29TH MEETING

OF THE

NATIONAL BIOETHICS ADVISORY COMMISSION

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I N D E X

P R O C E E D I N G S

WELCOME TO CHARLOTTESVILLE

DR. CHILDRESS: Welcome to the 29th meeting of the National Bioethics Advisory Commission.

As you can see, our chair, Harold Shapiro, is not here. He will be arriving tonight.

And our temporary chair, Alta Charo, is not here. She will be arriving in a short while.

But I want to take this opportunity to welcome you to Charlottesville and to the University of Virginia for those who are staying on for the Belmont Revisited conference.

At this time of the year since this is a period of garden weeks and other festivities, we usually have better weather than this so I hope for those staying through the weekend that it will improve considerably.

We arrived just after Thomas Jefferson's birthday so you were not here to celebrate that but for those on the commission we will visit Monticello tonight and if you have not talked to me about that,or by e-mail, check with me and I will talk about the plans for the evening.

And I, also, can provide additional information about Belmont Revisited. I gave you a new updated schedule at your seat for that.

So, again, welcome to Charlottesville and to this 29th meeting of NBAC.

We will begin with the Executive Director's report from Eric Meslin and then after that move into a discussion of the changes in the commission's draft of the Use of Human Biological Materials in Research with Kathi Hanna and Eric Meslin leading us through that discussion.

EXECUTIVE DIRECTOR'S REPORT

DR. MESLIN: Thank you.

Just a quick housekeeping announcement. We have microphones here that require that you push a button to speak and then when you stop speaking turn the button off. Apparently it only allows six microphones to be on at the same time and that will cut down feedback.

Harold will be arriving later and Alta is supposed to be here by 2:00 o'clock and I believe that Professor Capron is in the building and will be, also, arriving shortly.

I want to give you an update on a number of

things that have happened in the last month and be happy to answer any questions that you might have about them.

First and I think most important, as we move towards the end of the spring and early summer I want to take this opportunity to let the commissioners know that some of our research staff will be moving on to other career and academic pursuits so at meetings both here and in the next few to come I hope you will take the chance to speak with people like Sean Simon and Emily Feinstein who are here with us today.

I would like to publicly thank them for all the work they have done with the commission over the past couple of years and I know that the commissioners will share that view so we are delighted that you are here and happy to have the work that you have done for us be so helpful.

Secondly, I wanted to give you a brief update about some staff Hill visits that both Kathi Hanna, Rob Tanner and our communications consultant, Andy Burness, have been engaged in over the last couple of weeks. We have been meeting with staff from both the House and Senate principally to give them an update on NBAC's

activities, to perhaps respond to any questions that they might have about issues that are in development. I will certainly be happy to speak at length about this but principally there is considerable interest in NBAC's reports. Not surprisingly, there is considerable interest in our upcoming stem cell report but I think all in all the interest that the Hill expressed in both receiving the reports that we have sent and in our ongoing work has been extremely well received.

I have to say in honesty, though, there are still a great number of members who are unaware of NBAC's work and what we have been doing so I think the opportunity to be on the Hill was an appropriate one and that Dr. Shapiro intends to follow-up with members in the not too distant future.

That is a good seque to mention what I think you already all know. There is another hearing that is coming up on the 21st of April by the two subcommittees of the House committee on Veterans Affairs, the subcommittee on Oversight and Investigation, and the subcommittee on Health. They are examining the questions arising from the suspension of research at the VA hospitals in Greater Los

Angeles so testimony will be given next week.

Fourth on my list of eight, if you are going to keep track, there have been two meetings recently held over the -- in the past week on stem cell research. The AAAS has convened a working group to develop a statement on stem cells. That group intends to produce a statement on or about the 27th of May. It is intended to be widely circulated and available for public comment. That meeting was held on the 7th and 8th of April.

The very next day, the 8th of April, NIH convened a subcommittee of the Advisory Committee to the Director to produce a set of guidelines, which are in your briefing book, a draft set of guidelines that they hope to have completed within the next short while. The time table has not been firmly established but the intention is for the NIH Working Group to produce a set of guidelines, to pass them on to the advisory committee to the director for permission to then submit them to the Federal Register for 60 days of public comment, after which the ACD will provide those revised documents to Dr. Varmus, and my understanding is that shortly thereafter they will be finalized.

That timetable if you are keeping track roughly parallels NBAC's timetable. My understanding is that with the 60 day public comment period the NIH would not have its stem cell guidelines in place much before July and I am really just guessing. We are hoping to have some materials from NIH sent to us that will clarify exactly what timetable but at our present rate of intending to have something completed before or by June we will be paralleling that quite nicely.

I wanted to inform you that with respect to the comprehensive report that is not on our agenda today we are very fortunate that an old friend of all of our's, Jonathan Moreno, has agreed to come to the commission over the summer months and provide some substantial writing support for that. At previous meetings we were asked about the status of other committees.

Again the NIH has an advisory committee to the director looking at the location of OPRR and my understanding is that that report will be presented to the advisory committee to the Director of the ACD on or about June the 3rd. We might, therefore, as a group invite some of those members to come to our January -- I am sorry, our

June 28th or June 29th meeting. And to the extent that we can get their report sooner rather than later we will pass that on.

I am almost confident that I can say we were -- we will be fortunate to have Ruth Macklin also join us over the summer months to help with the international project. This was so recent that it is an e-mail that we exchanged just yesterday and the details have yet to be finalized. I have not had a chance to share that information with Professor Capron yet but I think we will all be delighted to have Professor Macklin on staff for a couple of months over the summer.

A couple of other quick items and then I will be done.

This is now the time that the commission should begin to think about new topics for its work. Part of the purpose of going to the Hill was to find a congressional interest but we expect to put on the agenda for June another round of discussions with the commissioners about topics that they think are appropriate for putting on our agenda.

There is an existing set that have not gone

away so those -- staff will be preparing that list and working with commissioners. This does not have to be a formal exercise waiting until June. If commissioners have ideas and topics that they wish to send on so that we can prepare a document please do so.

And I think the only other thing that I was going to mention is we have some new materials that are being literally put on your places as we speak. Materials that have come in from Lori Andrews, with whom we contracted to do a state survey for the stem cell project. The revised or a revised chapter 4 of the HBM report is being printed now and it will be circulated to you.

Obviously we do not expect you to have read it having not received it but I wanted to at least forestall any commentary about how the current chapter 4 does not seem to match with chapters 1 to 3 and 5, and that was not an intentional oversight. That was just the nature of the writing process. We had to make some research priority decisions and the chapter 4 got a little delayed so you will have that material by the end of the day and you can give us some comments.

And other things will be coming up from time-

to-time to your tables.

Those are my quick remarks unless there are any questions that commissioners may have about any of the items that I have raised.

MS. KRAMER: I have a question. At the inception of the commission we received a lot of materials on the issue of gene patenting and then it seemed to go away. Now are we charged with considering that issue? Do we have any choice on that?

DR. MESLIN: I am going to --

MS. KRAMER: Certainly -- it is mentioned specifically in the enabling statute.

DR. MESLIN: I am going to give a very short answer and I do not want to put her on the spot but I may ask Rachel Levinson to say something about that.

The short answer is that the specific language of the executive order says that we should as a first priority direct our attention to considerations of the protection of human subjects and the management and use of genetic information not limited to gene patenting.

I am not going to interpret whether that means we must or we should not but that is what the charge is.

There are other factors that have come into play. That item has not been taken off the agenda. We have simply been working on the reports that we have been given but I think it is an entirely appropriate question to raise in the sort of next round of topics but maybe I can let Rachel add to that.

DR. LEVINSON: Eric is quite right that it does appear that the words "gene patenting" do appear in the executive order from the President but that is not enabling statute. Otherwise there would be no way around considering it. That does not preclude the commission from looking at the issue of gene patenting and determining whether or not it has ethical concerns that need to be addressed by the commission. So there was some discussion of it early.

It was not considered as high priority as some of the other issues, including human biological materials, which was felt to be most pressing. So that if the commission looks at that again and says that it has either been overtaken by events since that time or there are certain ramifications that do need to be considered or do not, that is certainly well within your prerogative to

make that decision.

MR. CAPRON: Well, I suppose in that regard it would be sensible to have some technical preparation both in paper and perhaps by a witness. One of the people we heard from when we were in Portland and whom we would have heard from, and indirectly, I guess, heard from his staff when we began, was Senator Hatfield.

And the origin of the commission, as you know, is, in effect, a legislation -- an executive response to an effort that Senator Hatfield and Senator Kennedy and others were trying to bring about on a statutory basis. And I think one of the assurances to Senator Hatfield at the time was that his particular area of concern, gene patenting, would be addressed by this commission. And three years into things if, as Rachel says, it has been overtaken by events, that is to say if the patent office or others have resolved the issue in a way which satisfies the kinds of concerns that lay behind Hatfield wanting to have a commission on ethics as the subject then we should know that and we can report that there is no need for us to do this.

On the other hand, if that is not the case

then I think we should have some background rather than just going into it naively as to what is the state of play on that issue.

DR. MESLIN: Were there other questions about any of the remarks?

I think we will just move on to the agenda and let Kathi -- sorry, Larry has a question. Yes?

DR. MIIKE: One last thing. A word about the extension of the commission and whether even with an extension that we should plan on our studies ending by the end of the year 2000 since there is no assurance since there will be a new president and we serve at the pleasure of the president.

DR. MESLIN: Again I will give perhaps a part answer and maybe let Rachel give the other part of the answer. As we have planned the research products that we have in the pipeline right now we are planning for everything that we are doing to at least have an end date of September the 30th, 1999. That would be unfair to our contractors with whom we have an arrangement.

Having said that, many of the projects, particularly the international project, for example, which

is taking longer to achieve because of some administrative things like OMB clearances, has to have a -- perhaps a longer deadline. So we are preparing for the possibility of having to issue whatever data and reports we have by the end of September and for the possibility of having more time both to complete those reports, which I think will probably be necessary, and any of the other reports that we are going to put on our table.

Did you want to --

DR. LEVINSON: I guess, all I could add is that it is standard procedure for all federal advisory committees to have charters that only last for two years. This is not unique to NBAC or any other group and that ordinarily the Office of Management and Budget renews all of them. It happens that they do that in September and because our's happens to run out October 3rd we have asked for that to be expedited and to move that process along faster. They are moving it along. There are no objections so far but it is just that it has not been executed and I would not second guess anyone as to say whether or not that is a foregone conclusion but ordinarily it is considered to be a formality.

DR. MIIKE: One last comment is that I am less concerned about that than the end of President Clinton's term for two reasons. One is that with a new president anything goes but the other is that I think we need to have some deadlines for this commission. We tend to dawdle and I would like us to have a fairly firm ending for any of the studies that are going beyond the two that are contemplating now.

DR. MESLIN: Any other comments or questions?

I am going to turn it over to Kathi to walk you through where we are with the HBM report. I think everyone received the memo from Harold regarding our plan, hopefully, with this report to try and work through as much of it as we can with our intention of coming to final agreement at our next meeting in May so I will turn it over to Kathi.

REVIEW OF CHANGES IN COMMISSION DRAFT

DR. HANNA: What I would like to do with the time that we have until Alta Charo arrives is just go through some of the -- explaining some of the editorial changes in the draft and to tell you what you still do not have, what might be jumping out to you as missing from the

draft, and then if we could spend some time going through chapter by chapter. If you could give me -- obviously if you have copy edits or you have found typos or that kind of thing I would appreciate it if you just handed that to me but if you have substantive concerns about anything in the chapters one through three, because you have not seen the revised four yet, maybe we should just focus our time on that.

The changes that have occurred in the draft are mostly significant shortening of the chapters. Also, I went through and read all of the 97 comments we received fairly thoroughly and tried to incorporate, where appropriate, corrections or where people had concerns about tone and tried to make changes there, and we have already -- at the Princeton meeting we talked about what the reviewer comments were so I will not go through that again.

The comments that were in the preceding chapters, not in the recommendations chapter, were mostly corrections of fact or requests that we include something or take something out.

In chapter one it is still -- I think can be

shortened a good bit. I appreciate your comments and your help on that. I think usually it is easier to write the first chapter after you have written the rest of the report so we might have to wait until we go back to that.

Chapter one is not an executive summary so if anyone thinks it is supposed to serve that purpose it is not. We have not written the executive summary. That will appear in the next version that you see in May.

Chapter two, which was very long, has been shortened a great bit. Most of the material that was taken out of there was in Lisa Eisman's paper that she prepared for the commission initially. We are going to take a lot of that material and put it in an appendix, although certainly not all of it, but material we think might be useful for people that are not as familiar with the science or not as familiar with how these materials are used. And then, of course, her complete report will appear in the volume two of the complete set of the report.

Chapter three and chapter four got reversed in this last version and the reason for that was that we thought that the ethical analysis or consideration of the

ethical issues should precede the final chapter. So chapter three, which used to focus on regulations and various guidelines and professional statements, now is chapter three, that, too, has been shortened a good bit. It also does not sound as repetitive to have it appearing in the middle of the report where you are talking about the regulations.

When it was in the fourth chapter you read about the regulations and then you got to the fifth chapter and you read about the regulations again. So we have tried to streamline that discussion a little bit. Anybody that has any comments on how we might do that even more, we would appreciate that.

So in chapter four -- you have just had a copy put in your place in front of you and I think we will probably need to talk a little bit about that in our discussion today even recognizing that you have not had a chance to read it yet. And since Eric so graciously volunteered to spend a lot of time reworking chapter four maybe we will turn it over to him when we get there.

Chapter five, the recommendations have now been placed back into the text so again any suggestions

you have for the flow, the reasoning, whether the recommendations are showing up in the right place, whether it makes sense as you go through it, I would appreciate that.

There will be probably four appendices. One will be the -- we are going to include the common rule itself as an appendix so we will be able to download that and put that in as an appendix. I think for people that are reading, particularly investigators or IRBs, that might be helpful for them to have everything in one place because we do refer to the requirements in the common rule and so we will just reproduce that in the report as a service.

Appendix B will probably have the material from -- that has been removed from chapter two. There will be an appendix that again summarizes the findings from the public sessions that were held and then there will be, as in the capacity report, an appendix that lists and acknowledges all the people that prepared commission papers and commented on the report.

MS. KRAMER: Kathi, I am assuming that the flow charts are going to be reinstated?

DR. HANNA: Yes. And there is -- we are trying to figure out -- Dr. Shapiro would certainly like to have a useful set of flow charts in the report. I think we are going to have to work it out before Sean leaves -- he is our flow chart expert -- how we are going to do that now and where we are going to put them.

I think it would be very useful to have the flow charts in the body of chapter five.

MS. KRAMER: I agree with you and I think if there is any way of incorporating references in the text to the flow chart to help people use them it would be -- that would be good, too.

DR. HANNA: It has almost become -- I have sat down a couple of times and have tried to figure out how to design the flow charts and it really almost becomes an informatics kind of an issue because there are so many decision points that you begin to end up with a piece of paper that is this wide that has arrows going all over it and it gets very complicated.

So we will try to make it as simple as possible certainly and as clear as possible, and it might be that we are going to have to have different flow charts

for different people, depending on whether it is the investigator or the IRB or a repository.

MS. KRAMER: Maybe this is a question for Sean. Would it be possible to have at the beginning of the flow charts a "how to use these charts" sheet?

DR. HANNA: Sure. We can try anything. Actually we would like --

MS. KRAMER: Sort of assuming just very, very rudimentary knowledge of what it is all about.

DR. HANNA: I think it would be helpful. It would be nice if we -- if Sean could develop an interactive CD. That would really be the best way of presenting it when you got to one point and then you dropped down and you had to -- I think that -- I mean, I know that that type of a system is used to train investigators on how to walk their way through the common rule so we might think about looking at that.

MR. CAPRON: Don't you think training should begin a little earlier? I would suggest we talk to Parker Brothers about a board game.

(Laughter.)

DR. MESLIN: Steve?

MR. HOLTZMAN: There is a board game now for the drug development process.

DR. MESLIN: He said there is a board game for the drug development process.

MR. HOLTZMAN: $15,000.

DR. MESLIN: $15,000. He did not push his button.

As we will probably go through this when we get to chapter five but since we are on those flow charts everyone seems to be in agreement that that is a good idea but Kathi did mention something and I do not know whether everyone was agreeing to it, which was focusing on the consumers of the recommendations and developing flow charts for the various consumers, IRB's, repositories, investigators.

When people were saying, "Yes, it is a good idea to have helpful flow charts," were you agreeing to that as well? That is a different set of flow charts.

MS. BACKLAR: Actually as you bring that up one of the things, and I may have missed it in my travels in the last few days and all the things that went on, I did not -- I saw the goals very clearly put out. I know I

am sort of leaping ahead but I did not see anywhere as we had in the capacity report a little sort of section which said who we are directing these towards so that exactly as you said that is something that needs to be early on in there. I would put it in that final chapter five.

MS. KRAMER: Eric, to back up to your question, I think that a how to "how to use these charts" page, if it was done at a very rudimentary, you know, very sort of very minimal understanding base, it would be helpful to everybody, for those, you know -- for those who understand it and can just move through it quickly, they will move through it quickly. For those who have more problems -- and then perhaps in that way we could just develop one -- sort of one guide for everybody.

MR. CAPRON: Could I follow up with that? The notion of having separate charts for separate functions, that is to say there is something that an IRB does that an investigator does not do or conversely makes pretty good sense. That is what has to be done at that point.

The notion of having separate charts for separate people doing the same thing puzzles me and so I would want to see what you have in mind, why it is that we

would be having separate charts. Not in principle against it but puzzled as to what it would mean. So I think at an early stage with the next iteration of the draft if you could give us those alternatives.

One other technical question. I just noticed in what we were just handed that we now have the appearance of citations in the forms of parentheticals with names of authors and dates popping up here. Whereas, in the version that we read prior to the meeting we had some of that and then some footnotes to -- are we ever going to have a unified style with this?

I find that for reading for this kind of a report, the journal article format of having author's names with dates and so forth is not conducive to this being read as a report. I mean, the footnotes work better but we seem to be neither here nor there.

DR. HANNA: We have hired an editor and we are in the process of bringing on a desk top publisher designer and we have asked the editor to give us guidance on the style.

Now in draft form it is -- blame it on me if you wish -- to keep the --

MR. CAPRON: No, I understand. It is a place marker.

DR. HANNA: -- name. Right. Because we are still moving a lot of text around and when you are dealing with footnotes and endnotes. It can get very messy and you can end up with your numbering not correct. So for now we are leaving references in the body of the text.

We are going to use Chicago style referencing in this report. The -- I think the thing that has to be dealt with right now is the footnotes versus endnotes. It becomes a publication issue. It becomes a design issue. So any -- I mean, we would like to have the reports appear uniform but I have to say that between the cloning report, the capacity report, and this report they are not going to be uniform. They are not -- I mean, each one is going to have a different style.

MR. HOLTZMAN: Could I suggest the commissioners ask the staff to deal with those issues and if any particular commissioner has a particular interest in it they deal with the staff directly?

DR. HANNA: Okay. What I would like to do is just move chapter by chapter and talk about again any

major concerns, omissions, questions you have. As I said, we will be preparing a brief executive summary. We can do the same kind of executive summary that was in the capacity report, which is some summary text and then a listing of the recommendations. You might want to have a shorter executive summary. One that does not list all of the recommendations but lists the major recommendations. So that is the kind of thing we need to think about a little bit.

The executive summary will be published separately as a shorter document and I would not advise that we just publish chapter five as an executive summary. It is far too long. So chapter one -- the intent of chapter one is really just to kind of lay the groundwork and since chapter one has been written for a very long time and has been edited by a lot of people over and over and over again, it is beginning to get this kind of squishy feeling to it. So any suggestions that you have for how we can tighten it up or change the tone, why don't we just focus on chapter one?

Everybody likes it?

DR. CHILDRESS: The risk is that by proposing

anything we will simply add to the squishiness since you have already indicated that the things we have seem to do that and this may simply be a case where again someone, you or someone else, will need to go through and really reshape it according to this discussion and building on the text that is there.

DR. HANNA: Steve?

MR. HOLTZMAN: I actually mentioned this to Kathi before the meeting started in terms of a little of tightening of it and thinking about where we are going to go with our distinctions. If you go to the bottom of page three, and this carries over into four, where we talk about unidentified material that is not linked to an individual or his ongoing medical record, just being clear about the difference between when it links to the identity of the individual versus the information, which may not get you to the personal identity, and working through that.

In a related fashion when we talk about the ability to go back to the source, sometimes you can go back to the source, the tissue, because in the hands of the investigator the sample is linked to a specimen but

that specimen has been delinked from the person. And so just as you read it through thinking about what is at stake here, is it really going back to the specimen or going back to the individual, and just as you read through it being clear.

And then, you know, similarly if you looked down on page 20 -- at the bottom of page 4 in lines 22 and 23, when you are talking about "...when medical interventions are not available, having one's specimen linked with a disease predictor..." well, if and only if it can be tied to you and you are informed of it in terms of it being troubling. So again I think if you just read it carefully and ask what is at stake it will be clear.

DR. HANNA: Any other concerns in chapter one?

We have tried in this draft to -- I mean, we have been accumulating -- the previous full draft that you saw was the December 3rd draft that went out for public comment and we continue to collect articles and, you know, scan journals for information that is more relevant, that is more up-to-date and state-of-the-art. So we have tried in this draft to include much more recent references and double check the references that we already had but if

anything has crossed your desk that you think we should -- is important and should be included in here, please let us know.

DR. MESLIN: I wanted to, also, point out what you have already seen and that is that there is an additional box that is placed at the end of this chapter which refers to the Iceland decode case and the question arises whether you think it would be -- that is chapter two. Sorry. Never mind. Pardon me. I was going to ask you this question anyway. Whether there are people that you think we might want to ensure that we have on board at the next meeting so you will forgive my jumping ahead.

MS. BACKLAR: I am wondering, and I am a little afraid that I may have missed it, but is genetic information different from other medical information in that section on page 6. Do we actually -- do you actually make clear that one of the issues that makes it different -- that may make a difference is the uncertainty that there are only some pieces of genetic information that are certain? I am not sure that I found that in there.

DR. HANNA: In this section that Trish is referring to does anyone have -- I mean, this is an issue

that obviously has been percolating for some time in the origins of even separating genetic information out at all come from the fact that there used to be or in its last days a genetics subcommittee, and so that group started its work with that focus in mind and then started to broaden the scope of its analysis to include other types of medical information.

I have tried in this draft to eliminate, wherever possible, the distinctions or inappropriate distinctions between genetic information and other types of medical information but I know that there were some commissioners who expressed the opinion that they thought that there were some distinguishing features about genetic information so that is why we have left this section in here.

So if anyone has any concerns or feels that we need to change the wording in any way I would be happy to hear about that.

MR. CAPRON: On page 12 we have the section entitled "Moral Significance of the Relationship Between a Person and His or Her Body or Body Parts." Now at one level that is one of those headings that is going to have

a zing. I mean, in the sense of the relationship between the person and his body or body parts, well without the body parts the body, the person is rather an abstract notion but that idea itself could be explored. I mean, is there a sense of personality and personhood that is quite independent of body and, you know, we get to the whole question of, if so, where does that reside.

But it struck me that I expected to see and maybe I have missed later on in the report some further exploration of the ideas that are raised in lines 11 through 17 there where it says something about "...selective Western religious traditions offer some insight into the significance of the human body." And then it goes on to say "...but cultural differences can be significant because of the different symbolic nature or status cultures attach to specific body parts or tissues." Yes. I mean, have I missed that? Is that fully elaborated elsewhere?

DR. LEVINSON: On page -- I was going to bring this up, too. On page 97 where there is a discussion about commercialization and property rights that comes up again and it talks again about some of the issues that you

are raising. I am not sure whether this really answers your question but it talks about conflicting religious and philosophical traditions and so it is discussed a little more. I was concerned at one point about whether or not things were redundant but they are not but they also are not well-tied together with one expanding on the other.

MR. CAPRON: Rachel, my concern is not redundancy here but that I do not come away from this knowing even topically what divisions there are. So, so what in a way. I mean, if we were later to say some of these divisions are so extreme because of views about the burial of body parts with the person or the ability through this information to gather information that has portent for a person's life and, therefore, the way people fear being photographed at one point because your spirit was captured in the photograph. I mean, also, I do not know where this is going. It is just sort of an illusion that, yes, there are cultural differences. I do not even know topically is what I am saying.

The only thing that is referenced here is that the traditions generally favor the transfer of human biological materials as gifts and I had not -- I did not

go and look at whatever this piece by Courtney Campbell is and what he says there, and I am not sure whether the gift that he is talking about is primarily the transplant use of body parts, which is not at all an issue here, or the notion of a gift of the information contained. You are answering it is the former. Then it is really irrelevant here largely it seems to me.

I mean, the notion that when a family member dies one is moved to say, 'I can make a life-saving gift of the heart or whatever to someone else' is very different than the notion of 'When my pancreas was removed and put in a jar in the pathology lab I am, thereby, gifting the scientific community with the information campaign therein.' I mean, it seems to me a little apples and oranges.

So I found this frustrating particularly because the heading of the section for all its ambiguity that I suggest that exists in it, the moral significance -- I mean, this sounds like our home territory, doesn't it? I mean, that is -- we are commission on ethics and yet it does not -- the paragraph does not say anything other than there are issues there and they differ culture to culture

and by religious views and so forth. And I think we are almost saying that we knew this existed but we have not taken it into account or told the reader what it consists of.

DR. MESLIN: Steve?

MR. HOLTZMAN: First off, if I remember correctly the Campbell references to that wonderful paper that was written for the commission, which will be attached in appendix 2, and does go into great detail about how the transplant gift model should be construed or thought about as a model in the context of biological materials. Now whether one embraces that or not, it will be in the full report in the sense of the appendix there.

MR. CAPRON: Steve, may I respond? I agree we do not have to repeat in the text everything that is in the appendix but if what is in the appendix has, in fact, informed our thinking I think there should be some reference to it and it may be that chapter four -- and that is why I say having not read the new chapter four I was flipping through it to see, well, is it here. I mean, that -- this is -- that is the chapter on the ethical perspectives on it. Is it there? And it may be the

answer. Is it, yes, that it is there?

MR. HOLTZMAN: I do not disagree with you, Alex. I am thinking in terms of here to keep a concise first chapter I think what is at stake here is we are trying to explain why this is an issue now.

If you read the first sentence of this paragraph really the subject of this paragraph is increasing awareness in the medical community and I think one could give a few more examples here such as the one you are indicating to say that there is more of an awareness that we just cannot take these tissues and do anything we want willy nilly, all right, because of such things as cultural practices about burying body parts, et cetera, et cetera, and that might be enough here but we then in chapter four want to go into a deeper discussion, I think, would be appropriate.

DR. CHILDRESS: Yes. Maybe part of the issue is that in the chapter four in the ethics part, and I promised Eric I would help him revise this, this time, but I have just become a conference planner so I do not do substantive work these days, and I hope to help rectify that on another turn but it does seem to me that perhaps,

in part, because chapter four is set up to focus only on the secular side of things that we may not attend to some of the larger philosophical, religious and cultural things that are very, very important if we are ethically about the matter. It is not simply in a broader sense.

Now we do try to attend to some of that in our effort to think about community views but it does seem to me that we might in trying to put this in final form ask whether this kind of conceptual philosophical question, which also has parallels in theological discourse, might be something we would want to at least do a little bit more with in chapter four.

MR. CAPRON: And isn't that particularly true because the community concerns that we talk about primarily are stigmatization concerns?

DR. CHILDRESS: Right.

MR. CAPRON: Not cultural differences and views but just the uniform view that any identifiable group has that they do not want to be singled out and hurt by this process.

DR. HANNA: Trish, did you want to say something?

MS. BACKLAR: I thought that the point you have just made is important and probably want to look at this a little bit more in number five so that one revisits it in a few places. I think that is right.

DR. HANNA: I had a question about this section myself and that is I was wondering if -- I mean, I actually considered just taking it out at one point because I felt that it was -- it led you to believe there was more in the report than there actually is. But then when I reread it I thought it might also be useful to not just talk about the relationship between various cultures and their views of the body and parts of the body but also about medical information and health status because I think there are also cultural differences there as well and it is not just -- it is not just the body or the blood or the tissue. It also has to do with medical information or what can or cannot be revealed about health status.

I was wondering if we do expand this whether it would be useful to tie that in as well.

MR. CAPRON: I think that is a topic to address. I do not think I would put that under the moral significance topic in the same way about the moral

significance of body. That really is -- if -- in your cultural view either information about families is very sensitive. I mean, some families -- everybody talks over the back fence about the illnesses in the family. It is topic A. In some families it is a disgrace to recognize the existence of an illness in the family for cultural reasons.

It does not seem to me it comes here but it should -- could certainly come out if we are having a discussion later on of the type that Jim talked about where we are saying that there may be community -- different communities may view this differently as well as all being concerned about not being stigmatized. They may regard the notion of information about people or families or whatever somewhat differently.

DR. MESLIN: Maybe I should just say a quick word about four. We are not there yet but when you read four this evening or tomorrow or at some other point you may want to focus in on two items.

One is in the list that we give, it turns out to be on page 70 of the document that was handed out, we provide this set of interests and do a bit of work there,

I left on line 26 of page 70 the phrase "concerns about commercialization." It just is staying there. It has not gone anywhere and it really picks up part of what Rachel was saying.

But if you were to flip to page 80 you will see that that phrase has not been used. The phrase that I inserted as a placeholder are "concerns about inappropriate co-modification of the body and its parts," which is a kind of way of addressing what was in chapter one and your questions, Alex, and tying some of what Rachel had said.

So you may suggest to us by e-mail and we will certainly get Jim's input because there really are questions about gift giving and donation and what it means to give one's body or its parts that are not simply the kind of commercialization question that our public comments have drawn to our attention even though you are focusing unnecessarily on simply the "making money" off of these parts as if that was the only property based worry. There are other types of cultural issues so any input that you can give us there I think will be helpful.

MR. CAPRON: You might want to look at the

work of Margaret Jane Raden on this. Her primary concerns were not body parts but were people as such becoming co-modified but she made clear that you can have co-modification without having commercialization, which I think is what you are tying in.

DR. HANNA: Any other comments on chapter one? Okay. We will go to chapter two.

MR. HOLTZMAN: Just as a process question, do you want to just say -- anyone have -- when we are doing contracts we will say does anyone have comments on page thus, thus, thus or where is the first comments.

DR. MESLIN: Page 25.

MR. HOLTZMAN: It actually gets agreement. Silence means you cannot say anything further. My first comments is on 30. Are there any before that?

DR. MESLIN: Anything on 26? Anything on 27? 28? Going once. 29?

Mr. Holtzman?

MR. HOLTZMAN: Well, this schema we introduce starting on 29 is very important throughout the report and so you might think of some sort of way you want to unbury its first appearance potentially from just the middle of

two. I do not know if it belongs up front or you do it in a box or something along those lines. You might think about that. I think you should use certain typographic conventions like one 31, line 13, when you have "...that is specimens..." and then parenthesis, bold, "specimens." Again I think it can be -- a lot of the work in this report is hanging on how these terms are being used. So I just -- I think you should think about those conventions.

MR. CAPRON: Excuse me. Could you explain -- I just missed typographically what you were --

MR. HOLTZMAN: I was just suggesting bolding the word "specimens" on line 13 on page 30, for example. But again I do not want to get into the detail here. Just I think it is important. A lot of people are just going to go and read the recommendations. You do have it in the back there and maybe that is sufficient but just give it some thought.

I have a comment on 32 as well but go ahead.

MS. BACKLAR: It is just on line -- it is a minor comment. On line 7 I think you meant to write "affect" and not "effect."

MR. CAPRON: Are we engaging in -- if Dr.

Holtzman is going to be engaging in what font we put things in I will engage at the level of words. I was going to suggest we take the word "specimens" out of that, the "i.e. specimens." I mean to say human -- "Repository collections are of one of two types, unidentified specimens and identified specimens." We do not have to have said "i.e. specimens" in the first place. We already at the beginning of the report said that specimens is a word we use, I think, for the collection.

MS. KRAMER: I want to contradict you. I like it the way it is because I think it is confusing. We have been doing this for two-and-a-half years and we still get confused and I think that anything that lends clarity is helpful to people who are reading it.

MR. CAPRON: And I am suggesting it does not lend clarity as you are reading along and are about to be told that human biological materials are either unidentified specimens or identified specimens to pause on the way to say that they are specimens. Of course, you are about to learn that they are specimens, identified or unidentified. So that is why I would not use that word right there but perhaps this would go on too long if we go

word by word.

MR. HOLTZMAN: I have a comment on page 32 in the section on "coded samples." I am not trying to change anything. I just want to make sure we have this right. So if we read it we are dealing with things that are linked by a code. The paradigm in mind is the researcher has specimen X back in the repository. They know that X equals John Jones, right, "...with a code rather than..." reading "...a code rather than a name or any other personal identifier...where the repository retains information linking the code to particular human materials..."

Again I think it is linking it to the person that is at stake as opposed to the particular materials. You, the investigator, got it from this paraffin block. It could be an anonymized paraffin block. So I think that it is important that the tie is to the person here.

"...or where the extent of the clinical or demographic information provided with the sample..." I almost found that this was -- you were sliding over into a case where, in fact, in virtue of there being such extensive information it became what is number four,

"identified."

So I would ask everyone to read it clearly and see if we just slid those two cases together because if the investigator can do it then it is identified.

Right, Kathi?

DR. HANNA: Yes.

MR. HOLTZMAN: So that cannot be right. So again I would just encourage you to look at that carefully to see if it distinguishes the cases.

MR. CAPRON: I think Steve has an important point. Shouldn't we see exactly how identified samples, number four, would read if that point is to be made because, in effect, what we would be saying is it is irrelevant whether it is named or coded if it is identified through clinical demographic information provided with a sample sufficient that blah, blah, blah, "...could link the biological information derived from the research..."

MR. HOLTZMAN: Right, that the investigator could. I think we have always agreed to that, right, that it is going to be blocked. But clearly, you know, if I do not say it is Alex's sample but I say it is from the

bioethics guru from the University of Southern California, et cetera, et cetera, it is probably sufficient demographic information to -- and that would, therefore, be identified. That was complimentary.

MR. CAPRON: I would like to go on the record as objecting to that description but otherwise your point is taken.

DR. HANNA: Steve, do you want to suggest how we can fix that or does it just simply involve removing that last qualifier?

MR. CAPRON: I thought it was a question of moving it, not removing it, because if Steve's point is correct it is a matter of --

MR. HOLTZMAN: It is a matter of if it is a gene and it is identifiable. It is.

MR. CAPRON: Right. And it is different from the language we use down on line 13 where we say "...with a personal identifier such as a name or patient number sufficient to allow the biological information."

I mean, it is one thing to say your patient number, your social security number, your name are basically all equivalent because there are a lot of places

where the two of them are listed.

What we were saying up on lines 8, 9, 10 or 7, 8, 9, 10 is "clinical or demographic information" of the type that Steve was just describing. You know, a 34-year old mother of six with breast cancer and Hodgkin's lymphoma at Cleveland Clinic in July of 1998. There was only one person who fits that description. With that clinical information you do not need a name or a number to figure out who that is.

MR. HOLTZMAN: So there is two pieces, right. There is, is the information sufficient to zero in on the person? And the second, who can do the zeroing? Namely the investigator because by definition the person holding the code in the repository in virtue of having the code can only zero in.

So I think it is moving it but I think what is at stake, Kathi, and again I am doing this on the fly, is clinical and demographic information provided with the sample is sufficient for the investigator to link the biological information.

DR. HANNA: So you would say then you would remove the reference to the repository or a third party?

MR. HOLTZMAN: I think so. I mean, what makes it identified in the relevant sense of four is that the investigator knows who it is however they know.

MR. CAPRON: Would you accept "investigator or third party" as opposed to the repository that is because --

MR. HOLTZMAN: Yes.

MR. CAPRON: And so it is really a question, isn't it, of expanding line 13 with a personal identifier such as name or clinical information, clinical or demographic information, and then the sufficient to allow the et cetera, et cetera, and modify that to explain what we are talking about.

DR. CHILDRESS: Rachel observed, and I think rightly, that would just complete three and four.

MR. CAPRON: No. No. The rest of three stands. Coded samples that are -- that do not have that additional --

DR. CHILDRESS: But that part makes it identified in a sense, four, doesn't it?

MR. CAPRON: What we are saying is that that description does not belong under coded samples.

DR. CHILDRESS: It belongs under --

MR. CAPRON: It belongs here. That once you move there --

DR. CHILDRESS: Oh, so once you move -- okay.

MR. CAPRON: We are moving that text. I think we have to note somewhere here that is exactly what we have done either by a parenthetical -- clinical information or demographic information even when attached to a "coded" or even with a sample that does not have a name or a patient number. The idea is to say that something becomes identifiable through this process and the fact that it was coded with a unique code rather than with your social security number does not keep it from being identifiable, belong to an identifiable --

DR. CHILDRESS: This had to do with what you were adding before, I think.

MR. CAPRON: Adding the basic language of 7 and 8 where it says, "Clinical or demographic information." So that under 4 as I would see it, it would say, "Identified samples are those are supplied by repositories from identified materials with a personal identifier such as a name or a patient number or clinical

or demographic information sufficient to allow the biological information derived from the research to be linked directly by the researcher to a particular person."

MR. HOLTZMAN: That is exactly right.

DR. CHILDRESS: I guess I am not convinced that that latter addition makes a lot of sense for 4.

DR. MIIKE: I think what we are confusing is the rare exceptions that will break the rule and I think we cannot do it, Alex. I mean, you cannot -- we recognize the exceptions that in unlinked there are some samples that there are eight Natives in an Alaskan village. Everybody knows who they are no matter what, whether you have a name on them or not but we cannot put that in the category and I think we have done that in terms of saying there are exceptions where an IRB has to look and normally you would say it is anonymous or unlinked but they can be identified and you just have to look for these situations. I think we address that in the recommendations chapter.

DR. HANNA: Steve?

MR. HOLTZMAN: That may be -- so let's break it down into two problems. The first, I think it has to come out of the definition of coded. All right. That is

very clear that that is not what coded means. If the investigator has information in their hands descriptive of the individual such that they can identify the individual it is not coded. That is the first point. That is why this does not belong in three.

Now whether you want to rewrite four and expand with personal identifiers such as a name, patient number or sufficient descriptive -- sufficiently descriptive information to be able to identify the person, that is all we are saying. We are not trying to get at all the rare exceptions. And if you look at OPRR guidance on this, they actually say that although it is common sensical that --

DR. LEVINSON: So you are suggesting that tightening the definition in three and making it more restrictive but in a sense more usable by people who want to have their samples coded --

MR. HOLTZMAN: I am saying that this one is simply wrong and that what we meant by three -- I am not recommending any change from what we have meant all along in terms of tightening or untightening. Now maybe in terms of what got written here it is tightening.

DR. LEVINSON: That is what I meant. And transferring some of the information that could have been construed to be included under three and putting it in four to make it clearer. Not changing but clarifying.

MR. HOLTZMAN: You can transfer all of -- all of the information you ever could transfer you still can transfer. The question is whether or not that information is sufficient to say that is John Jones -- the investigator can say that is John Jones and if that is so you can identify the person.

DR. MIIKE: Wait, wait, wait.

MR. HOLTZMAN: We have said that all along.

DR. MIIKE: Wait a second. We are talking about conventions. We are not talking about individuals being able to be identified. We are talking about conventions when there is an identified sample. The intention was to identify a person and to send on the information with a patient name or some marker that identifies them and everybody knows that. The unintended identification should not be within the definition of what we are using here.

MS. KRAMER: Right. Exactly. I thought that

three -- three came out of cases where it was not going to be apparent who the information -- who the sample had come from but through collusion it could be divined. So to make those changes doesn't that make three too much like four and not address the other case? And if you want to tell me I am totally confused I will believe you.

DR. MESLIN: Bernie will.

DR. LO: Clarification suggestion. Let's try and keep the categories fairly clean and in the paragraph say the real world is not so clean and there are going to be instances come up where the line between three and four gets confused and even though the intent was not to identify individuals it may be readily available -- you know, it may be readily possible to do so because you have transferred so much clinical information and there are small numbers and that IRB's and researchers are going to have to puzzle and deliberate about those issues but not try and solve it as a definitional problem and just say definitions will not answer all our problems and there will be tough cases where ethical considerations that usually go in four actually may also be in play in things that seem to go in category three but it seems to me that

definitions have to be sort of clean to be usable and we have to try and -- not try and solve everything by making a definition --

DR. MIIKE: You know, this is a discussion we had in that conference call and I think it is addressed in a paragraph or so in the conclusions and recommendations section.

MR. CAPRON: I want to recant my agreement with Dr. Holtzman. His brilliance clouded my thinking. I think that Bernie's comments and Larry's comments really put the finger on the right thing. Coded samples are treated differently than unidentifiable samples precisely because of this potential, either that I will get the code book or, as it says here, that I have sufficient clinical information. I think since we end up for all intents and purposes treating three category three and category four very similarly for what we do with them it is still worthwhile to note that they are facially different and I would suggest we not change this and, as I say, I recant my earlier enthusiasm for Steve's suggestion.

DR. MESLIN: Any comments on page 33?

DR. CHILDRESS: Well, assuming we are

accepting some of the earlier changes.

DR. MESLIN: Right.

DR. CHILDRESS: Maybe we can --

(Simultaneous discussion.)

DR. CHILDRESS: -- repository, for example. You were not proposing that we --

MR. CAPRON: I was proposing that we not move from three to four the identifiable but --

DR. CHILDRESS: Potentially identifiable.

MR. CAPRON: Yes.

DR. CHILDRESS: I am starting to agree with that. I just wanted to make sure that what we were retaining, though, of Steve's earlier proposal and some of those other changes were accepted.

MR. CAPRON: Right. But the point -- the point of having the language "repository" under the coded sample would be repository has the list of names and code numbers. "Researcher" has the list of research results and code numbers. A person from the repository for innocent reasons, for malicious reasons, for whatever, going with the list of names and codes and taking the other information could put the two together and say I

know it is Mrs. Jones. So I do not think that repository is distinct from the --

DR. CHILDRESS: Well, I thought it was given the way we were distinguishing the specimen and the sample and that was part of the direction we were going here.

MR. CAPRON: This is just descriptive of a situation in which the information provided is sufficient where the -- someone from the investigator or the repository or a third party could, in fact, link the biological information derived --

DR. CHILDRESS: But being impressed with Steve's comments earlier I thought the point was that presumably if we are talking about a coded sample that is always the case it is somewhere in the repository and you can probably do that on a coded sample but we are not talking from the standpoint of sample, that is at is appearing for the investigator -- to go back to your comment about specimen. We are talking about specimen in a different way. We are talking about that from a repository standpoint. And I totally missing the discussion earlier? Steve, is that --

MR. HOLTZMAN: That was one part of my point

so respecting Steve's confusion as opposed to brilliance, I am happy to leave four as it is. I would be happy to just settle on the very simple point about three. All right. I do not think it is correct to say that a coded sample sometimes termed linked or identifiable are those supplied by repositories from ID'd material with clinical or demographic information sufficient to allow the investigator to identify the person. I have just taken out all the words in between but I have read grammatically what that says. I do not think that is the definition of coded and, therefore, my recommendation is leave four --

MR. CAPRON: But you have not read the sentence --

MR. HOLTZMAN: I did. I read the --

MR. CAPRON: No. If you do -- if you do sentence structure the "where" that you are referring to does not substitute for the with a code. It is where the repository retains information linking the code or where. So it is material -- it is supplied with a code rather than a name or other personal identifier where the extent of clinical information provided with the sample is sufficient.

Now you can still take the word "repository" out of there if your point is the repository has the code so it does not care about the extent of clinical information.

DR. MESLIN: I am going to make a suggestion that this is a good opportunity for some wordsmithing. If necessary, laptops are available as are tablets and pens, and I think if we circulate it, it might be helpful. We may not in a sense resolve it by a back and forth.

On the other hand I do want to remind commissioners that in the e-mail that was sent out a little while ago the attempt to try and make this more simple by removing both identifiable and unidentifiable from the text, where possible, and substituting the combined terms coded and identified and unlinked or unidentified where unidentifiable exists may help. Since that was -- I take it the silence on the e-mail was agreement with that convention I think that can help some of this and if Steve and/or Alex have text that they want to propose maybe we can bring it up for discussion as we move along. That is just a suggestion.

DR. MIIKE: One last comment. I think the

confusion between what we are talking about, if you look in three there is an "or". It is the "or", the second -- the phrase following the "or" is what is causing confusion and I think in the normal convention we are talking about a coded sample and that there is a possibility that the repository or third party investigator can find out who that person is and maybe we should just leave it that way by eliminating that little phrase that follows the "or."

MS. BACKLAR: Yes, that is exactly it and, in fact, because what you are talking about is human materials and where, and then you might want to take out repository because it is kind of redundant. They know already. So that is it because you still want -- what you are linking this second half of the sentence to is to the coding. Because you have the coding these other things can add to the information or a way to get back to who it is precisely.

DR. MIIKE: Alta, we are on the stem cell now.

(Laughter.)

DR. MESLIN: Alta, we have been walking through page by page and we are at approximately page 33.

<u>DISCUSSION OF DRAFT REPORT</u>

MS. CHARO: Okay. Thank you. I apologize. My puddle jumper was late coming in from Dulles.

MS. KRAMER: Are we on page 33 now?

DR. MESLIN: Yes.

MS. KRAMER: When I read this, which was a week ago, several days ago, it seems to me that the example that is given beginning on line 12 conflicts with the statement or with the sense of the paragraph that begins on line four and goes through ten because the last line of the example, lines 22 and 23, says, "May retain a record of a group of 100 samples used."

Steve, didn't we in discussing this in the past -- we could go -- the researcher could go back and get samples again from the entire field of specimens from the repository. So doesn't that make that then conflict with that paragraph above?

MR. CAPRON: I think that this was an example that we talked about where we hoped that the number was large enough and that we meant that you really could not make much of a statement about these hundred people at all from the data and that all you could be told by the repository was we will give you -- we kept enough of a

record that if you need another sample from all 100 of those people we will do it but we cannot tell you which one is which.

MS. KRAMER: I think -- now I remember what bothered me. It says -- on line 9 where it says, "Therefore, there is no way to go back and get more information about the source or to get another piece of the same sample," which I believe is understood the same particular individual sample. But you could go back and get -- since the repository has retained a record of the group of 100 samples you could go back and re-sample the entire group. So I just wondered if anyone else has a problem with that. Do you see a conflict?

MS. CHARO: Bette, are you asking about the -- I mean, there is two things here. There is the information and the other is a sample. You are right, they could always go back and get more material. And is that what you feel is causing the conflict?

MS. KRAMER: Yes. In my mind, as I read it, there was a conflict there.

MS. CHARO: Bette, would it clarify things if it were to say that there is no way to go back and get

more information about a particular source or to obtain an additional sample linked to a particular person?

MS. KRAMER: Right. What I added was, right, that there is no way to go back to get more information about the source or to get another piece of the same sample other than to sample again the entire group.

MR. CAPRON: I liked Alta's adding the word "a particular" instead of "the" before "source." It is a "a particular source or another sample from a particular source."

MS. KRAMER: Right.

MS. CHARO: Other than to sample the entire group is also very good because it clarifies what you actually do.

MS. KRAMER: Well, then it connects it to -- if anyone is reading that carefully.

MS. CHARO: Right, exactly.

MR. CAPRON: Yes.

MS. CHARO: Were there other comments on this page? Continuing on in the chapter.

Any comments on the description of the Iceland Health Records Database? I would like to offer up one

comment on it then if I may. This would be the box which follows the final page of this chapter, page 49. What would then become page 50 is a box on the Iceland Database Project. The box describes some of the privacy concerns about the database.

I was wondering whether people thought it might be helpful to mention something about the social background in Iceland with regard to the availability of health insurance coverage to citizens and the possibilities concerning unemployment so that there be a little more social context to understand the magnitude of the risks associated with a breach of confidentiality or whether people thought that might be over kill.

MS. KRAMER: I like it.

DR. MESLIN: I agree.

MS. CHARO: Of course I do not. I know that they have got universal health care but I do not know anything else about Iceland except that they have got a very cool language.

MS. KRAMER: Zero unemployment.

MR. CAPRON: A general question for Kathi and I guess for everyone. We have had discussions about the

way in which repositories of information are likely to respond to the growing interest in having current access to materials. There is description here on various repositories and their behavior.

What I do not think I saw here and I would be happy to have it pointed to me because I missed it is a description of something that Steve set forth at some point maybe as long as a year ago or more ago, Steve, about the ways in which companies in the kind of work that he does are developing relationships with sources of materials.

And what I have in mind is making clear that there is, in effect, the potential for ongoing business relationship which can then be responsive as it were -- that part does not have to be in this chapter but it forms the background -- to the kinds of forward looking recommendations we have in our report because the image that one gets here otherwise is of individual researchers in a university who have a colleague in the pathology department whom they call up and say, "Can you get me 50 tumors of this or that sort."

And there is -- that, I gather, is, you know,

one model and it will be an ongoing model but I gather that the commercial companies are developing relationships in which they are going to have all sorts of specifications as to what they want and so forth. And our sense, I think, is that part of what that relationship should be built around are a set of expectations of what is going to be told to people whose material is going into that repository and means of continuing to contact them if they have checked off boxes indicating that they are willing to be in research if they are notified of the research or if they get the research results, et cetera, et cetera.

And if that structure is not made clearer here people may wonder, well, what do we -- are we presupposing bigger changes in the industry as it were or really just adding rules to an industry that is already developing because of the commercial potentials here?

DR. HANNA: Steve?

MR. HOLTZMAN: That is a good point. Actually the paradigm for this is not so much that they may partially be driven by companies but it is more from the research institutions recognizing the potential research

and maybe commercial value but also research value of their specimens and the need to gather specimens. Have I got that right? Their specimens. The need to have collected them pursuant to conditions which allow them to use them in research. So Mayo is a model pursuant to the state statutes themselves.

And I provided to staff the consent form used by the -- did I actually say what university that was from? I cannot remember. Okay. But I could tell you it is a university major transplant center with whom we are collaborating and how they wanted to establish a tissue bank and the consents now specifically anticipate that they will go into the tissue bank and that it will be used in research broadly. It names panels of investigators who might be used. It mentions that it is co-funded by a commercial firm and that we will have access to it.

So I think we want to convey -- it struck me elsewhere in this report as well we have gotten a lot of focus on the individual in the consent and maybe recommendations and thoughts about how institutions can start to put in place policies is not actually a very useful thing for us to be making recommendations about.

MR. CAPRON: Could I just have a follow up? I am sorry. Go ahead, Alta.

MS. CHARO: Are you responding directly to Steve? Why don't you let Bernie go first and we will get back to you?

DR. LO: Let me just follow up on that. I think the use of these boxes can be very effective and I think a couple of other boxes we might put in are a box that shows institutional arrangements that we think are exemplary for sort of having these ongoing relationships and then a box on some sort of work towards these tiered consent forms out of the NIH or one of the Breast Cancer Action Coalition groups is doing to sort of give people a flavor for some of the positive things going on that address the ethical concerns people have had going in.

MS. CHARO: Alex?

MR. CAPRON: Yes. I just wanted to be clear. I think that the examples of the consent forms or the like might be here but it seems to me those would -- could come up in either chapters three or four but what I am asking here is just either add a box with a particular example or as a paragraph or so the kinds of things that Steve has

told us just about this is a world which is changing because of the value both to universities and to others of the material and that it is being organized somewhat differently and that there is a structure there and that what we are recommending is something that fits into that structure and not something that demands that the structure be created.

I guess, I mean, the point is taken that you think you have enough material or Steve can help or others can help, Bernie or Carol or whatever.

DR. LO: But just to sort of add on to what Alex just said, I think it is really important that this report convey that what we are asking -- what we are recommending is actually consistent with what some people and organizations are already trying to do so we are not necessarily asking people to do things that they think are impractical or wrong or whatever.

MS. CHARO: Just a question then. Would you -- I am asking this now of Kathi. Would you want or need text prepared by Steve, David Cox or others who have had experience working with these in order to flush something like this out and insert it or is there enough

material in the files?

DR. HANNA: I think it would be helpful to ask Steve for some suggestions. I will not ask him to write something up but if you could point us in the direction of some sources.

MS. CHARO: Alex?

MR. CAPRON: And it seems to me that -- I mean, we have on page 36 the heading "Past Research Uses of Human Biological Materials" and then we have those examples in italics. And then on page 38 we have a section called "The Value of Human Biological Materials to Current Research," and we give specific examples of areas of research and Steve's larger point which could come at the end of this section in light of this growing use and sort of the richness of the potential scientific work people are beginning to organize things more formally and with anticipation of ongoing collections and so forth to enrich the value of what they have and those relationships are now subject to examination of have they maximized the ethical component as well as the potential research value. So it would fit very naturally at the end of that section.

MS. CHARO: Bernie?

DR. LO: One of the things that has concerned me in general about this report is it does not capture a flavor that a lot of good work is going on that we want to encourage and sort of hope gets amplified. I think when we talk about current uses what does not come through are some of the examples that Steve and others have given of how you might have collected specimens or a database for one purpose, for one disease, and then find that it is really useful for something totally different.

That kind of sort of serendipitous uses I think does not come through and if that does not come through people are not going to understand why it is so important to have these data and the examples we give on pages 36 and 37 are nice examples but they are from the past. They do not really speak to the kind of research that is being done with large, large collections where you are going to go looking for candidate genes.

I think to give people a sense of why you need these very, very large databases with everybody in, with very few opt outs, is really going to strengthen the report if we can do it.

DR. LEVINSON: Yes. I was going to make a

similar suggestion and in the interest of timeliness of the report given the news this morning of the Snipps consortium that that be given perhaps later in this section on page 40 to 43 to just update it slightly. You are almost there but not mentioning it and it could be useful because it is something that is in the news now. People could tie it to what they hear in the paper.

MS. CHARO: You are referring to the Snipps consortium that was discussed in the New York Times today.

Bernie, if I may, I have a question to clarify what it is that you were asking for.

Would you be looking for a series of italicized scenarios that are illustrative of the kinds of arrangements that now exist ranging from giving some samples from the local path lab to the organized repository collections that are being created around various kinds of cancers, several scattered in key places, or are you looking for more of the kind of empirical evaluation of the percentage of repositories is growing from X to Y?

DR. LO: No. I think what I am looking for are some of the examples. The availability of a

repository that was originally conceived of for very, very different purposes and where it is going to be really tough to go back and get consent from people to use their samples for a very, very different purpose.

The availability of such repositories are really essential or highly useful for finding a candidate gene on an important illness that would have taken much, much longer if you had to assemble the database.

MS. CHARO: Is the collection that was developed for Tay-Sachs screening an example of what you are talking about where they have begun using it for colon cancer screening?

DR. LO: That is a good example. Steve has given examples of other databases he has put together or someone has put together to investigate a specific clinical problem and then later on people realized that for some other clinical problem it is a tremendous resource.

MR. HOLTZMAN: Yes, and you have got the range. Tay Sachs is a good example of that. One has the example of the twins registry for the people entering the Army in World War II. Those people have been gone back to

and back to for multiple different things. Initially maybe psychological was the thought of the study. You have got the example of Framingham where here you might still be interested in heart disease but now you are using different kinds of testing methodologies going and doing genetic testing whereas in the past you did serological testing.

So I think it just -- two points you are making. One is the technology changes and the nature of the tests you are going to perform change, number one. And, number two, as now we have a better understanding of the molecular mechanism of disease we start to reclassify disease in terms of the underlying biology instead of the phenotype and hence what was collected phenotypically can be many different things. That is the generic point.

DR. LO: Yes. Well, also, I think that -- there is a point, I think, that you, Steve, have raised at previous meetings that if you take a Framingham study you can argue that, you know, if you had studied apo-E that had something to do with heart disease that it becomes something for a totally different organ system and to not sort of pursue that on the grounds of, well, they were

really talking about letting themselves be used only for the risk of cardiac disease and if you want to do risks of other diseases you need to go back. That becomes really unwieldy and unworkable.

MS. CHARO: Okay. Any other comments on this? Okay.

Kathi?

DR. HANNA: I just would make a request since we have been trying valiantly to make chapter two smaller and smaller and smaller and now we have just made it larger, if you can suggest parts of the chapter now that you think we can eliminate to make room for these new ideas that would be helpful. You do not have to do it now but if you could hand it to me.

DR. LO: Well, one thing, I mean 36 and 37, I think that is way down -- I mean, that -- those were put in to say, you know, archives are good for old-fashioned pathological clinical research and that is really not what we are talking about and we can sort of cite it as a strength side or something.

MS. CHARO: Bette?

MS. KRAMER: Kathi, it is only 12 pages long.

I do not think that is terrible. I know it used to be 45 but I do not think 12 pages is excessive. I do not think we need to worry about cutting that any more.

MS. CHARO: Any other comments or shall we move on to chapter three?

Chapter three, comments?

Jim?

DR. CHILDRESS: A very modest one. On 62 we have varying -- on line 8, "Varying Definitions of Identifiable" and yet that paragraph focuses to a great extent on anonymous and so forth and not just saying varying definitions or else add all the other terms and I think "varying definitions" would be sufficient.

MS. CHARO: Yes, Bette?

MS. KRAMER: Going back to page 52, line 10. I do not understand what that clause means. "...even if they are outside the commonly accepted practices."

MS. CHARO: I suspect it means even if they are experimental procedures and maybe we can just rephrase it that way to avoid the usual -- the common confusion between research and experimentation. An experimental procedure may not be research.

MS. KRAMER: I think that needs to be clarified.

MS. CHARO: Clearly. Okay. Easy.

I had one before we get back to the section that you were talking about, Jim, which is kind of a broader.

On page 58, at the bottom of the page where we discuss expedited review, we make the point that expedited review, which is a way to get the IRB review to be done in a more expeditious fashion, right, so it is a good thing, one makes the point that there are going to be two requirements. One is that something be minimal risk and we talk about that later. The second is that it has to be present on an officially published list so even if it is minimal risk if it is not on the list it cannot be made -- it is not eligible for expedited review.

I wondered if we might consider having a recommendation that had to do with the amendment of that list to accommodate minimal risk protocols that use human biological materials in order to cover that loophole. Not loophole. Sorry. To cover that omission.

DR. MIIKE: Would you explain how you would do

that?

MS. CHARO: I think we will probably have to try it out in writing on e-mail first to get the language right but I think it would be a direction. It would probably be recommendation aimed at OPRR which --

DR. MIIKE: What I mean is that if minimum risk is not the only exclusion then what do you do to generate a list of the other categories?

MS. CHARO: Well, you -- I am sorry.

DR. MIIKE: Shouldn't it be more that if it is minimal risk we should not have categories? Shouldn't we just dispense with the second --

MS. CHARO: Well, we could recommend that that particular regulation be changed. That is separate from trying to simply work within the regulations and make them accommodate our own work.

The regulations already require that something must be on an officially published list in the Federal Register to be eligible for expedited review. That list gets amended periodically. It was amended just this past year to add a few additional things. MRI's, for example, are now on that list, which was important in our

discussions having to do with research on the decisionally impaired.

We could recommend that OPRR in its next go round on the revisions of that list consider adding as many forms of research on human tissue as it can knowing that if it is on the list and an IRB finds that it is minimal risk or believes that it is minimal risk that they can expedite the review.

DR. MIIKE: The alternative is just to say that any kind of research of minimal risk on human biological tissues should have expedited review rather than coming up with a list.

MS. CHARO: That is an alternative. It would mean that we would have to consider the effect on a wide variety of research areas not having to do with biological materials. There are many forms of minimal risk research.

(Technical difficulty.)

MS. CHARO: Goodness gracious.

To make a recommendation like that would mean we were recommending that with regard to areas of research that go beyond this report and we are saying we would have to discuss that further. Is that what you would like us

to do?

DR. MIIKE: No, no. What I am saying is that rather than expanding the list simply make an additional category any research that is minimal risk on human biological materials.

(Technical difficulty.)

MS. CHARO: I am going to -- yes. I think the table has suggested it would be a good time for a break while they work on the sound system. We will pick up right where Larry left off. Why don't we give it 10 minutes and it will be fixed by then.

(A break was taken.)

MS. CHARO: If I can make a suggestion, please, with regard to how to move through the chapter. A couple of questions have arisen concerning what is currently on that expedited review list as well as whether the list as revised in November, which is after this chapter was originally drafted, still requires every particular procedure to be specifically listed or if it is now geared only to a series of examples of the kinds of things that can be expedited.

It might make sense to simply skip this for

the moment and come back to it after we actually have the text of the revised -- the most up-to-date list and then we will be able to be more precise. So without objection I will just suggest that we continue moving on with the chapter and we will come back to that.

Were there other comments having to do with the description of the regulations or with the discussion on pages 60 et seq. about the application of the regulations to an imaginary protocol?

Moving along to pages 62 et seq. Comments on the description of how other professional societies have been handling this in addition to Jim's comments.

May I ask then in the spirit of collegiality if there is anybody here who shared the feeling I had about this section and, if not, then we will go without any change? I found myself finding this section difficult to read. Its point, I understand, was to highlight the variability of the approaches of the different professional societies but I found that in an effort to be comprehensive it began to feel a little bit like a laundry list and since they were inconsistent with one another it was becoming an incoherent laundry list.

Bette?

MS. KRAMER: I agree with you and I was wondering -- if we make some general statements about inconsistencies, consistencies, along with some examples, is it necessary to run through all of them?

MS. CHARO: Other people?

MS. KRAMER: What happened -- at one time we had a diagram, a chart about that. I mean, if we put that in the appendix and referenced it and just took the language in the chapter and, therefore, were able to abbreviate some of that.

MS. CHARO: So this might be a place where we could --

MS. KRAMER: I did not find that it really added that much to it.

MS. CHARO: Anybody who -- Steve?

MR. HOLTZMAN: Question: Did we intend to have an appendix which would collect all of these statements? Have an appendix which collected the statements. I think one of the things we had discussed was we were not working in a vacuum and it is important to acknowledge the hard work of others and that we

contextualized our own against it. The diversity of views provides a rationale for our report to try to have surveyed the territory and then come up with a classification that says we hear you all and here is a way to provide a human -- maybe on a go forward basis a singular uniform nomenclature.

And so I think there might be something to think about in terms of collecting those statements into an appendix and then you could shorten this down and reference the appendix.

MS. BACKLAR: Or --

MS. CHARO: I am sorry.

MS. BACKLAR: -- or --

MS. CHARO: Thank you.

MS. BACKLAR: -- I like that idea but I think what would be very interesting is perhaps not have this chapter at all in here and put a little guide to the various -- arrows to the various different opinions and one could do that just in a page or two ahead of the collection of the different sources.

MS. CHARO: So am I understanding correctly that you are suggesting that one would actually drop the

text that begins at page 62 about the various groups, drop all of that and use some form of it as an introduction to appendix with all the statements?

MS. BACKLAR: Right.

MS. CHARO: Kathi, can I assume that that has been enough of a discussion for you to have some ideas about what to do next with this material?

MR. CAPRON: Say a little more.

MS. BACKLAR: If I could say a little more I would write it but I cannot. What I am suggesting is that you get all of these different statements and do as Steve just proposed and you put them together and then you take a few pages, which is a guide to what you would find where the different statements are and maybe a tiny little synopsis so somebody knows where to go to look for which opinion and what statement it would be under. It is just like a very short road map telling you where to go to. Do you understand what I am saying?

MR. CAPRON: I do. The whole notion of separating out the other statements and treating them as a separate document -- as a separate part of the chapter -- was, as Steve said a moment ago, intended to say we are

not operating in a vacuum.

Another way of doing that is simply to acknowledge when we first raise our own definitions that we are operating in a world in which there have been variable definitions and that we realize that our own definitions are not presumptively better than anybody else's but we have crafted them because they make sense to us and as we talk about them just cross reference those that agree so that -- I mean, this stuff would end up going up to chapter two, I guess. Some of it could go up. Not so much the federal, which is the separate, but the stuff -- so that we say the Canadians, for example -- when we talk about sometimes referred to as anonymous, drop a footnote to the Canadian policy. They refer to it as anonymous. And then we do not -- you know, we do not have to say, "Well, there was this tri-part commission. They developed broad standards," et cetera, et cetera.

MS. BACKLAR: Right.

MR. CAPRON: Now is that --

MS. BACKLAR: Well, there are two ways you could do it.

MR. CAPRON: Yes.

MS. BACKLAR: You could either do it -- make it much shorter and still include it in this chapter or you could say -- or you could put that with --

MR. CAPRON: Right.

MS. BACKLAR: -- this packet of the various --

MR. CAPRON: Right.

MS. BACKLAR: -- opinions.

MR. CAPRON: See, I -- if we are going to have the materials themselves in an appendix, the major statements, which I think -- or a series of appendices, I think that makes sense. My sense is that if -- there is value in having a chapter where we say what the current federal regulation of this is.

MS. BACKLAR: Absolutely. I am not --

MR. CAPRON: Yes, right.

MS. BACKLAR: -- disagreeing.

MR. CAPRON: So that part of the chapter makes sense as a chapter sort of to show why isn't this already handled well.

MS. BACKLAR: Also, particularly because we use that later in chapter five saying what it is that we need to clarify from the federal regulations. I mean,

that is very important to have here so one knows where one is.

MR. CAPRON: Yes.

MS. BACKLAR: As they are now, right?

MR. CAPRON: Yes. So I would suggest that one -- then the way of shortening would be using the other stuff just as relevant to our own terminology either to acknowledge the terms others have used and link it there and not worry -- we do not really care what the whole structure of the Hugo (sic) ethics committee statement is.

MS. BACKLAR: Right.

MS. CHARO: Steve?

MR. HOLTZMAN: I agree with the direction of this such as the last comment about we do not need to care about the Hugo structure. But beyond the nomenclature issue we also did gain insight into ways of thinking about certain things. For example, the National Breast Cancer Coalition. So it may not be simply it drops out entirely. There may be a little bit of discussion about the issues that people -- those statements reflect as being important, which we have taken up as being important as well.

MR. CAPRON: As issues, not as --

MS. CHARO: Alex, your microphone.

MR. CAPRON: As issues and not as a separate, well, here is what organizations say and here is what other countries say.

MS. CHARO: So together what this would suggest is that where these materials provide contrast or consistency with a key point that we are making we would reference it. We would have an appendix in which the full text of these statements, the major statements is presented so that they are coherent policy, their definitions and the consequences flowing from them are presented in toto so that people can see them by way of comparison and that this textual discussion that goes from 62 to 67 -- where is the thing about consent again? 62 to 64. Well, okay, right. Sorry. 70. So 70 would wind up getting dropped out and parts reallocated to footnotes and text and parts eliminated.

Larry?

DR. MIIKE: I would not favor dropping all of those out. I think that what you need to do is at least identify those areas which are ambiguous or how other

people -- because here you are and you are saying here are the current federal regs but there are issues around them and collectively these various organizations have spot lighted those particular issues and, you know, we do not have to go into much detail but we should at least let people know within this chapter immediately following the current regs what are the kinds of things that people have been grappling with.

MS. CHARO: Now some of the material that highlights the ambiguities in the federal regulations was removed from this chapter and moved to chapter five in conjunction with the recommendations and that was many, many months ago. Would it make sense to reallocate some of that back here so that if you are introduced to the federal regulations you are simultaneously introduced to the key areas of ambiguity and again you would reference, where appropriate, other statements by professional societies that have grappled with that particular problem?

DR. MIIKE: There is not a problem with some redundancy in the sense that if you are talking about the regs as it currently is and you say here are some of the issues surrounding that, when you reach the conclusions

and recommendations it is perfectly logical to --

MS. CHARO: Okay. Other comments?

Bette?

MS. KRAMER: I just think it is important for several reasons to acknowledge the work of the other organizations and acknowledge their efforts to come to grips with it and that is it. I think it is important to acknowledge it.

MS. CHARO: And that can certainly be done both in chapter two and even in the executive summary and chapter one to acknowledge this is obviously an area we are working on precisely because so many people are working on it.

MS. KRAMER: No, but also in this chapter in some measure --

MS. CHARO: Right.

MS. KRAMER: -- it does not need to be --

MS. CHARO: Okay. Other comments? Okay.

We are up to page 71. This section is being revised and updated. Should we make comments on this portion of the draft anyway or would you like us to wait for the revised materials?

DR. HANNA: I think it would be useful to signal what you would like to say in this section on the privacy issues. There are now two recommendations in chapter five that refer to these sets of issues so it would be useful to know whether you think the material that is in here right now is still relevant, whether it is too long, whether we are missing things, how you would like us to focus the discussion so that it justifies the recommendations without trying to be comprehensive on the issue of privacy, which is an 800 page report and not a 100 page report.

I would add that in the discussions that Eric and I had with several committee staff from both the House and the Senate they are very interested in what NBAC has to say about privacy as it relates to research generally and they see human biological materials as king of a case study and this is because they are all rushing to get legislation through by the end of the summer so that they can preempt the Secretary and her efforts.

So there is a bit of a horse race going on right now. Many people are looking to NBAC for some kind of guidance when it comes to privacy concerning research

and research subjects. So I think it is important that we include something in here and if we can just find a way to narrow this discussion so that it is very clear that we are referring not broadly to the many issues that are being dealt with when people talk about medical records privacy but specifically how when somebody is considering human biological materials research they should be thinking in terms of other issues having to do with privacy.

So we can think about it from the perspective of the human biological materials research and where it touches or intersects with more general medical privacy issues then we can figure out actually what we want to say in this section.

MS. CHARO: Eric?

DR. MESLIN: While you are thinking about what you may want to say this is another opportunity to mention that the privacy issue is raised in chapter four so you have a couple of places where the issue can picked up. One can be the regulatory model here. Another can be the sort of ethics model which chapter four is attempting to say something about.

We got a lot of public comments on the privacy discussion and you will have a chance obviously to think about it some more but there are places to bring this up and I would just encourage you to think constructively because we have to draw a line somewhere. We will not be able to say everything that the entire House of Representatives and the Senate would like us to say about privacy protection.

And I also put in a plug that this could be the kind of topic that you may feel is important enough that it requires either a separate report or another full thinking through so when we talk about priority setting and other types of projects there are a whole set of issues that this can spin off. We do not have -- you do not have to answer every question in this one report.

MS. CHARO: Bernie?

DR. LO: I would like to make a few general points on topic. First, notwithstanding the keen interest among senators, congress people and staffers, I would suggest that because we really have not thought about this issue that we not take this on at this time. I am really concerned that we need to get this report out and to sort

of take a major new topic on I think is really unwise.

Secondly, I think there are some very focused things that have implications for the congressional privacy debate that come directly out of what we have said and I would suggest we try and draw those out and it seems to me that there is a lot of concern as to whether you should have explicit authorization or full informed consent as requirement before you can use medical records for research. So this is the Minnesota debate and we have clinic rebuttal and so forth.

And it seems to me if you draw out what we have said with regard to stored biological materials, which I think is actually somewhat different than using my medical records for research, one of the things we are saying is that we think there are a rather wide range of situations where we really do not think it is necessary to go back to the individual subject to reconsent them so to speak in order to carry out this research in an ethical manner. I mean, it seems to me that is a real different position than what some of the -- for lack of a better term -- strict privacy advocates have argued for in terms of federal policy.

And now that I think we have thought about it and we have really kind of discussed it at length I think we can highlight that and I think we should to help people in this very narrow part of a much broader topic but I would really -- I mean, I would really discourage us from getting into the broader issue because I think that is a several month excursion that is going to sort of get us further behind on other topics that are more important.

MS. CHARO: Bette?

MS. KRAMER: I agree with Bernie although the threats to medical -- without the threats to medical privacy -- let me see how to say this. Very simplistically I think of it as though if there were not a problem with privacy and if we had universal health care we would not have to worry about all this anyway. So while I agree with Bernie that it is inappropriate for us to take this on at this time because, in fact, we have not taken it on, I do not think it is inappropriate for us to acknowledge that threats to privacy are clearly one of the reasons why this is such a problem.

And what? Then go on to applaud the efforts that are being made by the individual states or by the

congress to address it and urge that it be addressed, you know, or say that at some time in the future that might be an appropriate subject for NBAC.

MS. CHARO: Kathi?

DR. HANNA: I hope I was not suggesting that we have to in some way react to the environment out there because it is obviously evolving and it is very fluid and it is hard to say what direction things are going to go in.

I do think, however -- I went and spent some time talking to various people in OPRR to try to understand how they do medical records and what their perception is of IRB's practices when it comes to medical records research. I first asked them whether they thought of medical records and, for example, human tissue in the same way and they said, "Yes, in fact, they do." And if you look at several places in the regulations there are lists of things and it says medical records or blood or whatever.

I then said, "Well, how do IRB's consider medical records research?" Either you are going to the medical records to review records to do research or you

are going to the medical records to find people whose blood sample you then want to pull because of the information you get out of the record. And they said that most of the time they feel that IRB's really get hung up in this. Very often they do not think of medical records research as involving human subjects and, in fact, a lot of clinical investigators do not think that medical records research involves human subjects.

So I think that if we can try and not worry too much about, you know, the big picture and what all the legislative proposals are but if NBAC can say based on -- you know, kind of in a principle way what investigators or those who are sharing information from medical records because the research with the materials brings you there -- it is not the whole separate issue but in some way there is a connection between medical records and biological materials.

I think it would be a useful step. I think that IRB's might appreciate a little bit of clarity on how NBAC sees this kind of going back and forth to the medical record because of the research in terms of the greater privacy issue. I think it would be helpful.

MS. CHARO: Alex?

MR. CAPRON: I think those are very helpful comments and it seems to me that what you have described is something which ought to be in chapter two because in chapter two we are talking about sort of the clinical -- I mean, the scientific process. And what you are describing is something which I know has concerned members of IRB's and that is the sense that -- the word that is used is "trolling" like a fishing boat or something, I guess, going through medical records to find people that you want to do research on and they do not consider that step to be research. And whenever IRB members call me about it I say, "Of course, it is research." I mean, you are not -- it would otherwise simply be an invasion of privacy I mean for third parties to say, "Let me look at your medical records of people who are not my patients."

The whole justification is that they are now embarked in a research project. The first stage of which is identifying the subjects and so forth. So I think that if that is a process which -- indeed, I have heard about it mostly from people who want to go on and do health services research, they want to find patients who have had

certain kinds of health -- but if you are saying that that is also sometimes used not the way we describe it, which is first you get the genetics data and then you want to find out what the person's health status was but rather you are looking for people with certain health status and now you want to look at their biological samples to see what you can find there, we ought to make that clear in chapter two.

And none of this is pejorative. It is just descriptive at this point that the reader who does not know anything about the subject will come away realizing what we say in chapter five about that then becomes an issue that I do not think we have fully addressed and we may want to -- when we get to chapter five now say where does that fit because it is -- it deserves to be highlighted. I do not know that it is a separate recommendation but be highlighted when we are talking about research with identifiable samples.

MS. CHARO: Steve?

MR. HOLTZMAN: I found that Alex's description of what seems to be a paradigm case a little surprising because the paradigm case in almost all research that I

can think of that we do for drug research is that you start by asking the question do I have a population of subjects phenotypically characterized, that is having a certain clinical condition. So it always begins with going to an investigator or a center and saying do you have and can you ascertain people and a good starting point for that is they go and they go through the medical records typically, at least in our experience, pursuant to an IRB approval to do that first step.

Okay. But --

MR. CAPRON: That is an --

MR. HOLTZMAN: Right. No, but in terms of the first step -- but the way you described it. That is always first. Then you go to the biochemical interrogation of the sample or collect from the individual or if you are doing a drug study you start by saying so and so, Dr. famous cardiologist, how many heart attack patients do you get. Do you have enough to be able to provide for the study? So if it is not clear that that is normal or the most often case, we should make it clear.

MS. CHARO: Alex?

MR. CAPRON: I thought what we had described

was a process in which you say I believe I have identified a gene or something and I want to look at tissue samples that the repository will tell me came from people who had X, Y, Z condition and I want to see do I find this and so there you are not asking -- you are not looking through the person's medical records as it were. The repository already has sorted out samples that it can find of patients who had XY disease.

What I was understanding some people from Kathi's comment were doing was comparable to what gets done in health services research where it is going to a whole -- you know, look at all the patients who came in, in a certain month, and you want to look through their records to find certain people who fit certain parameters. For the purpose then of following up with those people and maybe, she says, going to them and saying we want tissue sample from you or maybe finding that you already have some place in the institution their identified tissue sample. And I just did not think we had made that process as clear as the other one.

MS. CHARO: Larry?

DR. MIIKE: I just want to remind you folks

that when we look at chapter five when we came up or when the staff came up with the recommendations about medical records there were a number of us here who said, "Wait a second, that came real late," and the only compromise it seemed to me was that we simply said what we said now, which is just make sure in the medical records confidentiality legislation that these issues around what we are recommending are taken into account so that they are not sort of thwarted in what we are doing.

And I think that was the limited way so it seems to me that in these chapters we should be descriptive about what is going on at the federal and state level in confidentiality of medical records and leave it at that and just sort of compare it to what we are saying.

I do not think we can go any further into that end and I think that many of us would object for us delving into a confidentiality area which we really have not discussed.

MS. CHARO: Let me see if I can just make sure that I at least understand where we are. That first it might be helpful in chapter two when we go back, as we

have already decided to, to try to present a better picture of what the practice currently is. What kinds of repositories are people working with and whose staff -- you know, who is there and how do you interact with them? How do you make a request?

That kind of case study and that that include some elements in the case study that have to do with if and when the medical records become pertinent to that process so that as people read the report they have got a good idea in their mind of some illustrative examples.

Second, chapter three as it now exists has, Larry, what you have suggested you would want, which is purely descriptive material that touches only on the extent to which current medical records or actually laws -- I think it is only state laws, state and federal law. I am not sure -- it does not really go into the regulations. That may be something that needs to be added. How the state and federal laws now exist do or do not mirror the law that we are now talking about with regard to human biological materials and that is the extent of the discussion in chapter three. It is not prescriptive at all.

Maybe we need to perhaps add a little bit of text about the current state of understanding about medical records under the federal regulations that we have been working with up until now for HBM.

And then finally when we get to chapter five we will look -- I think it is recommendation 25 or so -- at the language that is the latest language having to do with a statement about the degree to which these two bodies of rules should be coordinated or the degree to which people should have to think about whether they ought to be coordinated, et cetera.

Is there anything that is missing from that kind of collection? Okay.

Bette?

MS. KRAMER: Before you go on let me just raise a question. In the light of this discussion then do we need as much detail study -- as much detail description as we currently have of the various state initiatives?

MS. CHARO: Would people like to see it shortened up a little bit?

DR. MIIKE: I do not have a problem with it because I think there are -- we are not being exhaustive.

We are just using some states as examples of what is going on currently.

MS. CHARO: Sure. I am sure that it could probably be shortened here and there and made sure that it always stays tightly tied to the purpose of the section, which is to compare and contrast.

Alex?

MR. CAPRON: Can you tell us a little bit about the states that were chosen here? I had a sense that you were dealing with states that had done a lot. If these are merely representative -- and they are not, are they?

DR. HANNA: No, they are not representative. They are the outliers because they have done -- they already have laws on the books.

MR. CAPRON: Right.

DR. HANNA: Many states have proposals pending that were never signed into law.

MR. CAPRON: So that the question would be in shortening if we do not really need to come away with detailed language about the Minnesota statute are there points of commonality that raise the kind of issue that

Alta described and where do our suggestions fit into existing law rather than -- it is very much the same as we really did not need to know all the thinking of the Hugo ethics committee.

MS. CHARO: No, no, that is right.

MR. CAPRON: I keep picking on that because I am a member of that committee so I do not --

MS. CHARO: No, no, this was originally a memo prepared in reaction to requests from the commission table for information.

MR. CAPRON: Right.

MS. CHARO: And we see here a great deal of the information in the memo. Some of it -- some of the language is illustrative of the confusion around the definition, for example, of unidentifiable subject of research because you see the same debates about whether coded information is treated as identifiable or not taking place at the state statutory level just like it did in the federal regs. To that extent it is illustrative but that is all it is there for.

Steve?

MR. HOLTZMAN: I think it is actually a little

more than illustrative and, therefore, absolutely topical and pertinent whether we shorten it or not. And that is for anyone who has ever worked for a state legislature drafting legislation like I did once there are certain states when they come forward with a very robust bill it becomes the model bill and you start your drafting there and certainly I can tell you with all of the different bills popping up all around the United States these are the ones that people keep looking to when they go to the starting point.

So I actually found it -- I think it serves a public purpose to get in a little bit of detail of what are being perceived as the leading cutting edge here of where it is going. At least that is how I read the intent of why we did this.

MS. CHARO: That is interesting.

MS. BACKLAR: Coming from a state, which unfortunately believes it is at the cutting edge of this, I am actually interested in this only because I think that it illustrates how complex it is when the individual states go off making rules and regulations which do not fit together and it is such a patchwork. I actually think

it is exceedingly mischievous, much of the work that goes on. Some of it, I am sure -- most of it I would like to say is very well meaning but I think the importance here is that we look at that patchwork and in some way some place -- maybe not -- well, allude to it at least in this chapter and come back to it in our recommendations about the concern about the patchwork model that is going on in this country.

MS. CHARO: Other comments? Okay.

Chapter four. Now chapter four is being revised and it was just passed out and I am sure everybody has had a chance to read it. It was great, huh?

(Laughter.)

MS. CHARO: Would you like to hold that until tomorrow so that people can glance at it tonight rather than making comments on the old material?

Well, that actually moves us up to chapter five.

I always like to have happiness in the peanut gallery, Eric.

All right. Shall we continue simply moving through page by page and then into the individual

recommendations? Comments? Or while you are getting your thoughts together, maybe, Kathi, you would like to summarize again for people the changes that they are looking at here, especially the people in the audience. Some of that was pretty much done in your pink sheet.

DR. HANNA: Did you like that pink sheet?

MS. CHARO: It was a great sheet.

DR. HANNA: Okay. In chapter five we -- after the last meeting there seemed to be agreement that people wanted the recommendations to be scattered throughout the report and so much of the language changes you see in the recommendation -- the process was that I posted them on e-mail. I asked people to comment on them. And those who gave lots of comments got to be invited to participate in the conference call where some things were worked out where there were -- appeared to be disagreement on the wording or the tone or the intent of a specific recommendation.

So many people sitting here participated in the conference call and then I went back and tried to incorporate the further refinements of the language of the recommendations after that call and tried to put in the

justification language both leading up to and then following the recommendation the thoughts that I heard people expressing.

Now it might be that you have additional -- in addition to the wording of the recommendations you might have additional language you would like inserted for the justification for the recommendation. So maybe we -- I do not know. How do you want to proceed? Do you want to proceed with the language of the recommendation?

MS. CHARO: Well, let me just ask if there is anybody who has substantial comments that are aimed solely at the text that they would like to have discussed first? Otherwise we can go recommendation by recommendation focusing first on the language of the rec and then the explanatory language.

Eric?

DR. CASSELL: I have only just a really small thing. On page 110, the definition of an unidentified sample, just in general principle it is not such a good idea to define a word by itself and that is the way that is. Sometimes -- are those supplied by repositories from unidentified collections. It is just define it. That is

all.

MS. CHARO: Okay. Trish and then Alex.

MS. BACKLAR: I have something that I think that actually Alex may have brought up at one time and I am still concerned about, and this is just a general comment. I find it a difficult chapter to read because I never know what is coming before and after a recommendation and I am -- I tried to go through thinking if you started with a recommendation and had all the text to follow it could you do it because I see what you are doing sometimes. You are trying to explain it and then you come to why you had the recommendation. I still find that very, very difficult to deal with and if I was on the outside I would find it even more difficult if I was not part of this group that understood the process.

MS. CHARO: So what -- I am sorry.

MS. BACKLAR: I think that Alex a while back suggested that the recommendations come first and then the text follow. Do you remember saying that?

MS. CHARO: Alex?

MR. CAPRON: The commentary that is to say.

MS. BACKLAR: Yes. And it -- and now it is

hard to know which is where. There are some before, some after, and hard to look at in that way. That was one thing. The other comment I have is rather -- it is not really small. I forget which page but one -- it talks somewhere about premises and then you list something and those -- what you list are really not necessarily premises at all. They are concerns rather than premises. I can find --

MS. CHARO: Where there is a specific word change or copy editing that is probably best handling in writing by handing the sheets in.

MS. BACKLAR: Right.

MS. CHARO: Alex?

MR. CAPRON: Two comments. One is related to something you have noted in an earlier chapter. On page 104, line 6, there is italicized text. I am not quite sure why that sentence is italicized but maybe it is just for the purposes of emphasis, Kathi?

DR. HANNA: Yes.

MR. CAPRON: Okay. The first two words there say "Research on..." and I think what we mean is examination of stored materials undertaken solely as part

of the clinical investigation falls outside the purview of this report.

Just to be clear because otherwise we are using the word "research" in a confusing way.

The second comment was inspired by Eric's pointing to the place on page 10, the language on page 10, lines 3 and 4, Eric, is the same language that we have in chapter two. It is our now standard definition of these four categories.

DR. CASSELL: I was biting my tongue about commenting orally and I felt about it that way then, too. It is just --

MR. CAPRON: Yes. I am not arguing.

DR. CASSELL: Yes.

MR. CAPRON: But it was useful to me when you raised that because I then read it over more carefully and I was thinking initially, well, actually you are wrong because it is not a matter of defining a word in terms of itself. It says unidentified samples come from collections of unidentified specimens but that is not what it says. It says it comes from unidentified collections.

And so certainly the adjective is in the wrong

place. We know what the -- but maybe your broader point would be better incorporated if we did say, using language that we use, when we are talking about unidentified specimens themselves, is to use the language about -- it would say collections of human -- of biological specimens --

DR. CASSELL: That are not --

MR. CAPRON: -- for which identifiable -- I am now turning back to page 109, line 17, "...for which identifiable personal information was not collected..." Now what that does is that repeats the language and I do not know if it is right because the whole reason to identify the specimens as unidentified on the previous page was to have said it once.

But in any case the word -- if we do not do that the word "unidentified" should come before human and not before "collections."

MS. CHARO: Right. So the suggestion would be essentially to lengthen the definition by saying, "Are those supplied by repositories from a collection of human biological specimens for which identifiable personal information was not collected or if once collected is not

maintained..." et cetera, et cetera.

MR. CAPRON: Yes. That would be the way of doing it. I actually am not bothered by using the word "unidentified" because we just defined it about 40 words before there on the previous page, 109, but if it would overcome Eric's sense that we are just repeating the word to define it in its own terms.

MS. CHARO: Okay. Global comments before we actually move on to specific recommendations. Steve and Bette?

MR. HOLTZMAN: I am not sure what you mean by "global comments."

MR. CAPRON: Are you worried about global warming?

MS. CHARO: No.

MR. HOLTZMAN: I had a comment on --

DR. CASSELL: Just a little room warming would not be so bad, however.

MR. HOLTZMAN: -- on 101 turning over to 102. It is in line with a comment I made right at the beginning of today's session. If you look at the bottom we are talking about anonymizing samples. 101, at the bottom of

the page we are talking about rendering samples anonymous. That solution would, however, seriously curtail many investigations and we then contrast it with having clinical information. Again you can anonymize a sample and still have clinical information so I am not sure our contrast is correct there. Okay.

Moving down to line 6 on page 102. We say, "Assuming that adequate protections..." and then the parenthesis, "...(including informed and voluntary consent are present) such information gathering could include..." It seems to me it is possible that that could be pursuant to a waiver of consent and so that if we are going to keep the parentheses I think it has to move to after the "and" in line 8, "and (including informed...)" Whatever the request for -- if you have requests for subjects to participate and then you would need informed consent.

MS. CHARO: Others? Bette?

MS. KRAMER: Yes. A global comment. Going back to the comments about where the recommendations are placed in the text. I was just looking through it briefly and just -- I was wondering if we made a format change so that at the beginning of the language where we begin to

discuss what leads up to say recommendation one, if we entitle that recommendation one, and then when we got to the actual recommendation did it in bold and said, "The recommendation one," or something like that. And then it seems as though then there are other areas where there are several recommendations that come out of the explanatory text.

MS. CHARO: So that the use of headings might provide a --

MS. KRAMER: Exactly.

MS. CHARO: -- set of signals. Would that address your concern, do you think, Trish?

MS. BACKLAR: I am not certain. Let me think about this and try to picture it.

MS. CHARO: Okay.

MS. KRAMER: I am looking it over because it is nice the way it flows, the recommendations flow out of the language now. I found that very, very helpful. But it might be that if we break it up so that the sections indicate which text goes -- are followed by which recommendations --

MS. BACKLAR: Well, there was one thing I did

presume and that is that you were going to number the sections and I thought you were waiting to do that so that you would not have to keep changing the numbers as we made changes. Am I wrong in presuming that that was going to happen? There are eight categories rather than six as in the capacity report.

MS. CHARO: Larry, then Alex, then hopefully we will be able to actually move into the text of the recommendations.

DR. MIIKE: Just in terms of forming, you know -- I mean, there are many ways of doing this. I mean, you can, for example, if you are talking about one particular recommendation you can simply indent all the paragraphs relating to it and then -- you know, I mean, there are ways that will catch people's eyes to say that this discussion, whether it becomes before or after the recommendation, is related to this recommendation or you can just do it the way that many reports do is you start off with the recommendation and then have the discussion around it.

MS. CHARO: Alex?

MR. CAPRON: Could we have a little bit of

discussion about the points that Steve raised?

MS. CHARO: Yes.

MR. CAPRON: Because I do not think I agree with him about it and I would like him to illustrate particularly the second point.

The first point was that it -- one response that we think an informed reader might have would be if the concern is primarily harm from having information linked to you why not just make all samples anonymous. And then the answer is that would harm or reduce the value of a lot of research and maybe make certain kinds of research pointless. I was not clear, Steve, what your objection to that discussion was.

MR. HOLTZMAN: I agree with that statement. If you read the next sentence, "Instead the protection of human subjects should take account of the great value for many studies using materials of having access to a certain amount of personal and clinical data about the persons from whom specimens were obtained."

You could have that information. You could fill that statement and still have an anonymized sample because you do not know the personal identity.

MR. CAPRON: Well, so what you want to do there is underline that you might need enough data or enough currently collected data on an ongoing basis for certain studies that you are not really maintaining anonymity. It may be coded and so forth as we go through it but it is still in our broad identifiable category.

MS. CHARO: Kathi --

MR. CAPRON: I am trying to --

MR. HOLTZMAN: I was trying to say -- the point I was trying to be make is that I did not think was fully supported by what was written it.

MS. CHARO: Right.

MR. CAPRON: I understand.

MR. HOLTZMAN: Okay.

MR. CAPRON: But the point is that a certain minimal amount of personal and clinical data can go along with even an anonymous sample.

MR. HOLTZMAN: That is correct.

MR. CAPRON: And so the emphasis of the sentence might be clearer without a full rewrite, "Access to more than a minimal amount or more than basic or more --" I mean, in other words, you have data. This is a 36-

year old caucasian woman. Well, that is not -- that does not identify the person but it may be useful if you are looking at something that you think is linked to sex or linked to age or linked to race. Right? And that -- but at some point you are going to get enough information about the person that they move into our "identifiable" category or you are, indeed, engaging in the back and forth. You know, every time you go into the hospital I want the current medical records to see if you have developed a disease that I think you have the gene for or whatever. So it is the more than minimal. I am trying both to understand and to suggest a fairly simple rewrite of this.

MS. CHARO: If I can intervene for just a moment here. I find that part of my difficulty in following the discussion is because people are using the word "anonymous" or "anonymized" which is not a word we use frequently throughout the report. We very carefully have these defined categories and I worry each time I hear people using it that they might be using in a sentence different than I understand it. I wonder if we can try to avoid that language and be very specific and that means we

will --

MR. CAPRON: Well, we can say -- at that point we can say "unidentifiable" or "unidentified." Whatever our language is.

Now the second point you made around the sentence beginning on line 6 on 102 -- could you just illustrate an example where you think that information gathering in the sense of ongoing collection of medical record data would go on without the informed consent of the person involved?

MR. HOLTZMAN: If one reads the sentence that is in line 5 and 6, "To permit investigators to have access to sufficient identifying information to enable them to gather necessary data about subjects in the sense of continuous gathering such that there had to be the link..." All right. I think that is the sense in which this is. All right. That could happen in the coded situation. I believe an IRB could determine or could they not in a coded situation -- what have we said -- okay -- that they could waive consent and that there is minimal risk.

MR. CAPRON: The sentence in which the phrase

"informed voluntary consent" occurs gives two illustrations. Information gathering including ongoing collection of medical records and requests for the subjects to undergo tests to provide additional research data. I am asking you can you imagine either of those going on without having gotten the informed consent of the subject because that is the only sentence in which the including applies to?

MR. HOLTZMAN: So my question is under the rec's we have stated if you were dealing with a coded situation with what is deemed to be minimal risk research, could the IRB waive consent, including to getting updated information about the subject? If yes then I think we have to move the parens after the end. If not -- that was my question, Alex.

MR. CAPRON: If yes then I disagree with the recommendation we have come up with and I -- because I did not think we were going to let researchers go to people's medical -- current medical records without them knowing that they -- their current medical records are being turned over to someone with whom they have no relationship.

MS. CHARO: Actually we do not say anything about the consent requirements for research on medical records. We only discuss the consent requirements for research on the tissue.

DR. MIIKE: Can I interject here? We are still on page 102, are we not?

MS. CHARO: Yes.

DR. MIIKE: Okay. So then I do not understand this discussion. All this 102 from 101 says that we could make all tissue samples not being traceable and we are simply saying why it is not practical to go that way. And I think I would just simply use David Cox's statements that more and more research means you have got to go back to the well and get continual update of information and right now we are wandering off into informed consent.

MS. CHARO: Well, let me --

DR. MIIKE: That is what we are talking about here. We are not getting into the recommendations.

MS. CHARO: Let me just take the privilege of the chair to remind everybody that the recommendations that now exist refer only to research on the tissue. They do not specify whether or not somebody should have to get

consent under any particular circumstance with regard to going back to the medical record. And the only stuff we have in the recommendations about the medical records comes at the very end at which there is right now a recommendation that has to do with what people who are writing new rules for medical records ought to consider in light of what we are doing on biological material.

We can change that but for the moment we have no -- we are not recommending or controlling the researcher's access or the terms of that access to the medical records. That is highly variable. That was the point of the discussion of the state and federal laws on this. It is highly variable from place to place.

DR. MIIKE: I understand that all but all I am saying is that this discussion over the past ten minutes has been about page 101 and 102 and we seem to have wandered off into the recommendations themselves. All I am saying is that all this was, was a statement saying why, you know, the simple proposition is not tenable in a research setting for biological materials. That is all this statement is saying.

MR. CAPRON: Larry, I think that Steve's

concern was that this anticipates a recommendation or a view as to what the proper arrangement is, whether or not it is a recommendation. This anticipates that if you are going into ongoing collection of medical records linked to the biological samples you are studying or asking people to provide further samples for you, you would need at the outset to have gotten their informed consent through that process.

DR. MIIKE: Yes, of course, but what I am saying is dump the whole paragraph from one to 13 and make just a simple statement saying why we cannot go ahead with making all of this tissue material not connectable to any human being.

MS. CHARO: How about that?

MR. CAPRON: Well, I would disagree with that because I think it sets up the need for the chapter. Look at the last sentence. "Where identifying information exists, however, a well-developed system of protections must be implemented to ensure that risks are minimized..."

MS. CHARO: But that is not inconsistent with what Larry said. Larry suggested that it be -- that this entire paragraph be reduced to the following. Right?

Basically the first sentence, which is, "For most people, the central issue...is harm. One solution is to make it impossible to link the tissues to people under any circumstances. A problem is that there is value to being able to link information to people and, therefore, a more nuanced solution is to provide protections so that the linkages can be maintained and people's interests can be protected.

DR. MIIKE: And we will get later on into the issue that --

MS. CHARO: And later on we will get into the details of what those protections have to be and what the circumstances are that trigger each particular one.

MR. CAPRON: I thought he said cut everything on page 102 from one to 13.

MS. CHARO: Oh, he was exaggerating the way he always does.

(Laughter.)

MR. CAPRON: Oh. So what should I have understood him to say? It is only the sentence -- the assuming sentence that he wants to get rid of?

DR. MIIKE: No, no. I am saying that for this

part of this preparatory statement, this chapter, we do not need this long involved discussion because we are going to -- we are addressing those very same points many other places.

MS. CHARO: Recommendation 1, page 107.

MR. CAPRON: Well, Alta, we can walk away from this but if I were the staff director I would not know what the commission's wishes on this were. Larry has expressed a view about dropping this. I have expressed a view about not dropping it. Steve has a particular problem with the wording of one sentence.

DR. CASSELL: We need a referee.

MR. HOLTZMAN: I thought Alta came up with a nice compromise which was to get the issues on the table and then let us go forward the recommendations so I would support her if you are asking this commissioner.

MR. CAPRON: With all due respect we have been talking about this report for two years and we go away from meetings and we see another draft and the new draft is confused probably because the staff has not had clear enough guidance from us. We ought to be near the end of this report. We have language in front of us. If we want

to delete a sentence because we think it injects an issue then we should decide to delete the sentence. If we want to delete a paragraph we should. I would not be in favor of deleting it and I did not understand Alta to say we should delete it but I do not know where we stand frankly.

MS. CHARO: I think simply as a matter of reality it is impossible to edit a text line by line in a group setting. More than anything else the thing that is useful is to put down on the text specific changes one wishes or to provide alternative texts and these can then be distributed so the people can decide among the versions or they can be discussed on e-mail with people's reactions to them but the word by word in a collective setting is likely to take forever and not allow us to get on to the substantive recommendations.

MR. CAPRON: I quite agree. That is why I wrote the text that we are looking at in these pages here. I rewrote them because I found them totally unclear in the last draft. I circulated that. It went out by e-mail and then it ended up here. This is the first time we have had comments on it.

DR. MIIKE: Well, let me take one last crack

at what I am trying to say. Whatever we are going to use in terms of anonymous. It says, "One simple protection..." et cetera on the bottom of 101. Then it says, "...that solution would, however, seriously curtail many investigations." What follows is not an explanation of why it was seriously curtailed but it says about all the other kinds of things around -- the rest of that does not really follow that statement. It gets into informed consent, et cetera, et cetera, et cetera, and what we should end up here is simply at an -- a little bit of an explanation about the curtailment and the effects of the curtailment of these investigations. Not getting into these other issues. It does not really follow.

MS. CHARO: Eric, did you have your hand up?

DR. CASSELL: No, absolutely not.

MR. CAPRON: Well, Larry, I disagree with you. I think it follows. If you want to spend time on this -- if you want to draft an alternative paragraph, I think Alta's point is right, draft an alternative paragraph and submit it and we will see if people find one or the other a better expression.

DR. MIIKE: Fine.

MS. CHARO: Okay. We will do that.

Recommendation 1. Comments? Okay. Any other comments? No. Going once, going twice.

Recommendation number 2. On this one I do have a comment. I find one part of the language confusing here. The first sentence, as you can see, says, "Research conducted on unidentified samples, whether taken from specimens stored by personal identifiers or those rendered unidentified by some independent investigator." Because I am constantly testing the language back against our four categories of samples I was going to suggest that the language mirror those definitional terms and be replaced with "Whether taken from specimens stored without personal identifiers or those supplied to investigators without identifiers or codes," which is the language of category 2, unlinked samples. Right.

MS. KRAMER: So do you want to use the word "unlinked" so you are absolutely clear that that is category 2?

MS. CHARO: That would be fine or mirroring the language.

Bernie?

DR. LO: "Research conducted on unidentified or unlinked samples does not involve human subjects." Is that what we are trying to say?

MS. CHARO: That would be fine by me as well. Okay. Unidentified.

DR. MESLIN: Just to remind you the suggestion that was floated to remove "identifiable" and "unidentifiable" throughout the text wherever it occurred and to replace it with the paired terms that are relevant, and I will not repeat them, is the intention to make it extremely clear. If you have found that they are there they are probably there by omission.

MS. CHARO: Right. But it is not only that, Eric. It also involves deleting the words "those rendered unidentifiable by someone independent," which is a --

DR. MESLIN: A generic statement.

MS. CHARO: Right.

DR. MESLIN: But text cleaning, not concept.

MS. CHARO: Okay.

Kathi?

DR. HANNA: The last thing you just said, Alta, about removing -- if we take out the phrase

"rendered unidentifiable by someone independent of the investigator" we have lost that independent of the investigator requirement.

MS. CHARO: Well, in the language of the -- where is the exact language now? -- of the definition of unlinked samples. 110. So the samples are already having the links removed by the repositories. It is supplied by the repositories without the links. Do we need to say something even further? Is the concern here that the investigator may have a relationship with the repository? Because otherwise this is already defined to include the phenomenon of the link being destroyed by somebody other than the investigator.

DR. HANNA: Well, the investigator -- I mean, in some cases the investigator might already have the samples and the point was that you did not want the investigator to be the one that not only makes the decisions to unlink them but actually does the unlinking.

MS. CHARO: But --

DR. HANNA: So, yes, you are right if it is coming from a repository. But several of the public commentators said that that is not the only way people get

samples. Very often they already have them and they have them with names on it but to do the research they decide that they want to unlink them and earlier on the commission said that that unlinking should not be done by the investigator.

DR. MIIKE: No. But if we are using our definition of unlinked in this recommendation and our definition of unlinked is it is unlinked. Your example would not fall within this definition.

DR. HANNA: No. I am only saying that in the rewriting of recommendation 2 we lose that requirement and I -- it is fine if you want to lose it.

MS. CHARO: Bernie?

DR. LO: Again, in the interest of trying to move us on, I think someone articulated earlier on the principle that we should make the general rules apply to most cases and when there are foreseeable exceptions we should put those in text. So I would suggest just to make it more readable, "The research conducted on unidentified and unlinked samples does not involve human subject" into the text. We add sentences in commentary to deal with exactly what Kathi said. Investigators may sometimes have

samples in their own hands with identifiers and wish to render them unlinked and this is how we interpret recommendation 2 in that circumstance, namely you cannot do it yourself.

MS. CHARO: Jim and then Steve?

DR. CHILDRESS: I strongly endorse Bernie's proposal. I think it makes a lot of sense here and it would really move this forward.

MS. CHARO: Steve?

MR. HOLTZMAN: There may be also simple effects when you look at unlinked samples, our definition, we use "are those supplied by repositories." Maybe we should say are those supplied to investigators.

MS. CHARO: So that it does not specify from whom. It can be a path lab.

MR. HOLTZMAN: Because if the investigator -- I could get it myself and now in one role and when I am going to become the investigator it is applied to me, just flip flopped.

MS. CHARO: Are people agreeable with Bernie's suggestion? Okay. Other comments on recommendations? Kathi?

MR. CAPRON: Can you be clear about -- are you talking, Bernie, about modifying what is described in unlinked samples or putting -- and, if not, putting what you said at what point in the text?

DR. LO: Some place under recommendation 2. It could be new text.

MR. CAPRON: Before recommendation number 2 we have a description of the unidentifiable samples and on lines 8 to 10 of 111, would that be a place -- I am trying to be quite as specific as possible for the staff so we come away --

DR. LO: I guess I would -- you know, we have gone back and forth. We have two categories of four and we have four --

MR. CAPRON: This is not changing the categories. It seems to me putting it there on 111 on lines 8 -- that describes what we went into this discussion with before Steve's change in language, which was a fine change, to say "supplied to the investigators." But now we have recognized that sometimes the investigators have the materials already so it is not a matter of forwarded to a researcher without identified

codes. We are also willing to count as unlinked those which the researcher has and has someone else -- I mean the language which we are now deleting from line 15 and 16. Right?

DR. HANNA: Right.

MS. CHARO: Kathi?

DR. HANNA: My question was just that you have removed a requirement from the recommendation and you are putting it into the discussion underneath and I just want to make sure that that is what you want to do. You are going to make many of the public commentators very happy by doing that because there was a lot of objection to that requirement that the unlinking be done by somebody independent of the investigator.

DR. MIIKE: But I disagree because there is a definition of what we mean by an unlinked sample.

By the way, I guess these are still clean up things but the paragraph above the recommendation is about unidentifiable samples and I think we are not using that anymore, right?

I think what Bernie is suggesting is clear. We have defined what we mean by unlinked and what we mean

by unidentified and it is simply repeating that in there. And then what he is suggesting is that for the case that you are worried about we make it clear in a short commentary underneath the recommendation that that does not fall within this recommendation and that that is a different situation all together.

MS. CHARO: Bernie?

DR. LO: I mean, Steve then raised the point, which I actually agree but I do not think we have talked about, that maybe by unlinked we mean not just the repository strips it but someone else other than the investigator unlinks it and then we basically -- I think we are modifying the wording of the definition on 110 to include something that is hinted at in the language of recommendation 2.

I would actually agree with that. I actually thought as to how it applies to every single recommendation. And if we do that I think we have to have text as to who does the unlinking because it cannot be, you know, my co-investigator who, you know, keeps the decoding sheet on the desk.

MS. CHARO: Bette?

MS. KRAMER: Right. Apropos that. I think very, very early on, two-and-a-half years ago, we were alerted to cases where clinicians are actually doing research on their own patients so that raises another issue. You know, how do these get unlinked? Who unlinks them for them?

MS. CHARO: Steve?

MR. HOLTZMAN: If you look at our definition of unlinked we stipulated in it that it would be extremely difficult for the investigator, the repository or third party to get back to the identity. I do not know that the focus of how that is to be achieved such as I have to ask a third party -- oh, by the way, it cannot be my best friend who tells me all their secrets -- is really what is important in the recommendation.

We have said that is provided to the investigator and it is unlinked and by that we mean that investigator would not be able to tell who it was. Now whether they do that by simply stripping them off themselves, throwing them into a bucket, stirring it up and then pulling them out so they are randomly assigned, that might be better than having their friend do it.

So I think if -- I do not think we need -- I am thinking. I do not think we need to say anything more in the recommendation. In explanatory text we should just simply say that the method of unlinking should achieve the goal of unlinking.

MS. CHARO: This may be true but it has come up enough that it suggests that some text that talks to it specifically might nonetheless be helpful. One could simply adopt the recommendation as Bernie has amended it and then include in the text or in a separate recommendation, either, that an investigator in possession of coded or identified samples may render them unlinked by having a third party or having an independent person delete the codes and identifiers and thus delink the samples. And that would clarify the situation and allow the main recommendation also to speak to the most general case.

I only raised this originally because I found that the way it was written actually confused me as to its applicability to number 2 and I was not sure reading it if it was supposed to apply to number 2.

MR. CAPRON: Could I have just a linguistic

clarification on the revised? Line 14 on page 111 is now going to read, "Research conducted on unidentified or unlinked samples that does not involve human subjects and hence is not subject..." Is that correct?

MS. CHARO: That is the proposal.

MR. CAPRON: Okay. Kathi, what was the content of the objections that we got which we are going to relieve by this change because the description of the process here was, oh, it is, just as Alta's said, difficult to read it here. We are not clear what we are talking about but we are really moving the same idea over to the definition of unlinked. If we are, then those people should be no happier. If we are making a substantive change we ought to be very aware of what we are giving away, as it were, from what we originally were recommending.

DR. HANNA: It was just the person who was going to be responsible for unlinking. That is all I was referring to. Many people who submitted public comments, mostly from the scientific community, did not like the requirement that we said somebody independent of the investigator had to do that. My only point was if you

were going to take that clause out of that sentence and just put it into the text most people will read that as no longer being a requirement. And that was --

MR. CAPRON: In other words, they will not read our definition of unlinked as a necessary part of the requirements?

DR. HANNA: No, no, no. It is the act -- there is two things.

MR. CAPRON: Alta just said that she had the word "independent" still in the way she put it. Steve did not. Steve said that all that was important was the extremely difficult language on line 9 of 110. Is that right, Steve? And you said it might be, you know, who cares as long as they use some method that will make it extremely difficult.

MR. HOLTZMAN: I think that is what we should care about, yes.

MR. CAPRON: Okay. And Alta when she reiterated things as our chair and the person who is giving directions to the staff by way of consensus statements here used the independent person. Now if what you are saying is that if it is not in the recommendation

people will simply ignore it because they will think that the language on 110, which is a definition, is something they can ignore, I think they are wrong because OPRR, whoever implements this, will put the definitions into the regulations so then there really is not substantive change.

If we are making a substantive change by adopting Steve's view then what we are saying is that what they objected to was what they thought was a cumbersome process of having to bring in somebody outside. Is that correct?

DR. HANNA: Yes.

MR. CAPRON: Okay. Then I am comfortable with Steve's view if it is just a cumbersome process that really does not --

MS. CHARO: Larry?

MR. CAPRON: -- take it seriously but if you are saying if you take it out of the recommendation they are not going to take it seriously then I am not comfortable taking it out.

DR. MIIKE: A couple of things just to respond to Steve and Alta's comment just now. I would not support

it because that was not what we have been discussing over the past few months about what we mean by an unlinked sample and to suddenly switch back and say that the investigator could do it by whatever means and the IRB should look at it and see whether that is true or not, I would not support that.

The second part is simply an editorial comment. The last paragraph on page 110 and the first paragraph on 111 really should be changed now. We are not talking about those two categories. What we mean is the first two should be treated the same. The second two should be treated the same. We are not talking about unidentifiable.

MS. CHARO: Let me run through again the suggestions and get a consensus on each one of them separately. The first suggestion has to do with page 110, line 12, and that is that we talk about -- sorry, not line 12. Line 5. That unlinked samples are those supplied to investigators rather than by repositories but to investigators, no matter by whom, from specimens that lack identifiers or codes. It simply broadens the definition. Okay. And actually it would seem like we might want to do

the same thing on 11 and 12.

The second is that the current recommendation 2 would have its first sentence amended and put aside now whether or not -- the precise language of the text and/or recommendation that would follow.

The recommendation 2, which refers to categories 1 and 2, is going to read, "Research conducted on unidentified or unlinked samples does not involve human subjects and hence..." et cetera, "...consensus."

Third --

MR. CAPRON: You are going to state all these and then we are going to discuss them?

MS. CHARO: I am hoping to hear if there is an objection. I was going to move on to number 3, which is how to resolve the last part of this, which is the concern about an investigator who has an existing collection of coded or identified samples who would like to have them rendered unlinked and what we say about how that is done so that it can then be considered unlinked for the purposes of no longer having a known subject.

MR. CAPRON: Okay. It seems to me that if we adopt change number 1 supplied to the investigator, the

result is that the hypothetical situation in which an investigator already possesses samples because they are his own patient samples or something cannot qualify as unlinked?

MS. CHARO: No. The question is how can he render them equivalent to unlinked so that they can be considered no longer research on a human subject?

MR. CAPRON: Okay. So unless we add language which goes into that, on the face of it, it does not meet it?

MS. CHARO: That is right. That is why we are worrying about it because whether it is supplied by a repository or simply supplied to an investigator, either way, a researcher who currently had a collection of materials would not be able under this particular set of definitions to have those materials considered unlinked.

And yet, as Steve has said, there are circumstances under which investigators would like to render those materials into an unlinked kind of form and then have them treated as category 2 materials and the question is what is required to do that? Is it an independent third party or is it simply that it meets the

definition of difficult and do we want to put it in text or in a recommendation?

MR. CAPRON: And when we went into this discussion today it had to be an independent third party according to recommendation 2.

MS. CHARO: Well, actually when we went into this discussion today we had not realized that there was a little bit of a logical inconsistency buried in the recommendation vis-a-vis the definitions and that has kind of been revealed by the conversation.

Bette?

MS. KRAMER: I think it is unrealistic to think that an investigator who is working with samples say from his own patients if they are ever going to be unidentifiable to him or unlinked and they just have to go into the category of identifiable.

MS. CHARO: So -- Larry?

DR. MIIKE: I think that -- I am not clear what Alex was saying about whether -- Alex, were you saying that if the prospective investigator had these samples in his or her possession that they could not be -- meet disqualification no matter what?

MR. CAPRON: With the language -- if we simply adopted Steve's language vis-a-vis lines 5 and 6, we would say the only way you could meet it if you had the specimens and now you want only samples from them you would have to turn the specimens over to a third party so that they could supply to you unlinked samples from those specimens. Is that correct? If that is the only -- we only did change one and change two. We would, therefore, take the language about third party, which is explicit in recommendation 2, and make it implicit in the definition of unlinked samples. Is that a correct statement?

MS. CHARO: I think so.

MR. CAPRON: Okay.

MS. CHARO: And, yes, we --

MR. CAPRON: And that is consistent with what Bette just said because she said if you are dealing with your own samples --

MS. CHARO: Right. But what Steve has explained to us and I think David as well is that you might, for example, have a pathology lab that has several hundred tissue samples taken from several hundred surgeries that you have been involved with.

MR. CAPRON: Right.

MS. CHARO: And you would like to be able to do research on them. You have reasons why you do not want to, for example, deal with all of the issues surrounding traceable and identifiable samples and, therefore, you would like to delink the codes that currently exist on this collection of samples from the samples and just work with the biological materials and the question is how are we going to signal to people that they may do that and what are the details of that procedure.

Bernie and then Steve?

DR. LO: Actually Steve had his hand up first.

MS. CHARO: Okay. Steve instead of Bernie.

MR. HOLTZMAN: So in terms of the change that -- the first change of "by repositories" instead to "investigators," I think Alex actually was making somewhat of a grammatical point that you cannot supply things to yourself. And I actually did not intend that. I was implying -- I think that is what he has been driving at here. Since you cannot supply it to yourself it cannot be unlinked. Okay. And I never intended that and I do not think anyone else was reading it quite that way with Alex.

So my thought was really just confronting the issue of someone can wear two hats and so it may not come from a repository. Now what we care about is that the investigator not have the knowledge that comprises the link. So that was my idea of saying make it to the investigator. The important thing is that in the hands of the investigator, the individual investigator or researcher, they do not have the knowledge of the identity.

I think with respect to the substantive issue as we have discussed it in the past of having a third party perform the delinking, certainly as I thought about it since the goal is delinking, I always thought of the paradigm of, well, you have got to get someone else to do it.

I was literally just sitting here today and the kind of case I had in my mind, Alta, is the one you just suggested. We go to someone. We want diminimus pathologists. They have got 10,000 samples for prostate cancer. They just go grab 1,000. They rip off the names and they actually do some work up with this as a collaborator but they really have no idea of which they

came from other than the diminimus Gleeson score, that is degree of the cancer, right.

And it just struck me as we are sitting here is that when we really care about, and I feel it is generally lacking and we can come back to this, is that I do not think we have talked enough about institutions mandating that there be appropriate procedures, whatever they are, to ensure that when things are claimed to be unlinked they are, in fact, unlinked. When they are claimed to be confidential encoded, they are, in fact, appropriate confidentiality standards.

So that was all I was reflecting. Am I going to, you know, lay that in front of the commission, you know, and say we have got to not -- we have got to get rid of this third party? No, that is not the issue. I am just asking us to think about the substance of what we care about.

MS. CHARO: Bernie and then Larry.

DR. LO: Actually my comments follow along in some sense to Steve's. I think the problem -- I like the general definition that you just proposed that the unlinked samples are those which the investigator obtains

in a way that has -- does not have identifier codes and you cannot crack it. We are now sort of looking on a sort of special case, which actually turns out to be common enough that it has evoked a lot of public comment, where the same individual is both the head of the repository or the repository and the principal investigator or the scientist.

And as with everywhere else in research in human subjects when one person plays two roles things get really messy and I think what we are saying is that you -- when there is this role conflict you have to really be -- we are not closing the door and saying you cannot unlink them but we recognize the possibility that you may not be able to keep separate those two roles that you are intending to do and you ought to have appropriate procedures in place to make sure that what you are doing really ends up with an unlinked sample.

That is where I put Steve's comments that you do not have to pay attention to how you are going to do this and whether, in fact, the sample that you end up with really is extremely difficult to link back up. So I think there is a lot of explanatory text that needs to be gone

into here. There are obviously differences. If I am the director of a gigantic pathology lab with 10,000 samples I am not going to be able to sort of unlink. If I am just sort of at a little, you know, community hospital and I only have 50 samples and I am studying 25 of them I probably just visually can identify every slide as to who it belongs to.

I think we just have to sort of -- in applying general principles they do not always fit particular cases very neatly and we need to not let the particular sort of unusual cases sort of swallow up the entire general discussion but somehow keep it proportional so that we have a general rule and a little sort of mental footnote that, yes, in this special situation it generally will get a little bit tricky and here are some ways to help you through it. But make sure that we do not end up spending so much time on peculiar situations that we end up gutting the big picture.

I think it is really important to distinguish the individual pathologist who thinks that on Saturday afternoons and evenings she is going to sort of do research, genetic research, is not what we are driving at.

We are really talking about the bigger repositories where if you have got 10,000 or 100,000 samples that it is going to be tough to link no matter who does the unlinking.

MS. CHARO: Bernie, are you suggesting that --

DR. LO: I have got Alex all upset.

MS. CHARO: I just want to understand your bottom line. Are you suggesting that in our discussion, in the text that will follow, and if there is a recommendation, any other recommendation that follows, that the focus should not be on the precise specific requirement that there be an independent -- a person independent of the investigator who severs these links in order to render the samples into a condition where they can be treated as not, you know, a human subject but instead to pick up on Steve's language that focuses on appropriate procedures, guarantees, something that is as of yet unspecified?

DR. LO: No, no. I think the general should be unlinked samples are those the investigator receives in a format that does not have identifier codes.

MS. CHARO: Okay.

DR. LO: So it is changing from supplied by --

MS. CHARO: Right.

DR. LO: -- to received by or something.

MS. CHARO: Right.

DR. LO: Then we say there is a special tough case where the same person is both the supplier and the recipient and you have got to think about it a little bit because in some cases it may be trickier than in others to actually carry this out. And I think that, you know, given that it seems to me that most of the time -- I mean, to me it is still an exception. It is not the general case. So the general rule is most of the time when you have got the same person both being the repository and the investigator it is a little trickier and that deserves a little discussion but I am just saying make that discussion a little discussion and not the predominant discussion.

MS. CHARO: Alex?

MR. CAPRON: Two points. I am not clear from Steve's comment whether your assumption that this is a little infrequent occurrence is correct. I mean, he describes situations in which the repository becomes a co-investigator with the genetics or molecular biology group.

Is that not correct, Steve?

MR. HOLTZMAN: If you are talking about large scale genetics kinds of studies, more and more you are going to find in the major medical centers that the pathologists are clinician researchers and they have a tremendous interest in collaborating all of our studies. Having said all that, all of our studies are done not in unlinked but in coded and we end up getting IRB approval anyway.

MR. CAPRON: But I am not worried about whether or not you are doing it in a legitimate way but you are doing it in a way in which if the word "investigator" means anything it includes the person who was originally holding the materials.

The second thing, Bernie, is the example that -- the reason my hair stood up at the end of your example was, well, we are concerned about these big pathology labs and we are not concerned about the pathologist with 50 samples who decides in the evening that she is going to do genetic studies on them and she knows who those 50 samples are. I am concerned about that person and the notion that that person would proceed on the basis that she is not

dealing with human subjects when she knows who those 50 samples are and so forth, it just does not satisfy me at all.

DR. LO: Let me -- on the second point I agree. I am very concerned about it. I do not think it is going to happen that much. So the total number of people harmed because their privacy has been invaded I think is relatively small. I agree it is egregious when my next door neighbor, the pathologist, starts rummaging --

MR. CAPRON: Okay.

DR. LO: Absolutely. So I misspoke and I meant it in numerical terms and not in sort of --

MR. CAPRON: Okay.

DR. LO: -- severity of the insult and the wrong.

MR. CAPRON: If that is the case I would agree with you that we ought not to do something that totally distorts what makes good public policy sense for that one rare case.

(A) I have no basis for knowing how rare it would be and (B) since it is easy to anticipate that it

would not occur I believe we can address it in a way which does not distort it. I thought that is what we were doing when we came into the meeting today. I liked recommendation 2. I understand the view that as written, particularly using the word "unidentified" and not using the word "unlinked" as well, it was confusing.

If we think of our recommendations -- our descriptions rather of the four categories as eventually regulatory language, which seems to me the only way they make sense, then I think we should be fairly precise about what goes in there and we come down to the issue -- and I do not know where you stand on this issue. I heard Bette say that basically if you are dealing with the samples that you have collected about your own patients you ought to treat them as coded or identifiable to you and you should not have this out.

I do not understand the word "supplied to" as suggesting self supply. If people read it that way then I am not satisfied with the change in language. I would want to clarify supplied by some third party, a repository or otherwise, to the investigator.

The notion that you supply to yourself what

you already possess -- we could have angels dancing on the head of a pin around that but it does not seem to me at that point you are supplying it to yourself. You already possess it.

Therefore, to me the question is, is the description of lack of independence going to be overcome by some unspecified procedures that we are now going to be writing in for the first time here?

And I am back to what Alta said a while ago. Show me some well worked out language in the definitions and in the commentary and I can decide then. I cannot decide in the present confused kind of state of this discussion.

MS. CHARO: Steve?

MR. HOLTZMAN: Actually I think we can decide because I do not think it is really that confused because I think what everyone cares about is that when the investigator has it that it be true -- if it is going to be called and treated as unlinked that it is truly unlinked and that the investigator cannot tie the results to the person.

And it seems to me it is a very simple

question. Do we wish to mandate that the delinking is done by a third party or not? I think we intellectually recognize that a third party does not ensure true delinking. We also recognize that self -- the investigator delinking themselves can genuinely delink them. But having said that, one can nevertheless say we believe it should be done this way and it just really comes down to whether the commission simply wants to specify the what or wants to specify the how.

MS. CHARO: Larry?

DR. MIIKE: I actually now agree with Steve. I misinterpreted what he was proposing. Because the definition by the change to investigator still retains the fact that whether you are the investigator or the repository, if they are different or the same, still has difficulty or a mere impossibility in being able to link it. So I think it would cover the situation that Steve is talking about. If Steve is talking about I am at the pathology lab and I have 10,000 breast cancer cases and I pull out 1,000, strip them all and then pick it out, as long as it meets the test that that repository still is unable to do it, then it is an unlinked situation.

Because when we are talking about unlinked we were talking even in an independent repository that sends to an investigator, even that repository should not be able to link it.

So I feel comfortable with the change from "by repository to investigator."

MS. CHARO: What about the question, however, of -- as Steve was putting it -- whether we are going to insist on the language of a person independent of the investigator when we are talking about a situation in which an existing collection, which is coded or identified, is going to be transformed into one that is unlinked? This is probably not, in fact, exceptional. It is probably somewhat common so it is worth being real clear if we are going to, as Steve put it, to put how are the -- the how or the whom. I am not really sure they are all that specifically separated but --

MR. CAPRON: Steve, would you think it was responsive to the kind of direction you want to go for us to have an explicit recommendation in addition to what is here identifying the responsibility of the IRB to ensure that the process used fulfills that objective and further,

either in the recommendation or in commentary, to note that the IRB may -- I do not know if it is a matter of presumption but where the investigator is also the repository and is taking the responsibility on rather than giving it to someone else of developing a method of the strip -- following the stripping process through --

MS. CHARO: Alex, I am sorry. I do apologize for interrupting you but I think that there may be a misunderstanding here because there will not be an opportunity for the IRB to have that oversight since by delinking we are saying it is not a human subjects experiment and the IRB will have no role.

MR. CAPRON: Well, I am glad you reminded me because we have actually had that discussion before and what we are then saying is that there really is not assurance in the process that the standard of extreme difficulty is going to be fulfilled and I go back to Kathi's comment that there will be a lot of joy in Mudville or whatever when this change occurs because a lot of people will either think that we do not care about it anymore or we put it somewhere in the commentary and they just do not have to really worry about it.

So it is not the onerousness of the process of delinking, whether it is by someone else, it is really that they -- that this just falls off the radar and that they can say I had a list of 100 samples, I ripped them off, I numbered them 1 through 100 and I now no longer know -- oh, by the way, the list from which I took it was alphabetical to start off with.

MS. CHARO: Bette?

MR. CAPRON: It still is alphabetical.

MS. KRAMER: I am trying to think about the example that you just raised where the investigator is working with samples which are identified or linked and now wants to strip them of identifiers to what -- escape the regulations. Is it a valid assumption that if he -- the investigator has been working with them in a linked fashion --

MS. CHARO: They may not have been working with them already. It may be that this is simply a collection. For example, the Department of Oncology will probably have a collection of tumor samples that they -- or specimens, sorry, that they have collected over the years and a member of the department would like to do

research on them. The member of the department does not need to have the samples coded or identified -- coded or linked for her purposes, right, and so would like to simply sever the links and work with the samples -- with samples taken from these specimens.

We are now in a situation in which we are simply asking ourselves what is the responsible way to handle that knowing that as we currently have structured this, right, at the moment at which an investigator takes away those identification tags and those codes, we are declaring that her subsequent work on the samples is not work on a human subject and, therefore, she will never go to the IRB. She will not even have to go to her department chair to ask for an exemption from IRB review. She will simply make a judgment in her own case that what I have done now means I am not working with human subjects. Remember the process of stripping identifiers off in itself research. So that does not trigger a need to go to the IRB.

MS. KRAMER: But, Alta, aren't those specimens going to be -- I mean, in that case is the investigator and -- are the investigator and the holder of the

specimens one and the same because if it is the oncologist aren't the specimens going to be in pathology and there is going to be a separation?

MS. CHARO: Bernie?

DR. LO: There are a number of issues that may be worth trying to sort out. Steve raised the question of whether we are most concerned with the objective or the goal as opposed to the means of a process. Should we be most concerned? Should we focus more on whether, in fact, when the researcher gets the samples they really are virtually -- extremely difficult to link back or are we going to be concerned more with the process by which they got to that alleged state?

And I guess I would put my vote for trying to look at the outcome rather than the process because it is -- you know, that is the goal you are trying to get and the process is not in exact congruence with that.

Alex raised another question that is extremely important and that is what is the verification that, in fact, this is actually happening and he views the IRB as an important procedural safeguard to make sure that just because I call it unlinked it really is unlinked to some

objective consideration and I think that is an important concern because there are certainly ways of doing it that do not measure up and I should be held accountable of whether it has been done in a way that really renders them unlinked.

MS. CHARO: Steve?

DR. LO: Then -- let me just finish.

MS. CHARO: I am sorry.

DR. LO: There is a third issue because we are using terms, and I think the public commentators used terms that I think cover a vast variety of situations. When we say, you know, I have samples and I am an investigator, what does that mean? I mean, I may have samples in that I am the chair of pathology and I am, you know, responsible for all the slides and the samples at UCSF hospital. I do not -- it seems to me that is very different than a much smaller operation where I have personally been involved in the clinical care of that patient and particularly I think with pathology have a visual memory of what those, you know, that associates slides with individuals.

So I think that, you know, we need to sort out

the extent to which people can link samples that do not have, you know, name, social security number or anything else because of information that is actually in the sample and readily obtained without fancy genetic analysis.

And somewhere it says now I am an investigator. In what sense am I an investigator? There are honorific investigators.

I would, I guess, say to Steve that if my role in your research project is that I have supplied you a 1,000 or 10,000 samples from this data bank I have built up and we make an arrangement, and I want to further my career and I want to get my name on a lot of papers but all I have done is supplied you with the samples and did not really participate in the analysis of the research, which I think is what is meant, frankly, by a lot of people who hold a lot of specimens. I mean, frankly, I think they supply the raw data, either patients or samples. They are not really part of the investigation. I am less concerned about that than if I am actually involved with the analysis of the data and going back and saying, "Oh, actually by the way, number, you know, 374 I actually remember --"

(Simultaneous discussion.)

DR. LO: Right, exactly. I mean, see, that is to me the real concern. It is the -- in the process of what I am doing, is something going to be like that?

MR. CAPRON: (Not at microphone.)

THE REPORTER: Your microphone, please.

DR. LO: Then finally let me just say in terms of independent of the investigator, I am not sure what that means either. I mean, if I am heading a huge department -- I mean, you know, we are talking about large, large departments here and not something where I am the chief of pathology and I have one poor administrative assistant who does everything else. If it is a large department, in some sense they are not independent of me because, you know, I am their boss in some ultimate sense. It does not mean I can sort of put the screws on them and say, you know, slip me that list or else, you know, you are never going to get promoted or you are going to take a pay cut.

Whereas, I would say, you know, a very small unit where there is only that other person and me there is a lot of -- there is a lot more concern about kind of

letting things slip.

So I think I am not sure what the public commentators had in mind. If it is a big organization it seems to me, yes, there ought to be -- it just does not make sense to do the kinds of projects Steve is talking about without a lot of procedures and there ought to be someone whose job it is to prepare these samples and do it independently. Just like you have biostatisticians who look at your data in a relatively confidential way sealed off from the principal investigator.

So I just think we sort of sort out, you know, Steve's comment about is it the process versus the final outcome. We need to address Alex's concern about is there some oversight on a claim of an investigator that I have stripped them and now they are really unlinked and now the IRB does not have to look. And I think we need to sort of try and sort out what people are really, you know, concerned about when they make these public comments.

MS. CHARO: Steve, you had a hand up?

MR. HOLTZMAN: Partly in answer to a question. In a typical case the pathologist we are working with genuinely is a collaborator so it is not just the

honorary.

Again I think the idea of a third party is a typical kind of way to try to achieve the goal. Okay. And it is because I wholeheartedly agree with Alex's comment about anonymization gets you outside and you are no longer dealing with human subjects research and you are no longer subject to IRB so you ask who is the police person.

Again I keep coming back and saying have we paid enough attention to this report to institutional mechanisms and safeguards? And if we moved it up to there and had some recommendations about that, I think we might -- we could include if we wanted to about third parties but we might have something even stronger than just this one place where we are saying there is a third party.

I mean, it is -- clearly if any one of us was running a hospital and you read this rec and it did not even say anything about third parties and you cared about it and you thought it was important you would be sending out to your investigators, "By the way if you have got samples and you are going to use them in an unlinked way you better be using them in an unlinked way, here is the

policy in the hospital to ensure that it is unlinked."

MS. CHARO: Alex?

MR. CAPRON: I want to suggest that despite the fact that the regulations do not presently contemplate this since we are making other recommendations that they do not contemplate that we have separate recommendations on unidentified and unlinked. And as for the unlinked that the recommendation is that they presumptively do involve human subjects until the IRB has concluded. And if Steve has in mind other bodies within the institutions that would be more adapt at providing the necessary certification that they have met the standard of extreme difficulty, fine.

Steve, I would be open to --

MS. CHARO: Well, actually, Steve, can I intervene just for a moment?

MR. HOLTZMAN: Can I just ask a question? All unlinked would be presumptively not unlinked?

MS. CHARO: No, not at all.

MR. CAPRON: Not all --

MS. CHARO: Actually, Alex, please, because what you have suggested now is a discussion exactly on the

question of the status of exempt as opposed to nonhuman subject. I do not know if you realize you recreated that conversation that had not yet been shared with everybody.

MR. CAPRON: Okay.

MS. CHARO: Was that your intent?

MR. CAPRON: I think we have to get into that but probably not at 5:00 o'clock.

MS. CHARO: What time is it exactly?

MR. CAPRON: It is 5:00 o'clock.

MS. CHARO: What time were we supposed to end today?

MR. CAPRON: 5:00 o'clock.

DR. MIIKE: Alta, are you saying -- am I correct that what you just said is that we are going to have a discussion about that specific --

MS. CHARO: Let me -- let me give a headline news version of something people can contemplate overnight and then we can discuss it tomorrow at the time that Harold selects.

During the course of the commenting on all the recommendations many of us sent our comments directly into staff. We did not send them to the whole e-mail list. I

had sent in a comment suggesting that we actually should be treating unidentified and unlinked, category 1 and category 2, slightly differently. That category 1 is genuinely no human subjects. Nobody has a clue which human being on the planet is being studied.

Category 2, we know the class of people being studied. We know that it is these 50 particular people. We have got -- you know, we know who they are but we do not know which sample goes with which person. And that that really is the study of those 50 people. They are human subjects but that they should be -- but research on their samples should routinely be exempted by -- from IRB review because it meets all the qualification -- it meets all the criteria for exemption and that has to do with the personal identities not being readily ascertainable.

It allowed for us to have some flexibility with regard to the question of small groups where you actually can figure out who it must be. It allowed for some better consideration of group harms. And exemptions are granted in institutions by different people depending on the particular institution's choice as explained in their multiple project assurance.

It could be the department chair. It could be the president of the school. It could be the IRB administrator. It could be the IRB chair. Institutions have a choice of how they want to construct it.

And when this suggestion was made and then it was discussed with a couple of other people on a call having to do with the recommendations the conclusion was, well, this is complicated enough and it is kind of a change late enough in the game that you do not want to necessarily get right into it.

You might want to hold it and I was holding it until later on after we had gotten through the recommendations but since it was raised now it does in this particular case as well offer an avenue for addressing Steve's suggestion, which is for unlinked stuff -- somebody wants to unlink their stuff, all they have got to do is just have their department chairs sign off that this is a way to do it that is responsible.

That is not to say it is a good recommendation, this whole idea, but we should probably talk it out when there is more time.

Steve?

MR. HOLTZMAN: Just a question for someone who has been asking for months and months and months between -- about the OPRR interpretation, this is a way of distinguishing the 101 or 2(f) versus the 104.

MS. CHARO: For those of us who find it hard to believe that two phrases that say different things can mean exactly the same thing it was satisfying to find a subtle distinction in meaning between the two provisions of no human subject and exempt from IRB review but nonetheless --

MR. HOLTZMAN: Human subject research.

MS. CHARO: Human subject research which is exempt but that is just intellectual satisfaction. It is not necessarily good policy.

DR. LO: Just so we are clear on this, does this mean that some time tomorrow when we have a little more time we are going to readdress this issue that Alex originally raised and I take it was discussed in conference calls? If something -- what assurance do we have that something that is claimed to be outside the purview of IRB review really ought to be outside the purview in an individual case?

MS. CHARO: You know, when I raised it there was a conference call among the people who had given a lot of comments on the recommendations and when I raised it on the conference call, interestingly enough, it was Alex who actually seemed to be not completely enthusiastic about the suggestion at the time in that context. As a result the idea was maybe it is not going to be worth discussing or maybe it will not be worth doing. I think it is Harold's call tomorrow. It is certainly not the most essential thing for us to discuss with regard to the recommendations.

MR. CAPRON: As long as we have the independent investigator -- of the investigator language in 102 -- in our recommendation 2 I was satisfied in our not drawing the two categories separately. If we -- once we take that out I think it makes sense to say if we are going to take Steve seriously and say there should be an institutional mechanism for certifying that the unlinking process is a good process then that has to -- then the unlinked samples need to be addressed separately from the unidentified samples.

DR. MIIKE: Alta --

MS. CHARO: Larry and then Trish.

DR. MIIKE: -- since I was on that call -- but you raised the issue about treating them separately even with the independent investigator language.

MS. CHARO: Yes. This was not the provision that triggered my thoughts on this.

DR. MIIKE: Yes. So, I mean, but -- so that is quite a different scenario.

MS. CHARO: Trish?

MS. BACKLAR: And it seems to me that if you go that route then you take care of the disparity of the different kinds of issues that may come up from a very small group to a very large group that somebody is seeing that because otherwise --

MS. CHARO: Right.

MS. BACKLAR: -- I am concerned what Bette is saying and what Alex was saying, and what you were saying about the confusion between the investigator and the repository or the investigator and the clinician, and back to all those old problems. So I am for that and would be concerned if we do not do it.

MS. CHARO: Would it make sense perhaps to put

this off until tomorrow because to get into it now -- it seems late in the day to do it and it is being sprung on people out of no where and it will give you time overnight to consider the implications of it because it has implications for multiple parts of the report to have an opportunity for unlinked stuff to have somebody at an institution have to sign off and go it is correct, you do not need to see the IRB after all. Right?

We convene again tomorrow morning at 8:00 a.m. in this same room.

DR. MIIKE: Can I ask something? Can you just sort of ask us right here whether we are going to be having some major problems with the rest of the chapter?

MS. CHARO: We --

DR. MIIKE: That will give us an idea how much time we have on this.

MS. CHARO: Okay. Knowing already that we have got chapter 4 -- is that the ethics chapter? -- chapter 4 that was never discussed today, and we also have one detail having to do with the expedited reviews, are people anticipating major problems with the remaining recommendations? You can never tell because I would not

have predicted that recommendation 2 was going to wind up taking an hour's worth of time. Okay.

Are you still willing to come to the meeting, Larry?

Eric, do you have any closing comments before we dismiss people for the evening?

DR. MESLIN: I was only going to say that it is not absolutely essential that there be a long discussion of chapter 4 since it sounds like the discussion of chapter 4 will --

MR. CAPRON: There we go again.

MS. CHARO: No, that was me. I am sorry. That was a piece of paper on my microphone.

DR. MESLIN: -- will in some ways determine changes that we will be making so do not let that be your disincentive.

We also have some other materials that I think we will just pass out tomorrow rather than now. I think I will just stop talking and see you all tomorrow at 8:00 o'clock.

DR. CHILDRESS: And, commissioners, if we can gather at 5:30 just outside the door here.

(Whereupon, the proceedings were concluded at 5:06 p.m.)

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