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DAY TWO, January 20, 1999

Opening Remarks

Harold T. Shapiro, Ph.D. 1

Discussion of the Commission Draft Report, The Use of Human Biological Materials in Research

Thomas H. Murray, Ph.D., Kathi Hanna, Ph.D., and Commissioners 4

OPENING REMARKS

DR. SHAPIRO: Our schedule today calls for us to adjourn at 1 o'clock, but it seems a more realistic target for us to adjourn at 12, given some Commissioners need to leave. So let's try to move ahead as expeditiously as possible. Now, our next meeting will be held only a few weeks from now, actually less than two weeks from now: February 2 is our next meeting. And in terms of the Human Biological Materials Report we have to, depending on the progress of things, either at the next meeting or at the very latest the meeting after that, reach conclusions on which recommendations we're going to approve. Now the public comment period ended yesterday, or the day before yesterday, something of that nature, and we really haven't had a chance to fully absorb and think carefully about the many thoughtful comments we've received. And that should be a critical component in our thinking before we [INAUDIBLE]. So sometime between now and our next meeting we will have a summary of those comments from our staff, together with the staff's recommendations as to how that might impact our own recommendations. We'll have to make decisions about that after seeing that material.

So the discussion today we ought to consider contingent in the sense that public comments, some of which are extremely thoughtful and some of which we heard yesterday, might cause us to do more than simply alter language but in fact alter the substance of one or more recommendations. We want to leave that as an open possibility. So today's discussion will have to, I think we won't repeat it again, but we just all have to understand that it's contingent on looking at and absorbing and thinking through the public comments themselves.

Now I have, and I presume other Commissioners have, handed in or will hand in to Kathi or others all the various editorial comments many of us have regarding what I would call more or less editorial issues: which issues should be considered, in which order, what the wording is, what should be shortened, what should be lengthened, what ought to go in an appendix, the whole series of issues like that. Our next draft, I think, will in fact in that sense look quite different than the current draft. But I don't want to take time this morning to deal with those issues. So the staff will be receptive to any of those ideas you have, as I will be if you have any suggestions. We have a large accumulation of those already, some of them very good, so I believe our next draft which will come sometime after our next meeting as we won't have time between now and then to get a new draft out will look in some sense quite different.

There are two issues, however, that before we go directly to our recommendations, which is how I want to spend time this morning, going through our recommendations again one by one, see how we feel about them and structure our discussions around those recommendations there are two issues that I want to mention. One is really left over from our very early drafts of these documents and deals with what I guess is footnote 2 of page 2 or something like that; it's very early on. It deals with a use of embryonic tissue that we described in a certain way as being prohibited it's kind of a pre-stem-cell-era footnote. That is obviously going to have to change, and we'll have some more appropriate way of dealing with that issue directly in the text, although we may not take up the issue fully, obviously, in this report and so will indicate it will come in our next report that we are also working on. So I don't think we want to spend time on that today, but just to tell you that that issue will obviously have to be dealt with in a somewhat different fashion and not dispensed with quite so cavalierly as it is in the current report.

The second issue, on which I think we'll see some more notice and we'll be drafting material for this Commission to consider, is the relation of many of these

tissues we're discussing in this report to the medical privacy issue. The President mentioned that last night [in his State of the Union address], but as you know the Congress passed some legislation asking the Secretary [of Health and Human Services] to produce plans. Those plans have been produced, and it's a rather complicated set of issues. If the Congress fails to act then the Secretary must act, but all that has to unfold in the next year or so I think sometime in 2000 is the deadline for all this to be done. I'm sure it will be done. And so we have to find a way in our material to indicate that this is very much directly related to this, the medical record, and is in some sense analogous to this. Alta pointed out I don't know which meeting it was, Alta that there is a strong analogy between these tissues and the medical record and may even be a medical record in some narrow way of thinking about it. So we'll have to produce some material on this, which won't resolve that problem as there are other groups that are addressing that problem with the NIH's special task force and so on; that's not our job. Our job is solely to connect what we have here to this set of issues, which will of course be done in the next draft. So that's another issue I just want to flag, which I don't think we need to address specifically this morning. But just to tell you that those two issues both the, for lack of a better word call it stem cell issue for the moment, which is a very simple issue, and the privacy issue, a very complex issue need to find their appropriate spot in our report.

So that's all by way of introduction. My proposal is, and I'll turn over to Tom in a moment, that we go through the recommendations one by one and see how we feel at this stage about them, and a number of issues will come up, I'm certain, as we go through these. And we'll just wait and see, hope that discussion can advance. If I can make one last statement on what I referred to as editorial issues, one that came up last time and is still in the report in a number of forms. The issue that came up last time was to make sure, as Carol will remember, that we distinguish between Aspecimens and Asamples. We made a decision as to how we would define one versus the other. The current draft's a lot better in that respect, but there are still some issues there that need correction. And there are also issues of the systematic and appropriate use of such words as Archives, Repositories, Collections, Tissues, Cell lines, and so on. That's a major editorial issue that needs attention. If we have time we'll come back to that, but I'd like to put those issues also on hold at least until we begin going through the recommendations, and if they have to come up they will come up. Nothing is barred absolutely. But as I read the report as carefully as I could, this draft report I guess now it's a few weeks ago when I actually read it there are still some important issues there so we have consistent usage. Carol, did you want to say something?

DR. GREIDER: If we start off by going through the recommendations today, there are some things that I don't think are just editorial in other places of the report. Will we then come back to that?

DR. SHAPIRO: Yes, correct. No, I think that's absolutely right. That observation is absolutely correct. This is just a way to get our discussion started. Let's see how far we go and then we'll continue that discussion at the February meeting. All right. So let's turn our attention, then, to Chapter 5. I'm just trying to find the page on which the first recommendation.... Okay, let me turn the discussion over to Tom.

**DISCUSSION OF THE COMMISSION DRAFT REPORT ON
THE USE OF HUMAN BIOLOGICAL MATERIALS IN RESEARCH**

DR. MURRAY: Thank you very much, Harold. I hope that for the purpose of the discussion about the recommendations you wouldn't mind if we also included in the material under discussion Charts 1 through 4?

DR. SHAPIRO: No, I think that's important.

DR. MURRAY: It's a footpath through the various things and I think they're done well and will be extremely helpful and in preventing false information or inconsistencies that might create problems.

DR. SHAPIRO: Right. That's important.

DR. MURRAY: All right. Between now and noon we're going to try to get through all of this; let's see how well we do. I'd like to begin by calling attention to line 18 on page 126, the section actually beginning on line 18. I realize not everyone in the audience may have access to this: basically this is the question of the sentence is, A The current regulations in the NBAC's recommendations do not apply to purely clinical uses of such materials. Rather, regulation of the Commission's recommendations applies to research defined as... and we give the standard definition of research contained in the Federal rule. I noticed that one of the things Mark Sobel conveyed yesterday had to do with quality control work, where I presume one is attempting to make sure that the specimens have been accurately read clinically. It's not research. I just want to be sure, first of all, do the commissioners agree that that is not in our understanding of research? It is not a systematic investigation to create new

knowledge? And therefore quality control work as done in a typical pathology laboratory would not come under our recommendations? Does everyone agree with that? Okay, then I think all we need...if that's true, all we need is clarifying language just to

DR. SHAPIRO: Could I just ask a question about that? There's quality control in what I consider the classical sense, that is a section a pathology sample comes and either confirms or doesn't confirm the diagnosis and figures out whether the surgeon did or did not do the right thing and so on and so forth. I can't describe that well, but that's what I consider the classical quality control issue. There's a whole other and rather newer set of quality control issues, which are more like what some health maintenance organizations might undertake regarding whether which procedure works better given a certain diagnosis that would cover a whole long host of cases they might have. If in 10,000 cases of prostate cancer that was experienced by their members and diagnosed in certain ways and treated in alternative ways, they would try to figure out which treatment works better because they're interested not in publishing an article but in delivering quality service to their enrollees. And I'm just asking a question: Where does that fit in response to the issue you've raised? Maybe others are more knowledgeable about this than I am.

MS. RACHEL LEVINSON: That is called A outcomes research.

DR. MURRAY: Well, I think the kicker in Harold's question, as I understood it, was that it was not outcomes research with a view toward generalizable knowledge but it was more like internal corporate research with a view toward competitive advantages. So I'm not sure.

DR. CASSELL: Do these people who are doing this have responsibility to the group of patients on whom they're doing this?

DR. SHAPIRO: Yes. That's my intent.

DR. CASSELL: Okay, but in your example, if they have responsibility I don't think it falls under research. They already have access to the patient, they have a right to it, they're not intruding into the records and none of the other things. If you turn around and say, A Well, let's suppose we call this research, do the other caveats apply to them? Not really. The records are not blind to them; it is in the immediate interest of their patients that they do that and so forth.

DR. MURRAY: Steve?

MR. HOLTZMAN: There's another example of quality control, typically in connection with biological materials, having to do with quality control testing of diagnostic markers, for example. So I was wondering what Mark had in mind when he

DR. MURRAY: Yes, please, Mark.

DR. SOBEL: Actually, that's why I brought it up.

DR. MURRAY: Does anyone else find it occasionally amusing that the Commission dealing essentially with the implications of technology so often is failed by its own technologies?

PROF. CHARO: Not ours.

DR. SOBEL: The reason I posed the question is that I think there are very many different people's views, and I think they're deserving of hearing in depth. From my perspective, certain types of quality control studies, which are my primary concern, are those in which the laboratory must test to make sure the current testing procedures are correct. They will pull samples, retest them, and maybe even share samples across the laboratory to make sure the people are getting the same results, make sure the machines are valid and are appropriately quantified so that the testing is adequate within that laboratory. That's one type of quality control testing. Now, the example of Dr. Shapiro is different in that it does not really specifically the duty of the laboratory to make sure its equipment and its testing procedures are accurate for patient care. It is asking a different type of question, which, actually, to me sounds more like research, because that deals with outcome in terms of choices of which tests to take. And that comes more toward validation, which I think is closer to research than to patient care. I think you have to distinguish between quality control and validation studies. Validation studies are in the development of tests, and that's more like research.

DR. MURRAY: Thank you. I'm going to recognize David in a moment, and Bernie also wanted to speak. I'm wondering if we might, for the purposes of this report, handle this problem simply by switching the order and say, look, what we are talking about is research as defined by 45 CFR 46X that's our purview. Maybe it is not at this point our job to decide what ought to count as research and what ought not to count as research. If we wanted to take that on we could, but that seems to me to be an

interesting enough problem that we shouldn't get bogged down in it in an effort to run through this report. So I think we might be able to handle that textually, but if anybody has anything substantive they want to continue to add, please do. David, then Bernie?

DR. COX: My comments relate directly to this. On page 88 of the draft report, under line 12, it says the activity that constitutes research directly addresses this issue. And again, as has been pointed out here, research is defined as a systematic investigation designed to develop or contribute to generalizable knowledge. In that situation, I believe that Dr. Shapiro's example is clearly research. It's on clinical information from a subset of patients, but it's to generalize what the outcomes are to other patients. So in my view that clearly falls under the aspect of research. Dr. Sobel's example clearly doesn't because it's in the context of specific clinical care of that defined set of patients and not generalizable to others. And if you look at lines 14 through 16, it states: If the work on the stored materials is done solely as part of the clinical intervention, as might be the case in a pathology laboratory, and that could be extended to say, such as in the case of quality control. Then the Federal regulations do not apply. So it specifically, in my view, addresses Dr. Sobel's point, but perhaps it could be clarified.

DR. MURRAY: Thank you. Bernie?

DR. LO: I think we probably should not get drawn into this because we can get diverted. But we may want to pay some attention to some other activities that are sometimes confusing, such as if teaching of students, if we're going to start saying that by research we mean the results of quality control, the laboratory control. It seems to me the teaching to resident students is another activity that we may want to separate out.

DR. MURRAY: If we handle it by saying that, look, this report deals with research as defined by the Federal rule, and there are other activities in which these tissues might be used that do not count as research, such as we could mention a couple of examples would that be adequate? Do you feel for purposes of the report we can do that?

Beginning on page 127, we talk about exemption. We end up with a couple of recommendations, 1 and 2, dealing with the category of exempt research. So, does anybody wish to talk about the text leading up to recommendations 1 and 2? Problems with that text? Recommendation 1: The research conducted on human

biological samples that are existing and publicly available is exempt from regulatory oversight only when the samples are either unidentifiable or rendered unidentifiable by someone other than the investigator. Coded samples are considered identifiable.≡ I have one comment about that but I want to know if anyone else has anything to say about that recommendation. David?

DR. COX: Yes. Just to the point of clarification in the recommendation, because there=s been so much confusion about whether the present regulations have coded samples being identifiable or not identifiable. One could read that as though for the first time the NBAC is making coded samples identifiable. So in some way having language that basically states, Aas is presently the case the NBAC≡ just so that it is not that this is something new that we=re adding.

DR. MURRAY: Carol=s nodding. All right. I wonder if we might slightly revise this recommendation, not to change its meaning, just to clarify it a little bit. I found myself as I went through the report againXwe=re on page 129XI found myself thinking: Are we talking about specimens or samples? Remember, specimens are the way they exist in the repository; the sample is what comes to the researcher. Samples are taken from specimens. So I wonder if the recommendation might read something like this: AResearch conducted on human biological samples that are drawn from existing and publicly available specimens is exempt.≡ Anyone? Does that help? Is that unnecessary? I just found myself getting confused. Pardon?

DR. CASSELL: I don=t see why it=s necessary.

DR. MURRAY: Well, I got confused, Eric. Maybe it=s only necessary for me.

DR. CASSELL: All right, try this. Let=s presume for the moment that the sample is existing and publicly available and that. But the specimen isn=t?

DR. MURRAY: No, the sample is not existent. The specimen is existing and publicly available from which we=re going to draw a sample. I think it will help in the long run to keep what is a specimen and in the possession of the repository distinct from what is a sample that comes into the hand of the researcher. I think that will help.

DR. SHAPIRO: All right, let=s just try it.

DR. MURRAY: Okay.

DR. CASSELL: Change the word to *Materials* and it doesn't matter.

DR. MURRAY: That would be fine, too. Yes, that would be fine.

DR. COX: I'm actually in favor of that, because not all samples are actually derived from specimens. That's the problem I mean, sometimes researchers take a sample and there is no other specimen. Certainly that's the situation. In repositories there are almost always specimens, but not every sample has a specimen attached to it.

DR. MURRAY: I think *Materials* is fine. So we just change the word in the first line now: *Research conducted on human biological materials*.

DR. DUMAS: And the third. And the fourth.

DR. MURRAY: Well, I think we should do we need *Samples* there?

DR. CASSELL: It should be *Materials* throughout.

DR. DUMAS: I don't think so.

DR. MURRAY: I think we need *Samples* there.

MS. KRAMER: I think we mean samples because

DR. MURRAY: We do mean samples there.

MS. KRAMER: ...we're talking to it as it is now in the possession of the investigator, and that's a sample, we've said.

DR. MURRAY: No, that's the specimen. Oh, I'm sorry, the investigator has the sample.

MS. KRAMER: Okay. Thank you.

DR. MURRAY: That's right. Sorry. Kathi?

DR. HANNA: I think when we want to say A sample we should say A sample, because there's still, I would say, just generally from the comments that are coming in, that there's still a little bit of confusion about the status of the material as it's held by the repository versus as it's held by the investigator. And I think when we can be clear and use the word that signals clearly where that material is sitting, I think we need to be as clear as possible.

DR. MURRAY: Kathi, what would you have us say in Recommendation 1?

DR. HANNA: Well, I think it's okay to change the first to A materials. I think certainly in the last line, where you say, A Coded samples are considered identifiable, I do think you mean samples.

DR. MURRAY: What about the use above in the line above that? Because I think we're talking about samples, we refer to them being rendered unidentifiable by someone.

DR. HANNA: Right.

DR. MURRAY: Okay. This may seem a little nitpicky, but I think precision is really X this is such a complicated report. Precision may be helpful to everybody.

MS. KRAMER: A point of information: Are the specific terms and the ways in which we're using them listed anywhere earlier in the text?

DR. MURRAY: Earlier in the text, not later.

MS. KRAMER: Earlier and then later?

DR. HANNA: Earlier and later.

DR. MURRAY: No.

MR. HOLTZMAN: Do we have a glossary?

DR. MURRAY: Would a glossary be helpful?

MS. KRAMER: Yes.

DR. SHAPIRO: Yes, we will have a glossary.

DR. HANNA: That would be helpful.

DR. MURRAY: Recommendation 2: A Repositories should require that investigators in obtaining samples from their collections provide documentation that research using identifiable samples will be conducted in compliance with Federal regulations for the protection of human subjects in research.≡ Bernie?

DR. LO: A question about the A provide documentation.≡ I take that to mean they=ve gotten whatever IRB approval is necessary. Do we also want to put on the repository any sort of obligation to assure themselves that they have metXthat the researchers have met the spirit of the regulations and good ethical practice? Or is it just a matter of someone administratively saying they got IRB approvalX≡That=s the IRB=s job; my job is just to pass out materials.≡ So, do we want them to just be a conduit of samples, or to exercise their own judgment as well?

DR. GREIDER: It seems to me that if the investigator has gotten IRB approval for that particular study that you don=t need to have two separate IRBs approve the same study. And that=s what you would really be doing if you required then that the repository sign off on that again. So documentation that you have IRB approval seems to me like it=s sufficient.

DR. LO: Well, the one caveat is that people would have some concerns about whether IRBs that don=t do a lot of these sorts of studies are as expert in teasing through the issues as, presumably, a repository that=s seen a lot of these studies might be.

DR. GREIDER: I think that=s making an assumption about.... I don=t think you can correct deficiencies in some particular IRB by throwing another IRB on top of it.

DR. LO: Well, I=m not saying it would need another IRB. I=m just looking for some independent moral judgment on the part of the person responsible for the repository.

DR. BRITO: The responsibility rests with the investigator and then the IRB that the investigator=s going through. I don=t think responsibility is with the

repository. I mean repositories have some responsibility, but not ultimately. I think you're setting an extra level; I don't think that's necessary.

DR. GREIDER: There also isn't always a repository, right?

DR. MURRAY: Well, by our definition the holder of the samples is probably all

DR. GREIDER: But an individual holder of a sample won't have an IRB attached to it that can do this at every level of review.

DR. MURRAY: Yes. David?

DR. COX: The present situation is really sort of what's being described. Many repositories just want to be assured that researchers are going through the IRB, and what you do is send them evidence of your IRB approval, and everybody's a happy camper. So if that's the intention of this recommendation, then that's going through. But to single it out as a recommendation seems making it more complicated. Part of this has to do with the fact that right now as things are written, remember, we're putting the onus on the repositories that used to be on the investigator. And maybe we'll come back and talk about that because right now the way the draft report's written, it's not the investigator who chooses to unlink, but it has to be the repository. So that puts extra responsibility on the repository; if that unlinking could still be in the context of the investigator then, as the present regulations say, then it's not clear we need this recommendation.

DR. MURRAY: I'm a little uncertain about what you're asking us here, David. Do you want us to do away with this recommendation or do you like it as it is? Or do you want to do as Bernie

DR. COX: I'm simply making a statement. I see no reason to have this recommendation right now.

MR. HOLTZMAN: There's obviously an ambiguity in the reading of this recommendation. On one reading of A in compliance with as many people around the table seem to be initially taking it, it said that you produce evidence that you had your IRB review. There's another reading, which simply goes to you being in compliance by saying, A Well, this research is not subject to the common rule. And my question is

what is the intent, what is our intent here? So, for example, a private body may not be subject to the common rule. Are we recommending that if they're getting the repository sample that they should be subject to the common rule? There's a variety of kinds of research conducted by anyone that is not subject to the common rule. For example, if the research involves solely the study of existing data or specimens where the data or specimens are publicly available, the research already is exempt. Are we now suggesting here that it shouldn't be exempt? My point here is there may be a very clear answer to that, but my sense is that people reading this might find this not clear on what we're saying.

DR. MURRAY: Alta?

PROF. CHARO: Would it be clearer, Steve, if it simply said that repositories should require that investigators document that they have met all pertinent Federal regulations? Those that are not covered by the Federal regulations will simply say, "We are not covered for the following reasons." Those who are would simply have to document that they've met whatever the Federal regulations are at that time interpreted to mean.

MR. HOLTZMAN: Okay.

DR. SHAPIRO: I think that's clearly the intent of this recommendation. I think that's the intent. On whether this language—that's what I thought when I read this language. But I understand the point you're raising. The intent is not to

MR. HOLTZMAN: So in compliance with all pertinent, if any, Federal regulations is what

DR. MURRAY: "With all pertinent Federal regulations for the protection of human subjects in research." I'm sure we all mean that and not that it's our desire to enforce all Federal regulations pertaining to any institution. I like the suggestion, Alta.

MR. HOLTZMAN: I like "if any."

DR. SHAPIRO: Well, I'm not quite sure what "if any" means. I mean, "if any" means sometimes you get a waiver where Federal regulations say you are exempt; is that what "if any" is supposed to mean?

MR. HOLTZMAN: Hmm. Or Aall applicable,≡ maybe?

DR. MURRAY: I think Aall applicable≡ is better.

DR. SHAPIRO: Maybe Aall applicable Federal regulations.≡ Bernie, can I ask a question about your suggestion, and ask Tom what he thinks about it? The repository, whatever it might be, might have its own rules, regulations, consent forms, and so on that it may have accumulated, it may have executed in the accumulation of its material. And I guess they have a responsibility, in some sense, to deal with their own constraints if they create it in the collecting of material. They may have gotten consents, they may have restrictions, they may have all kinds of things involved that may not be consistent with what investigators request when they want a sample. Is that the kind of thing you had in mindXwhat the investigator wants may not be consistent with their own constraints on their own operations? Or is what you had in mind a separate evaluation of what the investigator was doing?

DR. LO: Well, I guess I was thinking that I could imagine a repository that had developed its own standards of practice that went beyond what an IRB might require. And again I was thinking of an example. Remember when we heard from, for instance, the Mayo Clinic that they felt they had to set up a separate IRB for genetic-based research because there just wasn't the accumulated expertise on their existing IRBs? There was also some discussion by the Academic Society of Pathologists of wanting to view themselves as trustees, I think was the word, of specimens rather than just holders of it. And I think to the extent that if people do want to develop standards that are better in a sense than the sort of minimal standards that an IRB might require, you obviously want to leave that open to the archivists to do that.

DR. SHAPIRO: The way I interpreted this Recommendation 2Xand the language doesn't say this directly, I just want to tell you how I interpreted itXwas to say that in addition to whatever requirements the repositories have they should require, they could have any requirements they want. It=s their material: They control it; they=re the trustee. I think that=s the appropriate language to use for it. So perhaps the language hereXI don't have any particular language, but maybe the staff could consider, or Tom you might consider, beginning the recommendations in something in that wayXthat is, in addition to any rules the repository itself may choose to impose, they must require.

DR. MURRAY: That would be a useful clarification. I certainly read it that way and I suspect most other people would read it that way, but it wouldn't be a bad idea to say.

DR. GREIDER: Could it be in the following paragraph rather than necessarily in the definition?

DR. SHAPIRO: I hadn't thought through it line by line.

DR. GREIDER: It says some repositories have additionalX

DR. MURRAY: Yes, let's go do that. Yes, Larry?

DR. MIKE: Let me ask a factual question. If a repository is subject to the Federal rules but the investigator where they're sending it is not, what rules? Does anybodyXAlta, do you know? Because it=sX

DR. MURRAY: Let me ask Steve. Is Millennium [Pharmaceuticals, Inc.] covered by the Federal rules? When it does research in-house?

MR. HOLTZMAN: No.

DR. MIKE: Well, it=s a big hole to drive a truck through, then.

MR. HOLTZMAN: Millennium contacts a bank or university if it wants samples from them. Does thatX

DR. MIKE: That=s what I'm asking. It seems to me that if the issue is about an identifiable sample, and it sits in an institution that requires it apply to the Federal rules and then it goes outside and all of a sudden they can do what they want with it, it doesn't seem like it=s very logical.

DR. COX: It=s better that we not have it. I would prefer not to have this recommendation.

DR. MURRAY: Alta?

PROF. CHARO: I'm not sure in operation, Larry, it has the effect that you're imagining. Many, I can't say all, but many institutions like universities where

collections will exist have multiple project assurances [(MPAs)] with OPRR that include, among other things, the following requirement: that anybody who is an employee of the university who wants to do collaborative research with an outside entity, right, must do the research with the entity following along with the same rules as the university. In other words, they have a kind of externalization of the Federal regulations through the vehicle of their multiple project assurance. And if the external entity, let's say Millennium, does not want to follow those rules, many of these universities would simply forbid their investigators from collaborating.

DR. MIIKE: Well, I understand.

PROF. CHARO: So this mechanism actually serves to minimize the frequency of the incidents that you're describing. It doesn't reduce it to zero, but it creates a huge disincentive for university investigators and puts a lot of pressure on the private companies. And that's kind of a back door to regulations that have been out there for years.

DR. MIIKE: But on the other hand, then, if many companies do it, the question for me is, Should we require it or should we maybe get a more standard procedure rather than living up to the good will of people?

PROF. CHARO: Well, more than good will. I mean the multiple project assurances are negotiated and signed off on and stay in place for some number of yearsXthe time will be one, two, sometimes five years at a time. So it's a little bit more formal than what you're describing, although I understand.

DR. MIIKE: I understand that, but what I'm saying is that we usually like to have rules for the people who without the rules won't follow the rules. I mean, what's the point of making rules if people are voluntarily doing it? It's the others who do not agree. Otherwise, we just need a voluntary system.

PROF. CHARO: Are you suggesting then that we use this reportXand I'm not opposed to the outcome here, you understand, LarryXbut do you suggest that we use the report as a vehicle to try to deal with the problem of the gaps in coverage generally on human subjects regulation in the United States? Because what this is related to is the fact that the private sector is not in and of itself covered directly.

DR. MIIKE: I'm just looking at the intent of this, and then against the reality that if there is an institution that follows the Federal regulations but it then provides samples to institutions that don't, then all of a sudden the game is on. You know XI mean the rules are off.

DR. MURRAY: Eric's been waiting.

DR. CASSELL: Well, I think if Recommendation 2 is logically related to Recommendation 1, then it seems that the simplest way to do it is to make it the adverse of 1: A If research conducted on human biological samples that are existing and publicly available is exempt from Federal regulatory oversight. Coded samples are unidentifiable, etc. And the second one is that when samples **are** identifiable, thus, research on those samples is not exempt from regulatory oversight, period. Now, regulatory oversight is what these rules are about. If you want to spell out each rule that's being exempted, I mean being subject to regulatory oversight means, that's yet a third clause. But you solve it, I think, if you just make it the logical next step after 1.

MR. HOTLZMAN: That's interesting.

DR. MURRAY: I'm not sure that's going to solve the issue. To simply declare unilaterally that all such research falls under Federal rules that's actually not true.

DR. CASSELL: It isn't?

DR. MURRAY: If the bank is private, the samples are held in a private collection, and the entity doing the research doesn't have that kind of general assurance, I don't think it does fall under Federal rules. Larry?

DR. MIIKE: Well, returning back to the original intent, I suppose its intent was that in the situation I described we're strongly encouraging the repository to have some kind of quality, or some assurances on the outside researcher's establishment, right? So the question is, Do we make it a voluntary urging? And assuming that those repositories that are not doing it will consider doing it, do we make it mandatory? I don't know where I would end up right now, but it seems to me that's the only choice.

DR. MURRAY: Alta.

PROF. CHARO: Larry, you know as much as anybody sitting at this table that I am totally sympathetic to the idea of universal human subjects research regulation in the private as well as the public sector, which was the intent of the resolution that we passed back in May of whatever year, but if I had to go to the mat on the extension of human subjects protection to the private sector, I wouldn't want to do it on this topic. I'd want to do it on other areas of research where the harms are more concrete than they have been to date in the area of research on archived materials. I'd want to do it an area where it would be undeniable that people could agree that it is wrong to use people without consent or independent review.

So I would like to offer an alternative to what you're suggesting. And that is simply to urge those institutions that are covered, whether voluntarily or mandatorily—that is, the ones that have decided that they're going to participate in the system, including universities that have undergone the MPA process to put research that's not ordinarily covered by the Federal regulations under the Federal regulations anyway—to urge them to put into place for themselves this kind of requirement that they collaborate only with people who are going to follow substantively the same protections as those that the Federal government requires. That's exactly what the MPAs now do, all right, when they say you can't go off campus and suddenly exempt yourself from the rules if you're a University of Wisconsin employee, to extend this kind of thing, to make sure that they have their investigators collaborating only with institutions that follow substantively the same protections. And their IRBs should ensure this. I think that it's about as far as we're going to be able to get realistically on a topic where there's not been some scandal to spur action to something more dramatic.

DR. SHAPIRO: I just want to remind the Commission, and I guess it's important to keep in mind because this has come up on every single recommendation, that we decided some time ago that we wanted to work within the existing Federal regulatory framework, which applies to only certain parts of this system. And we decided not to look at those parts that didn't apply to it, namely the private sector. Now that may or may not have been a wrong decision, but this whole thing is structured in that way, so we cannot look at these recommendations outside that context and say, you know, does it apply to X when we have declared that outside our purview for the moment. Now that may have been a good or a bad decision, but that's the decision we made. So I think we should focus for the moment and come back to the kind of suggestion Alta had that arose from Larry's suggestion. We can come back to the issue once we get these recommendations as straight as we can as to whether we want to urge

and/or require some other mega-change in this system for good and sufficient reasons if we have them. So I justX

DR. MIIKE: I don=t have a problem with urging.

DR. SHAPIRO: Okay.

DR. MIIKE: I just seeXthere=s a discrepancy here, that=s all.

DR. SHAPIRO: Let=s come back to that as an issue when we=re through because I think it is an issue, I think it=s a real issue. But let=s not try to deal with it inside each recommendation.

DR. MURRAY: Rachel and Rhetaugh wish to speak.

MS. LEVINSON: I just wanted to restate a point that David and Carol have made today about repositories and the fact that specimens, samples, and materials are not always going to be coming from repositories. And that if you=re going to give a particularly strong oversight role to a repository, keep in mind what happens to that role if it doesn=t exist. If someone=s doing research, a company or a privately funded person, on human papilloma virus, they=re not going to go to a repository; they=ll go to dermatologists= offices where there=s going to be no responsibility or no desire to take on any type of oversight role that comes into play on compliance with the regulations.

DR. MURRAY: Rhetaugh?

DR. DUMAS: I feel comfortable with the suggestion that Alta made and believe that although we believe that the existing regulations are adequate working in that framework, I don=t think that would preclude a statement that would urge agencies that are not covered by those regulations to establish their own in line with those principles. Would that be appropriate to put somewhere?

DR. SHAPIRO: I think we said we could put that somewhere, we just don=t want to do it with every single recommendation we come across here. We=ll come back to that issue. But I think it=s a good issue and we=ll keep it on theX

DR. MURRAY: Steve?

MR. HOLTZMAN: I think that this discussion highlights just how ambiguous this recommendation is in its current form that we could be having this discussion.

DR. MURRAY: I take your point. I don't think it's simply the ambiguity in the recommendation. I think it is the fact that we want to protect human subjects as individual Commissioners and as a corporate body we want to protect human subjects in all respects. The fact is the law doesn't the regulations don't permit us to do that at this point.

DR. DUMAS: Can I ask you a question? Are we to assume that all repositories would be covered by Federal regulations?

DR. MURRAY: No, I don't believe so.

DR. DUMAS: Then that recommendation is ambiguous.

DR. MURRAY: Why is it ambiguous because of that fact?

DR. DUMAS: Because you're saying that you're asking the repositories to require or insist that those who take their samples are going to abide by Federal regulations.

DR. GREIDER: Applicable.

DR. MURRAY: Applicable.

DR. DUMAS: What?

DR. GREIDER: Applicable. We amended it to say Applicable. So if there aren't any Federal regulations then there aren't any applicable ones.

DR. DUMAS: But if you don't haveXif the repositories are not covered, there's no authority to require them to do that. So what does the recommendation actually do?

MR. HOLTZMAN: Several possibilities are [INAUDIBLE]. It's the research that [INAUDIBLE]. It's the repository, not the subject.

DR. DUMAS: So you're saying that the repositories should be free to let the samples go wherever? And that there should be some things beyond the repositories= control of how they're used?

MR. HOLTZMAN: I'm saying that's [INAUDIBLE]. It's my understanding that we would have to include them in the concept of a...was a repository. In such an instance you're right: We are asking the local pathology department, when researcher X says, "Give me some samples," to have researcher X certify to that pathology department that researcher X is definitely doing research in compliance with the regulation. And I think you're right, the local dermatology department or pathology department has no idea what the regulation is or what it means to get that assurance.

DR. MURRAY: David, and then I'd like to try to pull the threads together and move on to the rest of the recommendations.

DR. COX: I think these discussions really make the point that the central question is: What are we gaining from this recommendation? Certainly we all want to protect human subjects and see that the work's being done. But does this recommendation achieve that? In my view, because of the points that have been brought up by discussion, it doesn't.

DR. MURRAY: I actually disagree, David. It depends actually on what you say, what you mean to say. If you say that this doesn't provide assurances that all uses of all tissues involving all human subjects are covered and protected, the answer is you're right. But nothing we say is going to accomplish that because we're constrained, as Harold reminded us, by the terms of the Federal rules and the entities upon whom the Federal rules fall. Not all entities are under the Federal rules governing the protection of human subjects, so that's a given. All we can speak to are those areas about which we have any authority to speak. So I want to ask the question: Does this recommendation, suitably revised, add some protections, assure some protections for the human subjects about whom we can speak? And I guess my answer is that with the insertion of a term like "Applicable," I think it does. But I suspect why don't we take another crack at revising this, maybe adding some explanatory language, and if you still don't like it, well, we can still strike it. But if you continue to like it and think that it adds something to those protections, even if it be a finite amount, then we may wish to keep it.

MR. HOLTZMAN: Can I just lay out the argument why I think it doesn't add anything and is not useful? I think the model that was in people's minds when this was drafted was the statement by Coriell that they seek an assurance from the person receiving that they are in compliance. And ask yourself: Why does Coriell ask for that? I think it's mostly that this has to do with containing legal liability. So when you make the request to get or provide documentation, are you asking for a simple statement, in which case anyone can make a statement? Or are you actually looking for real documentation, in which case you are asking for the repository to play an active role in assessing whether that documentation is adequate? It's nothing more than saying that the investigator asked for itXsays, AYep, I= m in compliance.= What exactly has it done? So that would be the argument against why this is really not operative. Or if it is operative and real, it's imposing the requirement and request on people who are not in the position to implement it.

PROF. CHARO: You know, at this point I wonder if it makes sense to distinguish between what we are going to be writing and what a regulatory agency that's attempting to implement our recommendations would be writing. Because if we are able someday to understand what we want to say well enough to actually articulate it, I think that we might be able to allow the pertinent regulatory agency here, probably OPRR, to then issue its guidance or regulatory implementationXregulatory language if it comes to that, to spell out the kind of detail that you are now focused on, Steve, because I have a feeling we will never be able to get down to that level of specificity on every recommendation with agreement and still make it through this report.

I would like to suggest that we stay about one level of generality up from where you are. So if the point is that we would like repositories to take some responsibility to make sure that they're working with investigators who handle the material in a way that we consider to be ethically responsible, that's what we should be saying. And beyond that, it's somebody else's job to figure out which pieces of paper have to be signed and photostated.

DR. MURRAY: If the Commissioners will allow me to do this, I'm going to ask Kathi to say a word about what the public comments on this recommendation have been. And then I'd like us to move on to the next set of recommendations. I thought these were the easy ones. We have some tough ones ahead and we're going to need time to deal with them. SoXKathi?

DR. HANNA: There have been some questions in the public comments about this, and obviously we've not gone through all the public comments thoroughly at this point. But I can just say from the ones that we have looked at so far that people have questions about this recommendation and they tend to be more procedural. I haven't really heard anyone say, 'Get rid of this recommendation'; there doesn't seem to be a consensus for that. The questions seem to be, actually, from the people who are responsible for large collections: They don't seem to have a problem with this recommendation; they already do this. The questions seem to be more from smaller collections—people who pass samples from lab to lab without really possibly documenting or thinking about how they're doing that or whether they're passing information back and forth that they shouldn't be passing back and forth. So the questions seem to be more concerned about people that don't have the large Coriell-type system in place. What they're required to find out from the people who they're passing their materials to is in terms of should they just ask them, 'Did you get IRB review for this?' Or should there be an exchange of paper or something? Those are the kinds of details that are being raised in the public comments. We do have to figure out how to deal with that.

DR. MURRAY: Can we move on to Recommendation 3 which appears on page 134? Carol, we're on Recommendation 3.

DR. GREIDER: This may or may not fall under the idea of editorial comments, but in the text leading up to Recommendation 3—specifically, on page 131 where we talk about identified samples, unlinked samples, and coded samples—again, I feel strongly that we should have the language that is currently on pages 43 and 45 in Chapter whatever that discusses how we see a specimen, and then a sample coming from a specimen. That's not currently in here. All we have described in here are the samples, and that doesn't really make sense to me if you don't explain that we're thinking of these in two different ways. And again, on page 132, lines 2 through 5, we use the same language—'samples'—now to group two of our previous samples into one. And I think that that's very confusing, to have on page 131 'unidentified samples' and 'unlinked samples,' and then suddenly on page 132, without any further introduction to say all of these are 'unidentifiable samples.' And then the rest of the recommendations go on to call these 'unidentifiable samples,' and we're not explaining why we think these are different from each other.

DR. MURRAY: Jim?

DR. CHILDRESS: I'd like to speak to that also, because it seems to me that even if we end up saying the same regulations and guidelines will apply to both, that to take the language of identifiable or unidentifiable, to bring them together is really unfortunate because when we say that something is unidentifiable or identifiable I'm just going to take the identifiable one for a moment that means it's capable of being identified or can be identified. And if it is identified, it's not capable of being identified, it is identified. And it seems to me that when I read the report, each time I ran into Aidentifiable I had to stop and think: Are we talking in the broad sense or are we talking in the narrow sense, in which it means simply Alinked or Acoded. And it seems to me that that, at least for me, made it very difficult to be clear at each point where we're doing it. I'd much prefer that we, if necessary, go ahead and use the language each time of Acoded and Alinked and Aidentified, and I think the report would be much clearer if we did that.

DR. MURRAY: Point well taken. I agree. Harold?

DR. SHAPIRO: Well, I just wanted to make the point. It's quite fine with me to keep them not have the Aunidentifiable and Aidentifiable language and just repeat the other, that's quite fine with me. I just want to remind you how we got there. We got there when someone noticed that we were treating them the same. The exact same rules applied to these two categories, so there was an attempt to aggregate them. But if it's clearer the other way, that's fine. I have absolutely no objection at all to doing that; that's relatively simple and straightforward and so we might as well just do it. But let me ask another question. I didn't understand, Carol, the first question dealing with the material on page 131 where you seem to be concerned we're only talking about samples. I may not have understood what

DR. GREIDER: On page 43 of the report, I'm just not sure what chapter it's in, but on page 43 we lay out the same language but we preface it by, ANBAC has determined that samples can either be as they exist in the world or as specimens, and be either identified or not. But then we further subdivide that as to what goes forward to the researcher. And that language is not currently in our recommendations section in Chapter 5 anywhere.

DR. SHAPIRO: So you want to repeat that language up here?

DR. GREIDER: Yes, briefly.

DR. SHAPIRO: Okay, I just want to understand. That=s fine; that=s a good idea. I just want to understand.

DR. MURRAY: We=re still on Recommendation 3. David?

DR. COX: I just wanted to say how much I agree with these comments about this. It may seem like just word details, but it=s exactly at this point where the world=s very confused, and where we have to do everything we can to clarify our meanings because that lack of clarity, I think, has led to a lot of confusion to date.

DR. SHAPIRO: Could I just ask a question? That would mean, for example, if I understand the objection to using this Aidentifiable≡ and Aunidentifiable,≡ one would go back to the language that=s actually laid out here? I certainly understand that. And that means in Recommendation 2 you would do likewiseXthat is, we would just eliminate that word and go to two words or whatever is necessary to do it?

DR. COX: Yes.

DR. MURRAY: Could we read that first sentence, to make sure we understand what you want us to do? This is Recommendation 3. The new version of it would start this way: AIn most cases the common rule provides adequate protection of the interests relevant to the use of unidentified and unlinked samples.≡

DR. SHAPIRO: Right.

DR. MURRAY: That=s how we want it to read?

DR. SHAPIRO: That=s how I understand the suggestion.

DR. MURRAY: That=s clear. Carol?

DR. GREIDER: Just one other point, back again on page 13, just to point out why it=s important to keep these distinctions. Currently, lines 14 and 15 read, Aor biological information derived from the research that would be impossible for the investigator, the repository, or a third party....≡ If it=s impossible, then why are we even concerned about some of these being unlinked? I think it=s very difficult. This has to do with codes now. Do we really think that any code that might be given is impossible to break?

DR. MURRAY: Kathi?

DR. HANNA: Yes. The word *impossible* keeps getting changed every version, and I would say if you took a vote around the room about which word you want to use, you would all come up with different words. So it is a word that's raising some concern in the public comments, and we've said anywhere from *nearly impossible* to *extremely difficult* to *very difficult* to... So I think it's important to clarify what you mean there and use the words that you want to use to describe the situation, because in every version I have to say I get at least five or six suggestions from Commissioners about what word we want to use to replace that. So it's obviously an important word.

DR. SHAPIRO: Where's that? I kind of lost it.

DR. GREIDER: Page 131, line 15. The very first word there is *impossible*.

DR. MURRAY: I was struck by that again just as you were, because I didn't think we were set [INAUDIBLE].

DR. GREIDER: Isn't it the point that if two people get together that they can break the code and that's what we're concerned about? That's not impossible then, right? If the investigator goes with his coded sheet back to the repository with their coded sheet?

DR. MURRAY: Then it's linked; it's coded, it's not unlinked.

DR. GREIDER: It's not unlinked.

DR. MURRAY: I'm sorry, Carol, now I am confused because what you just described is coded samples, not a linked sample. Bernie, you had your hand up?

DR. LO: Well, isn't the issue here that even though something is unlinked in the sense of using other information, like reverse telephone directories and census information, you may be able to go back and link something that exists now in a form with no identifiers or codes. And so it's there. It's not impossible, it seems to me, in the sense that if you had a big enough computer and a clever enough programmer you could probably do it.

DR. HANNA: We actually got a comment from an individual who knows something about encryption who said that given two or three data points X is it three, Eric? X that he can figure it out.

DR. LO: Probably can.

DR. MURRAY: To say nothing of your DNA fingerprint. I think A impossible ≡ is probably not the right word here. Who is it that put it into this version of the text, Kathi? Who is it? Don't tell me it was me that pressed you into it because I don't think it was.

DR. HANNA: No, I don't think it was you. I won't disclose.

DR. MURRAY: You won't name them. Does anybody want to go to the mat to fight for A impossible ≡ as the standard here, or can we go with the word that X

DR. GREIDER: A Very difficult. ≡

DR. MESLIN: A Extremely difficult ≡ or A practically impossible ≡ or something.

DR. GREIDER: No, don't practicalize. No, no.

DR. MURRAY: I don't think we should fight about the word. David?

DR. COX: Not about the word but about the concept. In fact, because of what just happened, the confusion about whether there was a code here or not, what we're talking about here is unlike a coded situation, with the information available that was kept by the investigator and/or the repository and/or anybody else, that if they all get together and take that information that they have and piece it together, it doesn't give you a link. Now, that doesn't make it impossible because you could use other information to sort this out. But the idea here is that the word should convey the idea that you put all these people together and it doesn't give you the key. So you need other information to have the key now. So that's the concept that I would like to see conveyed here, as opposed to A linked ≡ where it would link if you put those people together and it does give you the key.

DR. MURRAY: Eric?

DR. MESLIN: I was only going to suggest that if you're not comfortable with the feasibility language that the word *impossible* suggests, you might go with probability language. It might be easier to convey the Commission's concern about the likelihood of something happening. And if your focus is on when it occurs, it doesn't matter. The fact that it occurs is the worry that you're trying to express in this recommendation. And when it occurs, that means that information will be transmitted that you're concerned about individuals being identified. So then the possibility is low. If you want to convey it in certainty language it may be easier than to come up with a feasibility word.

DR. MURRAY: Steve and then Harold.

MR. HOLTZMAN: We had some discussion by e-mail where we gave the examples of maybe [INAUDIBLE] a cohort of 100 and in any sense in which we thought we bent on link, nevertheless you might be able to find out. So I wonder if what's important here is arguing between physically and logically possible versus potentially feasible, or rather going and contrasting it with where there is intentionally kept a code or a key, making that the driver of

DR. MURRAY: That's part of it, that's part of it. Obviously, if it's intentionally kept we know it belongs in the next category of *coded*. If we wanted to cover the case where even though no formal coding was kept, in that sense no formal linkage, where the repository was small enough or enough data went forward with the sample that in fact the investigator could with relative ease figure out who the person was anyway even in the absence of a formal linkage, we wanted to cover that. I think that's an important one to cover, and it was raised repeatedly in our deliberations prior to today.

DR. SHAPIRO: I think I may be the source of the word *impossible*, because I found it. I mean you can look at this another way. I understand the power of code-breakers and so on and they become more powerful every day, which is exactly my concern. Because I felt that if something is short I don't want to use *impossible* too often here, but if it is some one person says they need only three points, someone else needs only two points, now there's some new software where it supersedes all this anyway, then we might as well face the fact that these are *coded*, period. As I recall our discussion, it was yes, they were not, no intentional code kept, to use Steve's helpful language a moment ago but somebody finds something, and now they want to

go back. And the question is, Can they go back? And if they can go back, therefore, then, whatever harms [INAUDIBLE] that have been imagined are now opened up again. We might as well just treat it as Acoded.≡

Now, if it is always possible to go back, if theXI understand, of course, that in unidentified samples it=s not possible as there=s noXor even then it could be possible, I suppose, given enough information and so on. So that was the source of my concern. Now this is not a huge issue from my point of view; I don=t insist on the word Aimpossible,≡ but I am trying with the words I recall from the discussion, we=re trying to deal with the situation where people had not intended to go back but nevertheless left a road open. I guess what we=re struggling for here is many Commissioners feel that if that=s a difficult enough path to go through that they=re satisfied there=s enough protection. And if that=s how the majority feels, fine. But I just want to say that I=m responsible, I think.

DR. MURRAY: I remember.

DR. SHAPIRO: I may not be the only one, but I certainly was one of the people who pushed for the Aimpossible.≡

DR. MURRAY: I remember perhaps 20 years ago reading comments by investigators who were upset about, this strengthened informed consent requirement in research. I mean real research on human beings, not the use of retained samplesXdoing things to people. And they were creating consents like, AWe have to include on the form the possibility that a meteorite might fall on your head while you=re sitting in the laboratory.≡ It=s not impossible, but it=s pretty improbable, and we don=t think that needs to be part of the consent. I think we=re looking for something short of the meteorite perhaps, but some reasonable standard. And I have Carol and Bernie.

DR. GREIDER: Well, as you all recall there was a lot of e-mail traffic about where to consider this particular thing, whether it goes up above with the Aunidentifiable≡ or down below with Acoded.≡ And I think at our last meeting we pretty much decided we wanted it to go up above with the Aunidentifiable.≡ And I was just looking for language that truly said what these samples actually are while still keeping it up with the Aidentifiable.≡ And just thinking about it in reality being possible just didn=t mesh, even though we had agreed that the [INAUDIBLE] very difficult, etc. I don=t have a problem with protections, but just try and say the way things really are.

DR. SHAPIRO: I don't think this is impossible, so if we can find other... I'm quite happy with other language.

DR. GREIDER: And just to follow up on your saying that you're the one that pushed for the impossible, that is of course your job.

DR. MURRAY: Bernie? If you care to follow on that, Bernie.

DR. SHAPIRO: Okay, is it the consensus? No wording now, we don't want to spend too much time on the wording here this morning, excuse me, Tom. People want us to find a substitute to just move back from that sort of outlook criteria, but not too far. Is that the sense of things? They just want to make sure?

DR. LO: Let me just say there's a fair amount of experience with outcomes research and large databases. And typically what's done is that the information is changed around. So you don't get the person's birthdate, you get their age. You don't get the exact ZIP codes, you get, Ait's sort of in one of these three ZIP codes. And that's done, so that it's not impossible but it becomes much less likely that you can backtrack and do it. So I think it is useful to keep this separate, but often what it involves is again some responsibility on the part of the repository to give out information in ways that make it less likely rather than more likely.

DR. SHAPIRO: You can say A very unlikely that the investigator or anyone else would be able to, or something like that. Let's try to find some language that conveys that.

DR. MURRAY: I sense we agree in principle on what to do there: We'll just keep looking. Kathi says she's going to rip out her thesaurus.

MR. HOLTZMAN: Well, I have one right here.

DR. MURRAY: All right, is that point settled? We're settled on that. Bette, is this on that point?

MS. KRAMER: Well, I was just thinking, since the intention is for it to be unidentified, maybe we should just include language that says it would require some collusion between parties to identify.

DR. MURRAY: It may or may not. I mean it might be that rather than collusion that some brilliant database analyst could pick it up on their own. Although collusion is one of the things that we want to [INAUDIBLE].

MS. KRAMER: It would try to [INAUDIBLE].

DR. MURRAY: Okay. Anything further on Recommendation 3? We're going to revise it as Carol had proposed. Carol, you had something else to say?

DR. GREIDER: On line 11, starting on 10 and 11X

DR. MESLIN: What page?

DR. GREIDER: Sorry; page 133: ASome might consider it ethically problematic that by stripping identifiers the investigator eliminates...≡ Aren't we having the repositories strip the identifiers? Just the language Astripping identifiers≡ implies that the investigator is doing the stripping. I just want to change that to Aby having the identifiers stripped....≡

DR. MURRAY: That's fine, I think. No problem with that from anyone?

DR. BRITO: Or Aeliminates the possibility the investigator....≡

DR. GREIDER: It's just that it's not the investigator that's doing the stripping.

DR. DUMAS: Right.

DR. MURRAY: Good. Anything else about Recommendation 3, given that we are going to revise it toXactually, it will end up being shorter, I think, because it will now say, Arelevant to the use of unidentified and unlinked samples.≡ Then I think that we pick it up again a little later on. Good. Moving right along, Recommendation 4 appears on page 135. Carol?

DR. GREIDER: I think this recommendation should come earlier. We're pointing out what the current regulations are and that they're not necessarily clear. And I think that maybe it would help, for instance, if it came before Recommendation 3Xit might make it more clear why we're doing Recommendation 3. And I agree with that; I think that together the lines 8 through 16 on the same page, 135, really go with

Recommendation 4, and that also should go before Recommendation 3. I'm not sure if it should go even earlier than that, but that should be looked at.

DR. SHAPIRO: Well, text would have to go back with the...if we move the recommendation, the text would

DR. GREIDER: The text above it I think is referring to it rather than the text below it referring to it, which is how I read it.

DR. MURRAY: Yes, that's correct.

DR. GREIDER: And maybe we should think about whether it could go earlier and precede some of these other recommendations. But I think it should at least precede 3.

DR. MURRAY: I think generally we'll want to reconsider the order. What I would like you to do is offer your advice about roughly where it ought to go and then let the staff make some calls about how to reorganize the ordering of the recommendations. So we're not going to vote on which number it becomes at this point, if that's okay. But I agree. Anybody disagree with that?

DR. COX: Earlier exactly where I don't care, but that's the same context as my comment on Recommendation 1. Just so it's crystal clear that this isn't something that the NBAC is initiating.

DR. MURRAY: Anything else about Recommendation 4?

MR. HOLTZMAN: Yes.

DR. MURRAY: Thought we were about to escape. Go ahead.

MR. HOLTZMAN: Just a question I've asked a number of times in the past. I mean we do make it clear now that there are differences in interpretation of the rank out there and that there is a need for clarification. Do we have any sense at this point of the OPRR's interpretation of A coded is okay? The answer is no, we don't know to what extent the OPRR's interpretation of A coded as A identified and falling within the regulation is not current practice, and hence we don't know to what extent

this will occasion changes in practice. We don't, do we? These are my questions, and what additional burden therefore it may be putting on the IRB system.

DR. HANNA: We don't know. We know from the public comments that people do not interpret it the way we interpret it.

MR. HOLTZMAN: We interpret it as being OPRR here so that therefore we are recommending potentially a significant new and additional burden on IRBs and a change in current practice. And we are saying that the personal communication of the OPRR's director is what controls the interpretation of the regulation. Just let me be clear on everything I think we're saying.

DR. MURRAY: What is the last phrase I didn't catch, Steve. We're not the OPRR. We are the NBAC.

MR. HOLTZMAN: Right, but we asked the OPRR's, Dr. Ellis for his interpretation. We have a personal communication, which we cite in the footnote, and we are in Recommendation 1 saying that that is controlling. I'm not a lawyer maybe we've got a lawyer across the table shaking her head. I've got to get clear on what we're doing.

PROF. CHARO: I think that, yes, it is controlling. Somebody could challenge it and they might win, although a court looking at a challenge will generally be extremely deferential to the interpretation of the regulatory agency that applies a particular regulation. That's exactly how they handle this question on a routine basis. But as long as the OPRR interprets it this way, the OPRR is within its purview to go out to any of those noncomplying institutions that are sending in comments and saying, Hello, guys, you got it wrong and now we're telling you and now you need to get it right. And those institutions would have no choice but to comply or to try to formally challenge. So in that sense I would say the OPRR is in a position to be controlling.

MR. HOLTZMAN: Okay. And Kathi, you're indicating that at least from the public comment the question that has been asked for the last six months about to what extent is practice not in conformity with the controlling interpretation, the public comment so far would suggest it is not in conformance with the interpretation.

DR. HANNA: Well, obviously it's not a representative sample, and we're probably hearing from those who disagree and are saying, "This is how we do it, and we don't interpret the regulations in the way that's being presented in this report."

DR. SHAPIRO: As I recall our discussion on this, whether we call this official interpretation or not doesn't—I don't have any view on that issue. But as I recall, our discussion was that whether or not this was the official interpretation, this was something that we wanted and we consulted the OPRR and they said that was their official interpretation, so we're using that. But if that turns out not to be the right way to describe it, then we can describe it in some other way as a new recommendation. But that's how the [INAUDIBLE].

DR. MURRAY: Bernie?

DR. LO: Just to close the loop on Steve's comment, is it not the case that the Commission also believes that taking [INAUDIBLE] just said, that this is not necessarily standard practice, it may require changes in practice and a greater work burden on certain IRBs, and that those administrative burdens are appropriate and acceptable. Isn't that the real policy issue here? That we're aware of that but we think on the whole that it would be a desirable thing rather than a regrettable thing?

DR. SHAPIRO: Right.

DR. COX: In that context, my comments about it being an OPRR interpretation in no way means that the NBAC doesn't have its own opinion about it. And in no way does that mean that we should just say, "Guys, this is the OPRR, so we have to live with it." But there are two pillars to that. One is their interpretation, but then there's the fact that that's the way they interpret it, that the NBAC actually agrees with that. So Steve, I mean that if we do in fact agree with that it's to make those distinctions; it's actually agreeing with the [INAUDIBLE].

MR. HOLTZMAN: No, I agree entirely that it should be coming forward as we recommend that it be part of this way, and we think it's valuable that it be a part of this way, and that the burdens, etc., are worthwhile—and then we articulate why. For example, the evidence of the fact that using coded samples has led to harms: We should cite that evidence, which I'm sure we do in this report. I just don't see it in the report.

DR. MURRAY: Larry?

DR. MIKE: I mean just to address the question about feeling a little uneasy about the language about official interpretation: We should just change the beginning there, just about the Federal regulations and the OPRR opinion or whatever, just to make it less legalistic.

DR. GREIDER: So it would be an NBAC recommendation and then subsequently say the OPRR also agrees.

DR. MURRAY: Yes, I think that's what I'm hearing. And I'm not sure everyone agrees with that on the Commission, but it's near consensus. All right. We will revise the wording of Recommendation 4 to reflect the comments we just had. On to Recommendation 5, and the text leading up to Recommendation 5. Recommendation 5 itself appears on page 141. Carol?

DR. GREIDER: In the text on page 139, lines 13 through 16 are regarding current scientific practices and the fact that most investigators don't need to know the identity of the samples to carry out research. And this is given as sort of an underpinning for why it's okay to use stripped identifiers. My interpretation from what David has said in the past is that just because this might have been good current practice in the past, it's not what's coming down the line. And should we base some of our interpretation on something that we don't really think is going to be true in the future? So maybe David can comment on that, because this was highlighted for me because of what you've said many times in the past.

DR. COX: Yes, well, I'm very happy with the text the way it is, as has been stated by numerous people besides me. There's still a large number of researchers out there that don't care about the clinical information. So, I mean, I don't want to swing this pendulum too far in the other direction. But both are going to be the case and I think that the way this language is written is fine with me.

MR. HOLTZMAN: Carol, actually this is wholly within the scope of identifiable samples. It's really talking about coding, right, and everything David and I have said about the genetic studies, where there's a desire to get more information that works with coding where you still are not privy to the individually identifiable information. So that's the sense of what should be going on here.

DR. MURRAY: Harold, did you have a comment, and Alta? I have one.

DR. SHAPIRO: My comment can wait. It had to do with those exact same lines. I think they're not quite in the right spot in the report but that's a separate issue to come a few pages earlier, and I'll pass that on to Kathi.

DR. MURRAY: Alta?

PROF. CHARO: I'd like to speak to the notion of minimal risk that is incorporated into Recommendation 5. See, and this is linked to Steve's last jab at the report and its lack of clarity about the nature of the harms it's trying to guard against. I think the major reason for wanting to be extremely clear about how it is that most of this research, in fact by virtue of code, doesn't deal with identifiable individuals and therefore should be reviewed by an IRB is directly traceable to the need to have an independent oversight body exercise some judgment about whether or not a protocol does in fact pose some real risk to some real people, rather than having that judgment be wholly in the hands of the investigator. But having given the IRB that kind of ability to exercise oversight by having created what you once called, Steve, a chokehold here, or something like that, I think now's the point at which you want to make it easier for the IRBs to say, A You know, this particular protocol doesn't actually pose a real risk, and we would like to make it easier for people to go forward with their research.≡

Now we do part of it here by making a recommendation that the practicability requirement be omitted when you've met the minimal risk standard. And we've said that the minimal risk standard is one that probably can be met in many cases. But we've still not been as explicit as one would like to be about how one would meet it. We've struggled around this, and I'd like to put an idea on the table for discussion, not for immediate resolution: that we consider taking a position that is completely at odds with the ones that the Mayo Clinic has, where they testified that they presume all genetic research to be more than minimal risk unless it's shown to be unusual. I think that over time we've seen myriad examples of research on stored samples, genetic and otherwise, that is absolutely of trivial importance to the people whose tissues were used in terms of any real effect on their lives. And it wouldn't be inappropriate for IRBs to start with the notion that it's probably minimal unless there is a specific Ahot-button≡ issue.

DR. MURRAY: Probably more than minimal.

PROF. CHARO: Probably, no, probably minimal. The reverse of the Mayo.

DR. MURRAY: Yes, I was following you but then I just got lost in the grammar [INAUDIBLE].

PROF. CHARO: The Mayo Clinic presumed that all genetic studies were more than minimal risk. I=d like to suggest that we presume the reverse.

DR. MURRAY: Yes.

PROF. CHARO: That these studies on stored tissue are going to be minimal risk unless certain hot-button issues are raised. And those hot-button issues are going to be of two types, I think. One might be, as Larry has pointed out and David insinuated yesterday, studies in which the extent of examination of somebody=s private medical records is unusually great. That is, you=re going to look many, many, many, many times over many years at a wide variety of things in the medical record, and regardless of the fact that it might affect somebody=s insurance, it does begin to take on a certain invasion of privacy aspect that is worth our concern about the dignity of personal privacy. And the second is stuff that we typically thought of as being stigmatizing because it is either pertinent to your employability, to your insurability, or because it goes to things that are politically sensitive, which frequently have to do with race, ethnicity, class, etc. And if we could encourage IRBs to start by thinking that it=s probably fine to do the research without further consent, but that they need to check whether any of these hot-button issues have been raised, and if they have been to then say, Maybe this is not minimal risk. I think we will have made an appropriate balance between the burden of having to go to an IRB to get the independent review, but once you=re there making it as efficient as possible to separate those things that really need some extra care from those things that should be permitted to go forward easily.

DR. MURRAY: Let me agree not only in principle but probably in detail with what Alta just said. My own reactions were we had a useful discussion here but we didn=t give the take-away lesson clearly. Even in the discussion of the risks of daily life, we say, AWell, there are different ways of understanding that and it=s complicated,= then we move on. I think we should probably give at least our take-away interpretations on each of those points. And Alta, I wonder ifXwould you want us to say.... I=m trying to see what instructions we would give the people who are going to draft the next version that the presumption ought to be in favor of the proposition that the research probably is of minimal risk unless certain circumstances.... That should be the presumption.

PROF. CHARO: Yes.

DR. MURRAY: End of sentence. And then give a couple of examples of cases where it might not be true, using the examples you've just providedXnot saying that those are the only possible examples, but saying that the presumption ought to be that it is you want us to say that.

PROF. CHARO: I'd like us to consider doing that, yes. I mean, as a lawyer I'm used to working with the idea of presumptions. It's flexible but it moves things along.

DR. MURRAY: And I think we absolutely have to make a report that is friendlyXand I hate to use the phrase Auser-friendly≅ but so that IRBs and investigators can look at it and say, AWell, what are they telling me? What do they actually want me to do here? How should I be thinking about it?≅ And a clear statement of presumption would accomplish that, if that's in fact what we want. David and Bernie?

DR. COX: I personally very much like this idea because a lot of the public testimony that we've heard has been making exactly this point. It is that there are lots and lots of situations that probably are minimal risk but unless we sort of state more clearly what we think is not minimal risk and what is minimal risk, it's extremely difficult. And I think for each of us to sit down and say what we think is not minimal risk and make a list of those would be a very useful exercise. In addition, then, to go and follow on Steve's rejoinder, which is basically to cite evidence of why we think that's not minimal risk as clearly as we can.

DR. MURRAY: Bernie, then Eric and Harold.

DR. LO: I also agree with this line of thinking. I just want to point out there's a precedent for that in the way the current Federal regulations treat questionnaire research: If it deals with a sensitive topic like illegal activity, drug use, or sexuality, it doesn't get [INAUDIBLE] review. But if it's a whole bunch of other categories [INAUDIBLE] presumption, you have to bring it to the IRB, you have to have thought about it and justified why you're considering it minimal risk, but it gets an expedited review. I want to add that it's not just the nature of the research, it's the protection the investigators have put into place to safeguard confidentiality. So I think there needs to be something that I don't find in the report there, which is a sense of good practice of protecting confidentiality. And again, that can evolve rather quickly in a standard set of

things that investigators must do. But simple things like you don't use the hospital record number as your code, you don't leave the code lying about, it's got to be locked up, you have to destroy it in the [INAUDIBLE] I mean, there are all these things, almost like a checklist that makes the presumption that it is minimal risk. Then for the more sensitive issues you may want to take additional steps to safeguard confidentiality like keeping your computer off the Internet so someone can't hack into it. Again, there are precedents for this in, say, public health. And we want to make sure that investigators are actively thinking about what additional steps they need to take to make sure the risks really are minimal by taking appropriate safeguards.

DR. MURRAY: Bernie, just to capture that because I think that was a very valuable contribution. Are you asking us to say in the report that the protection of confidentiality is one of the considerations we would expect?

DR. LO: Protection for confidentiality and minimized risk.

DR. MURRAY: I think we all agree on that. You then went into some suggestions on how specifically that could be done. I take it you don't want us to include those specifics, like good practice guidelines, in the report. I wouldn't think you would.

DR. LO: No, I don't think we should be just spelling out things, but we should say in other areas of research that there are standard areas that have evolved, and that if you don't follow them you're going to be looked at in suspect ways as to whether it really is minimal risk. And we should also push the burden back on, both on professional societies but also on the NIH, to start to develop those practice standards. I think that's our role: to say, "Here's what we're doing; we're changing the way we look at this. We're not experts in how to make this work. You guys are. But we really want you to take this and run with this in terms of developing a set of standards and criteria that really do embody what we're trying to accomplish."

DR. MURRAY: It sounds to me like we could. In the text, not in the recommendation. Urge, say, that it might be beneficial to both investigators and the subjects to come up with a set of standards [INAUDIBLE], but we cannot specify [INAUDIBLE].

DR. LO: [INAUDIBLE].

DR. MURRAY: [INAUDIBLE]. Alta, did you have something to add?

PROF. CHARO: Yes, I want to go quickly over what Bernie just said because [INAUDIBLE]. There are two aspects to information flow that currently [INAUDIBLE] minimal risk. One is the breach of confidentiality; the second is the plan, or lack of planning, for [INAUDIBLE] an integral part of the research. And in fact in the text of the report we've discussed the fact that that is a troublesome moment, when there are tantalizing findings. Actually I would suggest, Bernie, that you might even want to make what you suggest slightly stronger, which is that a presumption of minimal risk, if we decide to take that idea seriously, should be premised on the absence of pop-up issuesXon the presence of an organized plan for the maintenance of confidentiality that goes beyond the usual kinds of stuff we've all seen in our IRBs even though we kept them in a locked cabinetXsomething that goes beyond that, and incorporates some of your ideas. And third, a proactive plan for how to deal with the prospect of tantalizing interim findings so that an IRB can evaluate whether or not this protocol really risks interim findings that are of ambiguous clinical significance that will aggravate the hell out of doctors and patients alike but you feel necessary to go back and try to figure out whether or not this is really a scenario they need to be worried about. And it could be a plan that says we're not going to do it under any possible circumstances. That might be the plan, but these are the elements that have to be present before you can comfortably buy into the presumption.

DR. MURRAY: Harold?

DR. SHAPIRO: Well, in listening carefully, I don't know that I think it's a good idea to begin with that presumption. I can't think of anything harder than defining minimum risk as defining what a hot-button issue is, which is in essence, I think, more controversial and more subjective and more everything than even what minimal risk might be, hard as that is. And I have a different approach to this, and if I'm the only one I'll say this once and I'll desist from here on in.

There are certain burdens we cannot be released from despite our desire to be released from them, and one of them is figuring out what a minimal risk is. It changes every day with every consideration that comes up, every new kind of scientific discovery, every new understanding about what human beings care about, every new example that comes along, and therefore there is a continuous heavy burden on IRBs to know what minimum risk is. My own view is that there is no way to release an IRB from this burden. I think making points like what you consider minimal risk may very well

depend on confidentiality issues and so on is very important, and we can give examples and so on. But I don't think we're going to be able to release IRBs from that burden. I think we can help them by giving more examples and so on and so forth and giving them whatever guidance we can, but to think that we could make that burden easy seems to me not achievable.

Now more directly, the issue of the presumption that genetic studies are sort of presumptively, and sometimes in separate ways, as you put it [INAUDIBLE] much more [INAUDIBLE] than I am, minimum risk. I don't quite understand it. I mean, we often say the genetic record is like the medical record, the material is like a medical record by itself and it's almost like stating the presumption that anything dealing with a medical record is of minimal risk. And I think that's very, in my way of thinking about it, hard to quite come to terms with, to say nothing of the continued fears that people have regarding the use of this material. So while I think it's an interesting perspective. It really is interesting and makes one think carefully about this and I'm very glad that you raised it, and maybe it's the way to go. It seems I'm having a hard time with that presumption. I don't know that I like the Mayo presumption either, which is at exactly the opposite end. But I think for my own self, just thinking for myself, if I just tell myself the IRBs have a hard problem that can't go away, namely establishing what minimal risk is in any particular situation. Investigators have a hard problem. We can help them by giving examples, but we can't. I mean the examples are infinite. Every new investigation is a different combination of things. Then I feel release from something. I feel I can't, so I decided I can't solve that problem, but I'm not going to say that again. And if I'm the only one who feels that way X

DR. MIKE: You're not.

DR. SHAPIRO: Then we ought to get on with this in some other way.

DR. MURRAY: I have Eric and Steve and another Eric on my list now. And I think this is a very important point and I'd like to follow up with it. Eric?

DR. CASSELL: I think Alta's attempt is that it wouldn't be necessary if what you said weren't true, that in fact that constant wrestling with the issue of minimal risk is where we have been now and will be, and clearly not because of a failure of ours but because of the problem that it presents. I agree that it shouldn't be done, but what she also suggested is that we ought to be clearer about what we think is minimal risk and

what's greater than minimal risk as examples, because obviously you can't lay it out, and that that ought to be part either of the body copy or of the recommendation. But I agree that by the end of this Commission somebody will bite the bullet and write what they think about the worst minimal risk. On the 33rd draft they may get some consensus.

DR. SHAPIRO: But returning to Alta's suggestion, to the very brunt of the suggestion regarding genetic research as presumptively minimal risk and that obviously had a lot of very positive reaction around the table, at least as I listened to what people say could you say more about it as to why that should be minimal risk as opposed to some other category of research?

PROF. CHARO: That's two reasons. And first, let me emphasize that I'm flexible. I'm not going to, you know, dig in on this. I really want to throw it out for discussion. It's two things. One, most of the genetic research that I've seen in my own IRB and that I've heard described here is genetic research that's on characteristics far removed from some obvious functionality or some linkage to ethnic or racial or regional origins. It's things like it's the equivalent of blood groups. It's a very unemotional kind of information, and then when we think about genetic research, those of us who are not scientists tend to jump immediately to the most dramatic, *Time* magazine version of genetics, and the scientists are talking about stuff that's much more like the journal *Cell*. So in terms of just the sheer magnitude of the research out there, most of it I suspect is of this more remote, benign, abstract type. Typing tumors for the prospect of looking at which drugs will work for which tumors is the kind of thing that I think of as not really upsetting anybody or putting them at risk for any particular consequence or an emotional, dignitary type of harm.

Second, in terms of consequences that are quite concrete, although for years people have been worried about the prospect of employment and health insurance discrimination based on genetic tests and genetic status, with the exception of one single genetic phenomenon we do not see any evidence of widespread discrimination. The only genetic phenomenon that generates discrimination is sex. The presence of a Y chromosome versus an X chromosome actually does have significant consequences for everything from how much you'll get paid to how much you pay to have your blouse dry-cleaned. [Laughter].

Other than that, genetics does not seem to make much of a difference, so we've worried about these consequences but we have rarely seen them in action. That

suggested to me that the likelihood of a concrete harm is low. When you multiply the number of experiments that could even generate some interest by a health insurer or employer times the probability that they'll use the information, especially with group insurance being the [INAUDIBLE] and genetic tests are not economically efficient yetXall those factors that fit into thisXI conclude that there are going to be very few instances where there=s a real harm.

DR. SHAPIRO: But everythingXI mean I agree with what you said. Everything you=ve said also applies to the medical record in general.

PROF. CHARO: Yes.

DR. SHAPIRO: And I agree. I would have no problem saying in the report that it is our observation that the vast majority of genetic research or something like that really seems very minimal risk to us and so on. I do thinkXI still don=t like the idea that we create that presumption because that=ll last a lot longer than our court and in some sense our thinking about it will last, and I don=t know what=s going to happen tomorrow. But I think making the observation that a lot of this genetic research, for all the reasons you mentioned, is minimal risk is what I believe is helpful not to be in the examples that deal with minimal risk.

DR. MURRAY: I=m sorry. I recognize the prerogative of sitting here with the microphone. I don=t think we should get hung up on whether this is genetic research or not. We began with doing this as Agenetic research.≡ Now, we decided long ago that although much of it, perhaps a great majority of it, might be genetic in some form, it=s not about genetic research per se; it=s about research on human biological materials, genetic or nongenetic. And so I don=t want to get hung up on whether it=s genetic or not, and one of the things I dislike about the Mayo Clinic standard is that they focus only on genetics. In fact, I guess without even being conscious of it I rewrote in my own head Alta=s recommendation to agree that research on human biological materials should be presumed to be minimal risk. I think it should have the adjective Agenetic≡ in there. So, I=d rather get away from the focus on genetics [INAUDIBLE]. I=m sorry. Eric?

DR. CASSELL: Well, just briefly, another example is (BRCA) 1 and 2, and that=s not just gender. We=re just at the beginning of what all of this is going to be useful for. If that weren=t the case, nobody=d be so hot to do it. So we don=t really know what the next step is and we should be aware of that.

DR. MURRAY: The other Eric?

DR. MESLIN: Just a quick comment from the public comments that we've seen so far, and these are just the public comments that we have seen. There is a request that we address the issue of minimal risk as clearly as we can, and this is an opportunity that should not be missed. The question that I ask the Commission, which will help staff in redrafting or rewriting or in responding to the public comments that we get in order to comply with that analysis, is: Is it a policy decision you want us to justify, irrespective of the evidence, or is it something else? In other words, if there is insufficient evidence to demonstrate harms of sufficient probability and magnitude, should we declare the presumption of minimal risk, as there's no evidence that says it's risky? Or should we take the busy-intersection-≡stop≡-sign model and put out the Astop≡ sign before the accident occurs rather than after the accident occurs?

I mean, there is an argument going on in the literature now that says you don't have to have a lot of evidence for discrimination. The potential is there. And the NBAC's work can endure long after the next several years, and we should think about the Mayo Clinic's presumption. I'm not taking a position on one side, but it will help us in drafting any response or any options for you to consider if we know how committed you are to the evidentiary standard of harm. It's a general question, not just to Alta.

DR. MURRAY: I have on my list Harold, Steve, and Trish. And I also want to say that at 10:15 we're going to have to break, or at about 10:15. It would be great if we could finish with Recommendation 5 before we go on the break. Harold?

DR. SHAPIRO: I just want to add I'm not answering Eric's question directly; I just wanted to ask whether if you look at Recommendation 5 itself right now, quite aside from some of the issues that Alta has put before us, the last sentence has me puzzled, and we don't have to debate it right now, which is that the practicability requirement may still go forward even for protocols that do not meet the waiver. It's a question for the staff to think about. I don't understand where the practicability requirement comes in ever again.

MR. HOLTZMAN: That's right. You're right.

DR. SHAPIRO: I believe that's not for debate at the moment, but I think it should be dropped out, is my suggestion. The staff could look at it. That's most easily seen in the flow diagram in the back.

MR. HOLTZMAN: You're right. You're absolutely right. I think the flow diagram actually is inconsistent. Chart 2 is inconsistentX

DR. SHAPIRO: I've forgotten what the numbers are.

DR. MURRAY: Whatever number it is, yeah. It's inconsistent with what we say here. It's not Chart 2; it's Chart 4.

MR. HOLTZMAN: Yeah.

DR. MURRAY: And that was one of the things I wantedX

DR. SHAPIRO: It's just a small point.

DR. MURRAY: All right. Steve?

MR. HOLTZMAN: This is a follow-up that is connected to Bernie's line of thinking, and maybe it explains where I come from on how I think about this in Recommendation 5, because I tend to think of A coded \cong and want to put them in with A unidentifiable. \cong Alta has suggested whether the point is that we wantX then they would not be subject to any kind of review, hence bring them into our purview under Recommendation 5. That increases the burden, pragmatically, on a number of things that will be reviewed, and therefore we start to think about what are potential presumptions of minimal risk so as to be able to deal with the overwhelming majority of cases. The overwhelming majority of cases will be with coded samples and will involve rather innocuous research, okay? I think that Recommendation 5X and I agree with the spirit of that, but I think that it doesn't...it's administratively not terribly useful, and I think it fails to provide the protections that are necessary because I locate the primary locus of minimal risk in the informational risk.

What I would advocate is a structure in which we made it very mandatory that the coding systems be strong, the confidentiality protections of the coded information be strong, and that penalties be associated with disclosure. And then you would have the presumption of minimal risk because you're protecting against the

informational risk. So, it's not to suggest that this research go forward willy-nilly without any kind of protection. It's quite the opposite. It's just locating the risk in the informational risk and giving less credence to the notion of the dignitary harm that occurs in the absence of it being identifiable. That's the more intellectual justification.

DR. MURRAY: And then it wouldn't be reviewed by the IRB at all?

MR. HOLTZMAN: What the IRB would be responsible for, if you would, was ensuring that the institution has in place the necessary apparatus to protect the confidentiality. This is not a new position. Several societies have advocated this way of thinking about it.

DR. MURRAY: This is substantive.

MR. HOLTZMAN: I'm not suggesting that we don't want to change the report at this point, okay?

DR. MURRAY: Okay. Trish and David are waiting to speak.

PROF. BACKLAR: I wanted to agree with Alta, but Steve has brought up something that makes it a little complicated. I believe, in fact, that this research is when you're doing research on intact people, that is different from doing research on pieces of people. And so one considers research on pieces of people, unless specified otherwise, to be minimal risk. The problem is that we also have this [INAUDIBLE] information, which is also there in our medical record or even if you know that I'm ill, if you see me walking around and, for instance, I said that I had some kind of chronic disease or it was clear that I did have some information that is out there.

The problem is that information that we want to protect if we look at what minimal risk is as we describe it in our everyday lives, we know that this is a problem in our everyday lives because those medical records and all of those things are available to people in ways that we wish they weren't. And this is what makes it very, very difficult. So on one side you do have the issue that most of the research will be presumed to be minimal risk, but on the other side you're going to have to find some way to claim the issues of privacy and confidentiality and show that even though people have access to this now, it shouldn't be that one should have access to it. And that gets into the problems of what we were discussing at breakfast about how one deals with the

privacy and confidentiality issues in this report without focusing too much on it, but admitting that this is a terrific problem.

DR. MURRAY: David?

DR. COX: To be as clear as I can with respect to why I'm uncomfortable with Steve's suggestion, and let's be absolutely clear about this point—this is a pivotal point, this discussion that we're having right now, because it in fact was the suggestion and the agreement of numerous people on the genetics subcommittee that Steve's formulation was the way to go. I was the person that felt strongly against that, and let me say why: because under Steve's formulation, if you had a really excellent encoding system—if I'm misrepresenting this, Steve, you can correct me—if you have a really excellent encryption system, then, and this is the same question I asked Dr. Sobel yesterday, then is it minimal risk if information from 50 years of your medical record comes through so long as it's encrypted well? And Steve told me yesterday, yes, that is in fact minimal risk research, all right, under his formulation. Under my formulation, that's not minimal risk research because it violates more privacy the more information that you get. This is the crux of the decision. If most people around the table in fact agree that with excellent encryption, no matter how much information you get that's still a minimal risk, then I think the formulation of our report is not correct. On the other hand, if most people around the table believe that at some level the amount of information flowing through, no matter how good the encryption, changes something from minimal to not minimal risk, then we're on the right track. Would you say that's a fair description of the

MR. HOLTZMAN: It comes back to the twin pillars of why you think stem cell research, for example, is important; it has to do with protection from harms and what has been called, variously, wrong or a economy right, okay? All right, and if you're correctly formulating it, then I would say that when we are dealing with samples as opposed to an intact [INAUDIBLE], okay? So long as you are preventing against the harm—not the wrong, the harm—such as by completing coding systems, then that's all that's at stake, because I don't think there is a wrong or a dignitary harm, as it were, in play because I don't locate the identity of the subject in the sample.

DR. MURRAY: Before, Steve, you described your position and you said you were not asking for a change in the report at this time. Did I hear you correctly?

MR. HOLTZMAN: The whole report is based around a certain kind of approach to this, which is distinct from the one I articulated. I lost this battle 12 months ago. I've been sitting listening to it. Right? But I'm just helping people. I hope [INAUDIBLE] why you reach conclusions like, A Well, since [INAUDIBLE], now let's think about presumptions of minimal risk. It's going to logically flow out of where you've come from to this point.

DR. MURRAY: Right. I just want to see what actual issue is before us to be decided, and you're not proposing that we go

MR. HOLTZMAN: I mean, I'll throw it out, but I don't think it has a snowball's chance of

DR. MURRAY: I think the thing before us to be decided at this time is some variation of Alta's proposal, that we give some advice about a presumption that Harold has spoken against, as I understand it. Then I have Alta, Larry, and Carol. Maybe we'll hear those three comments, then we'll go on our break. Alta?

PROF. CHARO: In some ways I think that although I'm absolutely not going to come on board now with your idea from 12 months ago, Steve, I think that your focus on your concern about what you call harms and I'm calling the concrete consequences for an employee in a job that's not been given to you or a health insurance policy you didn't get right, the distinction between that and the current issue is what I think may also underlie part of the different first impulses that Harold and I have had, for example, on whether or not a presumption of minimal risk makes sense here. Because the use of my medical record and the use of my human tissue for genetic or nongenetic research that doesn't involve having my name or identity apparent traceable, but not apparent it seems to me to be a little bit like the equivalent of somebody who's doing research on interior design and during the day while we're all at work they use a pass key to go into a series of houses and take photographs, and in some houses everything's neat and picked up and in mine, of course, the dishes are in the sink and the underwear's falling on the floor and you don't know that they've been there. You come back at the end of the day, and you don't know anybody's been there, right? And there's a real interesting debate about whether or not one wants to take seriously the notion that you've been wronged by having this person come lurking about in your house without your knowledge before or after, right? You don't even smell their perfume, but they've been there. And I think that you've made it very clear

that you would not like to see the regulations take that kind of thing so seriously that it creates any kind of regulatory burden.

I think that your concern, Harold, about the repeated investigation of medical records, even with codes and even without consequences for employment, these speak some concern about exactly that scenario, and I'm kind of in between. I'd like to see XI mean my instinct is that it's minimal in the sense that it doesn't rise to the level of losing a job, but it's not without consequence and you would like to have an independent body have an opportunity to say you've done it one too many times, you've abused the privilege, right? Or you've actually done it in a context where there is some actual concrete harm because it's more traceable than usual; you know, it's an unusual kind of house that has AIDS or some other kind of thing, and I don't know if XI would want to urge people to fight to the end on whether or not there ought to be a presumption, but I don't know that just a couple of examples in the text will ever satisfy either the readers or the IRBs that are struggling with this. If somebody has yet a different suggestion for a way to make a much more focused contribution to the discussion about what constitutes minimal and nonminimal risk in noninterventionist research, I'd be very open to it.

DR. MURRAY: Okay. Larry?

DR. MIKE: Well, I'm just trying to see what the practical consequence would be of Steve's. Let's take the example of going back 50 times into my medical record, and as long as there is really no substantial harm in a classical sense but I would feel offended, how is that to be decided? How is that to be decided about with the adequacy of the consent? It seems to me that the IRB would have to look at that anyway. So they may not be looking at the actual risk itself, but they still have to look at the [INAUDIBLE], so it seems to me it would still go to the IRB.

It would be as if you're saying that, okay, they're exempt if it's minimal risk, but if you're substituting minimal risk, probably substituting an adequacy of the consent for the minimal risk standard, it seems to me you still have to go back to somebody outside. It can't be left internally to say, A Well, we got adequate consent and therefore we satisfied all of the X. ≡ You still need some outside body to look at it.

DR. MURRAY: Okay. Harold, you have the last word before the break.

DR. SHAPIRO: Well, I think two things: one, I think we ought to keep in mind as we go through this really what the burdens are. The burdens are not very great. We are not asking people to do so much here, even in some of these contentious cases. If you go down our flow diagrams a number of times you escape out with doing hardly anything. It's overwhelming, and it reflects the fact that we all believe that a great deal of this research is extremely minimal risk and all the things that everyone has said. And if you just go through these flow diagrams you'll find out that the huge majority of research projects are going to slide through here with a very minimal amount of oversight. At least that's my own view, and we shouldn't lose track of that, so we shouldn't let our conversations imagine that we've got this tremendously burdensome requirement on everybody, which I think in most cases is just not there.

Regarding the issue of the presumption—not the presumption, but how we can handle the minimal risk, I have a suggestion for the staff and maybe it'll help out when we see another draft. And that is that we be much more explicit about the fact that we feel a great deal of research in human biological materials is in fact very minimal risk, not about to do harm to just about anybody and maybe, in fact, do an awful lot of good for a lot of people, and therefore it ought to go ahead with very minimal oversight, which is exactly what's provided for. We ought to be more explicit about that, and also be more explicit and try to be helpful despite the fact that I believe a struggle is inevitable.

Interesting examples regarding minimal risk research might serve as some preliminary guidance to IRBs. I think that is an entirely useful activity, and there are some examples in here. Perhaps they should be brought closer to where the recommendations are, so that's another issue, or we should add examples. But I believe there's a way to accommodate these various views. We'll have to see when we actually look at the material. I think that that might be a helpful way to proceed.

DR. MURRAY: By my watch it's about 10:23. Can we reconvene in 12 minutes, and begin at 10:35? We actually will begin at 10:35.

DR. MURRAY: We have about 80 minutes before noon, which is not a lot of time. It would be wonderful if we could get through at least a quick read of the remainder of the Recommendations chapter of the report, and I'm going to try to have us do that, which means we are not going to be able to explore every nuance as we have done with the first five recommendations. But let's go through and see if we have any major problems with the remaining recommendations. We had a good discussion about

Chapter 5. I've spoken with Kathi. She feels she has sufficient information to offer us a revised explanatory text about Recommendation 5, so that is what we will do. It will be in the next draft.

Let's move to Recommendation 6. Are there any comments about Recommendation 6? This is the opt-out recommendation. I don't hear anybody or see anybody wanting to speak about 6; we're going to assume that you find it acceptable.

DR. COX: Quick.

DR. MURRAY: Yeah, Number 7. This is: A When research is conducted using existing identifiable samples and if requirements to seek informed consent have not been waived, IRBs should evaluate any existing consent documents for applicability. Where the IRB determines that the proposed research was agreed to at the time the sample was obtained, there is no need for furtherance. The IRB...≡ And I had additionally, A...may choose to require that the investigator inform the sources about the new project to provide general news about the results and/or the choice of dissenting participation in the research.≡ Does anyone wish to change that recommendation?

I had just a quick question here, Kathi. Early on, I think all through our deliberations, we've said that someone has expressly chosen not to have their tissues used in research and has so indicated. That's always been a problem; I'm not sure we say that, so I'd just like to make the recommendation reflect that. Does anybody object to that modification? I don't think this is an effort to say otherwise, just that they did not express it fully. Steve?

MR. HOLTZMAN: I have a question about A The IRB may choose to have the investigator provide general news about the results.≡ So we're here in a situation using an identifiable sample, which assuming for the moment was consequent to a determination of minimal risk, no rights and welfare, and that therefore no consent was involved, so the individual doesn't know that their sample was used in this potential study. And where the IRB may say, A Well, you should go back and give general news to John Doe. Oh, and by the way, have you read the latest *JAMA* article that says, >Prostate cancer is indicated if you have an increase in expression of the following gene=?≡ I think the whole area of when you go back with a research finding is a very sensitive area and I think we have to make sure we're clear in our guidance here.

PROF. CHARO: Well, first I would point out that even where consent has been waived, and that is not the situation necessarily contemplated in Recommendation 7, right? But even where it has been waived, the current requirements for the waiver of consent not only have this practicability business that we're saying might be dropped, but it also as its fourth criteria currently suggests that you have to go back to people subsequently if possible, and let them know that they were involved in an experiment without their consent. So, that's actually in the current regulations. That's probably I'm speculating now something that was written with regard primarily to deception studies, but nonetheless is in there.

Even putting aside those regulations, IRBs are always free to impose more requirements than the regulations do. The regulations always represent a basement, not a penthouse, of protections, and I think this is exactly where an IRB can exercise some judgment about what news if any should be sent back. This is not required; it simply says, They may choose. And it's reiterating a right they already have as IRBs. If they see some particular reason why there's a need to send information back to people not individualized information, just general information they're free to do it.

DR. SHAPIRO: Could I perhaps ask a question, then, about this particular sentence?

DR. MURRAY: No, please.

DR. SHAPIRO: You're quite right, of course I mean, you're right to point out that IRBs can require anything at all, but it needs to be appropriate. But if we're going to bother to select this to say as an option, it ought to be because we feel they should, you know, maybe want to give this some serious consideration. Otherwise, it's just arbitrary to pick one item out of a hundred that they may choose to do. And so I think the requirement for leaving the sentence is that we think that this is something not compulsory, but it sort of rises above the hundred or thousand other things we might choose to do, and so I'd just like, and my recommendation is to Tom and Kathi, to see if we really believe that we as a Commission believe that this has got some special characteristics. Otherwise, we either put it in the text as an example rather than put it inside the recommendation. And I'm open, depending on how the Commission feels about it.

DR. MURRAY: Alta, how would you feel about putting this in the text rather than in the recommendation proper?

PROF. CHARO: I don't have any strong feeling one way or the other on that. Sure.

DR. MURRAY: That's my inclination, because I think Harold's right. It does sort of single out this particular situation as one where somehow we felt called upon to mention this, so, I'm persuaded by his argument.

DR. COX: I am also. I like the idea of putting it in the text, because if they've already agreed, consented to, then there's the additional sort of obligation to go back and tell them more about it. On the other hand, if it wasn't consented to, then I think it would be a nice trade-off to go back. But we deal with that in a different way.

DR. MURRAY: Okay. Anything else compellingly important on the recommendation

DR. MIKE: Well, I guess it's minor, but the second sentence really isn't required, right? I mean, [INAUDIBLE], so it seems gratuitous to add that second sentence. And rather than having that sentence, you should have a sentence that says if it's not applicable, then you have to seek consent.

DR. MURRAY: I'm sorry, Larry, if thatX

DR. MIKE: Well, if you read the first two sentences, the second sentence just sort of reiterates what the first sentence says. If you're going to have a second sentence it should say what happens when it's *not* applicable, not when it *is* applicable.

DR. MURRAY: Eric, Kathi's shaking her headXnodding her head [INAUDIBLE].

DR. SHAPIRO: Let me see if I can understand exactly, Larry, what you said, because I think you may be right. There may be a need for one sentence rather than two, although it may require some change in the first sentence. Rather than asking IRBs to evaluate any existing documents, it was to ensure that the requirements are being met, whether they evaluate existing documents or any other way. We're talking about that as if consent has not been waived, then IRBs have to have a positive responsibility here. Is thatX

DR. MIKE: Well, yeah. What I'm saying is that since we single out any existing document, if it's not applicable, then what? Because we only reiterate if it is applicable, it's okay.

DR. MURRAY: Alta?

PROF. CHARO: I think maybe if you were simply to delete the words "for applicability" at the end of the first sentence, it now makes sense: The research is using existing identifiable samples, informed consent has not been waived, and IRBs evaluate the existing consent documents. If they indicate that it was agreed to, there's no need for further consent. Does that take care of the redundancy for you?

DR. MIKE: Yeah.

DR. MURRAY: Okay. That's good. Now I understand that. Moving on to Recommendation 8. This is a long one. Any comments on Recommendation 8 on page 145? I will say that the text that follows this recommendation I think we need to go through, but we will not do it today. Where we use the word, the phrase "human biological materials," we will use the word "specimen" and the word "sample." Please convey those rewritings to us, but let us not get hung up on this. Let us, in fact, focus on the language of the recommendation proper. Eric?

DR. CASSELL: Well, I take it that there are really two questions that are raised in here. One is that consent needs to be obtained and, second, that the investigator must ensure future confidentiality. You could get consent and may not do that; you could not get consent and do that, so they're really separate actions, and it should be true no matter what the case is. Investigators should ensure confidentiality and there are a number of ways of doing that, by, for example, in Number 1. and in Number 2, subjects should give authorization for future research consenting to the specific protocol, excepting that it will be rendered unidentifiable and stating that the sample cannot be, or stating that the sample cannot be and/or stating that the sample cannot be used. In other words, it's two separate acts. Confidentiality and consent are two separate acts.

MR. HOLTZMAN: I think that the way to think about it is that the first issue is what is being consented to. So Number 2 is being consenting to the specific, or then consenting more generally. If you're consenting more generally it's because you're within the context of your sample being anonymized or being coded.

DR. MURRAY: Alta?

PROF. CHARO: I must confess I can't remember the thinking that went into the drafting of Recommendation 8 and why the first of the four subsections included all these particular provisions, because its intent seems to be a little simpler than that. I mean the intent, building on what Steve just said, might be simply that the subject can be offered the following options: to give authorization for all future uses of the tissue; to consent to a specific protocol only; to have it stripped; to have it not used. And I'm not sure I understand why there was the decision to condition this kind of blanket future authorization on all the confidentiality stuff, but I don't want to suggest we get rid of it without understanding why it's there.

DR. MURRAY: Bernie?

DR. LO: Yeah. I think we're trying to do too much with this recommendation. I think the first time when you say that when an IRB determines that informed consent cannot be waived and that you don't have consent, I think we just need to say you need to get consent for that specific protocol, which sort of gets buried in here. I would rather see that first as an absolute because, one, I think it's problematic and that there may be other studies in the future where you mayXyou know, is it clear that you need authorization if you're actually able to waive informed consent? So that I think that you're asking people to authorize something that they otherwise would not have to authorize their consent to. I think that's a little problematic.

Also, I think that as I recall thatXwell, what I would like to see is that someplace in the report we talk about consent for future purposes and go back to some of the discussions that there were in much earlier sessions on tiered consent and other innovative things people are doing. I would tend to put that more with collection of samples in the future as opposed to you've got the sample but you didn't really get consent, so now you have a chance to go back and talk to people. I'm not really sure that's where it's going to be, but I just think we're trying to do too many things here. I think we ought to first start by just saying if you need consent you've got to get consent, and then if in addition you want to get consent for future uses as in Recommendation, you know, 22 or whatever it is, say that, but not to sort of collapse everything down here. And in that future section, have a much richer discussion of different options and really encourage people to do that to make it meaningful. I think we need to see a lot more supporting text than we now have in the report.

DR. MURRAY: I'm going to recognize Alta in a moment, so part of what you would propose is that in that first sentence we really say A consent must be obtained. We end the sentence by saying A...consent must be obtained.

DR. LO: Yes. If you need consent and you haven't gotten it already, you've got to go get it.

DR. MURRAY: Then we may or may not choose to give the list of options. But you've got to go back and get consent.

DR. LO: You may want to do some other stuff. For other uses you can't [INAUDIBLE].

DR. MURRAY: I think I get the drift of what you're saying. Alta, Larry, and Harold?

PROF. CHARO: First, I agree with what you've said so far. Absolutely. That's a nice way to simplify it. With regard to how we handle the question of authorization for future use, I don't think it's only at the moment that we're collecting new tissue; I think it's at any moment that we're interacting with somebody who is a tissue source. And that might include at the moment that I'm now getting consent for this specific protocol, I now have an opportunity with this person, and this is the moment at which I can now give them a series of options about future uses of tissue repairs I already have, as well as interactions where I'm collecting new tissue from somebody. As for that richer discussion for that moment, then, we can incorporate [Recommendations] 1, 2, 3, and 4 as the kinds of things that they can opt for if they'd like to incorporate my reference to the materials that we had in the previous meeting [INAUDIBLE] that lists the kinds of things we believe are central to [INAUDIBLE] agreeing with that decision. You know, alerting them to certain aspects about future research, alerting them to the range of controversial research that may be implicated and thereby letting them make as good a decision as they can make about this range of future uses.

DR. LO: Right. And if I could just say, that's a much different discussion than 3 and 4, because we may be anticipating an option where you can use my research for all except the following, which is now included in 1, 3, and 4, which may be an option that people may take.

DR. MURRAY: Larry?

DR. MIKE: I think that Recommendation 8, in the simpler version, should be part of Recommendation 7. I don't know why we separate out when it's adequate consent and it's okay, and then have a separate Recommendation for when it's not an adequate consent. So Recommendation 7 just says you review documents. If it's adequate, it's adequate; if it's not, then you have to seek consent for the particular experiment.

DR MURRAY: I think that's an excellent suggestion, and we will adopt it. Harold?

DR. SHAPIRO: I think my suggestion is similar to what perhaps Alta and Bernie were talking about, and so if it's repetitive, I apologize. It seems to me we have 7 and 8. And straightening that out I think is very positive. But what we really have here is a special case of prospective authorization, and we're trying to use whatever occasions may pop up to get prospective authorization in, obviously, the appropriate way. So I think the way to handle that is actually to have a section somewhere on prospective authorization, and then you could refer to it when necessary. As Bernie said, if you need a fuller discussion that's absolutely right also. And then we could refer to it as we go through. And so I think that Kathi, is what we'll try to do; I think that's the [INAUDIBLE] thing. We thought this through in other venues. It's really pretty straightforward; we can encourage this and then researchers and others can take every occasion they can find to get appropriate prospective authorization.

DR MURRAY: These are very, very constructive points of [INAUDIBLE]. David?

DR. COX: As a coda to that, I completely agree with that. But in many ways it's even in addition to prospective authorization because it's our recommendation about consent. We don't have a recommendation in here about consent and our feeling about consent, that it's more than just words, that it's a process, and some language about that. And then this recommendation is basically pertaining to that. It's when you're consenting someone, the kind of information that you get. I mean, maybe I'm off on that, but it seems, Harold, that it just goes together with what you just said.

DR MURRAY: I think we've done it. Recommendation 8 will be slimmed down and combined with Recommendation 7. There shall be a new section on prospective authorization for research. And we will make appropriate reference to that. Good.

Recommendation 9, page 147. Eric?

DR. CASSELL: Where we say A particularly sensitive research, I take it that that means greater than minimal risk. If that's what it does mean, then that's what we ought to say; and if it isn't greater than A minimal, what does A sensitive mean?

DR MURRAY: Eric, do you really want to tackle that question? Alta?

PROF. CHARO: That's not how I understood it, but if it can be read that way, then certainly we need to rewrite it so it's clearer. My understanding had been that this is about research that is politically sensitive, where I might have a political objection to the use of my materials to facilitate this line of inquiry, or research that is emotionally sensitive, such as on certain diseases that I might have or have a propensity for that are particularly stigmatizing or sensitive. I think AIDS has always been raised as one of the paradigmatic cases. So I would think of things like X

DR. MURRAY: You can even look at the X

PROF. CHARO: I would think of research X right X I would think of the bell curve and AIDS as my two paradigmatic cases of research where I would very much appreciate an opportunity to say, A Not with my tissues, please.

DR MURRAY: So. Steve?

MR. HOLTZMAN: So then take those two thoughts together. Is it because it may trace back to you?

PROF. CHARO: No.

DR. MURRAY: No.

MR. HOLTZMAN: It's only because X

PROF. CHARO: It's [INAUDIBLE] to pick up yesterday's themes.

MR. HOLTZMAN: Right. Exactly. If that is the case, then that should be applicable not only with respect to identifiable samples but to unidentifiable ones, because as we've written this I can take your sample, strip your identifiers, and then go and do that offensive research. So if that's the basis of the argument, then this needs to be written to X

PROF. CHARO: This is undoubtedly true, and elsewhere in the report we've said that one of the dilemmas posed by the use of unidentifiable materials is that it can raise issues about personal and political sensitivity or group objections and that as a practical matter it's difficult to figure out a way to operationalize some opportunities for these individuals or groups to object, so we asked for a degree of self-restraint on the part of the investigators. And I would certainly hope that IRBs are going to be X maybe we can make this more explicit X urged not to allow investigators to choose to strip identifiers solely to make it possible to do sensitive research because it now eliminates the ability to invite objection and dissent or opt-outs, right?

DR. CASSELL: On the simplest basis, that's a definition to me of greater than minimal risk in the context of the use of human biological materials.

DR. MURRAY: But it's not necessarily a risk to the individual subject.

MR. HOLTZMAN: No, but that's the difference here.

DR. BRITO: Maybe we need to spell it out here, because one of the changes in the current draft X there were actually some of the public comments that I did have a chance to read X that was looked on favorably was that we emphasize a little bit less the group risk. And then in Recommendation 3 we have the last sentence: A Research should be mindful, however, that some types of research on uneventful samples, while posing no potential for harm to the sample source, might pose potential harm to groups of individuals and therefore should not be designed. ≡ Maybe we need a sentence similar to that here in this recommendation. I, like Eric, am not particularly fond of the phrase A particularly sensitive research, ≡ and I'd like to see it spelled out as A greater than minimal risk to these individuals or to the group. ≡ But anyhow, I think we need to spell out here what we're talking about in A greater than minimal risk either to the individuals or to the group. ≡ It needs to be very clear.

DR. MURRAY: I seek help here. My understanding is that the concept of minimal risk applies to the person, to the subject, not even to some group of which the

subject is a member. I think it conflates it's a difficulty we're confronting, but I think it conflates the concept of minimal risk with this notion of our desire to protect people from having their samples used in studies that they would object to on matters of principle not because they are at risk, but because they are offended by the very nature of the research.

DR. BRITO: I'm in agreement with that. We should spell that out, and in addition add a statement that well, and this is based on what Alta just said, that research can be considered sensitive or particularly greater than minimal risk for the group also, and

DR. MURRAY: Well, that I think we invite more trouble and confusion too early if we try to expand the concept of minimal risk here when we're trying to be more precise about it in other parts of the report. I understand the impetus to want to do that. I just think we lose more than we pick up if we try to expand the notion of minimal risk. Larry?

DR. MIKE: The text immediately before explains what we're talking about, and I would suggest that we also refer back to that first Recommendation that does talk about that again, so that it's clear what we are talking about.

DR. MURRAY: Alta?

PROF. CHARO: Is it possible that what we're trying to just whispered to me, Why can't we just say what we mean? So I was trying to figure out what we mean. [Laughter.]

DR. MURRAY: What a revolutionary idea. [Laughter.]

PROF. BACKLAR: What you've just described it as was.

PROF. CHARO: It's research that's likely to be objectionable to somebody is what it is. It's research where somebody might want to object that's what we're really getting at, and we'd like to give them the opportunity to say No. For example, research on whether or not law professors are genetically determined to talk too much is research that I would object to and I would want the opportunity to say, Not with my tissue, right?

DR. MURRAY: The rest of us would say, A You don't need to do that study, as the actual X ≡ [Laughter.]

PROF. CHARO: So maybe that's the way to get at it. It's not about the sensitivity of the research; it's about the likelihood that somebody would want to take advantage of the chance to object. Maybe that gets closer to what we're trying to accomplish.

DR. MURRAY: Carol and David?

DR. GREIDER: The problem that I see with that is that it leaves open such a range of possibilities. I mean, if I were sitting on some IRB and somebody proposed to look at whether law professors talk too much, I would say, ASure, why not? It's helping me. ≡ [Laughter.] No, honestly, I mean, you know, it could be, you know, who knows what somebody is going to object to? How can you X how do you define what that sensitive research is?

MR. HOLTZMAN: But since we're asked [INAUDIBLE] judgement for IRBs, right? And so, when, and as Zeke gave the example, and then we're looking at doing a study of [INAUDIBLE] and they said, A Time out, we need to think about this. ≡ So.

DR. COX: Exactly my point. I think Carol is right on the mark here, because it says A where particularly sensitive research. ≡ Well, who's figuring out if it's particularly sensitive? The IRB is. The IRB may not get it right, but it's not for each person to determine whether it's particularly sensitive. The IRB in its aggregate, okay, makes a decision. So, it's not the researcher that's deciding, necessarily, if it's particularly sensitive; it's the IRB. So, just in terms of direction for someone here, that to make it clear who's determining it, then I think will make it clearer how one operationally abides by this Recommendation.

DR. MURRAY: I like where this is headed and [INAUDIBLE] guided by Trish's injunction to say what we mean. What if we made this an instruction to the IRB, something to the effect that IRBs should consider whether given the nature of the study and the nature of the population which samples are drawn, individuals would be X would find this use offensive.

PROF. CHARO: Probably, um-hmm.

DR. MURRAY: Probab- Xwell, if it=s probab-, well, there is a proba- Xa distinct probabilityXwe=dXwe=dXwe=ll fudge with the language; we=ll get it right. We won=t be offended. Basically that=s the way we=d be redrafting, as an instruction to the IRB to consider in this particular use. Is that fair?

Okay, Bernie?

DR. LO: Yeah, no, I think that=s good, and then I would suggest that we put some more explanation in the text on 146, incorporate David=s point that this is something that someone other than the investigator should review. And secondly, I think it=s worth putting in if there=s a history in a historical context here with genetics research that we need to be aware of, and this I think does separate out genetics research from other types of research on medical record or storage samples. I think we need to make that more explicit.

DR. MURRAY: Although we wouldn=t instruct that this only happen when the research is expressly to that. That is an example of one kind of research. Fine. Larry?

DR. MIIKE: I would suggest for consideration also making some explicit statements here aboutXremember our old discussion about whether it was wise to seek group consent when we=re dealing with these, like the cancer gene-type project, and we said no.

DR. MURRAY: We do that later; we talk about that later.

DR. MIIKE: I know, but what I=m saying is that we opted out not to seek group consent but to encourage investigators to talk with them.

DR. MURRAY: Right.

DR. MIIKE: Or, maybe we can make a link to that and in this way since the individual sample is being used. It=sXI wouldn=t call it a substitute for group consent, but it=s responding to that sensitivity and allowing the subjects themselves to opt out if they need to.

DR. MURRAY: So, you would incorporate in the text following, perhaps, in reference to the discussion later on. I think that makes eminent sense.

DR. LO: Well, Larry, would you say that group discussion, which I really agree with you is desirable, would help the investigator get a sense of how likely is it that members would want that subjects would want the opportunity to opt out? I mean, is that one of those to get some sense of how potentially sensitive is this and to what is the likelihood that a particular subject would say, A Yeah, I'd like a chance to opt out of that?

DR. MIKE: Yeah, I think so because it's impractical to seek group consent, right? But it responds in some way to allow the individual.

DR. MURRAY: Are you, Trish, you had had your hand up earlier.

PROF. BACKLAR: It's alright. It's been addressed, more or less.

DR. MURRAY: I think we know what we're doing with Recommendation 9? Alright, let's go to Recommendation 10, also page 146. This is about recontact.

It's a long recommendation. One possibility is to have the bolded and italicized language be briefer than that and then explain below, but we also have the option of keeping something with the level of detail that we currently have. Is there any strong feeling about that one way or another? Carol, Steve, Bernie, and Eric.

DR. GREIDER: This comment is about placement of this. It seems like this recommendation goes together with the Recommendation that we just combined 7 and 8, because in 7 or 8, we're saying that there wasn't that the consent was not good enough and they should be asked to recontact. And then this is about how to that recontact. And, it seems like having this intervening Recommendation afloat doesn't go too well.

DR. MURRAY: Okay. Steve?

MR. HOLTZMAN: This is an agreement with Carol and to make an additional point. If you look in our [INAUDIBLE] notice five situations where you may be going back, I think one stands out as radically distinct than the other four. Four of them pertain to recontacting. One of them pertains to going back with potentially medically relevant information, and I think that needs entirely separate handling [INAUDIBLE].

DR. SHAPIRO: I'm sorry, I didn't hear the last phrase.

MR. HOLTZMAN: It needs entirely separate handling. I think the issues of going back for re-consent or new consent logically fall where Carol is talking about. I think the issue of going back to someone with a research result is potentially clinically relevant as a whole separate set of issues. We should be clearly distinct.

DR. MURRAY: Would you treat them, then, as separate recommendations?

MR. HOLTZMAN: Absolutely.

DR. MURRAY: Alright.

DR. COX: I completely agree with that.

DR. MURRAY: Okay. On that point alone, does anyone first of all, does anyone have anything urgent they need to say about that particular point?

DR. CASSELL: Rephrase it in one sentence.

DR. MURRAY: That, because there are two distinct sorts of purposes for which recontact may be desired, we should treat the two purposes separately. Purpose No. 1 is because you want more information or something to further the research. No. 2 is you may have something that you think is of value clinically to the source of the tissue. Treat those X

DR. DUMAS: So what?

DR. MURRAY: As separate recommendations. That was the request. Right?

DR. DUMAS: But so what? I'm not sure what Recommendation 10 does except, no matter where we put it, except it says that if the investigator wants to recontact they need to take their plan to the IRB for review. And then you're instructing the IRB what it should be reviewed for, the factors that they should pay attention to but to what purpose?

DR. MURRAY: Well, perhaps I shouldn't speak on behalf of the people who just made the suggestion. I think I understand what they're going for. Look

at the very last phrase there, Any incentives offered for allowing use of the sample. It will be completely irrelevant if I was going back to help them clinically.

DR. BRITO: I just want to make this clear. Steve was what we're talking about here is the first four bullets and then the fifth bullet, To divulge results obtained in the course of research is what we're talking about as a separate [INAUDIBLE].

DR. MURRAY: Yeah. To address them separately. David?

DR. COX: One of the reasons why I would see it be separate is the potential conflict when you're trying to get more information from a person and one of the ways to get more information from a person is to give them something for it, right? In this case it's not like beads; in this case, it's information. But the so, is that information, you know, valid and clinically relevant to them? And you don't want people to be recontacting for more information and getting them confused. It's like the therapeutic misconception again, giving people information in exchange for getting more stuff back from them. So, by having these two things separate, it prevents, or it makes that distinction.

DR. BRITO: I agree.

DR. MURRAY: Yeah, I agree with that. Bernie had his hand up. Is it on this point, Bernie? I think [INAUDIBLE] that's a good suggestion that we have right now still doesn't. Do you want to X

DR. DUMAS: No! I hate to do this, but it's still confusing to me. You talk about the adequacy of the information that will be provided. So, what if the information is not adequate? There's nothing in this recommendation that says any constraints are going to be imposed. It just says that it has to go to review bodies for review and what they should look at. But it doesn't say under what conditions the investigator should be approved to proceed. Does that make sense? That's completely lacking from this recommendation.

DR. GREIDER: But that's true whether it's two recommendations or one, right?

DR. DUMAS: That's right. That's right. Yeah.

DR. GREIDER: So, if you had two recommendations as a separate issue in terms of them saying those recommendations.

DR. DUMAS: Wherever you put them, however you divide them up, the recommendation for me is inadequate because it doesn't say under what conditions the IRB should approve or disapprove recontacting.

DR. MURRAY: I think you've used your getting agreement among the Commissioners.

DR. DUMAS: Okay.

DR. MURRAY: I should note that we do something here in that we actually require that if you have any plan for recontact, or if you're contemplating the possibility of recontact, you have to bring that before that IRB. I'm not sure that's currently a part of the rules of current practice. That in itself is I think a contribution. But it would do we want to go into detail about what the IRB takes into account as they consider these plans for recontact? I see Eric has his hand up and Alta is nodding.

Eric, then Alta?

DR. CASSELL: Well, I actually think that there's too much detail in what we've written already. That's the IRB's job, and in every piece of research, every aspect of every research protocol, this is exactly what they do for a living. They don't get X

DR. MURRAY: Don't you get paid if you're doing something for a living? [Laughter.]

DR. CASSELL: You mean we're doing it because you don't get paid? We would do this to you if we gave you [INAUDIBLE]. But, so if there are separate issues [INAUDIBLE] but whether they should do it by mail or not by mail, I think that's local prerogative. I really don't think that's for them to X

DR. MURRAY: Okay. There's no detail, there's too much detail. Alta's going to explain to us the right path.

PROF. CHARO: I'm looking at the bulleted items above Recommendation 10, which identifies at least five situations where the Commission=s already identified the possibility individuals need to be recontacted. Some of them have been addressed in other Recommendations. The one that really stands out as never having been addressed anywhere in a systematic way is divulging results obtained in the course of research. My personal experience has been that this is a deeply problematic area, and although it=s true that it is up to IRBs to struggle through it, Eric, if we have anything valuable to say we should certainly do it. If we have nothing valuable to say I completely agree we should shut up. But, we hint at this just a little bit when we have a sectionXI don=t remember anymore where in the report it isXin which we discuss the phenomenon of interim conclusions, whether they actually constitute information that then becomes part of a consent process or whatever. We mention the fact that interim information itself can be a form of harm because of its ambiguities and its anxiety-provoking possibilities, and there=s actually a little bit of literature on this, and it may be worth sometime digging into it, if we can identify it, about what level of certainty is understood to be necessary before there is an ethical obligation to inform people about things, and that helps you to understand what that balance point is.

DR. CASSELL: I agree with that.

MALE VOICE: That we should do that?

DR. CASSELL: No, but IXbutXbut, what Alta=s effectively saying is that that is a separate issue entirely from the other one to go before it and this is what we said before. I tell you you can get a truth bomb in the mail, right? Your specimen shows that you have an early form of HIV about which not much is known. That ought to take care of you for quite some time. [GROUP LAUGHTER]

DR. MURRAY: Harold?

DR. SHAPIRO: As I see the issue that we=re discussing right now, that is around 10, there are two issues, and let me try it. One is the issue, which I think is raised by Rhetaugh, which mightXif you look at the second line, line 21 of the recommendation where it says AIRB should review,≡ this recommendation would be different if we said Areview and approve.≡ That would give the IRBs X

DR. DUMAS: A little teeth.

DR. SHAPIRO: A little teeth. So, one question is whether we should put A review or A review and approve. I think that would at least go some way to dealing with the issue of concern. The second issue is whether the clinical feedback issue, if I can describe it that way, should be handled separately from the recontacting or ongoing research feedback that also makes sense to me, simply because the examples you give would be quite different and not mixed up. The examples that we give here are all appropriate, but they're not appropriate in every category here. Some are only appropriate for what Steve called the recontacting stream and some are only appropriate for the clinical stream—the mail bomb that Eric talked about a moment ago. So, it seems to me there might be some profit in separating these, although in a very, hopefully, not too wordy way. But there's a real—that's just a pedagogical issue in some sense. It's not—but there is a real issue vs. the A review and A review and approve. That's a real issue. And we need to [INAUDIBLE] where people's feelings on that go and maybe if you don't mind telling people to express themselves on that issue.

DR. MURRAY: Sure. Bernie?

DR. LO: Yeah, I would agree with saying A review and approve. If I could also just speak to the point about separating out recontacting for the purpose of conveying information. A lot of those come up after the study's done as opposed to the preplanning. If we're going to separate them out, which I think's a good idea, we should also say that when the study's over and you hadn't planned [INAUDIBLE] people with the results but you have some findings which you think warrant recontact, that do we want to say the IRB should be involved in review and approval at that stage, because I think it's very hard at the onset to predict what's going to happen and what circumstances you're going to want to recontact people.

DR. MURRAY: I want to push something. Harold made, I think, a very useful distinction. Do we agree that the language of A review and approve—is that in fact what we wish?

DR. CASSELL: Yes.

MR. HOLTZMAN: Okay, for recontact.

DR. MURRAY: For recontact for research. So we can put that one—we've done that.

DR. CASSELL: And take all that detail after that.

DR. MURRAY: [INAUDIBLE]

DR. DUMAS: For whatever reason.

PROF. CHARO: Right.

DR. DUMAS: Let me see if I understand where we are. Any plan to recontact subjects? I mean, whatever, donors would be taken to IRBs for their approval period. Now, that means that you're going to recontact them for any of these reasons listed above.

DR. MURRAY: Now, we're—we want—we're trying to distinguish now. We are trying to distinguish now,

DR. DUMAS: Why do we need to? Why do we need to distinguish them?

DR. MURRAY: Because you've had a variety of arguments over the past 15 minutes.

DR. DUMAS: Oh, I'm sorry.

DR. MURRAY: No, that's okay. But you may not be persuaded by any of them.

DR. DUMAS: I might not have been in the room.

DR. MURRAY: No, you were in the room, Rhetaugh. But, you may not have been—maybe people weren't clear.

DR. DUMAS: I might not have been in the room. [GROUP LAUGHTER]

MALE VOICE: Tell 'em.

DR. MURRAY: I'm with you. Steve?

MR. HOLTZMAN: One of the reasons—aside from them being different, these two scenarios from going back, the other reason I think it's important to split

them is it's not immediately evident and either the IRB is the right body to consult with if you're going back with potentially clinically relevant information. As Bernie suggested, you don't contemplate coming up with this information pre-study, but you come up with a piece of information and now the question is should you go back and how you should go back. And I don't know enough about how hospitals operate, but I think there are things like ethics advisory boards and whatnot that might get invoked at that point at opposed to IRBs.

DR. CASSELL: [INAUDIBLE] paying attention. Just send out a letter telling me about your HIV status.

DR. DUMAS: It would be a terrible thing to do it that way.

DR. MURRAY: I'm not. I didn't hear you.

MALE VOICE: [INAUDIBLE] people will not go back to the ethics board for that. They just don't have. Unless we say you've got to do something like that, seek consultation, that's something we can say that would be [INAUDIBLE].

DR. MURRAY: Well, let's say it. That's what I'm saying. Alta, if we have a recommendation let's make it, and then Bernie.

PROF. CHARO: Two observations from the conversation. First, the scenario that you just described, Steve, only reiterates the importance at the outset when research is being designed and approved by the IRB, and its risks are being minimized to whatever level they finally fall, that the researcher have a plan for what to do if the temptation arises to transmit clinical findings back to the subjects. The moment to figure out how to handle this is when the research is being designed, not after the results have been generated, and that's very much part of what controls the ultimate risk because that's the moment at which you might decide you'll never go back. You'll only go back through an intermediate body that's going to accumulate information and make a judgement. All [INAUDIBLE] adverse events are sufficient to begin to rethink the approval of a drug, right?, and controls that information for a little period of time when the first few event reports come in. That kind of mechanism.

The second thing has to do with the separation of the recontacts to get newer or updated consents, etc., and recontacts that involve the transmittal of information. Although they're largely separable, Harold, I completely agree. They're

not entirely separable. One of the scenarios I've seen is that a researcher is looking at a particular condition—let's say cystic fibrosis—and they're testing for it by particular methods that is the gold standard at that time. Might be the sweat test was the gold standard and they were doing sweat tests on kids and they've got tissue samples from them—from newborns or from young children. And, then, Delta 508 comes along. You can begin to do genetic testing. You want to go back and you want to see what the frequency of Delta 508 is in this population, and now you're going to go back to people and you're either going back to people with—there is tons of clinical information from previous studies that they may never have been informed about, because that was never part of the plan for that previous study. To get consent to enroll them in a new study, specifically because they met some criteria based in the first one. You found out what interesting population to study further. These are like your tiered experiments, David. So that it is in fact a request for new consent. It is a request to get additional consent for an additional study, but the fact that you're being selected to participate in a subsequent study is directly related to the fact that you've got some clinical phenomenon, and ordinarily when you recruit people you tell them why they're being recruited. You're being recruited because you have [INAUDIBLE] therapy or you're being recruited because you have failed on bone marrow transfer and we're trying to get another [INAUDIBLE]. What are you going to tell these people. You're being recruited why?

DR. MURRAY: Yes, but I think that—doesn't that still fall under sort of subset one, that is—

MALE VOICE: I'm recontacting you with whatever information >cause I want you to be in research.

PROF. CHARO: Well, not exactly, because I think that we just—when we separate things, I just don't want you to create this kind of absolute wall between the notion of sending back information from previous research that's clinically interesting from other forms of recontact information, because in the process of recruiting people and getting new consent for new studies you may ordinarily be conveying clinical information you wouldn't have conveyed otherwise.

DR. GREIDER: But not necessarily, right? You need the controls as well.

PROF. CHARO: Well, but you X

DR. GREIDER: You know, but didn't X

PROF. CHARO: This is absolutely, but this is the reason why the IRB has to review and approve the plan and the consent form and the whole Mishigass, right? Does the transcriber need to know how to spell Mishigass?

FEMALE VOICE/MALE VOICE: Yes. Yes.

PROF. CHARO: Double S at the end. [LAUGHTER]

DR. MURRAY: David?

DR. COX: Yes. Alta, I think that you are putting together clinically interesting or clinical information from clinically relevant information and relevant by relevant I mean information on which a position or the person would act with a different type of treatment so that when you are or that a physician would act on, right? And so when we're talking about a clinically, it doesn't mean we put all clinical information into the second category. But we put a particular type of clinical information, that is, information on which one would clinically act on in a different way. So, it's not all clinical in one category and all other in another category. It's the type the physician would act on, on behalf of the patient.

PROF. CHARO: Right.

DR. MURRAY: This has been a very useful discussion. I think the point of we've I believe we've agreed that the review and approve, that that language should certainly be in at least part of this Recommendation. The suggestion was made to divide it into two, but and as a function of the intent of the recontact, one intent being to continue research with this individual in one form or another; the other intent being that as a result of what we learned in a prior research project to convey clinically relevant information. That strikes at least enough members of the Commission as distinctive enough that they [INAUDIBLE] broken into two. Let us try to see if we can divide it into two and put it before you again and see if you think that this is worthwhile or whether it ought to be combined into one.

DR. CASSELL: Including Steve's suggestion that if you are going to transfer back clinical material, even for the purpose of getting further consent, you ought to get the approval of or the help of or something or other.

MR. HOLTZMAN: Right. And I think that's consistent with what Alta is saying. In your initial research protocol you would say to the IRB something to the effect that if a clinically relevant finding comes up we would go through the following course of action to ensure appropriate [INAUDIBLE].

DR. MURRAY: Thank you for that very rich discussion about the issues raised by Recommendation 10. Recommendation 11 on page 149. Any comments on Recommendation 11?

Now, this is one case I think where if we are not careful begin distinguishing between specimens and samples we're in difficulty. I think that this is what this is saying is or am I just misreading this? What we're really talking about is rendering existing identifiable specimens unidentifiable.

DR. GREIDER: No.

DR. MURRAY: We're not talking that. Okay. Never mind.

DR. DUMAS: Is the purpose of this to say that where there are questions that the goals of the research may be compromised, that the investigators need to take the project back to the IRB?

PROF. CHARO: Would you say that again, Rita? I'm sorry?

DR. DUMAS: Well, it there's as it reads it says Investigators are encouraged to discuss IRB with the IRB in advance their rationale for removing identifiers if they believe that such would compromise the research. If *who* believes this would compromise the research?

DR. MURRAY: I have the same question. Who's the they are concerned?

DR. SHAPIRO: The investigator or the IRB.

PROF. CHARO: Investigators?

DR. DUMAS: So, I think the intent of the Recommendation needs to be clarified and then it can be reworded accordingly. If the intent is that whenever

anyXwell, whenever identifiers are removed, and I [INAUDIBLE] would be subsequent to an initial review. No? Okay.

DR. HANNA: It might be that the conditions of the research or the availability of consent of the ability to get consent might beXand I=am thinking again of the idea that Mary Clark King gave in Portland where the decision was made to just not have to deal with the IRB review by just stripping the identifiers and therefore you don=t have human subjects.

DR. DUMAS: Oh, and X

DR. HANNA: And the secondary question then was in doing so, did she unnecessarily compromise her research in a way that if she had perhaps consulted with the IRB ahead of time they might have been able to find a way around it so she didn=t have to do that. So this isXthe intent here is really to X

DR. DUMAS: Okay, so the point for me here is that this Recommendation is really more advice to the investigator and maybe it shouldn=t be worded as a form of Recommendation because if the investigator has the prerogative to strip the identifiers, then there=s no need for the IRB to be involved in that. However, you=re suggesting that if the investigator, in stripping those identifiers, are concernedXif they are concerned about theXwhat this will do to the study, then a good ideaXyou know, a good source of assistance or whatever would be the IRB. But that takes a different order from the formal Recommendations I think.

DR. CASSELL: I mean, it=s a strange recommendation. It=s a strange sentence. If you=re having trouble doing your study right, come to us and we will show you how to do it right. And when it has to do with consent, well, we don=t usually do that in telling the IRB something. This is a recommendation to the investigator.

DR. DUMAS: It=s advice.

DR. CASSELL: It=s advice to the investigator. Now, you may want to say that somewhere in the body copy, but I don=t see how that=s part of a recommendation to an IRB.

DR. MURRAY: Following on with your comment, it seems to be the direction [INAUDIBLE] two recommendations in here. One isXthe first one is to the investigator

and it probably doesn't belong as a recommendation. The second really ought to be to the repository. Then we've added the repository so it's preferable that the repository strip the identifiers and not pass samples on to the investigator and count on the investigator to do the stripping. And, that's at least X

DR. GREIDER: That's already part of the Recommendations, right?
That's already X

DR. MURRAY: Which I thought already was part of the investigations, so I'm not X I'm also confused.

I've got Larry. David, is your hand up? Larry, David, and Alta.

DR. MIKE: Aside from the fact that there are two different issues being addressed here, in Recommendation 1 we say the only way you can get unidentifiable is to have the repository doing the stripping, and this one would say it's preferable for the investigator to do it, so we're inconsistent.

DR. MURRAY: Right.

DR. CASSELL: It's not the whole recommendation now [INAUDIBLE].

DR. SHAPIRO: There are really, I think, two issues here. I think the second two sentences are either redundant or confusing, one of the two I think as I look at this, and are not directly related to the recommendation in any case. It takes on another issue which is already supposed to have been covered before so it has to go somewhere else and can be combined. The issue then is, as I see it, whether it's worthwhile us saying anything regarding the issue that surrounds [INAUDIBLE] this one. Now, it could be considered gratuitous advice amongst a long series of other bits of gratuitous advice that investigators are responsible for getting their projects right and IRBs ought not to approve any project using any human material that they don't think is scientifically interesting or valuable [INAUDIBLE] use here. And here's an example of that. But whether the IRB is actually the best source of advice for that problem I think is an open issue. It's an issue of study design.

DR. MURRAY: David and Alta?

DR. SHAPIRO: And maybe that's not required.

DR. COX: I actually am in favor of having this concept of have it be not as a recommendation but in terms of advice, and to me this falls into the same category to researchers as listen. This isn't as big a deal as you think, and in fact that most things really are going to be minimal risk and talking to the IRB isn't going to be a lot of hoops to go through and right now, because a lot of researchers think it's hoops, what they do is sacrifice what they could be getting out of their research for something that's not such a big deal. So, that's the message here. But that's not a recommendation. That's just text in the beginning.

DR. MURRAY: It's education.

DR. COX: Yes.

DR. MURRAY: Okay, David, that clarifies things. Alta.

DR. CASSELL: Recommendation 11.

PROF. CHARO: Consistent with that I think actually it might be advice that's aimed not primarily at the investigators who after all have an interest in doing its research with [INAUDIBLE] possible. It's really aimed at the research institutions and at the IRBs toXif we ever come up with a set of recommendations here that are really clear, to then educate their own investigators about the fact that this is the current understanding of what the rules are if you're using things that are stripped or things that are coded and linked, and here's how you go about using things that are coded and linked and here are the ways in which it may not be as much of a problem as you might have imagined it would be so that you are not encouraged to go ahead and come to us and not go stripping things off because of all the many ways in which there's value in using materials that still have some kinds of links. So, it's really not aimed at the investigators so much as at the institutional level as a matter of PI education. And a lot of them are going to have to do that. They're going to have to issue some kind of guidance to their investigators about how these new understandings are going to be implemented in their institution, what does and does not come to the IRB, and it's consistent I think with the view taken elsewhere in the report that we would like to encourage investigators to keep the identifiers on because of the kind of unforeseeable value of being able to go back and use those links in the future. So there's kind of aXthere is a general preference throughout the report making it possible to use linked materials.

DR. MURRAY: We're going to need to move on. Alta, I'm wondering, would it make sense to try to rephrase this as advice towards institutions and possibly professional societies and put it in the last section, which is Public and Professional Education and Conduct?

DR. DUMAS: Um-hmm. Yes.

DR. MURRAY: That reasonable?

DR. DUMAS: Yes.

DR. MURRAY: Everybody agree that we'll take a shot at that? I don't know if we'll be able to do it properly but that I think Alta's advice is good as to where to what the meaning of [INAUDIBLE].

DR. SHAPIRO: I think the Alta's given the reason why we might have an interest; that is, we society might have an interest in the identifiability of samples and not losing them just on the because someone says, you know, skip the informed consent, the heck with it, for my problems I don't need it. There might be an unexpected cross to that.

DR. DUMAS: Yes.

DR. SHAPIRO: So that we'd want to highlight that somehow. The more I think of it, however, I don't think that inside a recommendation is where we should do it. We should just find some other spot for that, but it's an important point.

DR. MURRAY: Alright. We'll take a crack at that. Bernie, is this on the same point?

DR. LO: Yeah. Well, it's on something else in Recommendation 11: that second sentence about who does the stripping.

DR. MURRAY: We're going to take it out.

DR. LO: That's good. Take out X

DR. MURRAY: We're stripping it. Yeah. Okay.

PROF. CHARO: And Tom, do we have here or any other place the comments about wanting to discourage PIs solely to avoid the opportunity for people to object to research?

DR. MURRAY: Probably not.

DR. CASSELL: Isn't that what you're going to put in your education section?

PROF. CHARO: Yeah.

DR. SHAPIRO: That's what I hope X

PROF. CHARO: Okay. That's it.

DR. MURRAY: We probably don't say that as directly as you've just thought it, Alta. I think we would want to do that. Thank you. That will go in the Education section.

Okay. It is not quite 11:45, so we're doing really quite well and we're on to Recommendation 12, page 150. Could I just say, I think in line 20 we should say, A when human biological materials are donated in the course of clinical care.≡ (INAUDIBLE) ...procedures. This can be accomplished by using separate consent forms for separate sections on aXthat deal exclusively ofXin other words X

DR. MURRAY: Right. Shorten it. Tighten it. Rhetaugh?

DR. DUMAS: What you've done here is make one recommendation and a list of suggestions or advice.

DR. MURRAY: Yeah.

DR. DUMAS: Again, so X

DR. MURRAY: So we should pull the suggestion, sort of the detail into the commentary that follows the recommendation? Is that X

DR. DUMAS: The information that follows the recommendation, yes.

DR. MURRAY: Eric was doing such a lovely job of providing us a supple text here that I think we should give him the task of redrafting this recommendation.

DR. CASSELL: I'll be glad to do that.

DR. MURRAY: Thank you, Eric. Trish, then Larry. Trish?

PROF. BACKLAR: It seems to me Xare you sure that you want to say that you Xdon't you want to say A using a separate consent form ≡? I'm concerned when you get this in one consent form and the inflation of clinical treatment, again, the therapeutic misconception. One would want to separate that very clearly.

DR. MURRAY: Eric will take that into Xgoing to take that into consideration as he redrafts this recommendation.

PROF. BACKLAR: Okay.

DR. MURRAY: Larry?

DR. MIKE: I think it's a convoluted way of Xright now it's a convoluted way of saying that there really has not been consent in the past, because it's been buried in a Xit's really been a clinical consent which happened to have a clause in there. But I think we should be Xjust directly address that is that I really don't believe there actually has been consent in a clinical setting for the research use and that Xand that Xthat knowledge should be made explicit. I'm not wedded a two consent form. I suggested that after you sign the clinical consent there's another sentence or two right under there and you sign again or you don't sign again.

DR. MURRAY: Right. That's typical. It may be that we can clear that up with either a brief paragraph inserted in the commentary proceeding attached to the recommendation or even a couple of sentences, but I think I Xgo roughly where line 9 application on page 150. I think that it's a good suggestion, Larry. We should just be up front about it and say it's been inadequate in the past, a lot of it. Carol and Bernie?

DR. GREIDER: It seemed to me in reading this section on page 150 to half of 151 where Recommendation 12 is discussed that we go a lot into this issue of consent in a clinical context and we completely omit consent Xconsent in the research

context, and it would be nice to have a separate heading that discusses something about the kinds of things that we heard about people designing consent forms in the research context just to separate out those issues since we deal with them separately. Right now they're very intermingled and it's unclear at the top of page 150 where the research is and where the clinical is.

DR. MURRAY: But would you actually have us do two separate recommendations?

DR. GREIDER: I don't know about a recommendation, but two separate headings under this area and maybe only have the recommendation about the clinical. I just think that the way that it's worded right now it'd be nice to separate out consent in the research context and consent in the clinical context. And then we can determine whether or not we need a recommendation about consent in a research context or not.

DR. SHAPIRO: As I recall some of the text, I know Bernie, excuse me, Bernie, we heard testimony during our, a couple of our meetings about problems with consent in the research process. Even directly in there. So, it can [INAUDIBLE] separate others. We had some testimony.

DR. MURRAY: I'm inclined to follow that recommendation.

DR. LO: Yeah. Along those same lines, I think we, there's a lot of material here, and we don't really do as good a job as we might of sort of laying out a lot of issues. I think one issue is what I take the first part of Recommendation 12 to be that when you're signing up for major surgery, the kind of consent that's been obtained in the past is not really very robust consent. That's Larry's X

DR. MURRAY: That's Larry's point.

DR. LO: That's Larry's point, yeah. The second point, it seems to me, is that even if you separate it with a different consent form or a different part of the consent form, the issue is what you actually say your consenting to. And so it's not just the timing's off and it's just buried in there, but do we want to say something about give more information about the types of studies that might be done, or is it just sort of blanket consent, you can do whatever you want with my tissue for research. So, that's a separate issue from when you do it on which form it is. And I think Carol's point is, it actually seems to me further along the path. If you're really going to talk to people

about getting their consent for future research projects, how shall we set that out. I think this is where I'd like to see us encourage kind of the use of tiered consent forms; working with patient groups, advocacy groups to try and figure out what is meaningful information; having NIH and [INAUDIBLE] sponsor work studies. There's just a lot we can do here to sort of push this whole sort of enterprise of figuring out how to discuss these with potential subjects in meaningful ways. It needs to be unpacked here.

DR. MURRAY: David and Larry? I'm going to ask people to really be concise. David?

DR. COX: I will try, because I wasn't before. We'll see if I can get it this time. I'm very much in favor of having two different sections dealing with consent one dealing with consent in the clinical samples and another consent in the research context. Previously when we were back at recommendation 8, we broke off certain issues of prospective stuff, and at that time I had hoped that that stuff could be in a section dealing with consent in the research area, and so and melding all of that together in the context of consent in the research area, then having the separate issues of consent in the clinical area and what that consent should be.

DR. MURRAY: Larry?

DR. MIKE: I'm concerned about any kind of a detailed consent form in the clinical setting because we do have safeguards on the back-end side when you do actually design a study, and if it's going to anonymize or whatever your unidentifiable [INAUDIBLE]. If it's not we are now recommending the IRB look at the original consent form to see whether it was adequate or not.

DR. MURRAY: Right.

DR. MIKE: So, I would rather just if I were basing, and let me personalize it, I would say I would be comfortable with saying that they may use my tissue for some research in the future as long as I know that the back-end safeguards are going to be in place.

DR. MURRAY: I'm going to move us on to the next one. What I'll say is this. We're going to do what I think several people suggested, David nicely encapsulated. We will try to develop subsections. Remember the title of the section is Collection of Human Biological Materials. In the future we'll have a subset about

the clinical context and a subset in the research context. [INAUDIBLE] We may or may not end up with two different recommendations. We'll see how we can work it out.

Recommendations 13 and 14. But let's do them together. Let's do 13; page 152. Yes, Bernie?

DR. LO: On 14, I was wondering if we want to see X

DR. MURRAY: Can we do 13 first?

DR. LO: Okay.

DR. MURRAY: Any objections to 13? We'll probably take the quotes off to identify X

PROF. BACKLAR: Doesn't that sort of connect back to the sensitive research in Recommendation 9?

DR. MURRAY: No, not strictly I think, Trish, because it could be actually not just because it is politically sensitive, it could actually reveal confidential information about the individual.

PROF. BACKLAR: Um-hmm. Um-hmm.

DR. COX: I think a lot of people don't even think about how this is connected to people that you don't even talk about, and this highlights that so that's why I'm in favor of [INAUDIBLE].

DR. MURRAY: Right. A politically sensitive thing is a subset of that but it's not the entire gamut.

DR. SHAPIRO: I don't have any particular recommendation at the moment, but that I just want to do have some still lingering concerns about phrases like consider the implication of [INAUDIBLE] research. Such results may identify individuals at harm. And so on. I'm not quite sure in my own mind what kind of constraint that we're encouraging people to think about on the publication of information. I understand there's an issue here that needs to be dealt with because I don't want to reveal private information about individuals and so on and the legislation

and/or regulations that govern this, and I don't have anything yet to propose here. It's just to say that I'm not yet comfortable with the way that it's phrased. I hope we can find a way to phrase it or explain it in some way.

MR. HOLTZMAN: Is the discomfort with this seeming implication about you may not publish and is it really that we want to get the two that the form of the publication should be one which doesn't disclose the sensitive information?

DR. SHAPIRO: Well, it's well now, when one thinks about sensitive information as private information about an individual, I can understand this extremely well and can see that, but supposing the sensitive information is a controversial piece of information about a group? It may not be wrong; it just may be controversial if people want to consider it controversial. And some people may feel offended by it indeed. And I'm trying to sort of get a better sense of feeling about that. This is not a freedom of speech issue we're trying to deal with here. Right? That, you know, that's why we have that. Offensive speech needs some kind of protection. And, so I'm just trying to I haven't resolved that tension in my own mind yet, and I think there's probably a way to do it [INAUDIBLE] it's a big issue in the end. It's and I don't have the language to suggest. I won't say anymore now.

DR. MURRAY: Could you suggest something after the meeting?

DR. SHAPIRO: I will. Yes, I will.

DR. MURRAY: When you've had a chance to think about it.

DR. SCOTT-JONES: I have suggestion for language. Instead of saying "Consider the implications of publishing research results," we could simply say, "Consider the implications of possibly identifying individuals at risk of harm," so you don't put the focus on the publishing of the results but on the possibility of identifying. Just omit all reference to publishing because the issue is not publishing per se, but it's identifying the individuals at risk.

DR. MURRAY: Rhetaugh.

DR. DUMAS: I recall somewhere where in the initial review of the protocols, the IRBs would consider as one of the important factors the potential for harm in the broadest sense not only to the donor but to identified groups of

families or whatever. Is that in here, or am I remembering that from somewhere else now?

FEMALE VOICE: It=s one of the recommendations.

DR. DUMAS: It=s one of the early recommendations. It=s here.

FEMALE VOICE: Yes.

DR. DUMAS: So, it seems to me that if we haven=t taken care of the concern that=s being addressed in 13 earlier, then we shouldXshould incorporate it in the initial reviewXnot the X but not the initial review necessarily but in the IRB=s review of the protocol.

DR. MURRAY: One of the rea- X

DR. CASSELL: Wasn=t that sensitive [INAUDIBLE]?

DR. MURRAY: It=s in Recommendation 3.

FEMALE VOICE: Yeah. It was [INAUDIBLE].

DR. MURRAY: Recommendation 3.

DR. DUMAS: See, this is an issue of potential benefitXthe balance of potential benefits to harms.

MODERATOR: I=m not sure we talked X

DR. SHAPIRO: Three.

DR. DUMAS: Three. Is it 3?

DR. SHAPIRO: Three talks about X 3 talks about research design, right?, and to try to get research designs that are sensitive to these issues, as I understand them. That=s what that deals with. What this talks about directly is dissemination of information, and as long as what we=re talking about here is information that relates to a particular individualXme or you or someone elseXthen I sort of understand what we=re trying to get at here. What I=m worried about is individuals might include a whole group

of individuals, like 10 million individuals, because they consider themselves a part of some group that they care about and feel part of and so on and so forth. And what this means about what we're trying to say here X and, again, I'm not objecting to it; I will try to get some other language. I'm just telling you that I'm not yet comfortable.

DR. DUMAS: What about a statement that refers to plans for disseminating the results of the research should include attention to these issues here?

DR. SHAPIRO: Maybe that would work.

DR. DUMAS: Because it's dissemination.

DR. MURRAY: I think X if I am correct in remembering the context of Recommendation 13, we really had in mind the biological relatives not large groups of people.

MALE VOICE: That's correct.

DR. MURRAY: But people who were intimately connected. In fact, the very next section talks about risk groups. But we don't say that expressly in there. Maybe we need to say that. That might help in setting context. Bernie?

DR. LO: I think this is just a specific example, the general idea that you shouldn't publish X in your publication results you shouldn't publish results that will identify specific individuals without their express consent. So, it's sort of like posting a picture of someone that they can identify their pedigree. So, it really does X

DR. SHAPIRO: I have no objection to that. Obviously I have no objection to that.

DR. LO: X so it does these separate out these sort of other [INAUDIBLE].

PROF. CHARO: That's right. But don't think it's going to be easy, because X

DR. LO: Oh, absolutely.

PROF. CHARO: In a case that was described to me, which might be a good one to keep in mind as we try to work around how you're going to say this, was a disease that's very unusual and somebody's studying it with a pedigree study in Utah,

and in pedigree studies or course you always list the number of births and abortions, and, you know, they had miscarriages and abortions and births, and because there was only family in Utah that had this disease everybody in the family suddenly discovered that there was one particular person in that family who had an abortion, which as you can imagine in that particular country was a big deal. And it was a big secret and it all got revealed in a journal article. And the family knew who theyXthey could recognize who they were in that article. So, this is very tricky stuff. Even when you=re dealing only with the pedigree studies.

DR. COX: But there=s literature on it, Alta, and it=s been dealt with by professional society, so it=s not that itXthat doesn=t make it any the less tricky but it=s not that it hasn=t been considered. So we just want highlight to it and perhaps in the text X

DR. MURRAY: I think we=ll find a way.

MALE VOICE: We=ll do that.

DR. MURRAY: Bernie, earlier you had a comment about 14?

DR. LO: Yeah, I think I did. With 14 I think we could do a lot more. I would separate this out and say scientific medicalizationsXI think primarily professional and personal societies should do all this. But actually I=d like to see a recommendation, and maybe this isn=t the place, its later, for the NIH to get involved. And again, they have a lot of things they could do through consensus conferences, center grants, training grants, to really educate investigators, develop good practice guidelines. I think we should really make a specific recommendation to encourage them to keep doing what some of the institutes but not all are actually doing in this regard. For instance, with a training grant, what they can do is make a requirement in a training grant that all this be included as a condition of getting the grant for their P30 center grants. It=s, again, a traditional thing. They=ve used it before. And, it=s a very simple thing they could do, but it really reaches a lot of investigators and future investigators.

DR. MURRAY: I think thisXmy sense is people like your idea, Bernie. Could you suggestXI think it just involves rewriting the first part of that sentence, actually, to make it broader than just scientific genetic organizations. And, somethingXand not just guidanceXit mightXyou might actually have some

requirements so that NIH might post them. Could you revise for us, give us aXand then IXwe=ll include that in the next version. Anything else on 14? Go ahead.

DR. SCOTT-JONES: It seems that 14, in addition to what Bernie just said, might be grouped with 15 and 16 because they=re all about educating the research community; it=s about standards that general editors should hold persons who submit articles to. It seems that they are better together.

DR. MURRAY: We=re all nodding. Yes. Good pickup. Steve.

MR. HOLTZMAN: It follows on Bernie=s idea, and I=m just wondering about current practice if one could recommend something even stronger. Specifically, in my company anyone who=s involved in the [INAUDIBLE] research, we require them to go through a training course where they=re exposed to the CPR and its requirements. I don=t know whether the NIH wrote people who are receiving NIH monies, whether there is any requirement that those individuals who are exposed to such training.

DR. MURRAY: Actually there is. Now, if you goXif you accept training funds, anybody that you train within the NIH or I presume it might be the same with other agencies= funds, must go through a curriculum and scientific integrity which would X

DR. GREIDER: But it doesn=t necessarily include anything aboutXI=ve never heard of 45 CFR 46 before this Commission and I=ve been doing this kind of stuff a long time.

DR. MURRAY: Yeah, you know the rules. You just hadn=t heardXprobably hadn=t heard the X

DR. LO: But if yourXif your training grantXif your training stipend is not supported by the NIH, there=s no requirement but it=s if you=re footed by Howard Hughes=s money or something else, there is no requirement unless the university says, AAll our trainings have to≡ X

DR. MURRAY: But what if in the training is completely left up to the institution?

DR. LO: Absolutely.

DR. GREIDER: And, you know, it might just be a general discussion about general ethics, nothing about actual requirements.

DR. LO: I think you're right. More specific we can try and set practice standards. I think a more likely [INAUDIBLE] is to get people to change.

DR. MURRAY: Would that require an additional recommendation or can we do that as part of the revised 14?

PROF. CHARO: [INAUDIBLE] language.

DR. LO: Yeah. I will try and do it in revised [INAUDIBLE].

DR. CASSELL: Well, let me just a commentary on we come back again and again to the necessity for educating IRB investigators. Sooner or later we're going to have to write something that's specifically addressed to that because it keeps coming back up again. At Cornell, incidentally, the investigators aren't interested in any of this stuff. They try to figure out how do they get what do they do when their boss steals their work. That's the ethics that they're [INAUDIBLE].

DR. MURRAY: We haven't heard that in the sessions we conducted at my current university. David, we're going to jump to 15 and 16.

DR. COX: This is addressing the issue of combining all of these. The one downside of combining all of them is by having them separate you can give recommendations to specific more specific recommendations to separate groups and there are actual physical merit in that, giving responsibility and recommendation to OPRR, giving responsibility and recommendation to professional organizations and then giving responsibility and recommendation for education in other settings.

DR. GREIDER: I understood the recommendation to be that we not combine them as one recommendation, but rather group them together under the heading of education but keep them as three separate recommendations. That's what I X that's what I X that's what I nodded my head to.

DR. COX: I misunderstood, then.

DR. MURRAY: Well, there was an ambiguity there because someXI think the way BernieXI understood my instructions to Bernie, what he=s going to write might pertain to both to professional associations and the NIH and others.

DR. LO: Let=s put them down as 14(a), and maybe we should do them as separate recommendations.

DR. MURRAY: I think that=s actually a good suggestion. We will, as Carol said, be moving them and grouping them together in this last set.

DR. COX: Otherwise it=s alreadyXit=s always somebody else=s responsibility to do it, so.

DR. MURRAY: Yes. Right. Diffusion of responsibility was the subject of my master=s thesis.

Okay. Recommendation 15. This is to OPRR. Anybody have anyXyes, Laurie?

MS. FLYNN: I just wonder whether it=s here or somewhere as we think about trying to raise the level of awareness and sensitivity around these issues if we want to include some of the health advocacy organizations that patients turn to when they=re dealing with serious illness. Often those organizations encourage tissue donation and participation in that, but I think this kind of discussion is largely not going on in that community and that somewhere here or in the appropriate place I think we want to specifically encourage getting outside the box of the research community to those who represent those potential donors.

DR. MURRAY: Laurie, this recommendation is a burden we place on OPRR. Do you want to place the burden on OPRR to work with these voluntary agencies?

MS. FLYNN: I do. I do.

DR. MURRAY: So we can includeXwe can basically add the voluntary organizations, the patient organizations into this.

MS. FLYNN: That would be my suggestion.

DR. MURRAY: Okay. You don't want a specificXyou don't want to recommend to them that they do this but to OPRR that it develop educational programs for them?

MS. FLYNN: That=sXit=s difficult for me to be certain whether the OPRR is the best place to develop these. What I want to see is some connection made between the research community and the OPRR, which is going to be helping to define what these new standards and practices look like. if that=s the locus of the initiative, then I want them to connect as they do this with some of the patient organizations.

DR. MURRAY: Do you want someone on the Commission other than yourself to do a redraft and then show it to you, or do you want to do a redraft yourself?

MS. FLYNN: I=m willing to do a redraft. I think I=d probably need a little input from those who are more familiar with the OPRRXthe range of the OPRR=s role.

DR. MURRAY: How about if I let you and Kathi work together on coming up with a redraft?

MS. FLYNN: Okay, because we=ve talked at other points about changing the OPRR and elevating it and so on. Some of this would depend upon how far that goes.

DR. DUMAS: Well, I=ve done work recently with the OPRR and I was very impressed. I don't know how much we need to elevate it. I think maybe we just need to understand what it is they=re already doing.

DR. MURRAY: Alta?

PROF. CHARO: Consistent with what we did in the capacity report, we might also make some suggestion to the federal government that it provide the OPRR with the resources in terms of funding the personnel to do the education that we=re calling for.

DR. DUMAS: That=s fine.

DR. MURRAY: That would be a recommendation, then, to X

PROF. CHARO: God. [GROUP LAUGHTER]

DR. SHAPIRO: I knew we=d get to that sooner or later.

PROF. CHARO: I think probably a recommendation to the secretary of HHS.

DR. MURRAY: Okay. That we can handle. Okay. Do you want toXokay. Good. I thinkXI don=t hear any dissent from that. Okay. Who else wanted toXDiane?

DR. SCOTT-JONES: I want to agree with what Rhetaugh said about the OPRR. I think they already do some things. They already have regional conferences that they hold in conjunction with the universities, so I would be in favor of when Recommendation 15 is revised to make it read not as if the OPRR would be beginning education programs but perhaps expanding their activities to include, because they already are doing some very good things.

DR. MURRAY: Good point. Anything more on 15? If not, 16.

DR. GREIDER: Yes.

DR. MURRAY: Sixteen and last. Carol.

DR. GREIDER: This is just a rewording. Right now it reads AWhen submitting research for publications, investigators should be required....≡ I think that what we=re requiring is of journal editors so I think it should read, AWhen submitting research for publication, journal editors should require investigators to indicate.≡

PROF. CHARO: And so I can mark that down X AWhen reviewing≡X≡when reviewing.≡

DR. GREIDER: Right.

PROF. CHARO: So whatever it is, it should be the adviceXit should be advice to journal editors, not advice to investigators.

DR. MURRAY: Go ahead, Alta and Steve.

PROF. CHARO: I think you might also want to consider taking out the whether and to what extent informed consent was obtained. There are many circumstances we've identified where consent does not need to be obtained. The key elements here are: Was it something that should have gone to an IRB, and if so did it go to an IRB? And then trust that the IRB did their job. So, if they were identifiable human subjects, then it should have gone to an IRB and the investigator should be able to provide an IRB review. Kathi's pained at this.

DR. HANNA: Well, I mean, I think you're going to run into the dilemma of what people consider to be identifiable. I mean, just because it's identifiable, I don't think it's correct to assume it went to an IRB. Just because people do not think coded is identifiable.

PROF. CHARO: This is true. I guess what the question is whether or not you want journal editors to help duringXsee, you want you the journal editors to be part of the transition period which there's a deep education of people that their understanding of the rules has changedXhas to change as opposed to simply journal editors going along with the enforcement of the rules as we now pronounce them?

DR. MURRAY: Eric?

DR. MESLIN: The former. No choice. Most mainstream journal editors now, but not all, have certain requirements to assure the readers that research involving human subjects has met certain standards. And all that will be is a letter attesting to the fact that it has gone through an IRB. This proposal is one that is in that spirit but requires, since we do not know and in our own research are not aware of whether the samples that are the subject of published reports were obtained from identifiable sources or not, or whether consent was obtained for their use. So, this is a educational function, but it is our responsibility that the journal editors could exercise to comply with what rules you would expect of investigators anyway. I think we all know cases where investigators have conducted research without their IRB approval either accidentallyXthey weren't sure that it was research. I will leave the flip side of whether it wasn't accidentalXand then have gone to a journal and the journal has quite reasonably inquired whether this has gone through IRB review. So this allows yet another opportunity for that oversight function in the chain of oversights.

DR. DUMAS: So, this recommendation is to professional journals.

DR. MURRAY: Yes. Diane?

DR. SCOTT-JONES: I'd like to comment on this as my role as editor of *The Journal of Research on Adolescence*. I agree with the spirit of Recommendation 16, but I believe it's a bit too specific for what journal editors do. For example, in the journal that I edit, each person who submits an article must state in their cover letter, at the time of submission, that they have complied with all the standards of the American Psychological Association [(APA)] for conducting research with human participants. Beyond that, we don't get into many [INAUDIBLE] details, so I think a more general statement like that instead of one this specific is warranted. Also, reviewers in the review process point out whether in the Method section there appears to be something that is not in compliance with the APA standards. So, I think that leaving it at a more general level as opposed to saying that journal editors are going to ensure that these specifics are done. I think the more general statement is more appropriate. I don't know what other journal editors already do. Some of you who have performed those roles as journal editors may know, but in my field this is done at the general level and researchers always are required to state that in the cover letter.

DR. MURRAY: Carol?

DR. GREIDER: Most of the journals that I submit to have no requirement whatsoever about any of this.

DR. MURRAY: So, this would be advice to journal editors that isXthat in certainXwhere you're doing research on human subjects routinely, people=s consciousness has already been raised. Where you're working with tissue samples, consciousness may not be there. It just strikes me, Diane, that you are perfectly positioned to be the member of the Commission to help redraft this recommendation.

DR. SCOTT-JONES: Okay. And another point I would like to make is sometimes the professional society that sponsors the journal will have a publications committee that might be in a position to set the policy here, not just the particular journal editor; it would be the society=s authoring journalists.

DR. MURRAY: Okay. Would you be willing to help redraft?

DR. SCOTT-JONES: Yes, sir.

DR. MURRAY: Thank you very much. Anything else on Recommendation 16?

You were wonderful, incredibly efficient, and cogent, and I want to turn it back to Harold=s care.

DR. SHAPIRO: Thank you very much. Let me make one X just an announcement. For those of you that are planning to attend our next meeting, you all have a note as to get your room reservations in. That=s by this Monday I think it=s required. So please do that if you are planning to attend the next meeting.

Eric, do you have any other business issues to tend to? Bernie?

DR. LO: Can I ask you a logistic question. How does one get from an airport to Princeton?

DR. SHAPIRO: From any airport, or X

DR. MIIKE: Or from Newark.

FEMALE VOICE: San Francisco.

DR. SHAPIRO: We=ll send out aXsome more information on this, but there are rental cars and a shuttle. Those are the two best ways to do it, but we=ll send out some specific information with some phone numbers and so on, and when we take a look at the schedule that some of you are riding together, we might be able to make some very specific arrangements.

DR. MIIKE: if you fly to Newark Airport.

DR. SHAPIRO: Newark is the best PhiladelphiaXNewark=s about 50 minutes from Philadelphia, about an hour and five minutes from Trenton, if you can find anything to take you there.

END OF MEETING.