

GENETICS SUBCOMMITTEE OF THE  
NATIONAL BIOETHICS ADVISORY COMMISSION

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## 1 P R O C E E D I N G S

2 DR. MURRAY: If the commission would all be  
3 seated, we would like to convene this meeting. Welcome to  
4 the meeting of the Genetics Subcommittee of the National  
5 Bioethics Advisory Commission.

6 Today's meeting will be devoted principally to  
7 a discussion of the Report on Tissue Samples.

8 Tomorrow there will be a meeting of the full  
9 commission, and the day after, the morning after that will  
10 be a meeting of the Human Subjects Subcommittee.

11 I have been asked to remind all the members of  
12 the commission to please, please pull your microphones  
13 forward when you have something to say. You can leave  
14 them there. That is fine.

15 I wonder if Dr. Harold Shapiro would have  
16 anything he would like to say in welcome?

17 DR. SHAPIRO: I simply would like to welcome  
18 all members of the commission and once again, for those of  
19 you I may not have said so directly, happy New Year to  
20 everyone. I look forward to working with you during this  
21 year.

22 I will make a somewhat more formal  
23 announcement tomorrow morning, but I do want to indicate  
24 that Dr. Eric Meslin has been appointed executive director

1 of the commission and so we are all very pleased. Eric,  
2 why don't you stand?

3 (Applause.)

4 DR. SHAPIRO: I know Bill Raub will be only  
5 too happy to go back to his regular full-time job. I will  
6 take this moment also to thank him, although he is not  
7 here, for his work on our behalf during a good part of  
8 last year.

9 So I will ask the staff to make sure that we  
10 all have coffee prepared by tomorrow morning. And I will  
11 have more to say at that time.

12 But, Eric, welcome. It is great to have you  
13 with us. I look forward to our discussions.

14 DR. MURRAY: Good. Let me join you in  
15 welcoming Eric aboard. It is good to have you here, Eric.  
16 My regrets to the ELSI Program, but tough.

17 DR. SHAPIRO: That is the spirit.

18 (Laughter.)

19 DR. MURRAY: Well, they would have done it to  
20 us if they could have.

21 DR. SHAPIRO: Right.

22 DR. MURRAY: No question. Let us get to--

23 DR. SHAPIRO: They did do it.

24 (Laughter.)

1 DR. MURRAY: That is true. That is right.  
2 They have been recruiting in our midst, haven't they, so  
3 it is only fair.

4 DISCUSSION OF TISSUE SAMPLES REPORT

5 KATHI E. HANNA, Ph.D., AND

6 SUBCOMMITTEE MEMBERS

7 DR. MURRAY: We are going to talk about the  
8 Tissue Sample Report, and we have-- Commissioners should  
9 have a draft of sections of the report. They should have  
10 had it for a week or two now. No? One week or so now.

11 Kathi Hanna has been working hard on it,  
12 including over the holidays, and I want to thank Kathi on  
13 behalf of all of us for what you have done. But we should  
14 jump into the report.

15 Now, Kathi, we want to go over each of the  
16 sections, I think, both the ones of which we have a draft,  
17 and the ones that we just have still an outline. I am  
18 going to ask Kathi in a moment if she has any specific  
19 needs that she would like us to address.

20 I have two things I want to mention. The  
21 first is I have a series of specific questions that I  
22 think we probably haven't talked enough about, even as a  
23 subcommittee, to know precisely what we want to say in the  
24 report, and I want us to get to them. You may have other

1 candidates.

2                   The second thing is, and I will try to resist  
3 the temptation myself even as I remind my fellow  
4 commissioners to resist it, this is not the time for copy  
5 editing. If you have large comments about organizational  
6 scope, yes; about sections that need to be in there, yes;  
7 but this is not the time to correct spelling or the  
8 precise words. Write it down, give it to Kathi, and she  
9 and I will make sure it is taken care of.

10                   Is everyone in agreement with that? Now, the  
11 temptation is very great because that is something we can  
12 fix on and do, but it is-- I think we are better off  
13 using our time to talk about the larger issues.

14                   Kathi, what would you like to see us do?

15                   DR. HANNA: Well, I think it is pretty obvious  
16 which sections need to be discussed. I think that the  
17 overview is obviously just my first attempt to try and  
18 forecast what issues are going to be covered in the  
19 report, so anything that is missing from that section I  
20 would appreciate your input on.

21                   I think that the second chapter, which is  
22 really just a slightly condensed version of Elisa Eisman's  
23 report, there I think you just need to make decisions  
24 about how comprehensive you want to be. I think it is

1 still too long, but I left a lot of the examples in there  
2 so that there was at least information for people who were  
3 looking at this for the first time.

4 For the third chapter, the moral and religious  
5 perspectives, I think we have a lot of information to work  
6 with from Courtney Campbell.

7 We still are waiting to hear whether we have  
8 someone lined up to write a commissioned paper on some of  
9 the other issues that are not necessarily, that don't  
10 necessarily have a religious orientation.

11 So that really leaves-- I think where we need  
12 to do the most work in is Chapters IV and actually VI,  
13 since Chapter V will be mostly descriptive and that is  
14 going to be fairly straightforward.

15 Other than that I think I just, you know, this  
16 is very patchy draft at this point and I think we need to  
17 focus. I can work from the transcripts and previous  
18 discussions on Chapter IV, but I think Chapter VI, where  
19 you really have to operationalize your recommendations, is  
20 where we need to do the most work.

21 DR. MURRAY: Okay. Trish?

22 MS. BACKLAR: I just would like to say that,  
23 in Chapter I, that we shouldn't forget that we really need  
24 to look in some way at the issue of minimal risk as we are

1       also looking at the Human Subjects Subcommittee. And you  
2       may not want to do that now because--

3                       (Technical difficulties.)

4               DR. MURRAY: I know that has come up in some  
5       of the discussions about tissue samples, including the  
6       National Action Plan and previous discussions.

7               MS. BACKLAR: And we are--many of us--really  
8       considering the detail--

9                       (Technical difficulties.)

10              DR. MURRAY: Yes.

11              MS. BACKLAR: So we might share some of that  
12       together.

13              DR. MURRAY: Yes. Yes. Yes.

14              DR. GREIDER: I have a couple of comments, and  
15       the first is on the outline. And I apologize that I  
16       wasn't there for all of the discussion when we discussed  
17       the orders and what the actual tactics were going to be.

18                      But it seemed to me, looking over this  
19       proposed outline, that the public knowledge and beliefs is  
20       relegated to an appendix rather than a chapter, and I am  
21       just wondering if we would consider actually having that  
22       be part and parcel of the whole thing rather than putting  
23       that in an appendix at the back.

24                      And I am not sure what kind of discussion

1 occurred since I wasn't here at the end of the meeting  
2 when we discussed the outline why it is an appendix.

3 And my recommendation would be to have it be a  
4 chapter following the science Chapter II. So something  
5 along the lines of, you know, what are the public views on  
6 this, earlier rather than as an appendix.

7 DR. MURRAY: This is the time to talk about  
8 the overall organization of the report. I think that is a  
9 good way to jump in. We had a discussion about that  
10 organization at the end of the last meeting, but that was  
11 not having a draft in front of us and, you know, your  
12 ideas get more concrete the more you have to look at.

13 Larry?

14 DR. MIIKE: A couple of comments. The  
15 framework Chapter IV, if we are going to be discussing the  
16 issues around which we then reach our conclusions in  
17 Chapter VI, then that is okay, but the way I, the way I  
18 glanced at Chapter IV, it seemed to mix both.

19 So you are either going to have to combine IV  
20 and VI and make it follow V, or you are going to have to  
21 have a discussion of the framework and then the policy  
22 recommendations coming later.

23 But in either event, I think just in  
24 sequential things, the currently-proposed policy should

1       come before our framework because that sort of bores out  
2       there right now, and then we impose our own framework on  
3       top of that.

4               The other problem is that I don't what to do  
5       with the religious chapter because I don't see the moral  
6       piece. And if I don't see the moral piece I don't know  
7       how useful the religious chapter is going to be in  
8       balancing that off.

9               If we keep the religious chapter there, then I  
10       would take out the conclusion section and more or less say  
11       that the religious discussion leads to the same kinds of  
12       conclusions that we reach in the--for lack of a better  
13       word--the lay approach that the rest of us think, which is  
14       that it gives the same kinds of conclusions that we would  
15       have reached regardless of a religious perspective.

16              Do you understand? When somebody talks about  
17       confidentiality, community, et cetera, et cetera, and  
18       those are not things that necessarily-- Particularly from  
19       the religious standpoint, I think it is something that we  
20       have all discussed.

21              So I think that perhaps that we should say  
22       that, even when you come from this religious perspective,  
23       we sort of arrive at the same point, regardless of whether  
24       we are coming from a religious perspective, or from a

1 scientific perspective, or a social perspective, or  
2 whatever.

3 DR. MURRAY: Kathi, you had something to say  
4 before. Did you want to say it now?

5 DR. HANNA: Yes. I just wanted to respond to  
6 Carol's comment about moving the section on public  
7 knowledge to an appendix.

8 I think we are still not quite sure what to do  
9 with that section, and part of it is because I think there  
10 is some discomfort about the reliability and the validity  
11 of the mini-hearings' approach as a good gauge, other than  
12 just one indicator.

13 And so I think what Eric and I have talked  
14 about doing is trying to find some other opinion polls,  
15 surveys, systematic types of measures, that can then be  
16 viewed as complementary to the piece that is being done,  
17 the mini-hearings. So I think the--

18 The other thing is that there are some  
19 interesting things that have come out of the mini-hearings  
20 that I think we should try and incorporate throughout the  
21 report as they arise, and not just segregate public  
22 opinion to its own section, but really try and, if it is  
23 relevant, refer to it in the chapter where it is  
24 appropriate.

1 DR. MURRAY: Bette?

2 MS. KRAMER: Excuse me. I understand the  
3 concern about the--

4 (Technical difficulties.)

5 MS. KRAMER: --and I know it is important to  
6 put it into the body of the report as opposed to an  
7 appendix because if you think back to our concerns that  
8 led to the mini-hearings it was the fact that, even though  
9 all of the--

10 (Technical difficulties.)

11 MS. KRAMER: So I think that if you put it in  
12 the context of recognizing that this is not a full-blown  
13 scientific poll, such as--

14 (Technical difficulties.)

15 MS. KRAMER: --but put in a context of our  
16 attempt to get some feedback from the public. And then I  
17 don't know legally--

18 (Technical difficulties.)

19 MS. KRAMER: And I hate to see it regulated to  
20 an appendix because I think it indicates a lack of concern  
21 of the public--

22 (Technical difficulties.)

23 DR. MURRAY: Carol?

24 DR. GREIDER: I agree with you, Bette. That

1 was sort of why I initially brought this up.

2 I also wanted to respond to Kathi that I think  
3 it is also true to incorporate as much of it as we can  
4 into other chapters. I very much agree with that.

5 I was just responding to the fact that it  
6 seemed to me to be a relatively important thing to many of  
7 the commissioners that we get this information rather than  
8 sort of operating in a vacuum, and I didn't want that  
9 issue to be an afterthought the way the report came out.

10 DR. MURRAY: Zeke?

11 DR. EMANUEL: Two things.

12 (Technical difficulties.)

13 DR. EMANUEL: --and I suggested, one of the  
14 reasons I asked Janet Wells(?) to come up with those  
15 questions was really incorporate it--

16 (Technical difficulties.)

17 DR. EMANUEL: --sometime in the next few  
18 months, but not--

19 (Technical difficulties.)

20 DR. EMANUEL: Having those questions and maybe  
21 even including them during--

22 (Technical difficulties.)

23 DR. EMANUEL: My own suggestion is that we  
24 still have a lot of boxology--

1 (Technical difficulties.)

2 DR. EMANUEL: And my only suggestion is that,  
3 once we resolve that, at least we can more or less decide  
4 what the framework is. And at least on eye level there  
5 was some disagreement and uncertainty about the boxes, and  
6 I apologize for the boxes.

7 (Technical difficulties.)

8 DR. EMANUEL: But we had talked about whether,  
9 on previous samples, we were going to combine research and  
10 clinical care and we had talked about how we--

11 (Technical difficulties.)

12 DR. EMANUEL: I mean, I think that those are  
13 the most important issues for us--

14 (Technical difficulties.)

15 DR. MURRAY: Yes. I think, particularly with  
16 Zeke here, we ought to take what time we have with him to  
17 try to look at the boxes, but I want to recognize Bernie  
18 and David.

19 DR. LO: David and I are--

20 (Technical difficulties.)

21 DR. LO: --little bit while I was swimming  
22 this morning, so this may be all wet.

23 (Laughter.)

24 (Technical difficulties.)

1 DR. LO: But it struck us, as we sort of  
2 stepped back from where we are around the-- We were  
3 concerned we may have lost sight of--

4 (Technical difficulties.)

5 DR. LO: I didn't really have a clear picture  
6 until I spoke with David about--

7 (Technical difficulties.)

8 DR. LO: One has to do with, as I said, just  
9 sort of what makes genetics DNA research--

10 (Technical difficulties.)

11 DR. LO: And, on the one hand, I think I would  
12 ask that we stress this firewall that we started to talk  
13 about and the way that we address--

14 (Technical difficulties.)

15 DR. LO: One direction is, as the researcher  
16 discovers things that are going to have potential clinical  
17 significance--

18 (Technical difficulties.)

19 DR. LO: So I think as long as we have a  
20 possibility of--

21 (Technical difficulties.)

22 DR. LO: So I think how we handle that is  
23 important when we are thinking about it.

24 I think it also may fall under pressure in the

1 opposite direction, and this I--

2 (Technical difficulties.)

3 DR. LO: And David came up with a model of  
4 using a large--

5 (Technical difficulties.)

6 DR. LO: The problem I see come up, when I  
7 signed up for that study, I said, you can only use my  
8 tissue for the disease of interest and--

9 (Technical difficulties.)

10 DR. LO: And one of the things I would like to  
11 see is this notion that along--

12 (Technical difficulties.)

13 DR. LO: I think we should sort of try to  
14 think about all those and anticipate those sorts of  
15 problems.

16 (Technical difficulties.)

17 DR. COX: Yes. Well, I run a risk of saying  
18 anything--

19 DR. MURRAY: David, would you bring your  
20 microphone closer? Thank you.

21 DR. COX: Because in the past, when I have  
22 tried to articulate these things, I have been totally  
23 incomprehensible, so I will try yet one more time, but if  
24 I am incomprehensible yet again, please tell me.

1           The-- Bernie has helped me with some of the  
2 words and the concepts and I guess one of them has to do  
3 with that there is several different processes of doing  
4 research, different study designs, and to focus on what  
5 that study design is--cross-cutting what the boxes are--  
6 gives a more whole picture to me.

7           And so it really has to do with not sort of  
8 what most of the samples are that are in existence now,  
9 but what are going to be the use of the samples in the  
10 future?

11           It is an important issue to deal with the  
12 retrospective studies--don't get me wrong--but I think  
13 that, in large part, our job as a commission is to think  
14 of where we stand now but, more importantly, where we are  
15 going in the future.

16           So in the second chapter, which I guess is the  
17 science chapter, because Carol and I are involved with  
18 that, and I think it is good to document what samples are  
19 there, but then, just like happened in cloning report, go  
20 through what the scientific process is, what some of the  
21 study design would be that could lay out what the  
22 structure for the future is going to be.

23           That is not sort of what the ethical boxology  
24 is, but it is saying practically how the research is going

1 to be carried out. Then that makes for a more whole  
2 discussion of--

3 It really boils down, in my mind, to this  
4 relationship of the subjects to the researchers, and that  
5 relationship is different in different settings, depending  
6 on how you do the design.

7 My personal belief is that, in genetics, the  
8 relationship between the researchers and the subjects is  
9 like tight. It always will be. All right? And that is  
10 very different from what is going on in epidemiology in  
11 general. So why is it tight in genetics?

12 And it is tight because of this  
13 stratification; taking big groups of people and winnowing  
14 them down to a narrower stratified subset of which you  
15 collect more and more information. And how you can have  
16 that kind of a process, where you divorce--in the long  
17 run, to come up with a treatment--where you divorce the  
18 researcher from the patient, I don't understand.

19 So my specific suggestion is, is that Carol  
20 and I--and others who want to--but in specifics, Carol and  
21 I work on the second chapter to include that kind of a  
22 process of the kinds of research that may be going on,  
23 different types of research, and what is involved with  
24 that in terms of these relationships, because I think it

1 complements the structure of the boxology.

2 And then--I quite agree with what Larry said--  
3 that then putting those two together we come up with the  
4 recommendations on it.

5 DR. EMANUEL: I am a little confused. I need  
6 some context--

7 (Technical difficulties.)

8 DR. EMANUEL: And I think this is a situation  
9 where we are talking about it. You want to go back to the  
10 Physician's Health Study or to the Framingham Health Study  
11 and do genetics on samples that were not initially  
12 collected for genetic tests.

13 (Technical difficulties.)

14 DR. EMANUEL: There is no relationship between  
15 the researcher there and the--

16 (Technical difficulties.)

17 DR. EMANUEL: No relationship. Even if you  
18 did accomplish--

19 (Technical difficulties.)

20 DR. COX: Okay. I understand, Zeke.

21 DR. EMANUEL: So the issue that Bernie  
22 suggested, you know, now once--

23 (Technical difficulties.)

24 DR. EMANUEL: You don't know who these 10,000

1 are. They are just numbers.

2 DR. COX: That is correct. So let us back up  
3 for a second and say, ultimately, what is the goal of  
4 genetics research?

5 It is not to find a gene that predicts  
6 something. This is my personal view. It is not to find a  
7 gene that can predict that you are going to die when you  
8 are, you know, 43. Okay? It is to come up with  
9 treatments to improve people's health.

10 So that what is the process by which, in my  
11 view of the future, that this is going to happen? It is  
12 going to start with very large populations like the  
13 Framingham or NHANES.

14 The initial part of it is going to be finding  
15 associations of genes that do make predictions. All  
16 right? Not all DNA information is going to be highly  
17 predictive, but a subset of it will be very predictive.

18 But that is just the beginning because, when  
19 you get those predictions, then you have individuals who  
20 you can make predictions about but there is no therapies  
21 or any options.

22 How then is science going to proceed to come  
23 up with any therapies or options? It is going to be to  
24 enlist exactly that subset of people to do clinical trials

1 to figure out what works and what doesn't work. That is  
2 where the relationship comes in.

3 DR. EMANUEL: (Inaudible.)

4 DR. COX: So it is not stopping when you find  
5 the association.

6 (Simultaneous discussion.)

7 DR. EMANUEL: Right. It is also a completely  
8 different type of research protocol that is separate from  
9 going back to the stored tissues. Right? I mean, that  
10 is--

11 (Technical difficulties.)

12 DR. EMANUEL: Right? I agree with you. Then  
13 what you do is you go back, find the people who got that  
14 genetic alteration and--

15 (Technical difficulties.)

16 DR. COX: But see, now we are going to--  
17 Follow me one more step now. So now we are with those  
18 individuals and that one set of researchers is getting  
19 more and more information about them and are involved with  
20 clinical trials.

21 Now, another group of researchers, because  
22 these happen to be heart doctors because they are working  
23 on ApoE, but now another group of researchers says, "Guess  
24 what? Your ApoE is important for Alzheimer's disease, not

1 just heart disease, and so we want to enlist you in this."

2 All right?

3 So that what it means is that if, when  
4 patients get involved with us to begin with, they are part  
5 of an overall process that they may or may not want to be  
6 part of, but you can't inform them about it from the very  
7 get-go, so--

8 (Technical difficulties.)

9 DR. EMANUEL: --this kind of example because  
10 the question is, is it covered in a way we feel  
11 comfortable with or is it not covered in a way that you--

12 (Technical difficulties.)

13 DR. MURRAY: Yes.

14 DR. EMANUEL: Is that what we are here for?

15 DR. MURRAY: Yes. You are here until 2:30  
16 p.m.?

17 DR. EMANUEL: Yes.

18 DR. MURRAY: Okay.

19 DR. EMANUEL: I apologize.

20 DR. MURRAY: Well, I think we should use you  
21 while you are here as extensively as we can, so why don't  
22 you do that?

23 DR. EMANUEL: So let us say we have a stored  
24 sample, like the Framingham Health Study, so it is a

1 previously collected sample. Right? And we are not going  
2 to--

3 (Technical difficulties.)

4 DR. EMANUEL: Right? So I am not sure why  
5 that isn't on the boxology 1a. Is that 1a?

6 DR. COX: Well, you tell me.

7 (Technical difficulties.)

8 DR. EMANUEL: Okay? Now say you have found  
9 that and in your first study, you know, you notice, in the  
10 Framingham, it is associated with the Ashkenazi Jewish  
11 population, and you go to another Ashkenazi Jewish cohort  
12 that has--

13 (Technical difficulties.)

14 DR. COX: I don't want to go to a different  
15 cohort though Zeke. I want to take the people that I have  
16 begun to find in Framingham because there is not so many  
17 of them there, and it costs me a lot of money to find  
18 them, and I want to do more stuff with them.

19 DR. EMANUEL: Okay. So I think the issue is  
20 what does "more stuff" mean?

21 DR. COX: More stuff means collecting--

22 (Technical difficulties.)

23 DR. EMANUEL: Collecting more clinical  
24 information, if it is done in an anonymous manner with the

1 firewall, is perfectly fine--as I understood our agreement  
2 last time--is perfectly fine in box 1a. We want  
3 continuous information--b--as long as it is in an  
4 anonymous manner, and you can't identify that particular  
5 person.

6 Now--

7 DR. MURRAY: Instrumentally, as I understand  
8 it, to see if I am following, what this would entail would  
9 be the researcher, you, now wanting additional information  
10 and more samples, going back to the steward of the  
11 samples.

12 DR. EMANUEL: And who is the steward of the  
13 sample?

14 DR. MURRAY: Presumably it might be a  
15 pathology department.

16 And saying, you know, these were very fruitful  
17 samples. I would appreciate additional sample material  
18 and additional clinical information, but it can also be--  
19 It could still remain anonymous. Is this what you are  
20 contemplating?

21 DR. COX: Well--

22 DR. EMANUEL: But imagine two different  
23 circumstances. Imagine you have a research study, again  
24 like the Physician's Health Study or NHANES. You are--

1       That data is being dumped into this anonymous pool. That  
2       is the way you have created the situation. So you have  
3       got the data up until that point.

4                Say two years later they do another survey of  
5       these people--right?--to find out, you know, what diseases  
6       have happened in the intervening two years, the way they  
7       do in the Physician's Health Study. That data, as it is  
8       entered, gets dumped in and there is an update.

9                DR. COX: Yes. But what if it is not the data  
10       that I want, Zeke?

11               DR. EMANUEL: What if it is--

12               DR. COX: Not the information that I want.

13               DR. EMANUEL: So you-- So now the question  
14       is, you want to walk backwards, identify those particular  
15       12 people--

16               DR. COX: This is how genetics is done. So  
17       that you go and you stratify populations and you  
18       intensively investigate a smaller subset.

19               DR. EMANUEL: I think if you then want to be  
20       able to use it in an identifiable manner, you are going to  
21       have to get their consent. I mean, that is what this  
22       says. Then you move to 1b. And then you would have to  
23       get their consent.

24               DR. LO: Okay. But that is-- I think that is

1 important that you can't sort of say the trustee goes back  
2 to the patient and negotiates and then anonymizes it so  
3 that, when I get it as a researcher, it is anonymous.

4 DR. EMANUEL: Well, I think we are going-- I  
5 think we are-- I think by not having a good example, we  
6 are sloshing a little back and forth.

7 In my mind--and I am only one member here--the  
8 trustee situation is a-- That operates really in the  
9 clinical where you have got the sample from the clinical  
10 context.

11 Remember, in the Physician's Health Study, you  
12 have got freezers full, you have got it computerized, you  
13 have got a database. All right? There you have got an  
14 organization already.

15 In the sort of clinical setting where you have  
16 gone and you want, you know, like the Angiogenesis Factor  
17 Study from the Brigham, you want samples of breast cancer  
18 with, you know, five to 10 years of follow up, and they  
19 are the trustee who pulls them out, who knows which ones  
20 they have pulled, and has gone to the clinical record and  
21 added that information to you. That-- There is a  
22 trustee.

23 In a research setting, there is not a single  
24 person like that pathologist. Right? I mean, there is a

1 whole infrastructure to dealing with 30,000 or 60,000  
2 people. And that is a completely different setting I  
3 think.

4 DR. LO: Right. I think the point I would  
5 want to try to make is that we need to think through what  
6 are the characteristics of either the trustee or the  
7 decision-making entity within the larger study that are  
8 such that we would feel comfortable saying they can make  
9 these decisions and, in particular, whether there should  
10 be some input in these research studies from the community  
11 as to when you cross the line from 1a to 1b because I  
12 think there are going to be a lot of judgement calls.

13 And I think that, in the way this is  
14 interpreted in practice, I wouldn't want people to not be  
15 aware of the nuances and the controversies.

16 DR. MURRAY: Carol had something to say.

17 DR. GREIDER: I am going to agree with a lot  
18 of what you were saying, Zeke.

19 And I think that one of the things that would  
20 help us all out is just to define specifically how we are  
21 going to deal with each of the situations, what the  
22 scenarios are in box 1a and 1b and 1c and 1d, and what  
23 kinds of protocols we would like to see put in place for  
24 each one of those different cases.

1                   I mean, I think you are all bringing up  
2                   specific cases, and I think that they all are covered by  
3                   this framework. We just have to be very specific about  
4                   how we define what goes into what box.

5                   If we are having trouble here, that doesn't  
6                   bode well for other groups in the future. So if we can be  
7                   more specific and lay out the details. And I agree with  
8                   you; we have got to do the boxology to do that.

9                   DR. MURRAY: Bette?

10                  MS. KRAMER: I am wondering if we don't have  
11                  to go back further; thinking about what Bernie said about  
12                  people who have opted out who might, for the benefit of  
13                  further knowledge, have changed their mind.

14                  And if I recall correctly in the mini-  
15                  hearings, just about every group, there were a  
16                  preponderance of the members, the people there, who said  
17                  that they would want to find out. At least that is my  
18                  memory from the presentations and looking it over.

19                  So I wonder if what we really need to take a  
20                  look at is the opt-out process?

21                  DR. GREIDER: But that fits within one of the  
22                  boxes, right? That is one of the--

23                  MS. KRAMER: Yes. Right. But it is--

24                  DR. GREIDER: --criteria.

1 MS. KRAMER: It is more procedural than--

2 DR. GREIDER: It is filling in with what you  
3 are going to do in the specific instances; it is not  
4 changing the framework. I mean, I think it would be--

5 MS. KRAMER: So that doesn't change the  
6 framework.

7 DR. EMANUEL: I think again, Bette, we have to  
8 distinguish. If you are using a sample in an anonymous  
9 manner, you don't know. I mean, what that means is you  
10 can't link result A with person B. That is what it means.  
11 Okay? So you can't actually go back to that.

12 If you are using it in a potentially  
13 identifiable manner, which would make it 1b, or any of the  
14 b's, you can go back to them, but that would have required  
15 consent in the first place.

16 Now, I think we need to-- I am comfortable  
17 with that and I would-- You know, we can argue about  
18 that, and we did argue about it in the previous-- But I  
19 think that does cover the cases and how you can go back.

20 If it is truly in an anonymous manner. I  
21 mean, if that is what that firewall is about, you can't  
22 walk backwards. We get that information. We can't link A  
23 to B. I mean, that--

24 DR. MURRAY: Harold and Larry have been

1       waiting.

2                   DR. SHAPIRO: Thank you. I want to ask a  
3 series of questions just to test my own understanding of  
4 this because I haven't been part of all of these hearings  
5 and I just want to make sure that I understand what is  
6 laid out here. And I will try to do it within the context  
7 of these boxes.

8                   I understand what is meant by use in an  
9 anonymous manner to have nothing to do with how it is  
10 collected, but it has to do with the nature of the  
11 researcher's--in this case--knowledge or capacity to go  
12 back to the original sources. In an anonymous manner  
13 means there is some kind of wall there so that a  
14 researcher cannot go back. Is that-- That is correct?

15                   DR. EMANUEL: Right. We think that is one of  
16 our breakthroughs.

17                   DR. SHAPIRO: Okay. No. I just want to  
18 understand. That is what I thought and I have no  
19 objection to that.

20                   And I think Bernie's point is that that wall  
21 is going to achieve a certain kind of dynamic over time  
22 and we may want to address that. I understand that we  
23 will come back to that a little bit after.

24                   I take it that it is true, in all these boxes,

1           that an opt out is always possible; there is no reason why  
2           anyone should-- Right? You have opt out in some cases  
3           and not in other cases?

4                     DR. EMANUEL: No. That is not true.

5                     DR. SHAPIRO: Okay.

6                     DR. EMANUEL: You have to distinguish  
7           previously collected samples.

8                     DR. SHAPIRO: Yes.

9                     DR. EMANUEL: The 238 million existent  
10          samples--

11                    DR. SHAPIRO: Right.

12                    DR. EMANUEL: --from the prospectively  
13          collected samples.

14                    DR. SHAPIRO: Yes.

15                    DR. EMANUEL: Okay? In the previously  
16          collected samples, when you went in for your breast  
17          biopsy, no, they didn't ask you about anything, right?  
18          You actually probably signed away your rights in a way  
19          that you had no idea.

20                    DR. SHAPIRO: Right.

21                    DR. EMANUEL: In the prospectively collected  
22          sample, we want to make that an explicit part of the  
23          process.

24                    DR. SHAPIRO: Okay. So the answer is that opt

1 out-- The privilege of opting out of a study, should you  
2 know about it, depends on where you fall in one of these  
3 boxes?

4 DR. EMANUEL: No. I wouldn't have put it that  
5 way. The privilege of opting out of any study is reserved  
6 for two categories. One is if your sample is going to be  
7 used in an identifiable manner, and, in general way, in  
8 prospectively collected samples.

9 DR. SHAPIRO: Okay. So it is only the right-  
10 hand side?

11 DR. EMANUEL: Well, and also all the b's.

12 DR. SHAPIRO: Along with some columns.

13 (Simultaneous discussion.)

14 DR. EMANUEL: All the b's. 1b, 2b and 3b.

15 DR. SHAPIRO: Okay. I will come back to that  
16 later.

17 Again, just for clarification, I don't know if  
18 we are all looking at the same table here, since there is  
19 quite a number of them at the end, but the one that is  
20 most fully filled out is the one that I am looking at.

21 If I look at 2a and 3a, or 2c and 3c, or 2e  
22 and 3e, or the bottom two squares in the anonymous manner,  
23 in each case, is it the case that they should read exactly  
24 the same as 1a, c and e?

1                   Because I can't understand why 2a, 3a, et  
2                   cetera--the bottom part of those columns where they are in  
3                   an individually anonymous manner--should be any different  
4                   from the bottom two squares and the top square.

5                   What have I lost here?

6                   DR. LO: Well, we do--

7                   DR. GREIDER: I don't think we are looking at  
8                   the correct version of filling in.

9                   DR. EMANUEL: Right. Right.

10                  DR. GREIDER: Right. What I have is the  
11                  filled in thing and what I think Zeke mentioned is that  
12                  this was a number we agreed on and--

13                  DR. EMANUEL: Right. I have revised that.

14                  DR. SHAPIRO: I am just asking a question. I  
15                  am not challenging anything. I am just asking whether  
16                  square 2a and 3a, properly filled in, are any different  
17                  than 1a?

18                  DR. EMANUEL: Yes.

19                  DR. SHAPIRO: Okay. Well, that I don't-- I  
20                  don't want to take up time now, since I don't understand  
21                  that, so one of the members will explain that to me later.  
22                  I am just--

23                  DR. EMANUEL: Actually, that is-- No. But  
24                  that is the heart of part of this boxology. Okay.

1 DR. SHAPIRO: Well, okay.

2 DR. EMANUEL: And now I think I understand.

3 The question is why isn't everything just 1?

4 DR. SHAPIRO: Not everything. No. I am just  
5 talking about a. Let us take column a.

6 DR. EMANUEL: Oh.

7 DR. SHAPIRO: Column a.

8 DR. LO: It is the community.

9 DR. EMANUEL: It is the community issue.

10 DR. SHAPIRO: But it is anonymous, so who  
11 knows anything about community?

12 DR. EMANUEL: Because sometimes you go to  
13 particular samples that identify a community.

14 For example, a colon cancer gene where you  
15 were trying to identify Ashkenazi Jews, you just didn't go  
16 to any sample, you went to a particular sample that you  
17 could associate with--

18 DR. SHAPIRO: So anonymous in this case is  
19 only partly anonymous; that is, you can't identify the  
20 individual.

21 DR. MIIKE: That is what we mean by--

22 DR. EMANUEL: By anonymous.

23 DR. MURRAY: You can't identify the--

24 DR. SHAPIRO: All right. I didn't understand

1 that. Okay.

2 DR. MURRAY: But it may well-- I mean, very  
3 little of these tissue samples are useful without some  
4 demographic information or illness history.

5 DR. EMANUEL: If you actually look at the very  
6 last table--this is I think not updated since our last  
7 meeting, but updated from our previous meeting--it now  
8 says to be used in an individually anonymous manner and  
9 the word--

10 Maybe we should have stressed or highlighted  
11 or bolded "individually" there, because what it means is  
12 that you can't identify an individual, but you might be  
13 able, through demographics, like Tom says, identify from  
14 which community they might come. You might have gone to a  
15 particular community to get the sample.

16 DR. SHAPIRO: Okay. So it just means I don't  
17 know their name; I may know something about their--

18 DR. EMANUEL: A lot about them.

19 DR. SHAPIRO: --religion, or about their race,  
20 or about something else?

21 DR. EMANUEL: Right.

22 DR. MURRAY: Yes, as an individual. Right.

23 DR. EMANUEL: To emphasize, again the current  
24 regs, the common rule only recognizes that box, 1a. It

1 doesn't recognize--

2 DR. SHAPIRO: Well, I assume--

3 DR. EMANUEL: --the other boxes.

4 DR. SHAPIRO: Yes. Okay.

5 DR. MURRAY: Larry?

6 DR. MIIKE: Yes. I want to get back to what  
7 Dave was having a discussion with Zeke about, which was he  
8 wants more information and so he wants to get back to the  
9 individuals who provided the original sample.

10 The variable in here is this trustee concept  
11 because it seems to me that that is an issue we have got  
12 to address. When is there a trustee who acts in place and  
13 just sort of a shepherd of the existing information, and  
14 when does the individual have to be brought in?

15 At a simplified level, one could say the  
16 trustee is there for information that is already in a  
17 record somewhere and does not need to be continually  
18 collected off an individual.

19 If information is being continually collected  
20 off an individual, that person is actively involved and  
21 should be--should be--sought after and said do you want to  
22 participate in these future research topics?

23 So it seems to me that the question that if  
24 you want more information and you are concerned that your

1 model doesn't--your particular instance--doesn't fit in  
2 here, it depends on what is the relationship between the  
3 test subject and the researcher or the clinician.

4 DR. EMANUEL: Bingo. And that is exactly  
5 what--

6 DR. MIIKE: But it would still fit in these  
7 because that would be--

8 DR. EMANUEL: I thought you articulated it  
9 right.

10 DR. MIIKE: Yes. Because it would fit in one  
11 of your boxes.

12 DR. EMANUEL: If you are getting information  
13 from an existing pool--

14 DR. MIIKE: Right.

15 DR. EMANUEL: Right? Existant data that you  
16 are going to use in an anonymous manner, then it is in the  
17 to be used in an anonymous manner.

18 If you need to go back to the subject and get  
19 additional information from that subject-- Right? You  
20 have got-- You are using it in an identifiable manner and  
21 you are wishing to collect special information that isn't  
22 extant.

23 First of all, that-- You know, 45 CFR 46  
24 doesn't apply to that. I mean, that is new information

1       you are collecting as part of a research protocol. That  
2       is a new protocol and that means you need to get their  
3       consent.

4                   DR. COX: No. Zeke, listen. It can fit into  
5       the boxes.

6                   What my difficulty is, is that do the boxes--  
7       What we, as NBAC, want to do with layout, you know, what  
8       the discussion, what the issues are--

9                   And if what we do is we say--okay--that,  
10       because of privacy issues and because of the difficulties  
11       of doing research that, what we are going to do is say the  
12       paradigm by how the stuff should be done is that there is  
13       a firewall between the people doing research and the  
14       patients, I have a problem with that.

15                   And the reason I have a problem with it is I  
16       think that the majority of the future research is going to  
17       require closer relationship, ongoing relationship, between  
18       the researchers and the patients because most of it is  
19       going to require more and more information and it is going  
20       to require continued consent.

21                   The trustees are going to be the community--  
22       not the individual patients--that you work with and that  
23       the researcher is very close with.

24                   And so that my concern is not whether things

1 can fit in the boxes or not, but whether we are sending  
2 the message that isn't sort of consistent with reality.

3 DR. MIIKE: But you are not suggesting--

4 DR. EMANUEL: I don't see a--

5 DR. MIIKE: --that, in a continual  
6 relationship between a researcher and a subject, that once  
7 a subject gives consent he can't back out?

8 DR. COX: Absolutely not. I am not suggesting  
9 that at all. But I am saying that there--

10 I think that the vast majority of genetic  
11 research, at least at the level where it is going to  
12 count--not at the level of finding associations--is going  
13 to require a very close relationship between the  
14 researchers and the individuals in the communities  
15 involved.

16 DR. MIIKE: Okay. But can I just--

17 DR. COX: Yes.

18 DR. MIIKE: Then I think that we are in a  
19 different scenario. We are not talking about a piece of  
20 tissue lying there; we are talking about the real patient  
21 now. The tissue was the entry into that patient.

22 DR. COX: Correct.

23 DR. MIIKE: But you are into a different  
24 relationship.

1 DR. COX: Correct.

2 DR. EMANUEL: And that is a different kind of  
3 research effort. That is not stored tissue research  
4 which-- So I think we are-- I don't think we are in  
5 disagreement at all. I think-- I mean, that would  
6 require a regular, every-day old protocol that you can--  
7 You already have to do now. It would require the  
8 patient's consent because they would be giving you  
9 additional information.

10 So I don't think it is-- I don't think it is  
11 the issue that we were addressing or, if it is the issue  
12 we are addressing, it requires informed consent.

13 And I now apologize for running out  
14 unfortunately at a very important discussion.

15 DR. COX: I agree with what you just said,  
16 Zeke, but I think that I would hope this is an issue that  
17 is on the table with respect to this because it is  
18 certainly broader than just dealing with the tissues that  
19 are sitting in somebody's freezer.

20 But when we are talking about the use of  
21 genetic information in stored tissues, I think that a lot  
22 of the action is in these broader issues and not just in  
23 what is in the freezer. That is my point.

24 DR. MURRAY: Thank you, Zeke. Sorry that you

1       have to leave, but I understand. We will see you  
2       tomorrow.

3                     DR. EMANUEL: Yes.

4                     DR. MURRAY: I had the bad form to cut Harold  
5       Shapiro off in mid-question, so let me give him a chance  
6       to finish.

7                     DR. SHAPIRO: Well, let me-- Someone tell me  
8       if I am not speaking articulately into this microphone.

9                     As I look at this table, which does seem to  
10       cover most of the cases I can think through one way or the  
11       other, although the problem of the wall remains and its  
12       dynamic nature, would it be true that if you look at the  
13       segment of the matrix that deals with existing samples,  
14       that is the left two columns, if I understand this  
15       correctly, that the nature of the original consent might  
16       somehow matter?

17                    And I don't have any suggestion to make. I  
18       just have an observation that we deal with those two  
19       columns. You may or may not have an original consent of  
20       some kind--I don't know the vast variety of things, I  
21       expect--and I am just suggesting that that might matter.

22                    DR. GREIDER: I think that we discussed that  
23       the last time and that we were sort of going for the least  
24       common denominator approach, assuming that it was the

1       thinnest possible, if any, consent and giving protections  
2       to that--

3                   DR. MURRAY:  When we were--

4                   DR. GREIDER:  --scenario.

5                   DR. MURRAY:  Yes.  Go ahead, Carol.  I am  
6       sorry.

7                   DR. GREIDER:  That is all.

8                   DR. MURRAY:  When we were being careful in  
9       spelling some of this out, we made the point that if there  
10      was, with the consent for a tissue sample, some reasonable  
11      indication that it would not have been, the person would  
12      not have wanted it to be used for X, then it ought not to  
13      be used for X.

14                   So if there is any indication with the sample  
15      that there was, you know, that someone checked the do not  
16      use my tissue for research, then you don't use it for  
17      research, or if there was some other question that was  
18      asked which would indicate someone wouldn't want their  
19      tissue to be used--

20                   DR. SHAPIRO:  Okay.  So the assumption is, as  
21      we go ahead here, that is a minimal consent, whatever  
22      minimal is.  Not being asked I guess is the minimal.

23                   Okay.  If I can make a few other comments.  
24      There is just related questions because I don't--

1                   And that is the issue of community consent  
2 becomes very large in these new rows here, the second and  
3 third row of the matrix, and I certainly understand why.

4                   The question I have, Tom, is whether the  
5 committee has given any consideration or talk about just  
6 what that would mean?

7                   We tend to talk about it as community  
8 involvement, which I understand much better than community  
9 consent actually. And one suggestion I have, which came  
10 out of really a conversation I had with Eric this morning,  
11 is that that might actually be a better word to use. But  
12 I leave that--

13                   DR. MURRAY: Which?

14                   DR. SHAPIRO: Involvement.

15                   DR. MURRAY: Well, where actually? I was  
16 disappointed to see it described as community consent here  
17 because I think we had moved to the notion of community  
18 consultation at our last meeting.

19                   DR. SHAPIRO: Okay. All right. So that is  
20 just-- I am sorry it hadn't caught up with me.

21                   DR. MURRAY: Okay. It wasn't in the document.

22                   DR. SHAPIRO: Yes. Another question that I  
23 have is--let me also just put it as a question--in your  
24 own thinking about this, on distinguishing from those that

1       have potential harms, and those that don't; that is,  
2       distinguishing in the second row and the third row.

3                     In your own discussions, how does that happen?  
4       Where does-- How do you decide whether to throw something  
5       in one box, the second row or the third row?

6                     DR. MIIKE: I think we punted on that and  
7       decided we could not be the body that could tease that out  
8       to the degree that would be satisfactory. Isn't that  
9       right?

10                    DR. MURRAY: Bette and Bernie.

11                    MS. KRAMER: I am having a little problem  
12       because I don't recall that we ever came to a final  
13       determination as to how we felt about community  
14       involvement, period. We seemed-- The last two meetings,  
15       as best I can recall, ended with those issues in the  
16       process of discussion but no decisions having been made.

17                    So if I remember correctly, on the basis of  
18       what--excuse me--what I remember, what is in these boxes  
19       is what Zeke had prepared for us around which to have a  
20       discussion, but we have never come to a final decision.

21                    Now, please correct me if I am wrong.

22                    DR. MURRAY: No. I think you are right,  
23       although I sensed--probably by mere projection--I sensed a  
24       growing consensus that some notion of community

1       consultation was sensible, even though we had to define it  
2       better, flesh it out, and defend it. But we still have  
3       some of that work to do.

4                   But Harold, I think, just asked a different  
5       question, which is how will we know, either in terms of  
6       substantive principles or some procedural arrangements,  
7       when to say that there is potential harm or no potential  
8       harm to the community?

9                   Bernie and Carol.

10                  DR. LO: Yes. If I can try and generalize  
11       from the last couple of comments, I think again I am  
12       concerned not with the boxes, per se, but who decides what  
13       fits into which box and who does that interpretation?

14                  And I think it is fine if you have Zeke on  
15       call to say, "Well, wait a minute, let me think this  
16       through and let me explain to you why it is really in the  
17       box here rather than the box there." But you can have  
18       zillions of IRBs and zillions of investigators doing this  
19       on their own and--

20                  DR. SHAPIRO: How many zeros are there in  
21       zillions?

22                  DR. LO: Yes.

23                  But my concern is that, unless we give this  
24       some guidance on these issues, the grid itself won't be as

1       useful. I mean, it is like any other sort of federal  
2       regulation on research. It is how the individual IRB  
3       struggles with it, and I think they need help on that.

4               One of the considerations they should take  
5       into account, deciding whether it is this column or that  
6       column, and I think just the issues Harold was raising;  
7       who decides? And, again, I would push to say that it  
8       doesn't make-- I would urge that we have some community  
9       input into whether there are potential harms or not, not  
10      just researchers or trustees, or whatever, or steering  
11      committees deciding it.

12             DR. MURRAY: Carol?

13             DR. GREIDER: I mean, just to directly address  
14      that issue, my understanding from our conversations was  
15      that it is the IRBs. That which box to assign it to is  
16      subject to IRB-- The researcher first says, "I think it  
17      fits blah," and the IRB says, "Yes, we agree with you,"  
18      or, "No we don't agree with you; it belongs in the other  
19      box."

20             And then there is a series of recommendations  
21      about what would be done if it were in one box or the  
22      other.

23             But to get back to the specific question that  
24      Harold asked, I don't think that we even agreed that there

1 was a difference between 2 and 3. We were in the middle  
2 of discussing that; whether you could even make a  
3 difference between 2 and 3, or whether we should have one  
4 column or row for all of the community issues. And we  
5 were in the process of discussing that at the end of the  
6 meeting.

7 And from my recollection, we never decided  
8 whether that should be a 2 and a 3, or simply a 2. So we  
9 couldn't have addressed how to decide which goes in it if  
10 we hadn't really come to that conclusion. And I certainly  
11 wasn't convinced whether it was 1 or 2.

12 DR. MURRAY: My recollection of our  
13 conversations and interim conclusions corresponds to the  
14 one that Carol just reported.

15 I want to mention that if we were to decide  
16 that the distinction between no potential for harm and  
17 potential for harm, if we were to decide that was an  
18 important distinction, one we wanted to keep in the  
19 proposal, we have got three things to do.

20 One was the procedural thing, which is namely  
21 let the investigator give the investigator's view. The  
22 IRB then makes a determination. So we did get that far.

23 We haven't provided anything by way of  
24 substantive guidance as to what we think counts as

1 significant harm, nor have we given examples.

2 Now, I think it won't be that hard to come up  
3 with some examples, and it wouldn't be dishonorable to  
4 stop there; to give procedure, to talk about some  
5 examples, and to give some very general guidance, if we  
6 wanted to have that. We don't--

7 I am actually-- I think you can sometimes do  
8 as much harm by trying to sort of precisely specify all  
9 contingencies--

10 MS. BACKLAR: Right.

11 DR. MURRAY: --which you will never do well--

12 MS. BACKLAR: I think so.

13 DR. MURRAY: --or perfectly, than you will by  
14 giving some fairly flexible and vigorous procedure and  
15 some general guidance.

16 And that is-- I confess that is my bias in  
17 these matters.

18 Bernie?

19 DR. LO: There is no-- There may be another  
20 option there, Tom, and that is not to try and specify all  
21 contingencies, but to lay out the considerations you ought  
22 to take into account and some of the problems that--

23 DR. MURRAY: Yes. That is what I meant by  
24 general guidance. Absolutely.

1 DR. SHAPIRO: Tom, can I just make a comment?

2 DR. MURRAY: Yes.

3 DR. SHAPIRO: If you considered pulling  
4 together rows 2 and 3, and maybe that is what some of you  
5 want to do, and you went from consent, as you have already  
6 done--that is just a mistake in the layout--to  
7 consultation, then, if you make that move, the distinction  
8 between 2 and 3 becomes much smaller.

9 Because if you put community consultation in  
10 both 2 and 3, then it is less and less telling, it seems  
11 to me, to make distinctions between 2 and 3, so maybe  
12 those things are not independent of each other, at least  
13 as I react.

14 DR. MURRAY: I think that is a good point.

15 David?

16 DR. COX: So I-- This is again for my  
17 understanding of how the boxes are being used.

18 So now I am over on the right-hand side of the  
19 research protocol where people get informed consent to do  
20 a specific study with respect to high blood pressure. All  
21 right? And their samples-- And they are informed about  
22 that. That is the reason for the research. It is just a  
23 standard, you know, informed consent.

24 Now is it the case then, when those samples

1 are collected, that if somebody wants to use that for  
2 behavioral genetics research, in an anonymous fashion,  
3 that the researchers have access to that material?

4 DR. GREIDER: How were they collected? To be  
5 used in an anonymous manner or to be used in an identified  
6 manner?

7 DR. COX: They were collected to be used in an  
8 identifying manner.

9 DR. SHAPIRO: You don't make distinctions like  
10 that. You just-- You don't distinguish when you collect  
11 it; you just distinguish only how they are used.

12 DR. COX: That is right.

13 DR. MURRAY: Right.

14 DR. COX: So they were used--

15 DR. SHAPIRO: It doesn't matter.

16 DR. COX: --in an informed consent in an  
17 identified way.

18 DR. MIIKE: But now you are asking to use that  
19 in a different research protocol?

20 DR. COX: That is correct.

21 DR. MIIKE: You would need--

22 DR. COX: In an anonymous fashion.

23 DR. MIIKE: Well, in the original consent,  
24 they would consent to the research as well as a general

1 consent for use in other research areas so, if it is not  
2 identifiable, they have given a general consent and you  
3 would be able to use it.

4 DR. COX: Well-- But that is why I want to  
5 know what the consent is. This is what-- Because this is  
6 the practical issue of where this stands right now. There  
7 is-- Patients are being collected under specified  
8 research protocols and other people want to use those  
9 samples for other stuff and they don't want to be bothered  
10 by going back and asking if it was okay.

11 DR. MURRAY: Right.

12 DR. COX: So I am looking at how that fits  
13 into our boxes.

14 DR. MURRAY: Carol?

15 DR. GREIDER: One thing is how it fits in the  
16 boxes and another thing is what we are going to recommend;  
17 the kinds of informed consent that one should get.

18 DR. COX: Exactly.

19 DR. GREIDER: Right? I mean where it fits in  
20 the boxes is very easy to answer.

21 DR. COX: Okay. So--

22 DR. GREIDER: And the IRB would review it  
23 because it is a new protocol and say it fits in this box.

24 DR. COX: Well, then tell me where--

1 DR. GREIDER: The question then--

2 DR. COX: --it fits, because I don't see where  
3 it fits in the box.

4 DR. GREIDER: It fits-- It would be f, 1 or 2  
5 or 3f. Research studies to be used so identification is  
6 possible.

7 DR. MIIKE: Well, he is talking about-- He is  
8 talking about anonymous. It would fit--

9 We had a--

10 DR. COX: It would fit under one box, and it  
11 wants to be used in another box.

12 DR. MURRAY: That is fine because we are  
13 focusing on the use.

14 DR. MIIKE: Use.

15 DR. MURRAY: When you are focusing on the  
16 manner of how-- In terms of-- In that set of our  
17 recommendations, which will deal with tissue to be  
18 collected in the future, we will deal also with the  
19 circumstances under which it is collected in the consent.

20 DR. MIIKE: Remember-- Yes.

21 DR. MURRAY: But our primary interest here is  
22 also--our primary interest, not is also--is with use, and  
23 whether or not a tissue is regarded as anonymous is  
24 anonymous in use or not.

1 DR. COX: No. But that is what I understand  
2 because that takes the participant in the research out of  
3 the picture.

4 DR. MURRAY: Right.

5 DR. COX: It is the user in terms of defining  
6 how they want to use it that has the control, the  
7 researcher. The subject no longer is involved unless the  
8 informed consent is appeared informed consent.

9 DR. MURRAY: Right.

10 DR. COX: That is the only point I am bringing  
11 up because--

12 DR. MURRAY: And I think-- We will look at  
13 possible ways that have been suggested about getting that  
14 consent, including getting consent say only for a  
15 particular study or a particular line of research versus a  
16 general consent to research which could not, at this  
17 point, be contemplated, the details of which couldn't be  
18 contemplated.

19 That simply are-- Those simply are some of  
20 the choices that exist right now, and we may or may not  
21 choose to recommend that they be incorporated in the sorts  
22 of consents that we envision once this report is in  
23 effect.

24 DR. LO: Tom?

1 DR. MURRAY: Yes?

2 DR. LO: If I could add one other point to  
3 this discussion, it seems to me that it is important that  
4 we keep clear the distinction between research context and  
5 clinical context; that we are pretty much in agreement  
6 that, in a clinical context, it is hard to imagine how  
7 practically speaking you can get a very detailed or thick  
8 informed consent.

9 And the only thing-- If I am conducting a big  
10 prospective cohort study where I am going to follow people  
11 over time, I ought to have ample opportunity to explain,  
12 have them ask questions, re-explain, and get a much more  
13 detailed consent.

14 And I think the thing that is striking about  
15 David's example isn't which box it fits in; it is the--

16 If I am asked to sign a general consent form  
17 and I am not really told what sorts of things I might be  
18 signing up for and, in particular, I am not told that  
19 there are certain types of genetic research that some  
20 scientists may be very eager to do that others find very  
21 controversial or down-right objectionable, if I am not  
22 told that, what I check off may not be very informed.

23 And I think that in our discussions of the  
24 extreme right-hand columns, which I think is different

1 than the clinical context discussions, we need to take  
2 into account that there is research and there is research.

3 And I think if I am thinking that it is all  
4 going to be for diseases like diseases I have, or things  
5 like cancer or heart attack, but someone else is really  
6 thinking of--whatever--behavioral things, or other types  
7 of really, you know, socially controversial and  
8 stigmatizing conditions, that ought to be part of the  
9 consent discussion.

10 DR. MURRAY: Yes. Yes.

11 DR. MIIKE: Well, I don't agree. I don't  
12 agree because what do we have-- It is not as though this  
13 is the only time that someone is going to review the  
14 research.

15 If it is going to be used in a controversial  
16 research topic sometime in the future, that is going to be  
17 reviewed by an IRB or other mechanism to see whether that  
18 is legitimate research, and the issues around that will  
19 come up.

20 DR. LO: Absolutely. But that is a different  
21 issue as to whether I want my sample used in that  
22 research. The research may be perfectly okay to the IRB,  
23 but I may, as an individual, say, "I choose to opt out."  
24 But you didn't--

1 DR. MIIKE: True. But you didn't-- But you  
2 have that choice if you are going to be identified. If  
3 you are not going-- If you are going to be anonymous, I  
4 don't see how you can-- I just don't see how, when you  
5 are being recruited into the research now, you can ever  
6 get any kind of a notion about possible uses in the  
7 future.

8 So, I mean, that is what our whole scheme is  
9 about, is about trying to protect that person if you use  
10 it in an anonymous manner or if you use it in an  
11 identifiable manner.

12 I mean, you know, what we are trying to do is  
13 trying to find a balance between the two, and I don't  
14 think you can use the entry into the initial research  
15 topic as the be-all and end-all about everything that will  
16 go on in the future.

17 DR. LO: Right. But see we draw different  
18 conclusions about it. So that depending on how much value  
19 you put on--

20 DR. MURRAY: Bernie, I am getting--

21 DR. LO: What?

22 DR. MURRAY: --clues that you need to act like  
23 a rock star and stick this right in your face when you  
24 talk.

1 DR. LO: So starting from that--

2 DR. MURRAY: Thank you.

3 DR. LO: --observation, you can either-- I  
4 mean, you can go two different ways.

5 One says it is so important that we not  
6 hamstring scientists that we are going to allow research  
7 to be used--material to be used--in an anonymous way even  
8 though the patient didn't really have very much idea of  
9 what they were getting into as opposed to saying some  
10 types of DNA-based genetics research may be so  
11 controversial we are going to bend the other way and make  
12 it a little harder for scientists and favorable to more of  
13 those subjects, albeit perhaps few--

14 DR. MIIKE: But that is a decision to be made  
15 in the future--

16 DR. LO: --who object.

17 DR. MIIKE: You can't make it at the time that  
18 someone is being recruited into a research topic, into a  
19 research protocol that has nothing to do with any future.

20 DR. LO: Well, can you at least tell me--

21 DR. MIIKE: I mean, sure. I mean, you know,  
22 I-- I mean, I will sign a form that says, "Don't use my  
23 tissue for unethical research." I mean, what good is it?  
24 I mean, there has got to be-- That decision has to be

1           made sometime in the future.

2                         DR. LO:  Maybe--  But my point is maybe we  
3           shouldn't--  I mean, another way to say it is that maybe  
4           we shouldn't--  It is not all clear to me that you should  
5           say that we are going to allow that research to be done  
6           because we can't go back and get consent later.

7                         I mean, maybe the scientist who wants to do  
8           very controversial topics is going to have to put a little  
9           more effort into recruiting their subject and selling it  
10          on the merits of the research subject, not because the  
11          sample happens to be there.

12                        DR. MURRAY:  Trish and Bette have indicated  
13          they would like to speak.

14                        Trish?

15                        MS. BACKLAR:  What is interesting about this  
16          is, of course, that we do use advance directives; the  
17          things in the future that we really don't know exactly  
18          what is going to occur.  So there is some history that we  
19          have of dealing with the future which is, of course,  
20          uncertain and often unanticipated.

21                        DR. MIIKE:  Well, that is a different question  
22          from what he has raised, Trish.  I can say it now; "I  
23          don't want my tissue to be used in the future."  It is a  
24          different question that he raises.  It is--  I agree with

1       you there are advance directives.

2                   MS. BACKLAR: Correct. But we also have some  
3 history of advance directives that don't just say no; they  
4 also say this is what I would agree to, this is what I  
5 wouldn't agree to.

6                   The problem with this is it becomes  
7 exceedingly complex. And I absolutely agree with Tom and  
8 Bernie in trying to keep this as open as possible. I  
9 didn't mean to direct you into this. I just wanted the  
10 point that there was something there; that we have some  
11 history.

12                   And we may find it useful to suggest it in  
13 some way; that it could be employed in this. Not to close  
14 it off though.

15                   DR. MURRAY: Thank you. Bette?

16                   MS. KRAMER: I am having trouble understanding  
17 Bernie's objection because, if it is going to be used in  
18 an identified fashion, then it requires a full informed  
19 consent.

20                   So if it is going to subsequently be used for  
21 a research study that had not been anticipated at the time  
22 that the subject was initially enrolled, then there is,  
23 without going back to that person, there is no way to get  
24 that full informed consent, so I think you have to make

1 the assumption-- You have got to I guess have to make one  
2 or two assumptions. Either it can't be used at all, or it  
3 can be used in an anonymized fashion.

4 DR. LO: That is a very different assumption.

5 MS. BACKLAR: Right.

6 DR. MURRAY: Right.

7 MS. BACKLAR: And I would like to go back to--  
8 I would like to go back to a discussion that we had, a  
9 very brief discussion--gosh, I don't know--two or three  
10 meetings ago and that was when we raised a question of it  
11 is hard--

12 Before this is all over, aren't we all going  
13 to be part of a group, a community, to which somebody  
14 might feel there is stigma attached, and isn't that just a  
15 part of-- Isn't that just a part of the risk that we all  
16 accept, I mean, or that we should all accept?

17 DR. MURRAY: I-- Yes. Let me see if I can  
18 press Bernie's point because I think I understand the  
19 point, but I may come to a different judgement about it.  
20 I am not sure. Let me see if I can just press it.

21 Is it possible, under the kind of thing we are  
22 proposing, someone's tissue gathered under one set of  
23 circumstances, to then become part of a tissue collection  
24 and to then have the use of that tissue requested, in use

1 in an anonymized manner so that my identity doesn't go  
2 forward but my tissue does, that it might be used in a way  
3 that I would, if I had known about it in advance, find  
4 offensive?

5 And I think the answer has to be yes, that  
6 remains a possibility.

7 Now, what are the alternatives?

8 One alternative is to go back and knock on  
9 everybody's door and ask them for consent again. For a  
10 variety of reasons, that is seen as incredibly  
11 inefficient. Also at times impossible for certain people  
12 who will be untraceable or dead or whatever else. And  
13 also, in some cases, it might do more harm than good  
14 because people don't want to be re-contacted about certain  
15 things. They may not want to be reminded of so and so.

16 I guess the issue is, yes, there is a  
17 judgement here. That could happen. Are there any  
18 safeguards against it? There are at least two kinds of  
19 safeguards.

20 Safeguard number one is the IRB. And frankly  
21 if I were sitting on an IRB with such a proposal, to do  
22 something which I thought was explosive, my inclination  
23 would be to say to the investigator, "Look, I could easily  
24 see many people objecting to this so you better go out and

1 get some new samples from people who are consenting  
2 specifically to this study." That is protection number  
3 one.

4 Protection number two is if it implicates a  
5 particular group and it, you know, we keep that category  
6 in our proposal, then we have to get community  
7 consultation. And if the community says, "Hold on a  
8 minute; this is outrageous," then presumably the IRB is  
9 going to listen to that and say, "You can't go forward in  
10 the way you planned."

11 So there are levels of protection, number one.  
12 One and two, really.

13 DR. LO: No. I agree with what you and Larry  
14 both said about the IRB. My concern is are IRBs, as  
15 currently constituted, really fitted to play that role?

16 And I think having community consultation is  
17 important, but I think we have all seen a lot of examples  
18 of IRBs composed predominantly of members with affiliate,  
19 institutional affiliations just overlooking things that  
20 more public and community input might have pointed out.

21 DR. MURRAY: Right.

22 DR. COX: So that, Tom, that you just gave,  
23 was a very clear answer to the scenario that I laid out,  
24 which is if somebody comes in for a specified research

1 protocol to work on heart disease and somebody wants to do  
2 behavioral research anonymized, the answer is they can do  
3 it--okay?--with different projections.

4 DR. MURRAY: Well, that you can make the  
5 request to use it. Absolutely.

6 DR. COX: Now--

7 DR. MURRAY: You may not be granted the--

8 DR. COX: But it is anonymous. But now let us  
9 go one step further.

10 And the one step further is that there is a  
11 really fascinating result in that behavioral research and  
12 people really want to go back and they want to look at  
13 these people. The researchers want to do it. But they  
14 can't because there is a firewall. "Oh, well, I guess I  
15 just won't go back and look at it."

16 Give me a break. They are going to find out  
17 who these people are. I guarantee you they will. That is  
18 how it works. Okay. And those people are going to be  
19 contacted. I guarantee you they will. Now, that is how  
20 it works in the real world.

21 DR. MURRAY: Will you give us a guarantee in  
22 writing on that, David?

23 (Laughter.)

24 DR. COX: Yes. So-- Because I know my

1 colleagues that do this work. Okay? They are like  
2 bulldogs with respect to if they have an interesting  
3 scientific finding, nothing will get in their way.

4 So it is not that they are going to violate  
5 the law, but they will go and they will identify the  
6 physicians who worked with those people. Is it so hard to  
7 find these individuals? No.

8 So I am just saying that the firewall-- Okay?  
9 You can do encryption, you can do any kind of coding that  
10 you want so that the researcher doesn't have access, but  
11 so long as there are ties, there are ways for that to  
12 happen under the table.

13 Now, I quite appreciate what you are saying,  
14 which is to have to go back and talk to the patients every  
15 time when you do different types of research, that is not  
16 practical.

17 All I am doing is talking about the other side  
18 of it which is that, when the patients are taken out of  
19 the loop and it is being done anonymous, are we really  
20 like talking out of both sides of our mouths on that, and  
21 is it in fact the case that those people aren't going to  
22 be re-contacted and you won't have more information?

23 And I am quite skeptical about it myself.

24 DR. MURRAY: Now, you--

1 DR. MIIKE: Can I--

2 DR. MURRAY: Yes. We have two comments, and  
3 then I want to say something.

4 Larry and Kathi.

5 DR. MIIKE: My question to Dave is, is that  
6 what you say is a standard practice, or is that  
7 aberration?

8 Because I always come back to the point that  
9 we cannot develop rules aimed at the aberration. We have  
10 got to develop rules aimed at the majority. And then you  
11 develop special sanctions for the aberrations.

12 DR. COX: I am sorry to say that I think--  
13 okay--although I use it in a really extreme example, that  
14 it is more the standard rather than the exception. When  
15 researchers have an interesting finding, they pursue that  
16 finding, period. And it is not the patients' interests  
17 that are the ones that take primary concern. It is not  
18 the subjects' issues that take primary concern.

19 DR. MURRAY: Well, you know what, David? I  
20 realize this is kind of an awkward thing to say at an  
21 ethics commission, but that is wrong.

22 (Laughter.)

23 DR. COX: I agree.

24 DR. MURRAY: Okay. Then we will put that on

1 the record.

2 I mean, I think part of what we are designing  
3 are systems, as Larry points out, not that won't stop  
4 every possible malefactor from doing something wrong,  
5 although we would also like to have them in backup systems  
6 and come and try to nail those people and punish them for  
7 it, but we-- But that is wrong.

8 And I don't care how enthusiast you are about  
9 your finding, you don't violate the protections of human  
10 subjects to get those findings. I thought we established  
11 that about 50 years ago.

12 DR. COX: I agree. But the problem-- The  
13 reason-- One of the reasons why NBAC exists is because  
14 all those things are written down and they work not so  
15 well because people give lip service to it, but they don't  
16 act on it with respect to human subjects research in the  
17 way that there are laws with respect to animal research.

18 So I have no problem with a firewall, but I  
19 would like not to see, you know, a fire go through it.  
20 And right now I am saying that I don't think our society  
21 has ways of implementing the concept of the firewall  
22 because I think that it is too leaky right now, socially  
23 and culturally.

24 DR. MURRAY: Okay. I have more to say but I

1 want to give my colleagues-- Carol, Steve, Bernie.

2 DR. GREIDER: I just have a quick question for  
3 David.

4 Thinking about it very soberly, what  
5 proportion of scientists doing research do you really  
6 think would have that sort of a bulldog attitude, knowing  
7 that there are people concerned with the kind of research  
8 that might be going on; that there are concerns with their  
9 research; that they would ignore it anyway and go ahead?  
10 A serious re-estimation of what you just said.

11 DR. COX: All I can tell you, and this is  
12 printed, and it was the head of a very-- The president of  
13 a prominent scientific society who, at the end of his  
14 presidential remarks, made the comment that if it is the  
15 patient's consent or our right to do research, I will go  
16 for our right to do research. It was a public  
17 presidential statement that is written down.

18 MS. KRAMER: David, I am sorry, would you  
19 repeat that. I didn't--

20 (Laughter.)

21 MS. KRAMER: I couldn't hear you.

22 DR. COX: That if it is the patient's consent,  
23 informing the patients, or being able to have the sample  
24 to do the research, I will vote for going and doing the

1 research.

2 DR. GREIDER: But that is one individual?

3 DR. COX: It is one individual as the  
4 president representing the society.

5 MS. KRAMER: And he made that remark in  
6 public?

7 DR. COX: In public. A presidential address.

8 DR. MURRAY: I skipped over Kathi in coming up  
9 with the list of speakers. Kathi?

10 DR. HANNA: I just wanted to make-- I wanted  
11 to make the point, and this ties into what I think David  
12 is trying to say, and maybe there is a more diplomatic way  
13 of putting it, which is that I think that, for some, I  
14 guess--

15 The question I would ask is how truly useful  
16 would anonymized samples be? And I think for most  
17 geneticists they would say not too terribly useful unless  
18 they are doing molecular epidemiology. They are just  
19 trying to find the prevalence of a marker in a population.  
20 And that the data--the clinical data--that are tied to  
21 that anonymized sample are probably insufficient if they  
22 want to go further and try and find gene function, or do  
23 reverse genetics.

24 So I think that it is not so much that they

1       have some malicious intent to go and find these people; it  
2       is more that the system that is being proposed would  
3       render these samples virtually useless to them unless they  
4       could go back, and so they are going to have to go back  
5       and they are going to find a way to go back.

6                 DR. COX:    Sure.  That is what I am saying.  It  
7       is not enough saying that these are bad folks at all.

8                 DR. MURRAY:  Yes you are.

9                 (Laughter.)

10                DR. COX:    Okay.  That is not what I am saying.

11                What I am saying is that if there are ways to  
12       get around the system, they will do it because of what  
13       Kathi said.  It is because in order to have things of  
14       utility, the system precludes what they need, and they  
15       will go and find ways of bending the rules to be able to  
16       get that.

17                DR. MURRAY:  Steve and Bernie.

18                MR. HOLTZMAN:  I am a little puzzled.

19       Speaking as an organization that spends \$50-\$100 million  
20       dollars a year on genetic research, we conduct all of it  
21       in an anonymized manner as we have been talking about and  
22       have no problem doing it in an anonymized manner.  So I  
23       think we have to get a little more granular in our detail  
24       in what you are talking about, David.

1                   It is one thing to say, "I want to go back and  
2                   get more clinical information." It may not be sufficient  
3                   for identifying the individual, hence it can still be in  
4                   an anonymized manner.

5                   If I collect it in the context of a research  
6                   study, prospectively, I probably address the issue of re-  
7                   consent, or rather re-contact, in that precisely because I  
8                   thought it might be the case with respect to a subset that  
9                   I found I might wish to go get more phenotypic  
10                  information. Okay? All of those things are consistent  
11                  with what we have been proposing now.

12                  You are suggesting that the paradigm case is  
13                  the instance in which you have phenotypic information  
14                  about a research sample collected, let us say, in a  
15                  clinical context with minimal consent--all right?--so the  
16                  individual had no idea they were participating in this  
17                  research, and that going beyond wanting to go back and get  
18                  some more medical information that is non-identifying,  
19                  rather the researcher has to get to that individual  
20                  presumably because they have to get another sample. Okay?

21                  DR. COX: Okay.

22                  MR. HOLTZMAN: And to me that is not the  
23                  paradigm case at all. I find that very infrequent.

24                  And so I am not sure what you are referring

1 to, Kathi, when you say that what we are proposing doesn't  
2 work for the majority of genetic research. I just-- It  
3 is palpably false to me.

4 DR. COX: But, Steve, I will tell you why I  
5 believe that is the paradigm case, or will become the  
6 paradigm case.

7 It is because that it is not the-- My belief  
8 that what genetics does is it takes big populations and  
9 stratifies them down to smaller groups, smaller groups  
10 that are difficult to find; to go out and to recollect  
11 because those people are fairly rare. They are maybe 1  
12 percent of the population.

13 So you maybe have 10,000 people but that 1  
14 percent is going to get a lot of attention, a lot of  
15 attention. Everyone is going to want to jump on and study  
16 that 1 percent of the people that have a particular  
17 genetic make-up.

18 So those people are going to get inundated by  
19 being studied and you say, "Well, do it anonymous."  
20 Right? Or go out--

21 I mean, I don't understand that if it is  
22 anonymous how you, as a researcher, who do you talk to go  
23 and get the extra information that you need to design your  
24 clinical trial or to ask about relationships between

1 different types of diseases? What is the process?

2 I mean, I am open to the process. I guess  
3 what I am saying now is I don't see that we have a process  
4 for doing this and I don't--

5 (Simultaneous discussion.)

6 MR. HOLTZMAN: You said two different things.  
7 If my desire is to go back to do a clinical trial,  
8 obviously I have to find the body, the person.

9 DR. COX: Yes.

10 MR. HOLTZMAN: If, on the other hand, as we  
11 have proposed, a one-way permeable membrane, so that  
12 additional phenotypic information, or clinical  
13 characterization can be available, I can go back and say,  
14 with respect to Sample 71, where you gave us the following  
15 phenotypic information, it would be really useful, given  
16 what we have discovered, to see if you have any additional  
17 phenotypic information of the following sort. And get  
18 that.

19 DR. COX: And I am with you. Okay? So--

20 But the only dispute that we have, in terms of  
21 the paradigm, is that most, is most of the research going  
22 to be in the context of doing stuff that doesn't relate to  
23 sort of clinical trials that are coming up with therapies?  
24 Is that going to be the most useful research or is most of

1 the research going to be focused more on clinical trials  
2 that involves the body of the individual?

3 And I would argue that the future is going to  
4 be more in the direction of clinical trials involved in  
5 the body than anonymized stuff where you get a little bit  
6 more information to publish another paper. Again, that is  
7 just a personal opinion.

8 MR. HOLTZMAN: Yes. I think it is highly  
9 improbable because, when we have looked carefully at the  
10 economics of thinking of doing family studies as clinical  
11 trial populations, it just doesn't make sense. It doesn't  
12 work. You can't get the numbers and if you can get the  
13 numbers, then the labeling you will get for your drug is  
14 so small that you couldn't economically justify it.

15 DR. COX: If I can make one more statement in  
16 this regard, and it is a front-page article in the *San*  
17 *Francisco Chronicle* last Friday, and the headlines to it  
18 was "Big Biomedical Budget Push by Clinton."

19 And in it were some statements from Richard  
20 Klausner, of the National Cancer Institute, saying that in  
21 the next year he has a \$3 billion dollar budget planned  
22 because he believes that clinical trials are really at  
23 risk in this country and that he wants to have more access  
24 to patients that want to be involved in clinical trials

1 and thinks that we need a new mechanism because that is  
2 the future of research.

3 So that, if he was correctly quoted, was the  
4 front-page news article from the head of NCI.

5 MR. HOLTZMAN: That is not inconsistent  
6 though. All right? If you are asking me whether or not  
7 there will be a pharmacogenetic basis for most selection  
8 of individuals for clinical trials, I think that is true.  
9 All right? But I don't think it will be necessarily  
10 familial or with respect to specific ethnic groups.

11 I don't want to get into the details here  
12 about snips and common variants, but you know what I am  
13 thinking.

14 DR. COX: All right.

15 DR. MURRAY: Bernie?

16 DR. LO: I just want to suggest that I think  
17 it would be really helpful, at least for me personally, if  
18 we could have some specific case scenarios. So I think  
19 David has some in mind. Steve, you clearly have some in  
20 mind saying that we can do a lot of really good research  
21 in an anonymous way. Kathi, you are concerned. I mean,  
22 to have that give flesh to the report would be helpful.

23 I also think it would help us as we deliberate  
24 because it is one thing to look at an abstract grid and it

1 is another thing to say, "Here are some typical research  
2 protocols that our best thinkers are saying are typical of  
3 what we are going to be facing." How well does our  
4 analysis fit?

5 DR. MURRAY: Right. I sense that issue has  
6 burned itself out, at least temporarily. Am I right?

7 DR. SHAPIRO: Could I just ask a question?

8 DR. MURRAY: Yes.

9 DR. SHAPIRO: Is the subcommittee decided on  
10 why you wanted two rows or three?

11 DR. MURRAY: I couldn't hear you.

12 DR. SHAPIRO: Is the subcommittee decided on  
13 whether you want two rows or three here? And I think it  
14 really makes some difference. And I don't have an-- I do  
15 have an opinion, but I would rather hear the committee's.

16 Or, Tom, if you think that is premature to  
17 even discuss now, by all means let us come back to it.

18 DR. MURRAY: I don't know. I don't think we  
19 have decided whether to have-- When you say two or three,  
20 I take it you mean-- We have all agreed, I believe, that  
21 where you have got an individual and there is no sort of  
22 group at risk, no community, "identifiable community,"  
23 that that is Column 1, and we all agree that that has a  
24 certain set of rules.

1                   The issue is, is there-- Where there is an  
2                   identifiable community, ought we to do things differently?  
3                   And do we need to have separate rows for--rows, not  
4                   columns--rows for when there is no likely harm or some  
5                   possibility of harm if, in fact, we intend to recommend  
6                   some model of community consultation, rather than a kind  
7                   of community veto? I thought it was a good question.

8                   MS. KRAMER: Tom?

9                   DR. MURRAY: Carol and Bette.

10                  DR. GREIDER: I just wanted to say something  
11                  because I think that Zeke was the one that was really in  
12                  favor of having three rather than two, so I was trying to  
13                  recreate in my mind what Zeke might say, just trying to  
14                  remind myself what his arguments were for having three  
15                  separate rows.

16                  And it might have been because the sort of  
17                  hoops that one would have to jump through would be  
18                  different for Column 2, Row 2 versus Row 3. And that is  
19                  why initially it was set out as three, to not put in the  
20                  extra added burden where one isn't needed. I am just  
21                  trying to think through why we initially had three.

22                  DR. MURRAY: Right.

23                  DR. GREIDER: And so that might be coming back  
24                  around to the issue of a consultation or community

1 involvement might change somewhat how we would address  
2 that if it is less of a consent versus an involvement.

3 DR. MURRAY: Maybe I should just add  
4 something. When we heard the-- I can't remember the  
5 fellow's name from the last meeting.

6 DR. LO: Jack Killen.

7 DR. MURRAY: Pardon?

8 DR. LO: Jack Killen.

9 DR. MURRAY: Jack Killen, yes.

10 One of the things that Jack Killen helped me  
11 to understand better was that community consultation did  
12 not merely constitute an obstacle or a punishment. Quite  
13 the contrary, in fact. It often contributed in some very  
14 substantive but also sometimes subtle ways to the design  
15 of a particular study, to the ability to access subjects  
16 for study.

17 And maybe one possibility then is to simply  
18 say not have two and three, just have two. Just so where  
19 community is involved, to then recommend community  
20 consultation be undertaken. Now, I think that is, at this  
21 point, where I would lean, but I would like to hear what  
22 others have to say.

23 And Bette and Trish and Bernie and Harold are  
24 all in line. Bette?

1                   MS. KRAMER: I just-- I want to understand  
2 clearly. When we use the term "consultation" as opposed  
3 to "consent," that implies that the community does not  
4 have the right to veto the project. Is that correct?

5                   DR. MURRAY: That is my understanding, yes.

6                   MS. KRAMER: Okay.

7                   DR. MURRAY: Although I think practically  
8 speaking, if your community with whom you were consulting  
9 said, "This is a God-awful thing and we would recommend  
10 that no one in our community cooperate with it," you would  
11 be foolish to go ahead with it. So I think, in effect,  
12 there is a kind of veto, but we are not going to call it  
13 that. We are going to call it consultation.

14                  DR. GREIDER: You might not be able to go  
15 ahead with it.

16                  DR. MURRAY: You might not be able to go ahead  
17 with it.

18                  MS. KRAMER: Right. And then I don't think we  
19 ever really addressed satisfactorily, at least not in my  
20 mind, what do we do when there are dissenting opinions  
21 within the community?

22                  DR. MURRAY: As I think it is not an uncommon  
23 feature of discussions with the various groups involved  
24 with HIV research, which is where a lot of our experience

1 with community consultation comes. You deal with it.

2 MS. KRAMER: And we have the problem--

3 DR. MURRAY: Negotiate.

4 MS. KRAMER: --of the Ashkenazi Jewish women  
5 in the Boston area who didn't want to consent to a study.

6 DR. MURRAY: Right.

7 MS. KRAMER: That was nonetheless being done  
8 in other places.

9 DR. MURRAY: Right.

10 MS. BACKLAR: I think if you go back to the  
11 first section, where you have community, no potential  
12 harms, and community, potential harms, the reason you have  
13 to get those boxes into one is because who is going to  
14 make the decision about what those harms are other than  
15 the community itself? That they need to address it.

16 I mean, it is not going to be very good if it  
17 is an outsider who is saying to you, "Oh, no harm to you  
18 in this particular case." So that is the argument that I  
19 would have for putting them in one box.

20 DR. MURRAY: For putting them-- For not  
21 separating them?

22 MS. BACKLAR: For not separating.

23 DR. MURRAY: Yes. I think it is a good  
24 argument, Trish.

1                   Bernie?

2                   DR. LO: I think, to follow up on a point you  
3                   made, Tom, I think we should try in the report to put  
4                   forth a position that community consultation is a  
5                   beneficial thing for the scientists and for the research.  
6                   It is not a hurdle. It is not an extra administrative  
7                   burden.

8                   That, in fact, anyone doing genetics research,  
9                   where some sort of ongoing interaction with patients or  
10                  cooperation of the community is needed, would be foolish  
11                  to try and plan a study without involving the community  
12                  from the onset, it seems to me. So that this shouldn't be  
13                  a conflict; it should be a congruence of interest.

14                  DR. MURRAY: Harold, and then Larry.

15                  DR. SHAPIRO: My main point was the same as  
16                  Trish's so I am not going to repeat that. I just want to  
17                  say one thing.

18                  When I looked over the overview of this paper,  
19                  as Kathi knows from the comments I gave her, I really  
20                  objected to some of the distinctions that were made there  
21                  between the researchers and clinicians. If I believe  
22                  David, I may reconsider my position there. But, in any  
23                  case, that we will come back to later.

24                  DR. MURRAY: Larry?

1 DR. COX: Some of these researchers are  
2 clinicians.

3 DR. MIIKE: Just on the issue of community  
4 involvement in a community consultation, that has been  
5 going on for several years now, even outside the genetic  
6 area, so it is not really a controversial issue and I  
7 think it is--

8 Anybody who is going to try to do research  
9 nowadays is not going to do it on separate individuals,  
10 and I think it is just a practical and an unavoidable  
11 process that one has to take up anyway, so--

12 And I agree with Trish that it is that  
13 consultation process that decides whether the harm is  
14 minimal or severe and then, even if it is severe, whether  
15 the research protocol should go ahead anyway so--

16 DR. MURRAY: Carol?

17 DR. GREIDER: When we first went through this  
18 grid and tried to decide whether there were two or three,  
19 I was thinking about it in the mode that we first started  
20 discussing it, which is the community consent and how one  
21 was going to get consent from a community.

22 But the discussion that we had with Jack  
23 Killen last time, about his experience in the AIDS  
24 community and how they really had a very integrated

1 involvement of the community with the research, really  
2 dispelled in my mind the sort of confrontational us-them  
3 sort of paradigm that had initially been set out.

4 And so I have moved from feeling like we  
5 really needed to have three to agreeing with what other  
6 people have now said; that two probably would fit the bill  
7 if we can articulate very clearly the kinds of things that  
8 Jack was laying out for us as to why community involvement  
9 is important as a part of our report.

10 Because he was very convincing to me about  
11 that it is not a hoop to jump through, but rather it is an  
12 integrated process of doing the research.

13 DR. MURRAY: Thank you. I think I hear a  
14 consensus that we are collapsing Rows 2 and 3. Are there  
15 any strong descents to that? Are there any weak descents  
16 to that?

17 DR. GREIDER: But what about Zeke?

18 DR. MURRAY: He is not here so we will have  
19 him defend it, defend that decision to the group tomorrow,  
20 right? That would be--

21 MR. HOLTZMAN: I mean, I was with Zeke as  
22 well. As persuading as I am by Pat's line of thinking,  
23 the issue was, to the extent that it was a burden for the  
24 kind of study that palpably couldn't be stigmatizing--the

1 number of whorles on your finger or what-not--it seemed  
2 kind of onerous.

3           Again, I think just to echo what two of you at  
4 least have said, it is conceived of as consultation. It  
5 is a very different kind of hoop and, in fact, it is  
6 positive. I think what we have to acknowledge, however,  
7 is the pressure it then puts on us to give some guidance  
8 here to whomever we are asking to make these decisions as  
9 to what is a community? What is a--

10           Kathi, I think in the intro, used the  
11 collectivity definition that was found in the Canadian  
12 report. Because we are asking the IRBs to say is there a  
13 community involved, number one, and, if so, to go get some  
14 consultation. So I think we will have to give some pretty  
15 specific guidance.

16           DR. MURRAY: That is an important point. I--  
17 We have-- I want to make two other observations.

18           One is that we may have achieved a kind of  
19 enlightened consensus, or we think it is enlightened--we  
20 know it is a consensus--about the value, potential value  
21 of community consultation in these kinds of cases.

22           My guess is that a lot of our scientist  
23 colleagues are going to have the same reaction that I am  
24 sure some of the scientists at this table had initially.

1 Be aware of that. Be prepared for it. We can do our best  
2 in the report to anticipate that and to explain, you know,  
3 why we think it need not amount to that. But there is  
4 going to be a certain amount of protests and a lot of  
5 education that will need to take place. Just be prepared  
6 for that, number one.

7 Number two is we are still going to have to,  
8 in line with Steve's suggestion, provide some substantive  
9 guidance--maybe also a little procedure--for figuring out  
10 when a "community" is involved. And maybe that becomes--  
11 We may need to say that that is, in the end, that is an  
12 IRB decision whether there is a "identifiable community."  
13 At issue here, if so, one needs community consultation.

14 Trish has been waiting, and then David.

15 MS. BACKLAR: I am struck, as we discuss this,  
16 of how so much overlaps with our discussions in the Human  
17 Subject Committee.

18 And one of the things that I noticed when Jack  
19 Killen was here last time was that we did not address the  
20 issue of therapeutic misconception, which can occur here  
21 and which we want very much to make sure that we get this  
22 into this report, and that when communities do become  
23 involved they do start to muddle up; that between  
24 treatment and research and what may be an advantage to

1           them and what may not.

2                           And we need to make sure that the researchers  
3           and the IRBs are very aware that, just because this is  
4           genetic research, the same issues obtain.

5                           DR. MURRAY:   David?

6                           DR. COX:    So I am very in favor of collapsing  
7           the three into two.

8                           DR. MURRAY:   Okay.

9                           DR. COX:    I think that while it may scare some  
10          people doing research to think that they have to have  
11          community involvement, in fact almost every paradigm that  
12          you look at that has been successful has involved  
13          community involvement when it had specific communities,  
14          whether they be ethnically defined, or even people with  
15          specific diseases.

16                           DR. MURRAY:   Could you help us by providing  
17          some examples of that--

18                           DR. COX:    So when--

19                           DR. MURRAY:   --to Kathi so we could actually  
20          put those, and name them, and describe them in our text?

21                           DR. COX:    Absolutely.

22                           DR. MURRAY:   Great.

23                           DR. COX:    So I am very--

24                           DR. MURRAY:   That would go a long way I think

1 towards making the point.

2 DR. COX: Yes.

3 DR. MURRAY: Bernie?

4 DR. LO: I also agree with collapsing the two  
5 columns.

6 I think that as we think about the report, I  
7 agree, there is going to be a lot of resistance among many  
8 scientists; this notion of community consultation.

9 I think, on the one hand, we do need to  
10 acknowledge that we talked at first; that both the  
11 scientists and the community people need to learn how to  
12 talk to each other, need to understand, you know, the  
13 languages the other people are speaking.

14 I think it is going to be acrimonious at  
15 first. I mean, the first couple of years are not going to  
16 be any easier than they were for the AIDS researchers.  
17 But you have got to get people to look at the long term,  
18 not the short term.

19 And then, to follow up on what Steve was  
20 saying, and Tom was saying, I think we should think  
21 through how far we want to go with this. I think we  
22 should do more than just say, "Do community consultation."  
23 We should at least, it seems to me, identify key issues  
24 that need to be worked out to make that meaningful. And

1 maybe this is just a process.

2 I don't think it should be left up to  
3 individual IRBs. I mean, they are going to all stumble  
4 around in the dark. I think the NIH and other national  
5 organizations need to take some leadership in calling some  
6 national meetings to achieve some guidelines on how you do  
7 community consultation. I am not so sure we need to do  
8 that, but I think we can sort of say someone else needs to  
9 do this.

10 You know, my own feeling is that we don't have  
11 to settle all the issues. We just have to point people in  
12 the right direction. If we point them in the direction of  
13 saying community consultation is a good thing, here are  
14 some issues that you need to address to make it really  
15 work, here are some procedural things that we think might  
16 help get scientists thinking about this.

17 There is going to be a lot of re-training. I  
18 mean, a lot of geneticists just really aren't that good  
19 talking to people and that is what this is about; talking  
20 and listening. They are going to have to re-train  
21 themselves.

22 DR. MURRAY: Thank you, Bernie. This seems a  
23 good time to take a 10-minute break.

24 If anyone wishes to do public commentary,

1 would you please tell Patricia Norris. Pat, would you  
2 raise your hand so that people know who you are? That is  
3 even better. Thank you, Pat. Would you please let  
4 Patricia Norris know that you would like to do so.

5 And we will see you--I have about 3:33 p.m.--  
6 so we will see you at about 3:45 p.m. We will start then.  
7 Bye-bye.

8 (Whereupon, at 3:33 p.m., there was a brief  
9 recess.)

10

11

NEXT STEPS

12

THOMAS MURRAY, Ph.D.

13

DR. MURRAY: We have an hour and a quarter.

14

15

We have one public statement scheduled to be  
provided, so we will need to reserve five or so minutes  
16 for that. And I think in all curtesy to that--and to that  
17 person--we should not wait until the end but try to do it,  
18 in fact, about the scheduled time, which was 4:30 p.m.

19

20

Among the things we need to do before we leave  
today are decide how we want to use our time tomorrow in  
21 the full committee.

22

23

If you look at your agenda for tomorrow--if  
you don't have it handy I can remind you what it is--we

24

have--

1 Harold will welcome everyone at 8:00 a.m.

2 We basically have until 9:30 a.m. to conduct  
3 our preliminary discussion.

4 We have two individuals, Susan Old from the  
5 National Heart, Lung and Blood Institute and Patricia Barr  
6 from the National Action Plan on Breast Cancer, who are  
7 expected to make comments and engage us in conversation.  
8 And that will go on until about a little after 10:00 a.m.

9 After the coffee break, we will then have  
10 until 11:30 a.m., which is the time for public statements.

11 At that point, we are finished for the day, at  
12 least as our subcommittee, so we need to use that time  
13 well tomorrow.

14 So as I calculate it, we have for ourselves  
15 roughly an hour and 20 minutes, and then about another  
16 hour and 10 minutes. We have about two and a half hours  
17 to do our presentation, when we are not actually also  
18 engaging scheduled speakers. So we want to use that time  
19 well.

20 And before we quit today, we need to figure  
21 out who is going to, how we want to use it and who do we  
22 want to lead the conversation. Do we want to divide up  
23 responsibility for different issues or different portions?  
24 So I will give you that warning.

1 Eric Meslin has also asked me to raise a  
2 couple of points, and I will do that.

3 One is whether or not--I think we did address  
4 this--whether or not we want to have a specific model  
5 consent form that we endorse or whether instead we should  
6 talk more generally about the elements of appropriate  
7 consent.

8 My recollection is we talked about it--we  
9 discussed that--and decided not to press a specific model  
10 consent form. Is that correct? Does everyone agree with  
11 that? Not as a statement of fact, but as something we  
12 actually would want to do.

13 MS. KRAMER: I think we had raised the  
14 possibility of maybe including in the report four or five  
15 examples of consent forms that had been presented to us.  
16 I don't think we resolved it, but we raised that  
17 possibility.

18 DR. MURRAY: Yes. I think we did talk a  
19 little bit.

20 Steve, did you-- No.

21 Carol?

22 DR. GREIDER: I just wanted to mention that it  
23 was pointed out to me by Elisa Eisman that, in her final  
24 report on the stored tissue samples inventory, she has

1 collected a large number of sample informed consent forms.  
2 And I don't know if anyone else got this final report, but  
3 there are a number of them in there if we want to look  
4 through those to continue the discussion.

5 DR. MURRAY: Right. Yes. I got my copy about  
6 10 minutes ago when Elisa handed it to me, so I haven't  
7 had-- And she pointed out that there are those examples  
8 of consent forms.

9 And we have the material from the National  
10 Action Plan and from the Primer(?) Conference and some  
11 other materials that we may wish to at least certainly  
12 refer to.

13 Bernie?

14 DR. LO: I guess I would be in favor of not  
15 trying to develop a model form because I think that is  
16 going to change over time and it is going to go through  
17 iterations. People are going to test forms, find out some  
18 things work, and some things don't. And I think we are  
19 better off sticking to the goals and principles rather  
20 than specific forms.

21 DR. MURRAY: I don't hear any descent from  
22 that position.

23 Steve?

24 MR. HOLTZMAN: Just you can go one step beyond

1 goals and principles to the elements.

2 DR. MURRAY: Yes.

3 MR. HOLTZMAN: Right? I think it would be  
4 very useful. The elements of the consent that are  
5 important.

6 DR. MURRAY: Yes. The consensus I thought I  
7 was agreeing with was something short of designing or  
8 voting on a specific model consent, but rather talking in  
9 somewhat more general terms about what consent forms ought  
10 to be like.

11 DR. MIIKE: There is also a practical  
12 obstacle, which is that we are suggesting general consent.  
13 I mean, the consent varies according to the situation.

14 DR. MURRAY: Okay. So I think we are in full  
15 agreement on that, and I feel very comfortable defending  
16 our position on that.

17 Another point that Eric has asked me to raise  
18 with you is to consider whether to regard the stored  
19 tissue report; to publish it first as a "interim report,"  
20 with a comment-limited, specified comment period, or  
21 whether to publish it, I presume alternatively, as our  
22 report?

23 Now, I have a view on this, but I want to hear  
24 what the other commissioners say.

1 DR. MIIKE: Can you say that again. As an  
2 interim?

3 MS. KRAMER: Can you say that again.

4 DR. MURRAY: Eric, why don't you--since you  
5 proposed this--why don't you describe what you have in  
6 mind?

7 DR. MESLIN: It occurs-- At least it occurred  
8 to me and some others that a report of this import, one  
9 that is being waited on by a number of organizations and  
10 which we have promised, cannot hope to enjoy the input  
11 from all possible commentators and that, since there is no  
12 specific deadline to get it out, except for as soon as we  
13 can in the highest possible quality fashion, that it might  
14 be useful to disseminate an interim or draft report which  
15 contains all of the deliberations and our recommendations  
16 and allow for a period of public comment, to be decided on  
17 as a reasonable amount of time, that would allow as many  
18 people as possible the opportunity to read it, to think  
19 about it, and to provide whatever comments or input that  
20 they felt appropriate.

21 That public accountability model I think is  
22 very useful, but it also I think provides an opportunity  
23 for the commissioners to hear views that they might not  
24 otherwise have heard by individuals who could not come to

1 the meetings, who weren't able to provide written  
2 documents. These would certainly be seen as comments and  
3 would be considered before the commission issued its final  
4 report shortly thereafter.

5 MS. BACKLAR: I think it is a great idea.

6 DR. MURRAY: Harold?

7 DR. SHAPIRO: I also am strongly supportive of  
8 that idea. And we have a model which I think worked very  
9 well and that is the Canadian group, what is called the  
10 Tricouncil, which publishes various drafts up on the Web,  
11 and it was extraordinarily improved from draft to draft,  
12 at least as I feel it.

13 And I think it was mainly comments from people  
14 who hadn't had an opportunity to be at the meetings,  
15 hadn't fully understood exactly what the recommendations  
16 were until they could see them laid out that way. And so  
17 there is an easy way to get it around now. And I think it  
18 would lend an awful lot more credibility and probably  
19 increase the quality of the final document.

20 DR. MURRAY: Bette?

21 MS. KRAMER: Well, it would also, if we in  
22 fact go forward with the public opinion survey, enable us  
23 to incorporate anything that we learned from that in the  
24 final report.

1 DR. MURRAY: Then the final report would be  
2 maybe in our lifetime. I mean, it is a while before I  
3 think we are going to have a public opinion survey to  
4 incorporate.

5 MS. KRAMER: No. I am sorry. I don't  
6 understand. Which is going to be further into the future.

7 DR. MURRAY: The wait until we get the results  
8 of the opinion survey, while I think it is within our  
9 lifetime--

10 I guess I don't have the same enthusiasm for  
11 doing it as an interim report. I understand the  
12 arguments, and some of them I find pretty good for doing  
13 it that way. People are looking for guidance from us.  
14 And are we going to say, "Well, here is our guidance, but  
15 it is not really our guidance because it is only an  
16 interim report and we might change things."

17 And it will mean, quite frankly, that a  
18 considerable portion of our energies after this report,  
19 when we are working on the next one, will have to go back  
20 and revisit this report. And I am very concerned about  
21 the time and the attention of commission members so I  
22 think there is a trade-off that we need to be conscience  
23 that we would be making if we chose this strategy.

24 DR. SHAPIRO: Tom, I think you are right. It

1 is a trade-off. But, one, I think the staff can be very  
2 heavily involved in dealing with this at the response  
3 level, and then bring some changes to us if there are any  
4 at that time. And, you know, I think your point is a good  
5 point. I mean, I certainly understand it. But I think on  
6 balance that we would still be well served.

7 I don't think we should give a long period for  
8 comments. I think we give a relatively short period for  
9 comments. I don't know what that means. I haven't  
10 thought that out. But it is weeks, not months, that I  
11 have in mind. But I understand the point. It does cost  
12 some--

13 DR. MURRAY: Let me actually mention one other  
14 virtue of doing it as an interim report. People are more  
15 likely to read it if there is a chance that they can  
16 actually make suggestions that will help shape, that will  
17 help modify it. That-- I have to grant that as maybe one  
18 of the strongest arguments in favor of doing it as an  
19 interim report.

20 DR. COX: Yes. And, Tom, that is actually the  
21 point that I was going to bring up. I am in favor of an  
22 interim report, but for that purpose. Because if Eric  
23 Cassell was here he would call it education. And by  
24 calling it an interim report, you are going to get many

1 more--hopefully--people involved.

2 I am pessimistic in terms of how useful the  
3 input is going to be because it is going to be not from  
4 people we haven't heard before, but it is going to be from  
5 all of the people we have heard from before, and we  
6 already know what they have to say. But that perhaps at  
7 least it gives the opportunity of education and having  
8 more people involved.

9 So I quite agree with your points in terms of  
10 the downside--and for me it is a fine line--but I am more  
11 in favor of it being an interim primarily for this  
12 education part.

13 DR. MURRAY: Carol?

14 DR. GREIDER: I agree. I think that if we can  
15 really publish it on the Web where people could really  
16 have access to it, then it would be a very useful thing to  
17 be able to get comments back.

18 I mean, I always circulate anything before I  
19 publish it to colleagues to get comments from them.

20 If we couldn't publish it in something that is  
21 quite that accessible, I would be less in favor of having  
22 a draft report that is just a paper report that is going  
23 to be difficult for people to get a hold of anyway.

24 DR. MURRAY: Bernie?

1 DR. LO: Yes. I will just put my vote in for  
2 having an interim report and getting feedback. I think  
3 patient advocates and the scientists are going to have to  
4 live with the report, so we should give them a chance to  
5 give us some feedback.

6 DR. MURRAY: If we publish it on the Web, that  
7 will certainly make it available to people with access and  
8 sophistication about getting--using--the World Wide Web.  
9 Will that get to all, you know, most of, if not all, of  
10 our relevant publics? To scientists I expect it would.  
11 Would the consumer groups, public groups, be able to do  
12 that?

13 DR. LO: I think a lot of the people would be  
14 able to, sure.

15 DR. MURRAY: Yes.

16 DR. SHAPIRO: We order pizzas on the Web.

17 (Laughter.)

18 DR. MURRAY: We order pizzas on the Web.

19 MS. KRAMER: You know, Tom, I suspect if there  
20 is a group that wants to pass it around to their  
21 particular audience, they can always-- There is nothing  
22 to stop them from publishing it themselves or printing it.

23 DR. MURRAY: Right. Right. Well, this sounds  
24 like I seem to be the only one who has dug-- I haven't

1 exactly dug my heels in. I am being dragged along though.

2 I think it might be well then to mention this  
3 tomorrow to the full commission, do you think? I would  
4 rather not have it take up part of our brief substantive  
5 time, but as we talk about strategies for publication, if  
6 we could mention this as a possible strategy that, if it  
7 worked well, I suppose could be a model for other reports  
8 where it was equally suitable. I am not making a  
9 judgement whether it would always be suitable, but I am--

10 Okay. I think actually we have gotten an  
11 answer to that question then.

12 DISCUSSION OF TISSUE SAMPLES REPORT (CONTINUED)

13 THOMAS MURRAY, Ph. D.

14 DR. MURRAY: Let us get back to the substance  
15 of the report, shall we?

16 Trish?

17 MS. BACKLAR: I am not sure that I made myself  
18 clear about one thing in terms of the Tissue Sample  
19 Report, and that is I have a concern about cutting out  
20 people from getting information about research that-- I  
21 am very concerned. Just as though it--

22 As a private person, if some of my tissue was  
23 used for research, I would want to know if something was  
24 important to me, so another reason for being very cautious

1       about a firewall. That is all I am saying. I don't think  
2       I made that clear before.

3                   DR. MURRAY: Let me see if I understand your  
4       point. As I-- And let me tie it into-- Because it is  
5       one of the things we need to talk about. There are two  
6       circumstances under which people may want to reach this--  
7       what we have called a--firewall. We probably need a  
8       better metaphor, but that is the image we are stuck with  
9       at the moment.

10                   One of them is this sort of-- It is David's  
11       cadre of researchers who really, really want to find out  
12       who those people are.

13                   DR. COX: The Spice Girls. They really,  
14       really, really want to know.

15                   DR. MURRAY: The Spice Girls.

16                   (Laughter.)

17                   DR. MURRAY: Well, listen I was in England for  
18       a week in December and they are already passe so how  
19       quickly-- How fleeting is fame?

20                   So that is one motivation, right?

21                   The second motivation though is one that I  
22       heard from the mini-hearing participants in Cleveland--and  
23       I gather it wasn't just in Cleveland that this was  
24       articulated--that there is a feeling on the part of people

1       who contribute to research, by whatever means, including  
2       tissue, that, if it is possible for that research to  
3       benefit them, then it ought to benefit them.

4                       That they sort of made a kind of contribution.  
5       If scientists learn something about them that they ought  
6       to know, they would like to have the opportunity to find  
7       out.

8                       I was surprised at the intensity of that  
9       feeling. Now that exists I must say with an equally  
10      intense desire to protect privacy.

11                      MS. BACKLAR: That is what I am referring to.

12                      DR. MURRAY: Yes. I thought it was that  
13      latter.

14                      MS. BACKLAR: Right.

15                      DR. MURRAY: Right.

16                      MS. BACKLAR: I just wanted to make sure that  
17      I said it.

18                      DR. MURRAY: We need to talk about that. I  
19      mean, if our recommendation said that this must be a  
20      firewall that is as absolutely unbreachable as human  
21      ingenuity can make it, then we have eliminated both those  
22      breaches, or we try to eliminate all those breaches if  
23      possible. Do we want to set up something less than that,  
24      at least in certain circumstances?

1                   Now, my reading of the summaries of the Primer  
2 meetings and the National Action Plan on Breast Cancer  
3 meeting is that there was some sentiment there as well;  
4 that--you know, particularly of this latter sort, the kind  
5 Trish was concerned about--that that ought to be possible  
6 when it was really, really important and clinically  
7 relevant, or some other intimate personal way relevant to  
8 the subjects. So we need to address that.

9                   Bernie?

10                  DR. LO: Yes. I think it is a really  
11 important topic, particularly in the context of anonymized  
12 versus anonymous samples; that we have in this grid the  
13 possibility of having samples that are anonymous to the  
14 researcher but linkable to somebody else.

15                  And so it is not a matter that you can't  
16 contact the person because you simply don't know. You  
17 could if you kind of could work backwards through the  
18 system. But we have constructed a system that says, "It  
19 is not going to be permissible to do that."

20                  And it seems to me there are a lot of reasons  
21 why you might want to get back to the patient. One is  
22 just the patient is curious, the patient wants to know,  
23 the patient thinks that is part of the arrangement of  
24 donating tissue.

1                   There is another situation in which clinically  
2                   the researcher, as scientist/clinician, thinks it really  
3                   is in that patient's best interest in that you have made a  
4                   discovery which is far more powerful than you had  
5                   anticipated, so rather than just a slight stratification,  
6                   you have got a combination of genetic findings that  
7                   predicts with--whatever--80 or 90 percent likelihood that  
8                   someone is going to develop a serious form of cancer. And  
9                   you didn't anticipate quite that at this stage of your  
10                  study.

11                  I think the pressure on the  
12                  physician/scientist to say this has clinical importance  
13                  and I would like to at least offer the patient the option  
14                  of learning it is going to be very powerful.

15                  Again, we saw this in the AIDS epidemic where  
16                  there was a lot of AIDS testing early on that was done on  
17                  anonymized samples, samples that were taken for other  
18                  contexts and then stripped of identifiers. And you found,  
19                  you know, 5 percent of people were HIV positive.

20                  And you could have contacted them had you  
21                  allowed the system to work. They were contactable at one  
22                  time. But for a whole lot of reasons, many of which I  
23                  actually argued persuasively at the time, you chose not to  
24                  do so.

1           I just think it is an issue. It is a dilemma.  
2           It is a real dilemma that we need to sort of sort out.  
3           And I think a lot of the concerns that were present in the  
4           AIDS epidemic, where you really needed to get an accurate  
5           picture of the epidemic--you were afraid of biosamples,  
6           scaring off people who were at highest risk--really don't  
7           apply to the type of DNA-based research we are talking  
8           about.

9           So the values that stay are sort of the  
10          convenience of doing the research versus either the wish  
11          of the patient to be informed or kind of a beneficence-  
12          oriented argument that it might be in their best interest  
13          to know.

14          And I just think the idea of a firewall sounds  
15          neat because it seems to solve some problems at the front-  
16          end. It actually makes, creates dilemmas after the  
17          research is done and you get--what we all hope for--  
18          smashingly positive results.

19                 DR. MURRAY: Steve and David.

20                 MR. HOLTZMAN: I just have a quick comment  
21          that struck me when you said the kind of DNA research we  
22          are talking about.

23                 I thought this committee agreed that what we  
24          were dealing with was medical research on stored tissue

1 samples, not just genetic research. All right? And I  
2 think that is just-- And I think we are going to have to  
3 come back to that issue. Just I think that is very  
4 important because three times I have heard that in the  
5 last half-hour.

6 DR. MURRAY: Let us nail that one down.

7 MS. BACKLAR: Yes.

8 DR. MURRAY: Do we agree with Steve that-- I  
9 mean, I think practically I can't find any other way to  
10 think about it. If we are going to come up with a set of  
11 policies and practices about research of stored tissues;  
12 to say they only apply if the research is "genetic" and  
13 not otherwise seems like a-- It seems like we are doing  
14 no favor to anybody involved in the process.

15 Is that-- Now, if there is any disagreement  
16 with that, please let it be known.

17 DR. GREIDER: I agree with Steve.

18 DR. MIIKE: Say that again.

19 MS. BACKLAR: I agree.

20 DR. MIIKE: Are we saying that it is tissue  
21 research? But a lot of the concerns that we have been  
22 discussing don't apply outside the genetic area.

23 MS. BACKLAR: But they might.

24 MR. HOLTZMAN: A lot of the concerns we have



1 position here and the compromise position is--I think this  
2 is what you are sort of trying to nail down, Steve--is  
3 that we had agreed that genetic information isn't  
4 inherently different from other types of medical  
5 information. That is-- I recollect that that has  
6 definitely been agreed to.

7 Having said that, it doesn't mean that there  
8 are not situations where genetic information has some  
9 different implications than other medical information, but  
10 that we don't--

11 (Laughter.)

12 DR. COX: We don't want to-- Is that better?  
13 Okay. I don't want this-- I am scared of them.

14 DR. MURRAY: Just remember all those Grateful  
15 Dead concerts, David. They were right up to the  
16 microphone.

17 DR. COX: So I agree with you, Steve, but I  
18 don't think we want to carve it out, you know, and just be  
19 talking about genetics. But, on the other hand, there can  
20 be special situations and we highlight those if we see  
21 that they exist.

22 And that was exactly the point, Tom, that I  
23 wanted to make in this context of the firewall, too, is  
24 that it makes us feel really good if we have a single box

1 we can put everything in and close the lid. But that is  
2 not the way life works.

3 So that if we could put most of the things in  
4 the box, but then delineate certain exceptions that we  
5 think are likely to happen, and we acknowledge that they  
6 might happen, and we say-- And if they-- And so these  
7 are things we have to think about because the box isn't  
8 perfect. Then I think that is reality.

9 And so I am more than willing to go with what  
10 you say, Steve, but then if there are specific examples  
11 that appear, you know, special for genetics, just  
12 highlight those. But it is not to say that genetic  
13 information is separate from other medical information.

14 DR. MURRAY: We may be flogging this more than  
15 we need to. I mean, I think if our report-- We would say  
16 in our report that we just-- We explored this issue of  
17 the use of human tissues in research because of the  
18 ability to extract large amounts of genetic information  
19 potentially from that tissue, and that is part of the  
20 opening of the report in fact.

21 We could then simply note that it would make  
22 sense to, you know, since tissues can--

23 DR. MIIKE: Aren't we the Genetics  
24 Subcommittee?

1 DR. MURRAY: Pardon? We are the Genetics  
2 Subcommittee.

3 I guess all I want to do is not ghettoize  
4 genetics and also not make people labor under two, sort of  
5 two radically different systems for not good reasons.

6 So we might just say, you know, we think what  
7 we are proposing would make sense as a general set of  
8 principles and procedures governing research with human  
9 tissues, even though we come into this from the genetic  
10 angle. I would I think be content to say that much.

11 DR. GREIDER: Why do we need to say that there  
12 are special instances in which genetics is different?  
13 That is what you just proposed, David.

14 DR. COX: I am saying that, if people want to  
15 say that, then we need to define the special instances.  
16 And I would give an example myself of what I would  
17 consider a special instance in terms of being different.  
18 And it is a quantitative rather than a qualitative  
19 difference. And it has to do with what the predictive  
20 power is.

21 So I would say that if somebody-- If genetics  
22 had a 95 percent predictive power, where most other  
23 information had a 25 percent predictive power, genetics is  
24 different. And it is different because it is more

1 powerful in that specific instance of prediction. Not  
2 overall, but in that one instance. There can be specific  
3 examples that the--

4 The specific example--it is a well worn one,  
5 but to make the point--is Huntington's disease. Okay?  
6 The power of genetic information in Huntington's disease,  
7 when you know that change in the DNA, is an unbelievable  
8 power.

9 DR. GREIDER: What about the predictive nature  
10 of somebody that is infected with HIV virus? There is a  
11 very high predictive feature there and you wouldn't say  
12 that that is a genetic. So there are predictive powers  
13 that aren't necessarily genetic.

14 DR. COX: Oh, no. And I agree with that. All  
15 right? So I am not saying this is unique to genetics, but  
16 it is unique to the specific case.

17 MR. HOLTZMAN: It is unique to a monogenic  
18 highly penetrant disorder.

19 DR. COX: Bingo. Thank you.

20 MR. HOLTZMAN: Okay. Which, when you think  
21 about HIV, is monogenic, a single genome, if you will--all  
22 right?--and highly penetrant.

23 DR. COX: Exactly.

24 MR. HOLTZMAN: So the point is--

1 (Simultaneous discussion.)

2 DR. COX: --is an example.

3 MR. HOLTZMAN: --and what we are concerned  
4 about-- What I always find very useful heuristically is  
5 to forget I even knew the word "genetic" and ask what am I  
6 concerned about? All right?

7 And you find that there will be cases where  
8 the analyte is DNA, the analyte is RNA, the analyte is  
9 protein, instances where it is heritable, instances where  
10 it is not heritable but it is communicable, instances  
11 where it is DNA but a somatic mutation. All right?

12 DR. COX: Exactly. And you use those  
13 examples.

14 MR. HOLTZMAN: And I think that was the whole  
15 conversation that we had in the meeting which Larry wasn't  
16 at when we talked about, yes, we are a Genetics  
17 Subcommittee--all right?--but all of it couldn't be  
18 instances of the papers that Zeke brought forward. And I  
19 think there was only one out of the six or seven which was  
20 a genetic study.

21 And the point he was trying to make  
22 heuristically was the kinds of studies that are undertaken  
23 and where the ethical engine could get going of concern is  
24 not specifically genetic. And I thought we had come to

1           that conclusion. All right?

2                           I don't mean to flog a dead horse, but--

3           DR. MURRAY: That is okay.

4           DR. GREIDER: So, Larry, why do you want to  
5           limit it to genetics if not limiting it to genetics is  
6           more inclusive, would include more things.

7           DR. MIIKE: No, no. I mean--

8           DR. GREIDER: What is the reason to--

9           DR. MIIKE: I am not limiting it to genetics.  
10          I am opposed to saying that the issue that we are looking  
11          at--tissue sample research--is separate from genetics, and  
12          it is not. To me it is essentially the same. I mean, the  
13          concerns that are being raised here.

14                        Are you telling me that the future of research  
15          is diverting away from the genetic basis of the tissue  
16          samples? Isn't that where the research is heading?

17                        I mean, you know--

18          MR. HOLTZMAN: I think research is--

19          DR. MIIKE: --look at me as the lay person.

20          And you are trying-- You scientists are telling me our  
21          concern about tissue samples is not primarily genetics or  
22          not solely genetics. Convince me about that.

23                        MR. HOLTZMAN: Whose concern? That the  
24          individuals, the lay people's concern or-- Whose?

1 DR. MIIKE: No, no. What you folks have just  
2 raised, which is that this is a tissue sample issue; it is  
3 not a genetics issue. I am saying it is a genetics issue  
4 within the tissue sample subject.

5 Or have I just been hearing everything wrong  
6 just lately?

7 DR. GREIDER: I think that it limits what you  
8 will discuss about something to say solely that it is a  
9 genetic issue. It is a biology issue, which is greater  
10 than just the term "genetics."

11 DR. MIIKE: Well, isn't that what the concern  
12 here is?

13 MR. HOLTZMAN: I think you just crystallized  
14 it. All right? If what I was proposing to do was to go  
15 in and analyze whether or not the tissue had an X and Y  
16 chromosome or X and X chromosome, I don't think there  
17 would be a heck of a lot of concern being generated and  
18 people wouldn't be exercised about the issue. So there is  
19 an example of genetic research which is non-concerning.

20 On the other hand, take the HIV example. If  
21 you are going into tissue and you are finding out  
22 something that is non-genetic, it does generate a concern.  
23 Okay?

24 So the only point we are making is that, when



1       resolve this is to try and say that there are certain  
2       types of research that raise profound ethical concerns.  
3       They have to do with telling someone who is relatively  
4       asymptomatic that we can very strongly predict what is  
5       going to happen to you in the future, and it is going to  
6       effect other people as well, and there could be some  
7       stigma and discrimination.

8                     DR. MIIKE: Right.

9                     DR. LO: Those are not exclusive to genetic  
10       information. And the HIV example and cancer and other  
11       things are examples. But I think what we want to say is  
12       that some of the concerns are genetic examples and we  
13       expect there will be other genetic examples.

14                    And to follow up on Larry's point, to the  
15       extent that there will be more and more genetics research  
16       being done, we want to kind of anticipate those problems.

17                    But the issues we are raising are not specific  
18       to genetics; they spread over a whole lot of other--

19                    MR. HOLTZMAN: And that is the point. What  
20       you just did is to forget you understood the word  
21       genetics. What are the characteristics--almost the social  
22       characteristics--that we care about?

23                    DR. MIIKE: No, no. I agree with that. I  
24       mean, I agree with that. But I am looking at this-- I

1 mean, when we talk about genetic information and the  
2 implications of that information, it is like other medical  
3 information. I agree.

4 But I am looking at the specific issue of  
5 tissue samples. Yes.

6 MR. HOLTZMAN: Right. There are all sorts of  
7 analyses that are going to take place on these, Larry,  
8 which are not just looking for heritable genetic  
9 mutations. You are going to be looking at somatic  
10 mutations, you are going to be looking at proteins, you  
11 are going to be looking at any number of different things.  
12 You could be getting all sorts of kinds of information out  
13 of this that are not--

14 DR. HANNA: Steve, I think-- You keep  
15 referring to this. I think you are misinterpreting what I  
16 am having a problem with and perhaps what Larry is having  
17 a problem with.

18 I don't think either one of us is saying we  
19 are only talking about heritable mutation or family  
20 studies or, you know, linear transmission of disease.

21 I think we are talking about the fact that DNA  
22 is stable in tissues. Other forms of medical information  
23 that you can get out of those tissues is not necessarily  
24 stable. And I think what-- It is-- Perhaps there is not

1 as much disagreement as everyone thinks there is, but it  
2 is-- Maybe we shouldn't say "genetic;" maybe we should  
3 say "DNA-based" information.

4 MR. HOLTZMAN: But-- But-- Now you are  
5 hanging the issues of the public policy on the stability  
6 of the analyte, which I really-- I am confused, Kathi. I  
7 mean, why is that important? I mean, if I flesh-- More  
8 and more of these samples are going to be frozen. All  
9 right? And so in fact you will be able to recover other  
10 analytes as well. All right?

11 With respect to urine, which you said doesn't  
12 belong in the report, I think maple syrup urine is a  
13 genetic condition which one can go and look at urine and,  
14 what is more, one can get proteins out of urine and be  
15 able to-- So in fact, in a relevant sense, it is tissue.

16 I mean, what we are talking about, or what we  
17 care about, and where the engine is going to end up going  
18 has to do with issues of informed consent, issues of  
19 potential predisposition, issues of stigmatization--all of  
20 those things--and the notion of one's relationship to a  
21 sample. And all of those issues are not a function of the  
22 analyte, are not a function of the nature of the test.

23 DR. HANNA: Well, I think that-- I don't  
24 think that the report so far is suggesting that these

1 issues are unique to genetics. I mean, in fact--

2 MR. HOLTZMAN: I am not--

3 DR. HANNA: --if you say repeatedly that they  
4 are not unique to genetics, then I would think your bases  
5 are covered. But I think maybe--

6 And I have asked for four months for somebody  
7 to please write, explain, give me a reference--or  
8 whatever--that I can incorporate that will counteract, you  
9 know, the tenor and the tone of what is disturbing you.

10 MR. HOLTZMAN: Well--

11 DR. HANNA: I can't-- I am not convinced, in  
12 a way that I can sit down and write it, so--

13 MR. HOLTZMAN: And that is why-- I am not so  
14 much referring to the report. It is just that I picked up  
15 a comment, or twice in the last 15 minutes that I was  
16 here--and I got here late and I don't know if it was  
17 discussed earlier--but I had thought that the committee  
18 had discussed the issue and had come to a position. That  
19 is all.

20 DR. HANNA: But the position has to be  
21 justified in the report, and we don't have that.

22 MR. HOLTZMAN: We--

23 DR. GREIDER: So, I mean, Zeke pulled out some  
24 very nice examples of where tissues were used

1       prospectively, retrospectively, and we had them all in our  
2       book, and he had labeled them. And, as I recall, most of  
3       those were not using genetic information by any of these  
4       definitions that we have given.

5               So if we can go back to those actual research  
6       papers that he pulled out for us and look at what are the  
7       issues that are discussed there--unfortunately, I don't  
8       have them with me--but my recollection is that most of  
9       them didn't have anything to do with genetics. That there  
10      are issues that go beyond the genetics that are important  
11      in tissue.

12             DR. MURRAY: David?

13             DR. COX: This is a very interesting  
14      discussion because everybody is right. And it is the  
15      relative weight that people are putting on these issues.

16             Of course there are papers that have been  
17      published in the past with respect to tissues that don't  
18      have anything to do with genetics. All right? And of  
19      course it is true that one of the reasons why our  
20      government and the public is excited about medical  
21      research is because they believe that genetics is going to  
22      offer something real special.

23             So it is where the relative balance is. And  
24      for this commission to say it is all in genetics is a

1 mistake, but for this commission to say that genetics  
2 isn't where the action is, and isn't where the excitement  
3 is, I mean, we would get laughed off the stage.

4 DR. MURRAY: I didn't hear anybody who wanted  
5 to say that.

6 What I-- I have a very simple-minded view of  
7 this, which is--I don't know--I think mainly that I want  
8 to keep things as simple as possible. And so if we are  
9 going to articulate a set of principles and recommend a  
10 set of practices about how to deal with research in human  
11 tissue samples, I would like to just do it as that.

12 The door which gets us in there is genetics,  
13 and clearly a lot of the action in the future will be in  
14 genetics, but probably not all of it. But all that is  
15 fine. I just want to keep it simple.

16 I think we do a favor to everybody involved if  
17 we don't segregate and sort of say if you are using this  
18 sample for genetic research these are the rules, but if  
19 you are using it for something else these are the rules.  
20 I think that would be a disaster.

21 DR. COX: Okay. But, Tom, then having said  
22 that--I am in favor of keeping it simple, too--but this is  
23 the point I made before and I will make it again now is  
24 that it is unlikely that we are going to have a single set

1 of rules without any exceptions that takes account of  
2 everything.

3 DR. MURRAY: Oh, yes.

4 DR. COX: And you will get--

5 DR. MURRAY: No argument.

6 DR. COX: And if there are some clear  
7 exceptions that we can easily identify, then I would  
8 rather face them up-front very clearly rather than pretend  
9 they don't exist.

10 And I am not implying that people are trying  
11 to pretend they don't exist, but I think that in an effort  
12 to keep things simple sometimes we don't want to think  
13 about the exceptions.

14 DR. MURRAY: Well, there is simple and rigid.

15 DR. COX: Yes.

16 DR. MURRAY: And there is simple that  
17 acknowledges the fact that, in an effort to keep things  
18 relatively simple, you may do injustices. And so you try  
19 to build in some probably procedural means for responding  
20 to obvious inequities.

21 DR. COX: Exactly.

22 DR. MURRAY: This is a problem that you find--  
23 and one finds--in the law all the time.

24 I have some good articles if anybody wants a

1 reference on it. Steven Tillman(?) has got a wonderful  
2 piece on the tyranny of principles about a decade ago and  
3 he sent a report on this.

4 I think we are okay on this. Now, there are  
5 differences of sentiment here. I am not sure there is a  
6 lot of difference at the end in the substance.

7 Kathi needs a reference. I will give you a  
8 reference. I have the reference. I will give you the  
9 article that I hope will at least articulate one view of  
10 this.

11 We have-- It is almost time for public  
12 testimony, but what I would like to do is spend a few  
13 minutes getting us back to the concern that Trish raised;  
14 that is, what happens if there is information generated,  
15 through research on tissues which had been used  
16 anonymously, that might be clinically relevant for the  
17 person who was the source of those tissues?

18 Just to recap where we have been on this. I  
19 mean, Zeke-- I think we are here articulating Zeke's  
20 position if we say--because I think he said it again  
21 today--he would like to see a pretty impenetrable or one-  
22 way penetrable wall, not being able to go back, partly on  
23 the grounds that if it is-- You know, at least a couple  
24 of grounds.

1           Number one, the kinds of "clinically relevant  
2 information" generated in research laboratories are not  
3 clear level, you know, they are not diagnostic tests as we  
4 normally understand them and standardize them, so there is  
5 some ambiguity there, number one.

6           And, number two, if it is really important it  
7 gets published and it gets disseminated to the health  
8 professionals taking care of these patients and so they  
9 will get the benefit; they will just get it that route  
10 rather than walking, rather than by breaching a firewall.

11           Am I right? Those are two kinds of standard  
12 arguments?

13           Now, over against that we have the kinds of  
14 concerns that Trish has tried to articulate, I think, Do  
15 you-- Why don't you pick up the thread, Trish.

16           MS. BACKLAR: If there is something wrong with  
17 me, I want to know about it. If there is something wrong  
18 with me and might affect my family, I may want to know  
19 about it. I certainly would want to discuss it with them.  
20 But the simple thing, if there is something wrong, I will  
21 want to know about it.

22           DR. GREIDER: But that isn't necessarily true  
23 for everybody.

24           MS. BACKLAR: That is correct. I didn't say

1           it was. I said it was a private--

2                       DR. GREIDER: So that is the issue that you  
3           have to deal with, is that some--

4                       MS. BACKLAR: Correct.

5                       DR. GREIDER: --people feel that way and some-  
6           -

7                       MS. BACKLAR: So I want to put that on the  
8           table because I don't think that I am the only person who  
9           believes that and, in fact, Bette-- Oh, no, it was  
10          actually Tom, I think, who substantiated that point of  
11          view--

12                      DR. GREIDER: But if you allow walking--

13                      MS. BACKLAR: --from the focus groups.

14                      DR. GREIDER: If you allow the walking back,  
15          because there are people that do want to know, then what  
16          about those people that really don't want to know? So  
17          that is the danger of walking back is that there are  
18          people who would--

19                      MS. BACKLAR: I thought that--

20                      DR. GREIDER: --want to not know.

21                      MS. BACKLAR: I thought that--

22                      DR. GREIDER: So where does the weight come  
23          down to--

24                      MS. BACKLAR: Wait, wait, wait. I did think

1       that was why we did all agree that the consent procedures  
2       were--the consent refusal procedures were--very important  
3       in the tissue issue so that if you refuse it doesn't come  
4       back, but I don't-- I would not want to be cut out  
5       because of some procedure that was put in place that  
6       didn't give me the option.

7                   DR. GREIDER:  What about the already-collected  
8       samples where there was no such--

9                   MS. BACKLAR:  Well, I can't live  
10       retrospectively.

11                   DR. GREIDER:  Well, I mean--

12                   MS. BACKLAR:  I am not--

13                   DR. GREIDER:  --we are dealing with that  
14       though.

15                   MS. BACKLAR:  Right.  Well, obviously I can't  
16       alter that in which there is no way back.  I mean, it is  
17       not--

18                   DR. GREIDER:  There is a way back.

19                   MS. BACKLAR:  It is like Orpheus and Eurydice.  
20       If you look back it is over with.

21                   DR. GREIDER:  Well, there is a way back--

22                   MS. BACKLAR:  There is a way back?

23                   DR. GREIDER:  --currently, but those people  
24       haven't said whether they would or wouldn't want to be re-

1 contacted. That is the issue. And if you re-contact  
2 them, you might be giving them information that they don't  
3 want to know and you are already--

4 MS. BACKLAR: You are giving them the option  
5 of saying yes or no, you see. You are giving them the  
6 chance to say yes or no. If there is a way that you can  
7 go back, you are at least--

8 DR. GREIDER: Not if you have a piece of  
9 information about somebody and you are contacting them  
10 because you know this information and you want to get more  
11 information from them. Just by contacting them, that is  
12 giving them some information.

13 DR. MURRAY: Harold wanted in on this.

14 DR. SHAPIRO: Trish, just ask the question.  
15 You are concerned with future samples. Do I understand  
16 that correctly or not?

17 MS. BACKLAR: Yes.

18 DR. SHAPIRO: And in all cases, therefore,  
19 there is individual consent, according to this.

20 MS. BACKLAR: Right.

21 DR. SHAPIRO: Therefore, does your issue come  
22 down--I am asking a question--to what we provide, what the  
23 nature of that consent form is in this respect; that is,  
24 whether a consent form contains some options in this

1 regard, or not?

2 MS. BACKLAR: Well--

3 DR. SHAPIRO: I am just asking a question. I  
4 am not--

5 MS. BACKLAR: No, no. I am actually not going  
6 to quite answer your question. It seems to me evident  
7 that one should have those options there.

8 DR. SHAPIRO: Okay.

9 MS. BACKLAR: I don't-- I have no difficulty  
10 with that.

11 I think that Carol has brought up something  
12 which is significant in this and that is that, if  
13 something was found out in tissue that was already  
14 collected that might benefit me and that I had not been  
15 able to give my specific consent to and there was some  
16 firewall built, I would be very concerned that I didn't  
17 have access to that.

18 DR. MURRAY: David, and then Bernie.

19 DR. COX: So, to say it in a slightly  
20 different way, but the same point that Trish is making, as  
21 a physician if I find out that my-- My oath as a  
22 physician is to do no harm. If I find out something about  
23 a person--that they are going to die and I have a  
24 treatment that can keep them alive--I have a real conflict

1       if I have a firewall that says I can't contact that  
2       person.

3                     DR. MURRAY:  And they don't know.

4                     DR. COX:  And they don't know.

5                     Because most of the patients that come to me  
6       as a physician don't know.  It is my duty as a physician,  
7       if I know, to act on that.  All right?  So this is an  
8       ethical dilemma.

9                     Now, it has recently come up in the context of  
10       genetics research--we heard it from Bartha Knopper and it  
11       was a big symposium at the American Society of Human  
12       Genetics meetings--if you have information, genetic  
13       information, from your patient, what is your obligation to  
14       tell their family members?  In this country, it has been  
15       very different from what the answer is in Europe.  Okay?

16                    Now, what was the conclusion at the American  
17       Society of Human Genetics meeting about this?  The  
18       conclusion was that--and it was a compromise position--  
19       that still you would respect your individual patient but  
20       there would be designated examples that would be  
21       exceptions of which you would be justified of going and  
22       telling the family member, examples that would put them at  
23       extreme risk.  All right?

24                    Thank you.

1           So the issue then is again coming up with  
2 exceptions, coming up with the examples of when it would  
3 be possible to breach the firewall. And it is the same  
4 situation of giving people information back. It is not  
5 that you have it open all the time.

6           Carol brings up a good point. Some people  
7 want to know, some people don't want to know. So you have  
8 to deal with that situation. We are not going to have a  
9 million of these different examples, but this is one of  
10 them. And just to deal with it.

11           Not that we are going to be able to fix it--I  
12 don't think we are going to be able to have a single rule  
13 that is going to fix it--but we have to open the  
14 possibility of going back because otherwise it doesn't,  
15 you know, pass the red-face(?) test. There is enough  
16 people that want to know and there are enough people that  
17 don't want to know that we have to have options for it.

18           DR. MURRAY: The queue is forming. Bernie,  
19 Trish, Larry.

20           DR. LO: Yes. I think this is a really  
21 important topic for us to think about, and I think we have  
22 some tough issues to think through.

23           One, I think we need to do a good job of  
24 elucidating what the conflicting ethical responsibilities

1 and principles are because what is most bothersome to me  
2 is the reason we built the firewall in the first place was  
3 really to further scientific research and make it more  
4 feasible by not putting too much burden on researchers to  
5 get detailed specific consent.

6 There are a lot of other competing--

7 DR. MURRAY: I would very much-- My first  
8 thought was to protect the privacy of the people whose  
9 tissues are being used. That would have been mine. But  
10 you don't think so?

11 DR. LO: Well, I may be more cynical. I hang  
12 around with researchers too much.

13 I mean certainly if you hear some of the  
14 professional societies, their biggest concern is they  
15 won't be able to do research that they think really  
16 benefits humanity and science in the long term. But, I  
17 mean, privacy of the individual is on that side, but then  
18 the right of some individuals to know, and the duty to  
19 protect, you know, give them information that may make it  
20 a benefit clinically.

21 That needs to be laid out because I think  
22 scientists and the public are very confused about those  
23 issues and don't realize that there are really pretty  
24 fundamental conflicts.

1                   Secondly, if we look to other situations--this  
2 goes back to Steve's point--this is not unprecedented.  
3 You know, HIV again gives you a lot of examples.

4                   The procedures for how you go back, under what  
5 circumstances, how do you bring in the private physician  
6 as opposed to the researcher cold-calling the patient  
7 directly, are things that we should all think about.  
8 There are better and worse ways of doing this kind of re-  
9 contacting.

10                  And then there are sort of different kinds of  
11 re-contacting. Trish, I think, was talking about  
12 clinically relevant information that an individual subject  
13 may or may not want to know, but should we at least offer  
14 them the option of finding out?

15                  Carol brought up another example, which is  
16 sort of a twist; that if I take David Cox's model of how I  
17 am going to do 21st Century genetic research, I start with  
18 a huge prospective cohort study and, out of that, I find  
19 the 1 percent of patients of interest, and I want to go  
20 back and study them.

21                  Now, either I can do it up-front, full  
22 consent, contact them a second time and say I would like  
23 to sit down and tell you about a study I am proposing, get  
24 your feedback, and get your consent.

1                   Or I can do it in an anonymized way where I  
2                   say I am going to not get involved like that. I am going  
3                   to have the steering committee of my prospective trial  
4                   add-on to the next battery of questionnaires that comes  
5                   out in six months some specific questions for that 1  
6                   percent that deal more with family history and other  
7                   phenotypic information.

8                   Technically, under our boxes, you know, I have  
9                   met the letter of the law.

10                  Carol brings up an interesting point which is,  
11                  you know, if the 1 percent, if I am one of those 1 percent  
12                  and my neighbor isn't, and we sit down and compare our  
13                  questionnaires, I say, "Hey, how come they are asking me  
14                  all these cancer questions and not asking you? Why? What  
15                  did they find out about me?" That is, you know, it seems  
16                  to me an ethically, you know, shaky situation.

17                  And the reason we got there is that there were  
18                  incentives for some researchers to opt out of a sort of  
19                  true dialogue with the subjects by sort of taking the  
20                  anonymized route rather than the full consent route.

21                  And I think that, you know, we are building in  
22                  some very, some incentives that are pushing us away from  
23                  the ideal of research as a partnership between the  
24                  scientists and the participant. And I think we just need

1 to be aware that that incentive is going to push some of  
2 my--

3 It is a lot easier for some of my colleagues  
4 to say, "I don't have to talk to the patients." Somebody  
5 else is hired to get the information, anonymize it, feed  
6 it back to me. It is a lot easier for me.

7 MS. BACKLAR: I think also--I said this as  
8 though I was a private citizen from a personal point of  
9 view, but I actually think there is another issue here  
10 which has been sort of touched on in terms of HIV and so  
11 forth--there are also public health issues. I just want  
12 to put that back on the table. Public health issues.

13 DR. MURRAY: You mean where third parties are  
14 affected by the results?

15 MS. BACKLAR: Where it may be necessary to  
16 give information to a group.

17 DR. MIIKE: My turn? I don't think you can  
18 have a practical policy with all those exceptions and all  
19 those individual decisions.

20 The way I would deal with your situation,  
21 Trish, is to say here is your informed consent form, in  
22 the beginning. And you say, "Can you assure me that if  
23 some research is done on my tissue and it is beneficial I  
24 will get it back; I will get that information?" My answer

1 is no. Then your choice is to either sign that or not  
2 sign it.

3 MS. BACKLAR: But we are talking about tissue  
4 that may have been taken without consent. That was the  
5 whole point Carol brought up.

6 DR. MIIKE: Well, but if we are talking-- Our  
7 proposed scheme is that, for prospective, you can't use  
8 it.

9 MS. BACKLAR: For prospective--

10 DR. MIIKE: You have to give a general or  
11 specific consent so, in that case, they would not be able  
12 to use it in our scheme. The way I understand our scheme  
13 being proposed.

14 MS. BACKLAR: I am sorry. It is very hard to  
15 hear in here. Can you--

16 DR. MIIKE: Well, what I am saying is that in  
17 the scheme that we are proposing--

18 MS. BACKLAR: Yes.

19 DR. MIIKE: --not already collected samples,  
20 but samples to be collected clinically or in research, you  
21 must give a consent.

22 MS. BACKLAR: Prospectively?

23 DR. MIIKE: If you don't give a consent--

24 DR. MURRAY: Yes.

1 MS. BACKLAR: Yes. I understand that.

2 DR. MIIKE: So what I am saying is though is  
3 that if you then say but if in the future something  
4 happens and it is beneficial to me, or if it is something  
5 significant and I want to be assured that I know about it,  
6 and can I give that assurance, then your choice is to say,  
7 "Okay, I won't sign," or you accept the consequences of  
8 that and sign the form anyway, given that knowledge.

9 But I don't think we can have forms and  
10 consents that vary all over the place.

11 One last comment is my disagreement on the  
12 tissue sample. I just suddenly realized that I was  
13 focusing on the community aspects of it and we are dealing  
14 with individual with no community, so in those instances  
15 then, then genetics is not the only issue. So I would  
16 agree with you when we are talking about individual harms  
17 and benefits without the community aspect.

18 DR. MURRAY: We are going to run out of time.  
19 Arturo and Carol had indicated a desire to speak. Let me  
20 just say how I would propose to play it from here on in.

21 To hear Arturo and Carol, and if there is  
22 anything urgent that must be said in response to them: we  
23 will have that.

24 To ask-- I believe we just have Mark Sobel

1 speaking as public testimony.

2 And then to use the remainder of our time to  
3 make our plans for tomorrow.

4 Arturo?

5 DR. BRITO: I just want to briefly respond to  
6 what Trish is saying. When I originally heard Trish make  
7 a comment, it made a lot of sense about of course if you  
8 take a tissue sample of mine and later on you find out  
9 there may be some information about me, of course I would  
10 want to know that.

11 But going along with what Larry says it seems  
12 endless; that there are so many scenarios--just looking at  
13 the table here--so many scenarios.

14 When we talk about anonymous, we are talking  
15 about anonymous really to the individual but not  
16 necessarily-- Well, we are also talking about the  
17 researcher, but it is a very paternalistic way of looking  
18 at it in terms of--

19 If you take a tissue sample of mine, unless  
20 there is a way of me having accessibility to that tissue  
21 sample in the future--me as the patient or as the person  
22 that the research has been done on--unless I have  
23 accessibility to that, then what you are doing is leaving  
24 it up to the physician/researcher to determine what is

1 good for me and what is not good for me.

2 So going back to what Larry says, it is just  
3 endless what you can do here. And I think that you really  
4 have to make the decision at the beginning whether or not  
5 you are going to agree to the research knowing that you  
6 are not going to have accessibility to that, or that no  
7 one is going to tell you of any problems with that.

8 I see Trish shaking her head, but unless-- I  
9 am not sure there is a simplified manner of doing this.  
10 It just gets so complex.

11 DR. MURRAY: Carol?

12 DR. GREIDER: I think part of the  
13 misunderstanding here is that, in some cases, we are  
14 talking about tissue samples that are already collected  
15 and, in other cases, we are talking about prospective  
16 collection of samples, which is part of the reason that  
17 Zeke laid out this nice grid, which now has two rows and  
18 multiple columns.

19 And so what I would find very helpful--we have  
20 had a lot of discussion about this--it would be very nice  
21 to have, you know, written down, so that we could look at  
22 them, what all of our recommendations are for each one of  
23 those different instances. And then we could discuss them  
24 piece by piece, rather than having misunderstandings about

1       whether it is prospective or retrospective and jumping  
2       back between the two.

3                   DR. MURRAY: I think we are there actually on  
4       most points. I don't think we are there on this issue of  
5       do we ever permit breaches of the firewall.

6                   DR. GREIDER: Absolutely. But to go back and  
7       forth and have these misunderstandings is a little bit  
8       frustrating.

9                   DR. MURRAY: Yes. Especially--

10                  DR. GREIDER: It would be nice to go through  
11       and discuss that issue, but on the right side of the  
12       prospective versus retrospective. And we have to discuss  
13       both of them.

14                  And I agree that I think we have talked about  
15       all of the boxes, but I don't think that, you know, we  
16       have ever really articulated exactly what is going to  
17       happen in each of them.

18                  DR. MURRAY: Well, maybe not, but I think we  
19       pretty much know, for each of them, what we are doing.

20                  DR. GREIDER: But this issue between Larry and  
21       Trish--

22                  DR. MURRAY: Not for every question.

23                  DR. GREIDER: --I see as one being a  
24       prospective issue and the other being a retrospective

1 issue.

2 DR. MIIKE: No, no. No.

3 DR. MURRAY: No. I think it is--

4 DR. MIIKE: No. It is a question about how  
5 much she wants to be able to know in the future, when you  
6 can't tell at the time that you are giving consent what is  
7 going to happen.

8 And I am saying that you cannot devise a  
9 policy that will satisfy the Trish's of the world in every  
10 instance that she wants. And so you must make a choice at  
11 the beginning about either to say, "Well, then I won't  
12 participate; I don't want to participate," or "I will  
13 participate given those limitations on what is accessible  
14 to me."

15 I mean, I think that is the only kind of  
16 practical choice that you can make. You cannot make these  
17 very specific consent-type agreements and promises down  
18 the road that cannot be fulfilled.

19 DR. BRITO: Can I just-- I know you want to  
20 get on to the next thing, but when we are talking about  
21 these boxes, we are talking about the--

22 What I am seeing here is the anonymous tissue  
23 and then the identifiable tissue. That is identifiable to  
24 the researcher. Unless there is a way to make it

1 identifiable to the individual involved in the research,  
2 then I would agree then there is a way. But I am not sure  
3 if that is logistical. Maybe David or somebody who does a  
4 lot of research can answer that.

5 But would it, you know, maybe at the  
6 beginning, you could make some access code or something so  
7 people can identify their tissue in the future. I don't  
8 know. But I think unless you can do something like that,  
9 I agree with Larry.

10 DR. MURRAY: Steve?

11 MR. HOLTZMAN: The sense in which we have been  
12 talking about anonymized is research conducted in an  
13 anonymous fashion by which the paradigm would be that  
14 there is a sample, it is associated with an individual, it  
15 is held by someone who is distinct from the researcher,  
16 the researcher knows it by a number--all right?--but the  
17 researcher doesn't have the ability to go and identify the  
18 individual.

19 So the issue boils down to here, in your  
20 consent process--we will come back to the retrospective  
21 ones in a moment; let us deal with the prospective--  
22 whether or not you are going to include in that consent  
23 either a statement that says there will be findings made,  
24 some of them might be relevant to your future health

1 status, but you will not know about these. You will not  
2 be informed.

3 Or rather you will create a process, such as  
4 for example Yale has a process which Levine describes in  
5 the notes from the national breast cancer stuff, the Arena  
6 Primer stuff or, as you see in what Primer struggled with,  
7 should we have something where it can be a very generic  
8 statement.

9 If a finding is made in the study which is  
10 potentially beneficial to you, or could be actionable by  
11 your physician, your physician will be informed.  
12 Whatever. A mechanism would be set up. You don't have to  
13 be specific. All right? Just say it is basically that  
14 you leave the avenue open to go back if there is benefit.

15 The downside on it? The downside is if the  
16 major concern is privacy--the major concern is  
17 discrimination based on privacy--have you put the, have  
18 you opened up, by opening up the possibility of going  
19 back, have you created more problem than you have solved?

20 What we clearly heard I think from the fora,  
21 the public fora, is people think, "Hey, I can learn  
22 something that, if it benefits me, I should know about  
23 it." It just seems like the human thing to do. All  
24 right?

1 DR. MIIKE: That is not the situation I am  
2 talking about. I am talking about the research down the  
3 road after that one.

4 MS. BACKLAR: Oh.

5 MR. HOLTZMAN: But if you think about-- In  
6 the case of the sample collected in the clinical context  
7 where there is no specific contemplated research, all of  
8 the research is down the road.

9 The national breast cancer example is  
10 specifically oriented to stuff collected in the clinic.

11 DR. MIIKE: Oh, no. That is my point. When  
12 you know what you are going to be doing in that research,  
13 of course you can make promises like that. But it is the  
14 subsequent uses that I am talking about.

15 MR. HOLTZMAN: Well, that is what I am  
16 talking--

17 DR. MIIKE: And those are the kinds of things  
18 that she wants to--

19 MR. HOLTZMAN: Which is what I am talking  
20 about, too, Larry.

21 DR. MURRAY: Yes.

22 MR. HOLTZMAN: I am talking about that.

23 DR. MURRAY: And I think that is what showed  
24 up in the Primer Conference and what actually showed up in

1 at least the mini-hearing that I attended.

2 MR. HOLTZMAN: Right. Because it is also the  
3 case it is in that future research and/or things that come  
4 up in the research that you find out which may not be the  
5 object of your study even to begin with. Okay?

6 DR. MURRAY: Trish has something to say on  
7 this--

8 MS. BACKLAR: It is just a--

9 DR. MURRAY: --and this may well be something  
10 we are going to have to talk about again tomorrow.

11 MS. BACKLAR: It is just a request. I would  
12 like to have in front of us--maybe tomorrow if it is not  
13 too difficult--Bartha Knopper's remarks that David alluded  
14 to because I remember them but rather vaguely.

15 DR. COX: Just very quickly, Tom?

16 DR. MURRAY: Yes.

17 DR. COX: I think you articulated beautifully.  
18 You responded to Carol's challenge and articulated  
19 beautifully where, with respect to the boxes, this point  
20 was. We were in prospective. And also the options. We  
21 either have a process for going back or we don't.

22 And a final point that you made that I would  
23 like to really emphasize is a motivation for doing this is  
24 different public interest groups and different IRB groups

1 really think that this is something that is worthy of  
2 consideration, even though it is difficult, Arturo, as you  
3 point out. It is very difficult.

4           You know, it is hard to imagine how you can do  
5 it comprehensively, but is it worthwhile thinking of  
6 mechanisms? Okay? Is there any mechanism that is  
7 possible? Well, these other groups are thinking of such  
8 mechanisms. In some ways, we should at least consider  
9 potential mechanisms.

10           DR. MURRAY: An historical note. I was on the  
11 committee of the ASHG(?) that wrote, with Bartha, this  
12 paper that she spoke from.

13           And basically the paper, as I recall, simply  
14 adopts the sort of points to consider of the previous  
15 President's Commission article about when, if ever, do you  
16 breach confidentiality under certain circumstances.

17           And I don't remember the exact list, but there  
18 are three or four things--some of you here may have them  
19 memorized--that might fit quite well in a kind of  
20 recommendation that we would make in these circumstances,  
21 so they would be the rare occasion when the firewall might  
22 be breached for the patients, for the tissue contributor's  
23 benefit.

24           But we don't have any more time to talk about

1 that today, I am sorry to say.

2 I think we owe-- I apologize to Mark Sobel  
3 for putting his testimony off but, Mark, may I ask you  
4 please to take the microphone? And if you don't mind one  
5 more time indulging us with the ritual of identifying  
6 yourself and your institution.

7 STATEMENTS BY THE PUBLIC

8 DR. MARK SOBEL

9 MOLECULAR PATHOLOGY DIVISION

10 NATIONAL CANCER INSTITUTE

11 DR. SOBEL: I am Mark Sobel of the Molecular  
12 Pathology Division of the National Cancer Institute.

13 I would like to address three issues based on  
14 the discussion that you have had this afternoon.

15 One is an issue that Dr. Shapiro brought up  
16 that I don't think you have really followed up on, and  
17 that is who decides what box things go into? And I would  
18 like to provide to you an example that occurs at NIH for  
19 intramural scientists, which is that the intramural  
20 scientist does not have the right to decide what box it  
21 goes into.

22 There is a triage system, which we call the  
23 Office of Human Subject Research, which I think exists in  
24 many institutions as well. Before it goes to the IRB,

1       there is the determination, by somebody--a third party--  
2       that it is or is not exempt from further review. And I  
3       think the commission might want to consider such a  
4       recommendation to be included as part of this mechanism.

5               The second issue is related to the discussion  
6       this afternoon about genetic information, whether or not  
7       it is separate or distinct from medical information. And  
8       I would urge you to include the general feeling that, in  
9       this report, that genetic information is just like other  
10      medical information. And there are many examples of non-  
11      genetic research that are potentially stigmatizing or  
12      harmful and vice-versa.

13              However, it has been pointed out that there  
14      are some specific cases which are potentially more  
15      dangerous or harmful to subjects. And I would urge you to  
16      consider looking at the National Cancer Institute's  
17      guidelines for giving out certificates of confidentiality  
18      which outlines a series of specific types of research that  
19      might be potentially harmful and that might lead toward  
20      the granting of a certificate of confidentiality.

21              And they have a nice booklet now that they  
22      have just come out with that summarizes the rationale that  
23      could be used, and you could refer to that.

24              Finally, I would like to address the most

1       contentious issue for this afternoon, which is the  
2       firewall concept.

3               The pathology consensus group did state that  
4       there might be situations in which researchers might come  
5       up with information that they feel would be potentially  
6       advantageous to the research subject, however the research  
7       was performed in an anonymous manner. And it was always a  
8       possibility that the firewall might be breached.

9               At the time we proposed an IRB or some  
10       clinical review board be in place to consider such  
11       specific requests but, once that request was made, that  
12       would really involve, if it was future research as Dr. Cox  
13       pointed out for a subset of patients, that would really  
14       involve a new proposal requiring specific informed consent  
15       for getting new information or new samples from people.

16               And in the case of patients or research  
17       subjects that would like information that they think might  
18       be clinically relevant to them, I would urge you to limit  
19       that scenario because, as most researchers know, most  
20       research in the early stages is quite speculative and we  
21       really don't know what the penetrance and what the real  
22       meaning of it is.

23               And so I think we need to educate the public  
24       and you need to include in your report information for the

1 public that stresses that, in the long term, research does  
2 people good, but in the short run there are very often  
3 misunderstandings and misinterpretation of research data.

4 And that is the whole point of peer review and  
5 letting things incubate in the literature until there is a  
6 consensus so that there should be rare situations when it  
7 would be necessary to go back to the research subject with  
8 clinically relevant information.

9 The reason that CLEA(?) was passed was to  
10 protect the public from the misuse of research data that  
11 was performed in non-certified tests or with tests that  
12 really do not meet the requirements of test validity and  
13 test utility.

14 DR. MURRAY: Thank you, Mark.

15 I can't help but note that we probably have  
16 helped to create that problem. How many times have we  
17 read an article that reports some very, very basic science  
18 discovery that says it might lead to a cure for cancer?  
19 Right? And subjects read that and they don't see all the  
20 steps in between. So we have to shoulder some of the  
21 responsibility for that particular misperception on the  
22 public's part.

23 CLOSING REMARKS

24 THOMAS MURRAY, Ph.D.

1 DR. MURRAY: We have a few minutes left. We  
2 have to decide what we are going to do tomorrow in our  
3 roughly two and a half hours that belongs to actually us.

4 I think we want to-- Let me just tell you  
5 some of the things I think we ought to do, and then I am  
6 looking for guidance as to how we should, who should sort  
7 of take the lead to present the various components.

8 We should explain how it is that we came up  
9 with this notion of research conducted in an anonymous  
10 manner and how that differs from the prior idea of  
11 "anonymized samples."

12 Are you with me on that?

13 DR. SHAPIRO: I think that is a really  
14 critical issue for the entire commission to understand so  
15 I hope whoever does it-- I hope you will--

16 DR. MURRAY: Do we have a volunteer who wants  
17 to explain that idea?

18 (No response.)

19 DR. MURRAY: I mean the option is, if we don't  
20 have a volunteer, is either I appoint somebody to do it,  
21 or I do it myself. I guess it depends on how generous or  
22 self-flagellatory I am feeling at that moment.

23 As you know, our fellow commissioners are  
24 fairly bright folks who are not inclined to take things on

1 faith, so be prepared to defend any position that you are  
2 representing us on. Because that is one thing I think we  
3 absolutely need to do. We need to present the boxes.

4 DR. COX: I nominate you for that one, Tom,  
5 because I think you would do a great job.

6 DR. MURRAY: Oh, thanks a lot, David. Okay.

7 We need to do the boxes and explain. I think  
8 we could do it historically--in so how we started out with  
9 so many--but that is not really the best way. Let us just  
10 talk about the ones we have and why we feel they make  
11 sense, and capture the significant, some dimensions at  
12 least of the problem.

13 And Zeke is not here.

14 DR. HANNA: He will be here tomorrow.

15 DR. MURRAY: He will be here tomorrow. Eric  
16 is willing to talk to him this evening. Is that right,  
17 Eric?

18 DR. MESLIN: Yes.

19 DR. MURRAY: I think my inclination would be  
20 to ask Zeke to conduct that part of the presentation. How  
21 do you feel about that?

22 DR. MESLIN: And just as a point of  
23 clarification, that part would be his corrected original  
24 form that you didn't get today that he regretted he was

1       unable to provide, plus the amended boxology--the reducing  
2       the three rows to two--so that the full commission would  
3       see what had originally been discussed and what had been  
4       agreed to.

5                       Zeke actually wasn't here when you agreed to  
6       that, but I will, with your advice and consent, encourage  
7       him to be pleased to present that, having not been here  
8       for the presentation.

9                       DR. MURRAY: I am going to suggest we not call  
10      it a "boxology." It has a--

11                      DR. SHAPIRO: People have been using matrices  
12      for years and we are the first ones, as far as I know--  
13      Maybe Kathi or somebody came up with that.

14                      DR. MURRAY: Let us call it a matrix. I mean,  
15      boxology has a faintly theological and even derogatory  
16      tone--

17                      (Laughter.)

18                      DR. MURRAY: No. I mean, some people might  
19      think of it as derogatory and I don't want to get into  
20      that. It is a matrix. That is all it is.

21                      We think we should talk about the community  
22      consultation idea. That is a key idea.

23                      Now, the Human Subjects group has been talking  
24      about this as well, I take it, so it won't come as--is

1       that true?--it won't come as a complete shock to them.

2       But I would be very grateful if Bernie would take a few  
3       minutes and just lay out some of our thoughts about that.

4                Is that-- How does that strike you?

5                I think the firewall issue-- The concept of a  
6       firewall, a one-way wall, will come up as Zeke talks about  
7       his matrix. The issue we were just trying to resolve, I  
8       think not fully successfully within the past half hour, is  
9       a substantial one.

10               I don't see any-- I don't see it as a bad  
11       thing if we simply lay out that we are having this  
12       conversation about when, if ever, or should we create an  
13       impenetrable firewall, or should we permit certain rare  
14       exceptions? If we couldn't just in fact put that before  
15       the full commission and ask for their input as well.

16               Because I don't think there is anything-- Not  
17       only is there nothing wrong with that, there is actually  
18       some advantage both in terms of they may have some ideas  
19       that we haven't thought of, and also it will involve them  
20       in a constructive way in helping to shape the report. So  
21       I would be in favor of doing that.

22               Is that suitable?

23               Are there other central elements--features--  
24       that we must specifically address tomorrow morning?

1 DR. SHAPIRO: Tom, it is not a direct answer  
2 to that important question, but in terms of the firewall,  
3 when it should be penetrable, if ever, and so on--that  
4 whole set of issues--I think it would be helpful if one  
5 could spend some time understanding whether being unable  
6 to penetrate it would put you in an ethically indefensible  
7 position.

8 Quite aside from the examples that have been  
9 given here, it seems that we need to understand whether,  
10 if you took the extreme position, which I am not  
11 suggesting for the moment, but it would really be helpful  
12 to understand if you could define an ethically  
13 indefensible position that would lead you.

14 So that is really an assignment for some  
15 future moment when we could discuss this.

16 As I look--and perhaps this is part of what  
17 you anticipate as Zeke's presentation tomorrow--that is,  
18 the current matrix of possibilities shows that consent is  
19 not required for some, under certain circumstances for the  
20 retrospective samples; that is, the far-left row.

21 And I just want-- I think it is important the  
22 commission understand that. I am not-- That seems fine  
23 to me just myself, but it is just I think quite important  
24 that Zeke outline that, draw their attention to that

1 issue.

2 DR. MURRAY: Yes.

3 As we talk about this, sort of the pro and con  
4 of whether to ever breach the firewall, lots of people  
5 were very articulate about it. Two in particular I  
6 thought were Trish and Larry.

7 Would the two of you be willing to just sort  
8 of present, you know, without necessarily, you know,  
9 feeling cemented into the position, to presenting the  
10 view, A, I mean, of Trish's view that it might be  
11 desirable to permit it and Larry's view, from a policy  
12 standpoint.

13 Would the two of you be willing to sort of set  
14 the debate off for us on that? Okay.

15 I think we have the four essential elements.  
16 There is a fifth which we could integrate into Zeke's  
17 presentation and that is the idea, which I thought was a  
18 very good one, about how--going forward from here, in the  
19 future--how we would deal with the issue of consent.

20 And, as I understand it, the way we would deal  
21 with it is to, you know, have a consent. We are going to  
22 talk about the features, et cetera, without giving a model  
23 form, but we are going to say that, in terms of the  
24 process, it seemed to us to make sense to have a consent

1 more or less at the time of tissue donation.

2 And if someone chooses not to consent then and  
3 there, obviously they are out.

4 But for people who do consent then and there,  
5 we also send them, or give them, to be sent back within a  
6 couple of weeks, if they change their mind and they want  
7 to remove their tissue from the research pool, they are  
8 going to be permitted to do that.

9 So it is you must have a positive consent,  
10 plus people get a second opportunity to change their mind.  
11 Is that-- Is that how you recollect our discussion about  
12 that? We should at least mention that.

13 Carol?

14 DR. GREIDER: In this presentation that you  
15 are saying that Zeke is going to make about the matrix,  
16 are we going to have him go through and discuss what we  
17 have suggested as how we would fill in that matrix?

18 DR. MURRAY: Yes.

19 DR. GREIDER: And in doing so discuss with the  
20 full commission what we believe each one of those ought  
21 to--

22 DR. MURRAY: I think we have to.

23 DR. GREIDER: Sorry.

24 DR. MURRAY: Yes. Without spending two hours

1 on each of the boxes, yes, I think we have to.

2 DR. GREIDER: Right. Because in the past,  
3 when Zeke has presented that, first we focused on should  
4 this be the matrix that we are discussing? Do we have the  
5 right categories?

6 DR. MURRAY: Yes.

7 DR. GREIDER: And I would certainly prefer if  
8 he says, "These are the categories that we have come up  
9 with. These are our reasons." But then go through with  
10 the commission and say what the different suggestions  
11 would be in each one of those.

12 DR. MURRAY: Yes. I mean, I think you are  
13 right. We have made the jump from are these the right  
14 categories to these are the categories we are working with  
15 now and here is how we plan to fill--

16 (Simultaneous discussion.)

17 DR. GREIDER: So first maybe just discuss  
18 that?

19 DR. MURRAY: Yes. It is important-- I mean,  
20 I am sensitive to the fact that people in the audience may  
21 not have had copies of the matrix to look at when we are  
22 talking about 1a, 2b, you know, et cetera. Let us make  
23 sure we have a transparency, or some way to show the  
24 people what we are talking about, and not just the

1 commissioners.

2 MS. BACKLAR: So have them make 2 and 3, 1? I  
3 mean, not-- No, no, no. I don't want to confuse things.  
4 One is 1. Two and three are--

5 (Laughter.)

6 (Simultaneous discussion.)

7 MS. BACKLAR: Yes?

8 DR. GREIDER: One and two and that is it.

9 MS. BACKLAR: Good. Okay.

10 DR. GREIDER: Right?

11 DR. MURRAY: There is individual and there is  
12 community, right?

13 DR. GREIDER: Right.

14 DR. SHAPIRO: Carol, if this weren't a Genetic  
15 Subcommittee, we could call the boxes "cells."

16 DR. GREIDER: Ahhh. Okay.

17 DR. MURRAY: All right. Anything else urgent  
18 that we need to do today?

19 (No response.)

20 DR. MURRAY: No.

21 ADJOURNMENT

22 THOMAS MURRAY, Ph.D.

23 DR. MURRAY: Thank you. It has been a very  
24 constructive-- Did you want to say something, Eric.

1 DR. MESLIN: Just very quickly--

2 DR. MURRAY: Before he adds that, let me just  
3 thank you all. It has been a very constructive day.

4 Eric?

5 DR. MESLIN: For those who were following the  
6 agenda and noticed the item which was "Future Commission  
7 Research Activities," we did not get to that today. That  
8 is only because of timing.

9 This is an issue that the full commission will  
10 be discussing tomorrow and it is the result of the  
11 informal discussions that a few commissioners have had at  
12 the request of the chairman to start strategizing about  
13 the future reports that the commission will take on.

14 So you may want to think about that a little  
15 bit this evening, but there will be time--a considerable  
16 amount of time--tomorrow afternoon devoted to that subject  
17 that will be led in the discussion by Eric Cassell.

18 DR. SHAPIRO: Finally, let me thank Tom for  
19 his Christmas cookies. Thank you very much.

20 DR. MURRAY: That is okay. See you tomorrow  
21 morning.

22 (Whereupon, at 5:03 p.m., the meeting  
23 adjourned, to reconvene as the meeting of the National  
24 Bioethics Advisory Commission the next day, Wednesday,

1 January 7, 1998, at 8:00 a.m.)