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GENETICS SUBCOMMITTEE

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P R O C E E D I N G S (11:00 a.m.)

DR. SHAPIRO: I'd just like to open today's meeting, thank commission members for being here. We have important work to do today and tomorrow.

Today of course our agenda focuses on what we think of as our general information activity, dealing with banked tissue and so on, tissue banking, this particular area, and I'll turn to Tom in a moment, because he will chair today's session.

We have at 12:15 set aside some time for public comment. We will reassemble after that to continue our discussion. Around 4 o'clock, or at least after the session on tissue banking is done, I will talk to commission members about certain matters of commission business. That shouldn't take too long, just to bring you up to date on budget, timing, other kinds of logistical issues, reports planned for the rest of the year. Then we will adjourn. And of course tomorrow we have a long day's session on human subjects. That begins at 8 o'clock and adjourns at four in the afternoon. We have quite a packed day tomorrow, going from 8 o'clock, as I said, to four.

Let's turn our attention now to today's business.

DR. MURRAY: Thank you. I want to welcome you all to the first meeting of the I Survived Dolly Club. You're here; that is the only qualification for membership.

We have until about 4 o'clock today to try to push

forward our work on the use of tissue samples in genetic research. This is work, you may recall in the distant past, that we were busily engaged in when we were rudely interrupted by a sheep. But we are going to pick it up again. Today is devoted in part to recovering our momentum, but also to making some progress over where we were before.

I have a number of comments I will make later about what I think some of the key choices are that we have to make. But I want to just quickly, in five or ten minutes, run through what I think are some issues in the preparation of the report, going from the timing of the report's release to issues of process, personnel and schedule. I'll do it briefly now, and then we can revisit it at the end of the day, when we have had a chance to really sink our teeth into it.

We have been saying that a release date for the tissue sample report tentatively would be the end of this year. I still think that may be realistic. We may wish to revise that, based on our deliberations today. But I would like to have by the end of today a pretty firm handle on at least our expectations about when the report would be released.

Now, end of the year, if you take it to mean literally December 31, may have some disadvantages as a release date. We may want to have our work finished in advance of that time, but that is a time of the year when, if you want to release something so that no one at all notices that you have done work,

that is probably about as good a date as you can find. If we feel that way, I suppose that is what we will go for, but I hope and expect that we won't feel that way. We may want to move it either up a couple of weeks, although even then, by mid-December, things are pretty lost, or we may wish to move it back a couple of weeks. I would regard that as no failure, particularly if we did it with the understanding that that was the better way to enhance the reception of the report.

About process. Based on our experience with the cloning report, and my gratitude to the staff of the commission, Kathi Hannah, various contractors and the commissioners, nonetheless I would like us to be guided by a couple of principles.

As commissioners, our job should be to guide the preparation and not act as primary writers of the report. Secondly, the meetings that we have ought to focus on key substantive issues, including the most difficult and controversial matters primarily, rather than on fine-tuning the language of the document.

I think we really had no choice working with the cloning report but to proceed as we did. But given six months or so to finish our work on this report, I would like to see us hand off more of that sort of labor to NBAC staff and contractors, and have the commissioners be more deliberative in the rules.

Those are not self-evidently true propositions, so let me ask if anyone wants to comment on those. Silence either means you're all asleep, you all consent, or the ideas were so stupid, nobody thinks they are worth commenting on.

DR. SHAPIRO: Well, there are other alternatives, but let me just say one thing. I think that those premises depend very much in my mind on the quality of people that can be identified to do the work. That is, those initial drafts as we all know are critically important and have a huge influence on the final outcome, no matter how deliberative we are in reviewing them.

So I certainly accept the premises, if we can do it with that proviso, that people can be found to carry on that job.

DR. MURRAY: Thanks, Harold.

DR. MIKE: I think we probably have to assess the other meetings, because we have a September meeting and we will probably have to have one more after that, and maybe you will throw in another subcommittee meeting.

The other comment I would make is that if we remember what our contract papers were like under the cloning and what our final report looked like, it is not a simple matter of taking the contract papers and coming up with a report.

DR. MURRAY: Yes, I agree with that. Is there general agreement among the commissioners currently present that to the

extent possible, that we can get professional staff and contractors to do the final drafting, that that is a desirable thing? Is that a role we wish to hold for ourselves?

DR. COX: Actually, Tom, I'm really keen on that, if we as a group can come up with an outline first. My only concern about it, if we don't have an outline, is that certain areas will fall through the cracks. So if we can lay out what the turf is, and then make sure that we have somebody addressing all the issues, then I would be very comfortable.

That is my only concern with what you suggested, which otherwise seems great.

DR. MURRAY: Right, I didn't see this as a hands-off relationship with the authors, but very much an engaged relationship with the commission members setting out what needed to be done, and providing lots of feedback.

DR. COX: Because part of it is that what the commission papers frequently do is, they rely heavily on what other people have already said. In these areas, what other people have already said is very heavily weighted towards certain stakeholders on one extreme side or the other.

DR. MURRAY: I hadn't noticed.

DR. COX: As in most things. But I think it in those areas where there is nothing written that we want to make sure that we explore to find out if there is nothing written because there is nothing to write, or because no one has bothered.

DR. MURRAY: Roughly, in terms of people that we need to work the report, including some current NBAC staff, we will want some contractors to write background papers. Wherever possible, we would like the background papers to be directly usable in the body of the report.

Secondly, I think we will need someone with advanced training in an analytical discipline, reasoning and writing, preferably in philosophy or the philosophical side of theology, someone who I would see in the best of worlds attached to NBAC, at a minimum for the period of time that we are working on this particular report. It might be a more continuing role. I don't have any reason to prefer one to the other right now, but I would like to have somebody there to see the report through to its conclusion.

I would like to have them on board, if possible, no later than the first of September. Earlier would be preferable. I would like to have their primary responsibility be to this subcommittee for the preparation of this particular report, so that they not be in a conflict of loyalties situation. It should be understood that they are there to work on this report.

Again, ideally, I would like to have a second person on staff at NBAC for the duration of our work on this report with advanced training in law and/or public policy, to work on those aspects of the report. We may not be able to have those, I don't know.

I would like to see in addition probably on contract a skilled writer-editor, preferably with experience in preparing an official report, similar to the one we envision, a Kathi Hannah, if you will. I suppose, depending on how people felt, we could talk to Kathi about this. I know she is here. She is hiding in the corner, but it won't work. Really, someone who can make sure the report, even though it is authored by many different people, will speak in one voice, will be coherent, will not be repetitive, all the things that a really fine editor and policy analyst can do.

Lastly, NBAC personnel to assist in the preparation of the report, both administratively and substantively. I know that at least one member of the NBAC staff has been assigned to help us with this report, and for that I am grateful.

That is how I envision the personnel. I think maybe we should hold off scheduling until later, but I can tell you that I envision three meetings. We'll go over that at 3 o'clock. It is almost 11:15, so we are not behind schedule yet. I would like to ask Sheri Alpert, who has been -- how is it described? Are you loaned to NBAC?

MS. ALPERT: That is as good a description as any.

DR. MURRAY: Okay. Sheri is going to loaned to NBAC by another branch of the government. I leave it to her whether she wishes to reveal which branch she is on loan from, or not. Sheri is going to help us sort through some of the privacy

issues, particularly the legal and policy implications.

PRIVACY ISSUES IN GENETIC ANALYSIS OF BANKED TISSUE

MS. ALPERT: Hi. As Tom said, I am on loan from -- I guess I have to 'fess up -- I am a policy analyst with the Office of the Privacy Advocate at the Internal Revenue Service. It is not necessarily an oxymoron, but I'll leave it to you to determine whether it might be.

What that office does is not only look at the legal questions of, does the law allow us to do X, Y and Z with personal information about taxpayers, we more importantly deal with the issues of, should we be doing these things to begin with. So we get into a lot of the ethical kinds of issues and do a lot of ethical analyses or whether or not the IRS should be doing various things that they want to be doing with personal information.

I have been there about six years. I have had an interest in privacy issues coincidentally since 1984, when I discovered my first computer database, or actually discovered how to make my own computer database, and have been interested in issues of genetics since my sophomore year in high school. So I have had a longstanding interest in all of the issues that you are dealing with.

I have provided an outline in small packet, if you want to follow along.

What I basically did in this outline was to come up

with as atomic bomb survivor a list as I could come up with, on the various types of privacy interests that are involved with banking of tissues and genetic analyses of those tissues.

I don't think it is going to be possible to cover all of them in a report by the end of September, which is the time through which I am assigned to NBAC. But I can certainly do a subset. The reason for giving you the longer list is so that you can determine which of the issues that you find are most compelling and most important for the work you want to do.

Just generally, I wanted to go over some of the types of privacy interests, just generally, not in relation to anything in particular, but just a broad philosophical kind of domain, what different types of privacy interests are.

The first thing to say about privacy is that there is no universally accepted definition of what it means. I describe it in the things that I have written as being related to notions of solitude, autonomy, anonymity, self determination and individuality. So it is a very personal notion. Within some socially and culturally defined limits, privacy really allows us the freedom to be who and what we are. By embracing privacy, we exercise discretion in how much of our personhood and personality we show with others. We generally feel less vulnerable when we can decide for ourselves how much of our personal sphere will allow others to observe or scrutinize.

Jeff Lyman, who has done a lot of writing on moral

aspects of privacy, has described privacy as a condition in which other people are deprived of access to some information about you or some experience of you.

Autonomy is the first of these interests that I have highlighted. That refers to the capacity of members of society to function as uncoerced individuals. That definition comes from a report that was done by the National Research Council, called *Private Lives and Public Policies*, dealing with statistical uses of information.

It is also related to respecting peoples' wishes not to be accessed in some respect. I am referring here to the philosophical dimensions of autonomy, as opposed to court interpretations of what autonomy is, because the interests really encompass more than the court addressed in *Griswold*, for instance, in its decision there. Further, that National Research Council report stated that the protection of personal or individual autonomy is really a fundamental attribute of a democracy. So it is important stuff.

Informational privacy. In the information age, it really is an information age conception of privacy. The less opportunity individuals have to limit access to their own personal information by others, or to limit the amount of personal information they have to give up to others, whether it is voluntary or by coercion, the less privacy they have. It involves when information should be communicated or obtained,

and what uses of it will be made by other people.

It is also useful in looking at informational privacy issues to distinguish between what has been called aesthetic versus strategic privacy interests. The language I am about to use will sound familiar to some of the people around the table. Aesthetic privacy means that personal information is restricted as an end in itself, that is, in instances where disclosure is inherently distressing or embarrassing. Strategic privacy, on the other hand, is the restriction of personal information as a means to some other end. The issue is not the experience of disclosing personal information, but the longer-term consequences of doing so. Both strategic and aesthetic informational privacy interests are at risk in the context of genetic analysis and stored tissue samples.

The next is freedom from intrusion and surveillance. To a large extent, this encompasses an individual's interest in anonymity. Ruth Gavison has characterized this interest by saying that we enjoy our privacy because no one is interested in us. The instant that someone becomes interested in us, they could find it very easy to take all that privacy away.

Now, freedom from encroachment on or violation of dignity, a lot of folks lump this together with autonomy interests. I break it out separately here because of the context in which we are talking about the issues. I am breaking it out here to accommodate notions of group interests or

collectivity interests. Whether interests related to cultural, racial, ethnic, religious or family groups, as long as people identify themselves fundamentally as members of a group, encroachment on that group can be viewed as a violation of the individual's dignity and the dignity of the group.

Next, I am moving on to different types of tissue banking storage. I'll go over these very quickly, because these will be obvious to most everybody.

DR. SHAPIRO: Can I ask a question?

MS. ALPERT: Yes.

DR. SHAPIRO: I don't know whether you want to be interrupted when someone has a question, or you want to wait to the end. Whatever you want is fine, as far as I'm concerned.

DR. MURRAY: I was going to ask the same question. How do you feel about it?

MS. ALPERT: Go ahead. Ask away.

DR. SHAPIRO: Do you and others who think about this carefully, how do you deal with the issue of what is asserted or speculated about in this area, versus what is -- I was going to say real; I understand that is the wrong word to use, but how does one deal with in these areas trying to assess any one of these issues, and deciding between just what is assertion -- is assertion reality? I guess that is what I'm saying here; individual assertion is reality here.

MS. ALPERT: To some extent, yes, certainly in the

context of -- when I deal with the issues in the IRS context, I often tell people within that context when they don't necessarily understand views that the public might have about some of these issues, the bottom line is, perception is reality. That is a different context, obviously, because it is a law enforcement context, so conspiracy theories rule the day, to some extent.

But to a large extent, yes, perception is reality in these cases, because the issues are so personal in nature.

DR. CHILDRESS: In your identification of privacy issues, it seems to me that one might distinguish an interest in privacy as a state or a condition, state of affairs, when people, for example, leave you alone because they don't give a damn. That is one thing.

Another kind of privacy interest though is in the right to privacy, that is, the right to be able to control others' access. So it seems to me that the privacy interests bring those together, but sometimes it may be useful to distinguish them.

MS. ALPERT: Yes. I tend to like to think of privacy in terms of access limitation as opposed to control, because it is -- in an informational perspective, anyway, control connotes a type of power that an individual may have over their own information, that they cannot possibly have or cannot exercise in the way things occur in the natural world or in the unnatural

world.

It would mean, for instance, that in a secondary use, I still maintain control over someone else's ability, or I can control what that person does subsequent to my disclosure of that information to them. That may or may not be part of my bargaining power in providing that information to someone.

So if I can limit the access, in other words, by limiting the amount of information that I give to them to begin with, which to some extent is controlled, but not quite, that turns out from a policy standpoint anyway to be easier to deal with.

Tissue storage types. Again, these will be pretty self evident. Clinical -- and in clinical I also lumped things as blood banks and bone marrow banks and those sorts of things, research, forensic, commercial and identification, like Department of Defense.

Now, I do want to show you something that was --

DR. HOLTZMAN: Sheri, what did you mean by commercial, commercial as distinct from clinical research?

MS. ALPERT: This is what I'm talking about. This is a printout of a Web page that is a commercial banker of DNA. Now, it will take you a minute to find it in here. It is right there, right next to campus colognes, if you want to know what your alma mater smells like. I don't know what that means. This is literally a Web page that is out there for people to

bank their own DNA. Then when you click on the one for gene line, this is where you go.

Now I'll read off some of the stuff at the bottom. This of course won't be on microphone. One of the things they promise is strict confidentiality, no insurance companies will find out the information. A medical advisory panel. It is safe, easy, non-invasive, although how I'm not sure, unless it is just a swab. There is even an 800 number and peace of mind about the future, all for \$174.95.

DR. MURRAY: Cheap.

DR. HOLTZMAN: But what do they do with it? Do they test it?

MS. ALPERT: Apparently they just bank it. It doesn't -- it is just for storage purposes, in case your grandchildren want to come back and blame you for their disease, right, exactly, assuming you have grandchildren in 25 years.

There are other companies out there, or at least one that I know of, that doesn't go at it this way, but they do offer -- or did anyway, about a year ago -- a storage facility for your DNA, for remains identification, if you want to bank your infant's DNA, for instance, or your own.

DR. SHAPIRO: But these categories that you have deal with reasons why this stuff was collected in the first place, as opposed to other ways of identifying the categories.

MS. ALPERT: Yes. So it wasn't necessarily, Steve, to

get to your question, dealing with pharmaceutical companies. When I say commercial specifically, it would mean to be more --

DR. HOLTZMAN: I think Harold's point is that some of your categories were in terms of the purpose, and you shifted in terms of the sponsor and who was doing the activity. I just needed to understand. So this would be a particular purpose in perpetuity, posterity.

MS. ALPERT: Right. Now, looking at the relationship of the privacy interests on stored tissues, the informational privacy interests are really among the nuts and bolts of the issues. It is what information is gleaned from the tissues. Obviously, this depends on the context in which the tissue was collected. The question of who has access to that information, how long the information will be used, how will it be maintained, how long will it be maintained, will it be disclosed, if so, how and to whom, and under what circumstances, et cetera, any possible permutation you can think of, of where information from the tissue analysis may go would be an informational privacy interest in stored tissue.

The autonomy aspects, this to me deals mostly with issues of notice and consent. How much and what the tissue source is told prior to the tissue removal, about how it will be used, who will have access to the tissue and the resulting information, and whether or not the patient has any rights with respect to his or her tissue.

I'm not necessarily talking about what is called ownership, I'm dealing with that separately. When I say rights to the tissue, rights in the case of a clinical trial, rights to remove their tissue from the trial at a later point. That is one of the things I'm talking about.

To some extent, these issues parallel the informational privacy interests. In the case of informational privacy interests, the information flow attaches to the analysis gleaned from the tissue sample. The autonomy interests, the same sort of interests surround the actual physical tissue itself, but the same sorts of interests are there.

Freedom from encroachment on a violation of human dignity. This is where I am placing the physical activity interests in tissue banking. Again, whether it is culturally, religiously, ethnically or family based, these are interests that people share because of their collective uniqueness.

For some of these groups, the interests may hold that the sanctity of the human body and its component parts and systems are inviolate. In other groups, the interest may simply relate to the fact that certain characteristics may be associated with them in ways that they find undesirable to disclose, again, back to the aesthetic versus the future privacy interests.

One aspect that I find interesting in the tissue banking discussion, or the whole issue, is that within it, you

have something that is unique to privacy interests when they are normally discussed in other contexts. That is, the artifact of the tissue itself, this thing, whether it is a spot on a slide or if it is a piece of an organ or a piece of a tumor, whatever.

From an ethical perspective, the relationship that we feel to that thing, that artifact, has not been analyzed a lot that I can find, anyway, and I'm not talking about within a context of medical or cultural anthropology. It could be that I just haven't run across the entire literature on it yet. But to a large extent, this would encompass the notion of how we view our own bodies and portions thereof.

It is a question of a fundamental interest any of us as in our bodies and our body parts. Do we care if someone has a part of our body, or a tissue from it, and which tissue or which part, and what the context is. Those are all variables that really have not been -- again, as I have seen it, and please, someone tell me if they have seen it and I have just missed it -- but I just haven't seen a lot of those sorts of interests addressed in much of the literature.

For instance, in the Moore versus University of California, the question would be, would he have cared about the use of his spleen and all of the other tissues that were taken from him had there not been a financial stake for him and for the doctors who were treating him. I'm not sure that that sort of a question has been examined.

Yes, Rachel?

DR. LEVINSON: If you will forgive the phrase, I think there is a body of literature on various religious beliefs and attachment to body parts. For example, when a leg is amputated for surgical purposes, it may often be kept for the time that person dies, and would be buried with him, and other parts of the body may be treated similarly.

MS. ALPERT: Right, yes. I was trying to distinguish between group identity, if you will, or cultural or religious identity and just trying to get to more fundamental -- and there may not be one, I don't know, but just trying to get to a more fundamental level of how, just as human beings, irrespective of any particular affiliation that we may have in our social sphere, whether or not we have any interest in -- if this was my tissue and it was sitting here, would I have any interest in this apart from my religious or my cultural or other sorts of interests that I have in my life.

I'm not sure if I'm making myself real clear.

DR. MIKE: My guess, not knowing anything about this, is that it is a matter of degree. If you got my arm in a formaldehyde versus a piece of my blood, my interest is going to be very different.

MS. ALPERT: Absolutely. And if I am providing either a urine specimen or a blood sample to my doctor, I will feel very differently about that than I would if I was supplying

either of those fluids to my employer. So it is not only tissue dependent, it is also context dependent.

MS. HYATT-KNORR: It also has a lot to do with knowledge.

MS. ALPERT: Sure.

MS. HYATT-KNORR: If you don't really know what is going to happen to it, and it is not really important to you, nothing will follow. But if you have an idea what it might be used for, or you might not agree with that use, then you have a whole different situation. So knowledge has a lot to do with it.

MS. ALPERT: Absolutely. Yes?

DR. CHILDRESS: In some ways it may be difficult to separate the individual and his or her interest in the tissue from his or her religious, philosophical, cultural and other beliefs. So I think that may be part of the difficulty. But there is a literature from the late '80s, particularly Tom Murray and others, contributed to a very important body of literature that tries to get at how we think about tissues that have been removed. A lot of the debate in organ and tissue transplantation obviously relates to it.

MS. ALPERT: Yes. In some of my thinking about this issue, in trying to divorce a person's interests in their tissues from their other influences, religious, cultural, ethnic, et cetera, it may be that what ends up happening, or the

interests that end up flowing from that tissue are inferential. In other words, yes, this is here, this tissue is right here, and my main interest in it is, I want to know who is going to have access to it and what they are going to do with it and what they are going to do with the information gleaned from it. So in some ways, you get back to the informational privacy interests, and that may be where the analysis ends up heading.

It was partly a question of whether there was anything that makes tissues unique from other things.

DR. MURRAY: Without going in detail, let me endorse that. There is something about bits of our body -- and as Larry points out, we don't feel the same about all bits of our body. William James, who provided the thought experiments, said, imagine if you filled a tumbler with your own saliva; would you wish to have it back again, and most people said no, whereas they might have different sentiments about severed limbs or such things.

So it depends very much on context. I think Jim referred to my work on the relationship between the provider of the tissue and the recipient and ultimate users of the tissue, on how that exchange is to be understood. So I think we can take the point that it is a useful category, but then we can move on to the next one.

MS. ALPERT: I would just add that the purpose for the giving of the tissue as well, if it is specifically for the

purpose of organ donation, that is very different than if it is to provide a blood sample.

DR. MURRAY: That's right. That is what I mean by the nature of the transaction.

MS. ALPERT: Oh, I'm sorry. Just because of the way the mechanics of doing the slides worked out, I am just reordering some of the things that were on the outline that I had provided. Now I'm going to be getting into specific privacy interests in stored tissue.

I suspect that the first two are fairly clear, so that I won't necessarily have to go into much detail, since much has been written about it, and the subcommittee has already had discussions on those two issues, being the right to know and not to know, the content of your genetic code, and whether or not that is even an option, depending on the context or the reason for which the tissue was given, and its effect on relatives.

These interests deal more with the genetic analysis of the stored tissue. I think you clarify that. So looking specifically at genetic analysis of stored tissue, then these issues I suspect become clearer.

The next thing I'm going to deal with is a blurring of the distinction between clinical and research uses. That is a process that is actually paralleled in the field of medical informatics, just how general medical information is treated.

The reason this matters is that trust is a very

fundamental part of the relationship between a physician or other care provider and a patient. If it turns out that a patient is an unwitting tissue source, or his information is gleaned from the tissue in a way that he hadn't anticipated, that patient upon finding out may be more inclined to withhold information important to subsequent treatment, or may be less inclined to seek care in the future. Or on the other hand, they may be pleased to find out that their tissue is furthering medical science. Again, it is a very personal sort of thing.

A lot of these issues are also very tied up in the consent process, and in what people are told about what is going to happen with various parts of themselves, and information about those parts, and I'll get into some of that a little bit more.

The liability issue. What I am referring to here is not legal liability necessarily, or -- yes?

DR. MURRAY: That is not corresponding to what is up there.

MS. ALPERT: Oh, thank you. Secondary uses. See, even I confuse myself. Secondary uses. I just got ahead of myself. Thank you.

DR. MURRAY: I was just confused.

MS. ALPERT: So was I. Not anymore. Thank you, Tom.

Now into the issues of secondary uses. These probably are among the most difficult, or the most -- well, definitely

the most difficult to deal with.

On the informed consent, it is mostly the process in this case of whether or not in a clinical setting, for instance, the consent form that the tissue source is asked to sign is coupled with the consent for treatment. In other words, when I go in for surgery or whatever, am I given one consent form that says you consent to surgery and, oh, by the way, you also consent as part of signing this document to having the tissue used for other purposes, educational, research, et cetera, et cetera, are those two things coupled into one consent form.

How the consent process is designed, how much information the potential tissue source is provided about what will happen to the tissue and the information gleaned from it, are fundamental issues relating to the informed consent process.

Custodianship and trusteeship of the samples. Notice I didn't say ownership. It is my contention that the custodial relationships, or looking at these from a custodial standpoint may be more appropriate than thinking about these tissues in terms of ownership. I say that, because the legal discourse of ownership, the way the courts have looked at these issues, have a lot of economic -- well, they are based solely on economic interests, and the non-economic interests really do not play much of a role in how these issues are decided.

Ownership of either information or tissues is a source of contention between privacy and patient advocates and those

with commercial or research interests in the information and the tissues, and the point of contention is often a conversation stopper, so it might be beneficial to try to steer that conversation away from proprietary and economic interests and towards the issues of what is at stake for the individual as well as the research community and others. It brings up issues, or it can allow issues to be discussed in terms of how individuals and groups should be treated along with their tissues and their information with dignity and respect.

DR. SHAPIRO: You want to avoid ownership, because the legal discourse on this focuses on economic issues, which you feel may not be so appropriate in this case.

MS. ALPERT: Not that they aren't appropriate; it is just that the economic interests are the only interests that are generally taken into account within the legal discourse that has run up around tissue samples and other interests or other issues where proprietary interests have been at issue.

DR. SHAPIRO: But I understand the suggestion that we might want to expand the rhetoric used in this, in order that other interests get accommodated. On the other hand, it is hard to know how to think about custodianship and trusteeship without solving the ownership issue. You are a trustee for something, you are a custodian for something, and you have to deal with it one way or another. But I understand the basic points; you want to expand the discussion. That seems reasonable.

MS. ALPERT: Yes, that is, basically trying to find a word that isn't quite as charged as the word ownership is, or property is.

DR. EMMANUEL: For the vast majority of situations, though, making money on the tissue is not what is at stake, right? There is something else. So whoever owns it, there is another purpose which we need to solve the procedures for.

DR. HOLTZMAN: I think another way it has been talked about by some is that using ownership as the fundamental concept is somewhat poverty stricken, in terms of the relationship in terms of which we stand to our distinct body parts in different kinds of contexts.

So for example, I believe in the organ transplant writings and the thinking about that, I think what was articulated was the notion that you don't stand in relationship to ownership to your donated parts, even if you donate them.

So I think to endorse your point, how do we get a rich enough discourse here that would then give us guidance without falling into a, who owns it and therefore they determine based on autonomy the private property right that they can do with it what they want.

DR. MURRAY: Let me see if I hear that correctly, Steve. What I take as an endorsement of treating it under the kind of rubric that Sheri has put up for now, without trying to evade the issue ultimately of ownership, but this is a much

broader way of thinking about it.

DR. HOLTZMAN: Yes. I'm not sure what the right term is. I think it is the broad issue of how do we stand in relation. It is fascinating to me, I can sell my plasma, but I can't sell my blood. I sometimes get into a different relationship to my plasma, at least in the United States, than I do my blood. I believe that it worth thinking about. DR.

MURRAY: The explanation is not in a matter of principle, it is a matter of the history of the two different parts.

DR. HOLTZMAN: But the history could be very important.

DR. MURRAY: Oh, it is, it is very interesting.

DR. HOLTZMAN: In where we wanted to store tissue, and we probably could learn from it.

MS. ALPERT: On decision making for subsequent use and analysis, I am thinking here in terms of how institutional decisions are made to provide others with access to tissue samples or to information gleaned from those samples, to what extent are the tissue sources' interests taken into account.

In some of my readings, it is sort of apparent that the IRB process does not always do an adequate job of taking those interests into account. That is not a criticism of the IRB process; it is to some extent the fact that so much of this technology and so much of the ability to do genetic analyses are occurring at a rate that many folks on local IRB are frenzied to

try to keep up with, to try to understand what some of the implications are of the research protocols that they are trying to make decisions on.

IRBs are increasingly faced with making decisions on the initial collection and subsequent use of tissues in genetic analysis, so that is what I am talking under there; there are other interests as well in that, depending on the purpose for which the tissue was collected.

Under liability, it is a question of who is responsible to whom for what legally and ethically. Again, I have liability in quotes, so that it doesn't necessarily connote just legal things. It involves questions of recontact for tissue sources for retrospective analysis of stored tissues. It could also involve issues of process oversight, to insure that tissue sources' interests as defined in the informed consent and the regulatory processes are kept in the forefront.

Now, a lot of the kind of analysis I do on privacy issues, and I have done a lot of public policy privacy implications sorts of things, mostly in the context of increasing computerization of personal information. To some extent, that dovetails with increasing sophistication of genetic analysis, the furtherance of these technologies, the implications they will have for personal privacy.

The first one is anonymity in research. I know you have discussed this one. Promises of anonymity are becoming, or

are going to become, forthcoming as genetic analyses become more sophisticated. That has obviously not only implications for individuals, but also for collectivities.

Under the group privacy issues, this is an issue that is distinctive in arenas where increasing technological sophistication makes the aggregation of information about groups of related individuals easier to accomplish. These are relevant issues, whether or not the samples are studied as anonymous aggregate samples or individually identified.

I also put up linkability with other personal medical information. I hesitated, because I don't want to get into the genetic exceptionalism discussion necessarily, of whether or not genetic information is different. But it is relevant to this discussion of what is likely to happen to the information that is identified and identifiable.

To the extent that increasingly sensitive and granular genetic information ends up in a person's medical record, that person may become more at risk in a variety of ways, simply because of how many people -- it is almost easier to say who doesn't have access to your medical records than it is to say who does. The universe of who doesn't have access is becoming much smaller than the universe of who does. As medical records are increasingly computerized, that will become more and more the case.

**PARTICIPANT:** Is it your view that genetic information

shouldn't be treated any differently than other medical information? Or is it your view that genetic information is the same as other medical information?

MS. ALPERT: I was really hoping to avoid having to answer that question. I haven't made my mind up yet.

DR. SHAPIRO: The Fifth Amendment is not an option at this point.

MS. ALPERT: I'm sorry.

PARTICIPANT: One has an objective standard, the other one is very --

MS. ALPERT: No, I realize that. In a clinical setting, I don't have difficulty with genetic information being part of the medical record; it already is. I just haven't figured out in contexts other than clinical how I feel about the issue yet, or how I would deal with it. So that is kind of a maybe answer.

DR. MURRAY: Sheri, I had a question about -- I'm not sure what the brunt of the point was in that last issue of linkability.

MS. ALPERT: It tangentially gets to some of the issues of bias and discrimination, and use of genetic information. The more sophisticated genetic information is that goes into a medical record, the more you are placing an individual at risk for misuse of that information or for just a wider variety of people having access to it, and being able to

use it in ways that the individual would not have anticipated at the time that information got into the medical record.

That is true with medical records or medical information generally, but it becomes more sensitive when you put more sensitive information in the record itself.

DR. MURRAY: All right, I understand.

MS. ALPERT: The rest of my presentation is going to speed up, because I haven't found a whole lot of current public policies relating specifically to privacy issues or privacy interests in stored tissue. I'm not talking about genetic discrimination in health insurance and genetic discrimination in the workplace. Leaving those issues out, because that is where most of the legislative action is, and I am still frankly in the process of digging through on a state level what is going on. But as far as federal laws, there really isn't a whole lot.

Proposed federal legislation mentioning stored tissue. Again, most of them deal mostly with workplace and insurance discrimination. There was a bill that was introduced by Senator Domenici, Genetic Confidentiality and Non-Discrimination Act of 1997, S. 422. It did deal with some of these issues, and was actually ~~modelled~~modeled after Jordennis' genetic privacy act, Jordennis et al. It has been withdrawn from consideration though in the last month or so, after the Senator's staff was fairly well convinced that it wouldn't have passed anyway in its current form. So the bill is probably being redrafted and will

be re-introduced at some later point.

Steve had provided a listing of some of the state laws that had passed, again mostly dealing with workplace issues or insurance discrimination. There were six states that in 1997 passed laws dealing with those areas, a couple that were not on this list. One was Indiana, and another one was Oklahoma, which just passed a resolution to form a task force to look at some of the issues. So there is a lot of stuff going on in the states. That is just 1997. There is a lot of stuff that has already been enacted.

As far as regulations are concerned, the most relevant are those that are dealing with informed consent from the FDA and from OPRR. That is all I'll say about that.

Under general practice and procedure, what I am talking about here are those procedures that have been adopted voluntarily. For instance, relevant to any standards that institutions have to meet to be accredited either by the joint commission or by another body. I haven't investigated enough to know whether there is a whole lot out there, but that is what I intend by that heading.

International policies. This would include the convention that was recently adopted by the Council of Europe and by Hugo, by World Health Organization and others. There is also a document that is out for comment, but I assume it is comment within Canada, since it is a Canadian document. It is

the code of conduct for research involving humans, and has got some very good information in it, and it looks like it will be quite a useful document. I have pieces of it here somewhere.

There is a chapter dealing with informed consent and with privacy and confidentiality, stored tissue samples, genetic analysis. So there is some good --

DR. SHAPIRO: What is the date on that?

MS. ALPERT: I'm sorry?

DR. SHAPIRO: What is the date on that?

MS. ALPERT: May 28, 1997. So it has just been out on the Web not too terribly long. It was put together for -- it was reported to the President's Medical Research Council, the National Sciences and Engineering Research Council and the Social Sciences and Humanities Research Council, and is waiting for translation of the final version, before it becomes final.

DR. MURRAY: Sheri, it might be useful, not right now, but if the URL for that be distributed to the commission later.

MS. ALPERT: Sure.

DR. SHAPIRO: I think we did distribute an initial copy of that. It sounds like a new draft. I think we have an initial copy, but it may have changed in some significant way; I just don't know. So it would be useful to have it. We had one back about eight, nine, ten months ago.

MS. ALPERT: The last couple of slides are areas where a lot of the analytical stuff needs to be done. These are

obviously not exhaustive, but on specifically identifying the consent process, because again, to me it is very important whether or not in a clinical setting the person who is going to be the source of the tissue has an opportunity to separately consent for treatment from consent for use of tissue, as well as other contexts, and whether or not the legal and regulatory protections that are currently in place or that are being proposed are adequate.

A lot of these obviously depend on what the initial analysis shows, as to what the solutions are. So I will leave it at that for the moment, but put that as a place marker of an analysis that can be done.

You have to follow up on that, whether additional protections are needed, whether the consent process needs to change or needs to be reconfigured in some way to address some of the issues the analysis will point to. Again, the custodial kinds of relationships and responsibilities analysis, and the oversight of the use practices.

That one to me is important, in that it allows an oversight process to insure that the terms to which people are agreeing to provide their tissues are being adhered to. There is really not much of an oversight mechanism now in place apart from OPRR. I am talking about something that maybe is not quite as formal as that, but that could get to a lot more than OPRR can get to, within the context of what they do.

That's pretty much it.

DR. MURRAY: Thanks, Sheri. Any questions or comments?

DR. COX: I have a comment, or comments. I feel overwhelmed, Sheri. I think that you have been atomic bomb survivor in the things that are laid out, but I have been sitting here, asking myself why I am feeling overwhelmed. To lay out for me the kind of focus in this outline that I am most drawn to, it is in the information and in the informational privacy.

Then we say, why did we as a group not pick on information, but in fact pick on stored tissues? Because we thought they may be more tractable to deal with. In fact, for me personally, they have the potential for information that hasn't even been realized yet. So they are actually deeper than just information, because it is information that is yet to be realized.

So in that context, it is not that these other issues are not important, but how all these issues relate to that, I think I am extremely interested in, so one can control the tissues in an attempt to control the information.

I guess what I am believing is, since the tissues themselves can have this yet to be realized information, that is a key issue I would really like to -- just personally. I am interested in other peoples' comments about this, but it is a

key issue I would like to really pay attention to, because it is one of the ones that is most troubling to me.

I haven't seen it addressed very much in that context. It is behind what a lot of peoples' comments and concerns are, also behind a lot of peoples' approaches, like, we will control the tissues so we won't have to worry about the information.

I think I have muddied this more than clarified it, but the bottom line is, out of all this information, I am looking for something to have be a life raft here. It is the potential information in the stored tissues that I would really like to focus on.

DR. SHAPIRO: David, are you saying that it is because this information has some unknown potential that makes it somehow different? That is, it might be used in things you perhaps cannot even imagine today?

DR. COX: I guess what I am saying, Harold, is not even potential, but what the information is. We don't even know what the information content is. Certainly in the context of genetics, we can posit a guess about the form it might come in, but in most situations, as complex as it is to talk about privacy with respect to information, we at least know what the hell the information is.

Here, we have tissue samples that we don't know what the implications of the information that might come out. That could be either for good or for bad. So in the case of for

good, we may not be able to contact people to let them know, if we haven't thought about it. So I'm not putting a value on whether it is good or bad, but just that it is an unknown. It is a source that sits there, allowing us to generate more and more information.

So that to me is what makes this different from just privacy of information by itself. Maybe it isn't different; I don't know.

DR. MURRAY: There is a useful distinction that sometimes gets blurred in discussions about genetic privacy. I think David has hit on it. I just want to see if it is the same one that I tried to make before.

That is, between genetic, quote, information that so-and-so has, a certain allele of a particular gene. That is information. It could be put into a computer code, it could be written in a medical record. That is information pretty much like any other information might be recorded.

Then there is actually genetic tissues, which are potentially unlimited forms of information that might be drawn even from a very small sample of tissue, including the individual's entire genome and perhaps other exposures to retroviruses in the course of a lifetime, not even what was inherent, but what has happened in the lifetime. Is that the distinction you would make?

DR. COX: Yes.

DR. MURRAY: Okay. It seems to be a very important distinction. In one sense, the tissues are -- the information may be there potentially. I suppose we should have a physicist here, talking about potential energy and kinetic energy. The information is potential, but it can't be extracted without a considerable amount of effort with current technology, nor can information be recorded electronically and easily accessible. It remains hidden within the tissue itself.

DR. COX: And I would just say as an addendum, Tom, something that has made this real to me recently is several research discussions, where there is lots of adjudication over who gets access to the DNA, because the DNA is limited. It is not in the form of a cell line.

So the research solution, one that I myself suggested, was, why don't we just make a cell line, and then we will always have plenty of stuff to do whatever we wanted to do. That is the specific example of what I am talking about.

DR. MURRAY: So there are bits of David Cox floating around in different test tubes?

DR. COX: No, not mine, but potentially, because it is a limited resource. Otherwise, -- it is a limited resource to glean information, as opposed to an unlimited resource, where even stuff you haven't thought about yet, you're going to have plenty of stuff to figure it out.

DR. MURRAY: Let me just hammer the distinction one

more time. In genetic information, where you have -- this is the sequence or this is the name of the allele this individual has, that is information easily codable, put in a medical record, et cetera. But in a way, that is the end of it, that is the information. You could correlate it with other information you have about the individual, perhaps, but that's it.

With tissue samples, you have this resource where the information is not readily available. Information per se is hidden within the tissue, in that sense. So one can get hold of a tissue sample and may have nothing useful, but if one had the technologies to extract information, one could extract almost limitless information from it. It is the potential to extract information, rather than the information itself.

DR. COX: From the point of view of genetics, we don't have the technology right now. With a small piece of tissue we could get all the information out, and we would be done. But we are technology limited right now, we can't do that. So we can't get it all out at once, so we need continual access. But it won't be that way forever, probably, but it is that way right now.

DR. MIKE: Maybe I'm just in another world here, but to me, the crucial issue here is that it is not the information aspects of it, but the linkage to individuals. All of the discussion I just heard could apply to endangered species and research on endangered species, or a search in pharmaceuticals

for rare plants and trying to propagate and store and those kinds of things.

So to me, the key in all of this discussion about stored tissue samples is the linkage to real persons. That is the key point, that it is no different than any other kind of scientific research.

DR. COX: That's right.

DR. HOLTZMAN: And I would completely endorse what you're saying. I look at the title to Sheri's outline, privacy interests in the genetic analysis of stored tissue samples, and I find myself rewriting it: public interest in the medical analysis of stored tissue samples. Then I say, if I am balancing those two issues, what would be the crux? How do I achieve the public benefits of medical analysis of stored tissue samples while dealing with potential privacy issues? It tends to lead one right towards the issue of anonymity and whether or not it is identifiable.

DR. MIKE: There can be simple solutions with complex consequences. We could anonymize everything, but then you end up with something that would be very valuable to the individual, but you are faced with a dilemma about, do you anonymize at the very beginning, not knowing what the consequence will be? And if you don't, what happens?

Anyway, we can propose very simple solutions to it, but as I say, the consequences are what we are worried about.

DR. GREIDER: But you actually lose information if you anonymize everything. You are choosing then to get rid of a large amount of information, so the information content per se changes if you anonymize.

DR. COX: Can I say, Larry, that I completely agree with you that the linkage to the individual is important, but I don't think that that is any different in terms of information, electronic or otherwise, or stored tissues.

What I was trying to do was say, what is different about the tissues themselves as opposed to the information. But linkage is a critical component, as are all these other issues addressed when we talk about privacy of information. There is a whole slew of them.

I agree that with respect to privacy of information, this public versus private balance and linkage to the individual is a critical point. But I don't think that is unique to the tissues per se. It is unique to the whole discussion of information.

DR. CASSELL: I'm intrigued by what David said. Anonymity may not be able to provide information to the individual at another time that turns out to be very important. We have had a number of occasions in which the price of the protection of the subject has been the loss of information, the inability to protect somebody in the future, just as the price of restricting cloning research has been, will we be able to do

this in the future. I think we are going to bump up against that throughout the whole term of this commission: the question of, what is the price in lost information, lost scientific advantage.

At the present time, what we tend to do is to say, it is not worth the price. The price is too high. You must be able to give that person information about them. You must be able to continue on.

Just as a statement about the future, I think there is going to come a time when we begin to shift, as, it may well be worth the price. After all, because you can't do something now doesn't mean you can't find your way there a different way. But this is another area.

I feel that the intrusions into the personal are so enormous, always rationalized on things like that: well, we want to be able to help them in the future. If we actually looked at the risk-benefit analysis, two helpings for 200 injuries, is that really worth it. That is something that we are going to have to keep in mind as we do this.

DR. BACKLAR: One of the things that is interesting about this is that we might want to give people their choice in whether they want this information to be available to them or not.

DR. CASSELL: Yes, but choice implies the ability to make a choice, the knowledge to make the choice, the

understanding of the implications of a choice. In these instances, people may not be able to make that choice. It isn't clear yet what the implications are. Sure, it looks like, I want anything that will help me in the future, against some vague loss, but the vague loss may be in fact much more destructive than the help is helpful.

So I think you're right, we always want people to make a choice. After all, it is their tissue, isn't it? It is their tissue. But it isn't just their tissue, it is a shared understanding of a relationship to the personal.

DR. MURRAY: Carol wishes to speak, but I have to ask Henrietta a question. Henrietta, I know there are public testimonies scheduled at about this time. Do you know how many there are scheduled for today?

MS. HYATT-KNORR: I haven't heard from anyone. Is there someone present who wanted to make --

DR. MURRAY: Most of the papers seem to have to do with the human subjects issues. I didn't know if any of the public -- I just need to know how many people intend to give public testimony today, so we will permit time before lunch for you to do that. I don't see any hands. Do you see any hands?

MS. HYATT-KNORR: No, but some material is in writing.

DR. MURRAY: Very well, so we may continue our conversation until 12:30. Carol?

DR. GREIDER: My point was a brief one in response to

what Trish said. That is, if we are dealing with retrospective analysis of stored tissues, there really isn't a chance to give people a choice, or there might not be.

DR. HOLTZMAN: Tom, I have a question. As we commented the last time, the genetics subcommittee met, before Dolly, I guess it was, took over our lives, we commented that there has been an enormous literature written in this whole area, with a lot of different and strong, good arguments on both sides, articulating what are the important distinctions.

We have a few pieces of representative samples handed out today. We could start with the Clayton Wright piece on the one hand, which may or may not have been redistributed, and the David Korn position on the other, and start to articulate what are the issues at stake, instead of having to re-invent them

I'm just wondering what our process is going to be. When I look at this paper about privacy, it is one particular take on it. Even if we wanted to look forever on this thing, I know where I would start. We want a very reasoned position which a lot of good people spent a lot of time on. So I'm just wondering, what is our process?

DR. MURRAY: We will be talking about the positions again today. Zeke is out of the room at the moment, but will be helping us to revisit the conversation we began back in March, about the ethical issues.

What Sheri was -- we were asking Sheri to do was to do

this particular take, say, look, if you see this as an issue about privacy, what might one say about it? What here is relevant and ought to be incorporated or acknowledged in whatever report we write.

That is really what I would like to turn to right now, in the 12 minutes or so. We have Sheri Alpert until the end of September, two and a half months. What would you like her to do? What would be the most useful contribution she could make to our report on tissue samples, given this synoptic view of how a privacy expert thinks about the issue of tissue samples? What question would you most like her to illuminate for us?

DR. MIKE: From a utilitarian point of view, I was not at the March meeting, but I reread the transcript. I think in terms of where the rubber meets the road, those issues we are going to discuss this afternoon again, is where we are heading in terms of choices.

So my preference would be that Sheri's analysis looks at how we are ending up in those choices and how the privacy issues apply in each of those situations.

DR. KRAMER: Just to pick up on what Eric was saying, in each of these issues we are going to have to give up -- and in each of the considerations, we are going to have to give up something to gain something else. If we had some kind of matrix to look at, that always works for me, if I can see it out there in black and white.

DR. MIKE: I think that is comparable with what I'm saying. From what I see right now, we have either four or two categories, or three, I guess, three categories. How you would implement any kind of regulations or policies, and given those instances of use and applications of the stored tissues, we would like to see where we would be heading in terms of the rigor of protection or obligation toward people to either protect their privacy interests or to give up their privacy interests, either in person or collectively by some kind of a policy judgment about that, just to show the balancing in each one of those situations.

DR. KRAMER: Just to finish that, I was not sure with some of Sheri's remarks whether she was talking about prospectively -- tissue that is taken prospectively as against the stored, or were you just looking at the issue altogether? Because it seems to me that that is very different, and I don't know -- in this first proposed paper of ours, are we going to take a look at prospective access of tissue, or are we just going to look at stored tissue? We conceivably could come up with two very different kinds of guidelines.

DR. MURRAY: My instinct is both, but understanding that there might be two quite different regimes for what tissue has been gathered already. Some tissue samples are a century old.

DR. KRAMER: Right, exactly.

DR. MURRAY: I think to require informed consent to look at all those tissues from sources would be a little unrealistic. So we may wish to have -- and standards are different; we may want to have different policies.

DR. KRAMER: Exactly. So one of the interesting considerations might be the imposition of a time line on a matrix as well.

DR. MURRAY: Right. I had Trish and Steve. Let's start with Trish.

DR. BACKLAR: I'm hoping we can also go back and look and investigate a little bit more the issues to do with ownership. I see that one of the states talks about ownership of genetic information. I think that really needs to be explored in terms of tissue, and analyzed maybe against organ transplantation, so on and so forth, and how we dealt with that before, and also in the prospective issues.

DR. MURRAY: So you would want Sheri to go back and do a bit more about --

DR. BACKLAR: The property issues.

DR. MURRAY: -- the property issues.

DR. BACKLAR: Yes.

DR. MURRAY: Okay. Steve?

DR. HOLTZMAN: I was going to make a suggestion which for me is very radical, maybe using Sheri's time to get some facts instead of some concepts. As a privacy expert, what we

have right now is -- winging its way through Congress, or about to, major national medical information privacy, and stuff going on in the states as well. If our work here is going to be useful, arguably we should have a sense of where the nation is going, where the Congress is going.

So if I'm looking at an assignment of a couple of months, it might be very useful from my perspective, the facts of what is out there specifically, how it touches on this issue, and where it does and where it doesn't, and what are the main concepts where it does, in terms of standards of confidentiality, means by which things can be anonymized or not anonymized, what is sufficient in that, how people are looking about maintaining confidentiality, because in certain of the approaches they had suggested that what is more important than consent, for example, is the maintenance of confidentiality.

I think that might be a very useful background for us when we are doing the conceptual and ethical work.

DR. MURRAY: Steve, would it be consistent with your request to do something that I have been wanting to ask Sheri to do, and that is, also to step down from the more conceptual level and to say, there are a few policies you said, for example, FDA and OPRR regulations, to have really good, concise descriptions of what they are, so that we know just what the current background is. And then, I take it, to extend to what she just described.

DR. HOLTZMAN: Right, that's what I mean. Layered on top of it is the mandate out of the Kassebaum-Kennedy bill for a broad scale -- you know more about this than I do -- broad scale medical confidentiality bill, and where is that going.

DR. MURRAY: I'm sorry to think that it may be boring for you, Sheri, but it may be helpful for us to have just that nice crisp description that we would fold right into the report.

MS. ALPERT: As far as Kassebaum-Kennedy, I have already done an analysis like that, so that is easily done. The state level is where it is going to get more difficult until a medical privacy bill passes, because there is such a conglomeration of stuff out there that you find in a myriad of different classes of legislation within a state. So that -- I would probably have to focus on specifics within the states to do something like that.

DR. MURRAY: But there are groups that can be very useful, in terms of the Georgetown Law Center, or there is Bio, which have collected all of this, and just pulling together synopses that are relevant.

DR. COX: These comments have been very helpful, because now I know what I would like Sheri to do. Primarily, I'd like to second what Larry said. I am primarily coming down very pragmatically, quite focused retrospective on tissue samples, but not because I am only limited in my interest to them, but they have the smaller subset of issues dealing with

general privacy of information and medical information.

Then what we can do as a group, why I'm interested in that, is that we can then do as Steve suggested: look at these other laws, other things that are out there in that context. It is going to be a smaller subset of the whole thing, but by being a smaller subset, we will be able to identify the things that it doesn't address, so we don't have an opportunity to address some of them, because it is retrospective as opposed to prospective.

But in doing that, we can then clarify the issues that we would really like to make sure that are present in the prospective studies, because we didn't have the possibility of having them in the retrospective.

There is also an immediate practical issue with respect to the retrospective, in that it is very divisive right now, in terms of people trying to figure out what to do. This is your point, Larry, that is pragmatic. There are these retrospective samples, and everybody is trying to figure out what to do. I'm not saying our ethical decisions should be based on having a need to act, but I think it gives us a narrower field within which we can deal with it easier.

DR. MURRAY: David, I want to be sure I understood what you are saying. Clearly, you want us to focus -- and as quickly as we can, responsibly focus on retrospective, that is, in currently stored tissues, correct?

DR. COX: Yes, correct.

DR. MURRAY: Do you want us not to deal with the issue of what practices should be in place for tissues gathered from here on in?

DR. COX: No, but I would like to have that come out of what we see when we focus on the retrospective. I don't want to be too much in series with this analysis, but I think that if we are looking at -- what I'm thinking is that it is an in-depth analysis of the retrospective, doing what Steve suggested, since we already have a lot written on there, but I'm not sure that what is written really covers all the issues.

So if we focus on that deeply, that can be our launching pad for the broader issues of medical information.

DR. LEVINSON: Just to add to that, there are other groups that are working on prospective and have decided not to work on retrospective. So you don't necessarily want to duplicate what they are doing. In looking at retrospective, you might come up with answers and suggestions that will be useful to be fed into the other groups that weren't thinking about that, because they are only focusing on prospective.

DR. MURRAY: Which groups are these?

DR. LEVINSON: The breast cancer action plan. They are developing an informed consent form for the prospective use of tissue. They are looking at it that way, in the forward look. They may not come to certain questions that you do if you're looking retrospectively. You say, if we had done it this

way in the past, we would be able to use this tissue in such and such a way. They can benefit from their discussion.

DR. CHILDRESS: I think there is a way in which Steve's two directions can be brought together, that is, the facts and the conceptual.

If one looks at the current legislation being proposed, some of it is medical privacy, some of it medical confidentiality, both terms have been used, you didn't focus very much on confidentiality. We ought to work on those concepts as they appear in the legislation and actually try to figure out what kinds of values are at work and how they are being balanced differently in medical privacy versus medical confidentiality legislation. I think that a lot of the debate falls under these categories sometimes, without a lot of reflection on what is at stake in choosing one or the other.

DR. SHAPIRO: I have a small point, and I don't know if it really would distract from the subcommittee's progress here.

I am trying to straighten out in my mind the difference between privacy and rights. That is, there are rights of various kinds which are established, and then there is the issue of privacy, which is claimed by individuals, asserted by individuals, felt by individuals and so forth.

It seems to me it might be helpful at some stage to distinguish between those two. People may have an existing set

of rights, either to know things about themselves, about others, what others know about themselves in one of the pieces of literature we have been reading. Then there is the issue of privacy, which might include rights, but it is a much broader, amorphous kind of thing. It might be helpful to make that distinction carefully in this area.

Now, I don't think this is a major issue. I just put it out there in case others think that it is useful to look at. Some philosophers have argued that indeed there is no such thing as a right to privacy, but it seems to me to make sense to say that yes, there is privacy as a state of affairs or a condition, but there could be rights to privacy, as has been recognized in our own legal context, or at least specify that in certain kinds of ways.

DR. MIKE: It seems to me that the only difference is that rights are societal recognition of certain aspects of privacy. So if we are going to look at that, and I agree we should look at it, the analysis should be what led certain privacy interests to be deemed as rights, what were the reasonings behind that. Then we might give some -- maybe we will find wild inconsistencies in there, or we might find consistencies in there.

DR. SHAPIRO: But like we have often said before in our discussions, there are a wide variety of moral views on the issues, some of which get ensconced into legislation and some of

which don't, because we feel differently about whether everyone ought to behave in a certain way or not. A similar analogy here might be useful.

But it is a small point, Tom. I didn't want to interrupt the flow.

DR. MURRAY: That's fine. Sheri, we are at the lunch break time. Do you have any quick comments or questions you want to ask us? This isn't your last opportunity. You can always reach us by the Internet or any of the old-fashioned means.

MS. ALPERT: I have a grab-bag of stuff to deal with, and I will put it together.

DR. MURRAY: We need to do better than just to give you a grab-bag. What I'm going to do is, I want to invite other members of the commission to partner with various people who will be working on the report. I won't name people around the table publicly, but anybody who wishes to volunteer to work closely with Sheri, to help shape her contributions to the privacy part of the report, I would be grateful. Otherwise, I will be twisting your arm to do that.

Thank you, Sheri. Thank you very much. We are just three minutes behind schedule. Let's reassemble in one hour.

(The meeting adjourned for lunch at 12:33 p.m., to reconvene at 1:30 p.m.)

A F T E R N O O N S E S S I O N (1:39 p. m.)

DR. MURRAY: We are a few minutes behind schedule, but I am going to ask everyone to please settle.

One of the most useful things we did -- it is not quite after Dolly, it was before Dolly, because Dolly had been announced but we hadn't yet plunged in -- was to take an initial look at some of the ethical issues, and how those issues were raised and framed in a variety of the position papers that had already been published on tissue samples.

Zeke Emmanuel led us through that conversation, which I had the opportunity to review, in a very helpful manner, and we want to revisit that and once again get up to speed and see if we can push further on it. So I have asked Zeke to lead this conversation.

ETHICS ISSUES IN TISSUE BANKING

DR. EMMANUEL: Because a number of commissioners were not actually at that meeting, the handout you have, I apologize, is slightly out of order. I had made the handout before I saw that not everyone had attended the meeting.

What I'm going to first do is go over some of the regulations, the appropriate passages in the common rule, then talk about the various proposals that are out there from that. Then we had made, I thought, substantial progress in our discussion on March 5. What I have tried to do is to summarize where we came to at the very tail end of that discussion,

through a variety of comments by people on the subcommittee.

Then, I have taken a bit of a leap to the next step. It is obviously my view, and it is more for discussion of the process. So I will try to talk fast here so we get on target.

There are two essential passages that deal with existing data that are relevant here, and that has been cited by many of the previous statements. The first is 45 CFR 46.101. That says that research activity in which the only involvement of human subjects will be in one or more of the following categories are exempt from this policy. That is the policy of IRB review. That involves research involving the collection or study of existing data, documents, records, pathological specimens or diagnostic specimens if these sources are publicly available or if the information is recorded by the investigator in such a manner that the subject cannot be identified directly, or through identifiers linked to the subjects. So that deals with the anonymous, anonymizable linked aspect.

The next one is that an IRB may approve a consent procedure which alters some or all of the elements of informed consent set forth in this section, or waive the requirements obtained in informed consent, provided the IRB finds in documents that either the research involves no more than minimal risk to the subjects, the waiver of alterations will not adversely affect the rights and welfare of subjects, the research could not practically be carried out without the

waiver, and whenever appropriate, the subject will be provided with additional pertinent information after participation.

Now, my own understanding for the stored tissue of that requirement is that currently anonymous samples can be used without informed consent or IRB review, since they are existing, and subjects cannot be identified. So that is for the currently anonymous. Then for the anonymizable sample, I think reading those they could be used without informed consent or IRB review, since they are existing and the information is recorded in such a manner that the subjects cannot be identified.

Then there is the linked or identifiable. Generally, you need IRB review or informed consent because you're not going to get all four conditions satisfied, at least in the genetic test area.

Others may have different interpretations, and I understand that.

You have this complicated chart. I tried to make it simple as possible and to digest the papers and the reports from which this is -- not all of these reports or recommendations are as clear as they might be in this area. What I have tried to do is divide the chart into two parts. One is the recommendation for those existing samples. So pathological samples, for example, that now are stored in the department of pathology at your favorite medical school. Then there are what to do about the future studies, prospectively, what rules should

we lay down.

I want to go through these serially. It turns out that there are slight but relevant differences on the existing samples, larger more substantial differences on the future samples. Let me preface before I go through this in detail, it was a general view of the subcommittee, I believe, that this chart did not capture everything we thought was relevant or important. That is the reason for the charts that are at the front of your handout. But it is useful to know what the standards are that are out there. And please, anyone interrupt me at any time if I'm not being clear.

The American College of Medical Genetics basically list a bunch of concerns. One of the more useful ones is the American Society of Human Genetics, which had a nice little algorithm, and they have a standard basically to continue with the current policy: no informed consent for anonymous or anonymizable, get informed consent except in the exception under the common rule that I just read.

DR. GREIDER: Zeke, can I ask you a question?

DR. EMMANUEL: Yes.

DR. GREIDER: When you have anonymizable or anonymized, I am assuming that where you are saying no informed consent, that is when one does anonymize those samples that are considered anonymizable.

DR. EMMANUEL: Right.

DR. GREIDER: Just because they are anonymizable doesn't mean there is no informed consent, but only when you exercise that.

DR. EMMANUEL: Right. And actually, part of what I want to get into later on when I talk about where I thought we had got to at the end is that what you take to be anonymizable, I wanted to articulate what I thought was underlying our view. You have to create a certain kind of firewall. It doesn't mean that no one in the world still knows the name of that sample, but it means that the researcher or investigator cannot walk backwards, nor can anyone from a published paper.

DR. MIKE: Am I correct to also assume that these recommendations are not based on the actual status of the tissue samples, but what happens to them in preparation for proposed research topics? In other words, since they talk about anonymizable or anonymized, identifiable, et cetera, they don't start with the actual way in which the data is actually stored, but they make their safeguards after a particular proposal is researched, and they have done something to the data set. Do you see what I mean?

DR. EMMANUEL: No, I'm not sure that I understand.

DR. MIKE: If you say that they have anonymizable or anonymized, that means that you have already taken something and changed the conditions, and then they apply the policy to it, because these are all coming from research based groups,

basically, so they are more concerned with the data as it would exist in a particular research proposal rather than taking one step back which other than researchers might do, and say how should we deal with the data sets as is, before we start talking about a particular application.

DR. EMMANUEL: Right, yes.

DR. KRAMER: Maybe it would be helpful to find out how the samples become either anonymous, anonymized, anonymizable, et cetera. When they are initially taken, they are identified. The vast majority of them still exist in an identified manner currently. So for example, the pathological specimens in a hospital have a number, the number corresponds in a book to a patient's name. You can go get the record, so you can get the medical history of the patient. Similarly in big research projects, like the nurses health study, you have stored tissue samples that got a number on it, that number corresponds to a patient, so you have the data that you collect on that patient.

So it is all currently linked, but the research would unlike it.

DR. KRAMER: Or it would be unlinked before it was given for research.

DR. EMMANUEL: Unlinked to an identifier, but not unlinked to a medical history. Is that clear? That is the important point, it seems to me. So that your name and social security number would be taken off, but the history --

DR. KRAMER: Would be attached.

DR. EMMANUEL: Yes.

DR. KRAMER: That would be called anonymized.

DR. EMMANUEL: Right, anonymized, right.

DR. SHAPIRO: Zeke, can I just ask a question about that 45 CFR 46 regulation? Do I understand that regulation correctly, that it has to be no more than minimal risk and so on, but also that it not adversely affect the welfare of -- that that is something in the minds of who? When you say it is not adversely affecting, as you think about regulation, is it something the researcher decides or the IRB decides? Who decides that?

DR. EMMANUEL: I think it is an attempt to make an objective assessment by the IRB. I think you couldn't solely rely on a subject; any patient, or the most extreme patient.

DR. SHAPIRO: Okay, thank you.

DR. EMMANUEL: The College of American Pathologists believes in no enforcement, no IRB review, all the way through, and then in the case of linked or identifiable, they want IRB approval, but they don't have to have contact with the patient or family and not give research results back.

In part, arguing that this is research, not clinical information, trying to hold the research clinical treatment distinction present. The ELSI working group has probably gone the furthest to make new recommendations on existing samples.

They suggested that under the anonymous, you don't need informed consent, but they wanted to have IRB review for scientific validity, to make sure that the research project actually was valid. They wanted no informed consent, but they wanted an IRB review, and they listed out five factors to whether you might get consent, and you might actually go back to the subject.

DR. HOLTZMAN: Is it really right to say they say no need for informed consent? It is only when all of those conditions are fulfilled, like you can't get informed consent, then no need for informed consent?

DR. EMMANUEL: It is a little more ambiguous. They are a little more hedgy. I think they would like it to be the way you have stated it, but they recognize that that is an important change in what we understand by the current rules of the common rule.

DR. HOLTZMAN: And I also seem to recall that their definition of -- there was no such thing as anonymizable. It was either anonymous or it wasn't.

DR. EMMANUEL: I think there was an anonymizable, but a lot of this is raising important questions as to what to consider anonymizable. If we can hold off for a second, because I think that is absolutely critical. Part of what I want to suggest I think we came to is that there should only be two kinds of samples. Sorry.

DR. HOLTZMAN: It's okay.

DR. EMMANUEL: Then if you will look at the anonymous, the future studies, there are some bigger differences here, in part because they center on how much consent you need. Maybe I'll just jump down so we don't waste too much time into the dichotomy between the College of American Pathologists and the ELSI working group.

The ELSI working group wanted a fairly extensive informed consent process on future samples that we collect. They wanted consent for all samples that would be used or might be used for research in the future, and they wanted a laundry list to be given that included whether they wanted to be recontacted with linked results, they might be informed of those results, whether they would permit their sample to be stripped of identifiers, whether the sample could be shared with other investigators, whether, if they were going to share it, it would have to be linked or anonymous, whether you wanted to limit the types of diseases for which samples could be used, limit the type of investigators with which the sample could be shared. So a fairly extensive informed consent subsequently.

You have to get this on everything, if you ever thought you might want to go back to a tissue bank, for example.

Conversely, the College of American Pathologists wanted a minimalist approach. On the anonymous and the anonymizable, more or less continue the same no informed consent required, or have a general consent that people sign when they

go in the hospital, I permit my samples to be used for research and education, as long as I'm not implicated.

Then they wanted a general consent for linked or identifiable, not anything more specific. That seems to me to be the most polar opposite approach. I think we heard from David Korn, passionately arguing for this minimalist approach.

That is part of what I presented last time. As a result, a very fruitful discussion, where it was clear that many brains in the room were much better than one brain working alone. I think we came up with something that I have tried to distill from the record and my recollection of my notes that looked like this.

We were not happy with the previous provision, because Steve Holtzman correctly reminded us that part of our concern is going to depend upon the kinds of research or the purposes of research for which the samples are going to be used. He quite clearly articulated what came to be three types of research.

In addition, we came to -- I think, having re-read my notes in the transcript, the idea that the anonymous and the anonymizable should not be made distinct, that there should really be one category, and the linkable or the linked, another category.

So what I have tried to do here is talk about first, samples of research without an identifiable community or group, random samples. The example of that that Steve used is going

back to random pathological samples of patients with colon cancer, looking for genetic alterations that are associated with colon cancer. No specific group, you're not looking for specific genetic traits that run in families or anything, or run in certain ethnic or racial groups.

I think the view we came to is that on the anonymous or anonymizable, we would have IRB review, but not for scientific validity, not for an assessment of the content, but for an administrative decision whether in fact the research proposed is of this kind. No informed consent of the patient or the person whose sample it is, and no need to get community consent, because there is no community looking at it; you are just going through random patients.

Linkable is a different issue. Again, IRB review and an informed consent, unless you have the four criteria met. I think we might be able to come to the conclusion that the four criteria by definition in a genetic test couldn't be met.

The next categories we identified were samples or research with an identifiable community or group, but where the research purpose doesn't have any stigmatization. I have chosen this example somewhat contentiously on purpose. It is an example actually which came to me for advice, and I think is a good example, creation of immortal cell lines from samples of patients who are enrolled in an AIDS study. The reason they want to immortalize the cell lines is that they stored blood on

all these patients, some of whom have died, but they are running out of samples because they want to do so many more tests.

So we had another example. Steve gave us another example, and I'm sure people in the room can think of others. Here, I think the conclusion we came to is that we should have administrative assessment by an IRB, not for scientific content, but to insure that this is the kind of research we have at hand, no informed consent for the subject, but community assent. Community assent is my term; we didn't actually use it there. I'll discuss in a second what I mean by community assessment.

With the linked or identifiable, you have informed consent for each individual, because it is linked and identifiable.

Finally, there is the samples of research with an identifiable community, where the research could have a stigmatizing effect. The example we had was looking at a particular community trying to find out genetic alterations associated with bipolar affective disorders.

Here, I think we had a higher standard, where we were IRB reviewed. If it is anonymizable, no informed consent, but community consent, where the community actually had to approve it. When it is linkable, you've got informed consent and community consent.

Now, maybe --

DR. MIKE: Can you then tell me what you mean by the

difference between us and --

DR. EMMANUEL: Yes. In your packets there are some definitions. I think it is appropriate now for me to try to go through -- because they are somewhat interpretative, based upon what they said, and I will freely and readily admit, there is a lot of my own -- trying to make coherent what we said.

Anonymizable, as I said, you could have samples that have identifiers, but the researcher, investigator, collects the data and sample in a way that makes it impossible to walk backwards and link the sample with the person from this research project or from the publication. But the stored tissue may still exist and could in the future be linked or continue to be linkable with the medical record or other source. It is just that the researcher couldn't do it, and no one from the publication could walk backwards.

Anonymizable therefore refers to the sample from the research project -- I think this answers your question, Larry. And a firewall is between the investigator and the identifying information, not between say a clinical pathologist in the hospital or any future researcher. So the same sample could be used for anonymous research and linked research. Is that clear?

Community assent. This would be, provide community leaders or organizations with information about the research project, mail information sheets to the community members if possible, not require any formal endorsement. The onus would be

on the community to respond or reject, and you might provide the results generally to the community of the research.

Now, obviously I am using the word assent, trying to piggyback on our notions of assent with children and with others through this context. Yes?

DR. KRAMER: Do you imply or want to imply that without that assent, it wouldn't go forward?

DR. EMMANUEL: I want to suggest that if the community did raise significant objections, you would have to reconsider the research. Part of it is where the presumption lies. Community consent would be to provide the community leaders and organizations with information on the research, mail information on the research to community members, hold some public forum or meeting, and modify research in consultation with the community, and receive some formalized endorsement. Much like the kind of system that Bernie had described to us at several occasions about research with the AIDS community.

The research advance I'll get back to in a second, because that is to talk about the future or our rules prospectively.

This is for the stored existing tissue samples now that have been collected without any rules, without any consent, community assent, et cetera. Maybe now with those definitions, we could look at it again.

The point I think is to try to say that samples that

have a high level of stigmatizing either of a community or members of a community, need a higher level of scrutiny, but don't need -- at least when they are anonymous, for people to go back to each individual sample holder. In many cases, it is going to be impossible because they are going to be dead.

DR. GREIDER: Okay, I'll bite. So why did you put the immortalizing AIDS samples under non-stigmatizing group?

DR. EMMANUEL: Well, for several reasons. I don't think that just -- the research itself doesn't have to be -- even though it is on a population, the research itself doesn't have to be stigmatizing, any more stigmatizing to the group. So just because you are a group that might have some stigma associated with them, the research itself might not.

In addition, it is an ongoing study already. So the people that have already participated acknowledged. So I think the hurdle of participation is already passed. That would be my analysis of that case.

DR. KRAMER: But do you always know before the research takes place whether the results are going to be stigmatizing or not?

DR. EMMANUEL: You have some sense of what you're fishing for, I think. I would say, compare this and this.

DR. KRAMER: Compare what?

DR. EMMANUEL: Compare the bottom two. Almost any result, when you're going to look at psychiatric illness, I

think is going to have some kind of stigmatizing effect, but part of what I tried to do in the second case is to think of a situation where it wouldn't necessarily have a stigmatizing effect.

You might for example be looking at cell surface markers in the immortalized cells. That should have no stigmatizing effect.

DR. SHAPIRO: The difference between the bottom two in terms of actions is, the only difference is assent versus consent.

DR. EMMANUEL: Yes.

DR. SHAPIRO: Otherwise, everything is the same.

DR. EMMANUEL: Right.

DR. SCOTT-JONES: I just have a comment. The way you are using assent here differs a bit from the way it is used with research with children. When you talk about child assent, you assume parental consent has already been given, and the child's assent is just the child's willingness to go along with the procedure on the day it is actually administered. So you assume consent already. It is not taking the place of consent.

What you describe here as assent is more like what is called passive consent in research with children and adolescents. That is, you simply notify the parents and the burden is on them to respond and object, which is how you have described community assent, but that isn't how it is used in

research with children.

DR. EMMANUEL: Well, fair enough. But assent is not used only on the day of a procedure. Sometimes it is assent on the whole research project. It also is -- it depends.

DR. SCOTT-JONES: The critical thing is that the parent has consented, and then the child gives assent as well. It is not taking the place of parental --

DR. EMMANUEL: It might pre-empt. I agree. Just as a matter of fact, in many cancer studies, you have a 14-year-old who is not going to assent even if the parent is going to consent.

DR. SCOTT-JONES: Exactly. The child still has the right to refuse, even if the parent has consented. The child can say, I don't really want to be in your study.

DR. EMMANUEL: Right. Part of what I am doing in the community assent is to say that the community can object or withhold.

DR. FREEMAN: I am wondering if the wording might be for the second one, presumed consent and for the third one, just full or active consent, as opposed to assent and consent.

Unlike what is called passive consent, in fact, what you describe under your assent, which I suggest be presumed consent, is actually a quite active process. The problem with passive consent, you send it out to the kids, you don't know if the parents ever get it or not. You are making sure that the

community is made aware in this very active procedure, but you presume their consent unless they say, wait, we've got an objection. Then the other one, the full one, is a very active process, as well as requiring them to actively state one way or the other.

DR. EMMANUEL: Right. It is active, but what it doesn't do is, it doesn't put the onus on the researcher for some formalized endorsement. It puts the onus on the community to object.

DR. SCOTT-JONES: Zeke, I'm sure you have already thought about this, so I am interested in what you have to say about it. Obviously, a problem would be identifying the community leaders. There could be multiple leaders who don't agree, who could be diametrically opposed to one another. So how does that work?

DR. EMMANUEL: That is a problem which I think we are going to have to talk about, the whole issue of bringing in community into research raises. It is an issue that the subcommittee is also aware of. I guess we are going to have to negotiate what the rules are we are going to agree to.

I don't think there is any settled lore on this yet. We are all working on it. But I think in some communities, it is more identifiable than others. It often depends upon how the community is structured, whether it is a racial, religious community with a political structure or a more ad hoc community.

DR. MURRAY: Zeke, since we are on the discussion about community, in thinking about it before I came to the meeting, we could get into deep waters here. You are the political philosopher in the group, but deep waters of two different kinds. That is a terrible mixed metaphor.

One is, how do you tell what the role of the community is, since most of us belong to multiple communities? And some of us might have different views about which one we belong to and how central that is to our identity. So A is, how do you identify the community, and B is the representational question, how do you figure who the relevant representatives of a community are?

DR. EMMANUEL: I think actually, those are the general and big problems with community. But I think in this case, it is less -- the first one is less of a problem. We are not asking you as the subject to identify which is the relevant community. If the research doesn't have any community component, or doesn't identify and circumscribe a community, then it is not relevant. Then you move on to A, the first type.

DR. MURRAY: I think that is a very good response. It doesn't take care of all problems, because the researcher may define the community either much more narrowly or much more broadly than the relevant community might, who then might want to respond and say, but you have said it is X, but we think it is X plus ten.

DR. EMMANUEL: I agree, and that is one of the reasons to get IRB review, to decide whether you are in the right category, whether you as the researcher, for reasons of self interest, say I am up here. It means I have to do less work. And the IRB says, no, we think it is down here. You can't have all checks, but I think the IRB review could make sure that you are in the right category here, does some of that work.

DR. MIKE: If a vocal minority or a vocal individual objects, would it drive it toward -- it would drive it in two directions. One is, what do we mean by assent, or it may drive it toward a third category, which is stigmatization.

DR. EMMANUEL: I think following up on Dr. Shapiro's point, we should try as hard as possible to have an objective definition here of the three categories, where it doesn't depend on what a minority says.

Again, part of the reason for the IRB review is to try to have an objective categorization of whether it is stigmatizing or not, rather than a subjective standard of stigmatization. If a vocal minority raises it, then you are going to be in a judgment call area: how much do they want of modifications, how easy is it to do those modifications, are they objecting inherently to all kinds of research like this, what are the alternatives.

It seems to me that maybe this is a little too stark, presumed consent is a little too stark. But I think unless they

have serious and good objections that are not just, we don't like this, --

DR. MIKE: I was surprised that you picked a specific example for number two about the AIDS study. Some people would say just the fact that it is from a group that is HIV positive or whatever, that in itself is stigmatization.

DR. EMMANUEL: But that was exactly what I wanted to get at. That is why I picked the example, so that just being in that group would not in and of itself qualify as stigmatization.

Correct me if I'm wrong, but I thought part of the import of what Steve raised, which I thought was very perceptive, it is not the group, it is the purpose for which the research could be used, the results of the research could be used.

Now, let's remember, the values that we think are at stake, that are bound up with stigmatization, are ones related to social isolation, discrimination. Those are related to the purpose of the research, not to the group you are part of.

DR. MIKE: But that may be acceptable among intellectuals, but will that sell on the outside?

DR. HOLTZMAN: But isn't it key to the example you chose, that these people have already been identified as HIV positive?

DR. EMMANUEL: Maybe yes, maybe no. I'm trying to think of other examples. Let's say you want lymph nodes from

HIV positive people, and the research you are looking at is not going to be stigmatizing. It is going to be cell surface markers or something, the genetics of cell surface markers. I don't think that in and of itself --

DR. SHAPIRO: It seems to me, the difficulty is whether or not one could predict whether the research could be stigmatizing or not. That is a hard issue, since the results of the research are not always predictable, on this ground. There is always uncertainty, and on these grounds it may not be predictable. Or do you think that is not the case?

DR. EMMANUEL: I think that is going to be the case for a small number of cases, but not for the vast majority. I am trying to think of all the kinds of information that this encompasses, like all the stored tissue samples for the nurses health study, the physicians health study, or breast cancer samples in my favorite hospital.

Under those conditions, if you are looking for a marker of, let's say, metastasis. How stigmatizing is that likely to be?

DR. LEVINSON: It depends on the figure. If you get a result that leads back to something --

DR. EMMANUEL: But you have to be looking for that originally, and that I think would put it into that category.

DR. LEVINSON: No, if you find it out later.

DR. BRITO: Sometimes in the process of the research

itself, you uncover something that could be stigmatizing.

DR. EMMANUEL: I agree, sometimes. My own view is, that might be overblowing most of the research. I think that may --

DR. BRITO: It might be overblowing, but even if it is a small percentage, that small percentage can have a large impact. I was going to suggest that this division is a nice division to start with, but I think at some point there has to be a caveat in there, or something that defines the gradation of stigmatization, and what happens in the process of research. Basically, you are changing the category. You're changing from category two to category three.

The example you are giving with the AIDS is a perfect example. You don't know with that cell marker. What happens if you find that in the process, a certain minority group has more of a propensity to have these cell markers for a particular retrovirus, or what have you. So then it becomes stigmatizing. So you have to go to the next category.

DR. EMMANUEL: I think that is a great example, but I think we should try to think of some examples before -- my own preference is not to worry about the hypothetical that is unlikely to happen, or where we can't think of a good example where it is going to happen, and yet create such barriers to this kind of research.

DR. BRITO: I think the hypothetical is likely to

happen. It is just a matter of time.

DR. GREIDER: It sounds like what we need is a process, as Arturo is saying, to move from one category to the next during the course of the research, that there would be some way to be able to say, wait a minute, it looks like this research might be headed to move me from category two to category three, and a process for re-review, or something like that.

DR. EMMANUEL: One of the things that I think the human subjects committee is -- to change IRB review from a one time effort to something that actually worries, once the conduct of research is going on.

One of the things that this assumes is that there are certain background confidentiality standards, certain standards of research review, et cetera. I think part of what we are going to have to do is specify the sort of common assumptions against which this kind of research is done. This kind of categorization and rules are not meant to cover all possible regulation of the research.

DR. KRAMER: What about the example of the BRCA-1 and 2? Was it envisioned that that would be stigmatizing to a group when that research was originally undertaken?

DR. EMMANUEL: That is a great example. They specifically went to a variety of stored tissues that had community identification with them, right? It didn't just

happen serendipitously to pop up, Ashkenazi Jewish women. They went to the Tay-Sachs repositories and looked, do Ashkenazi Jewish women have it.

So there, it seems to me what you've got is this, right? By the definition of how you framed it. Similarly, I don't know whether they did, but they were going to go to sickle cell banks, banks of tissues from sickle cell patients. It seems to me, you have already put yourself in category three, before you even started.

One of the problems may or may not be whether you think consulting with the community didn't happen. I can't speak for the process.

DR. GREIDER: How is that different than the AIDS case? How is being an Ashkenazi Jewish woman any more stigmatizing than being HIV positive?

DR. EMMANUEL: Because you are identifying a genetic cause of the cancer with a particular subgroup. The purpose of the research isn't to assign to the AIDS patients something. Now, it might be if what you're looking for is some behavioral actions that might be related to some physiological changes.

DR. GREIDER: I understood it before you brought up the example of the BRCA-2 and the Ashkenazi Jewish community. I don't understand it anymore. I don't understand the distinction between two and three.

DR. EMMANUEL: It seems to me that what you have got

in three is research which is going to be -- has the potential for being stigmatizing, or a high likelihood of being stigmatizing within a particular community. And that depends upon the research. Part of the point is, it doesn't depend upon the group.

DR. GREIDER: So it is the fact that they were looking for BRCA-2, not the community, that makes it --

DR. EMMANUEL: That they were trying to pin it to a particular community, it seems to me.

DR. GREIDER: So if you were looking for BRCA-2 in AIDS patients, then it would have been number three?

DR. EMMANUEL: No, they are both number three, it seems to me. If you were randomly looking -- in the first sample, they were randomly looking for BRCA-1 in any community, in any person. That is one, it seems to me. Everyone is agreed to that? Without stigmatization, I'm not sure, standing on one foot here in front of you, that I can instantaneously come up with an example. But it seems to me the other two go into this category.

DR. HOLTZMAN: Trying to reconstruct our thinking on this would be useful. We started with the basic way people think about this is that the sample can either be tied to the individual or not. We said that even though samples may not be tied to the individual, nevertheless they can be tied to a group. Hence, we needed to have a notion of, even though

individually anonymized, nevertheless community identifiable. That is the reason for the second and third category.

We then went beyond that, and now we are in a different conceptual bucket. That is one set of distinctions. The next set of distinctions is, what am I looking for, what are we looking for, what is the trait we are trying to ascertain, genetic trait, non-genetic trait, whatever. Would the identification of such a trait and its assignment to an individual or to a group possibly be construed as stigmatizing?

DR. EMMANUEL: Very helpful.

DR. HOLTZMAN: Right? So take the Ashkenazi women and breast cancer. Even though you have all of these individually anonymized samples, but they are all Ashkenazi women, can end up with a result, namely, that this group has this characteristic. So that puts it into the community identifiable bucket.

Then the question is, is risk of breast cancer potentially in our society considered stigmatizing in a way in which -- choose another condition, 25 freckles on your nose, wouldn't be? This is not to say that there aren't black, white and gray about what is and is not stigmatizing.

Now, if I understand Zeke's second example of what he is trying to say, the trait we are looking for is the presence or absence of cell surface marker X. People don't view people differently in the world based on whether or not they have this or that glycosylation pattern on a particular cell surface

marker.

I think it is getting a little confused, because I'm sitting here saying, yes, but we don't know if the study is that this group of people potentially has AIDS or is HIV positive, that could be considered a stigmatizing condition. But I don't think that is what you meant by the example. I'm not saying any of this works; I'm saying that is what our thinking was.

DR. CASSELL: But your thinking is correct, except that, if you don't stigmatize anybody, if it is really benign and yet it is a community, it is really like an individual for whom there is no risk in some cases. But you still want that individual involved, so we say assent, not consent.

On the other hand, supposing we use the example you just used, glycosylated cell surface markers. Three weeks after you have done your study, somebody links glycosylated cell surface markers to something that is stigmatizing.

I'm not arguing the motive, but the question is, do you need the middle group? Or turned around, who is going to do the consenting for the community? When you get assent, you in essence go to a community and say, listen, this is the kind of work we are about to do, and then you are getting opinions. When you get consent, you're not getting opinions. You're getting a community to say, no or yes. Who is the community, and are you going to get a community to do that?

DR. EMMANUEL: But part of the point is, they have

been doing that in certain communities. If you have an identifiable community of Native Americans, you can do it there. If you have lots of AIDS groups, which aren't politically recognized, aren't racial, aren't religious, also they have been getting community consent from them.

So I think the who question is a serious question, but in theory we may be making it more complicated than in practice it actually is in many cases. In some cases, it will be ambiguous, it will be hard. But I think again, partly by adding the purposes of the research for which you are doing it should help clarify and hone in on who that relevant community is. You're right, it may not have a political structure which you can easily get consent from.

It does seem to me nevertheless, I thought as I was thinking about it that this distinction was relevant for some kinds of research, and that the consent process does require an extra bit of work that for much research will not necessarily be relevant and will be a lot of work without a big inhibition to doing additional research.

DR. FREEMAN: Part of the problem seems to be people not understanding the process. Since I am in the Indian Health Service, as you all know, I take part of this process. This actually makes a lot of sense to me, and there is a process for it, I think what Dr. Shapiro was talking about, what Carol was talking about.

To give some examples, suppose we are in two, and we get asked to give information in the community, and the minority in the community says, wait, wait, we don't want to do it. This is what Larry was asking. Well, it depends on what the reason is that they don't want to have it down. If they say, you don't realize that this condition that they are studying is stigmatizing, the IRB should say, we blew it, and put it into number three.

So part of this becomes a process of interaction. Eric's example, where there is the previously not stigmatizing condition after the fact becomes stigmatizing, the IRB should say, wait a minute, it is now in a third category, and before it is published, even though the research has already been done, we put it in three and we need to go back to that process.

So there is an interaction between the IRB and the community, and what are the reasons that are being given for either opposition or support. I think this is very doable in that kind of a process, because we do it all the time.

DR. EMMANUEL: Let me take Eric's case of, three weeks later we come out and we find that what you looked at is now linked to something which is stigmatizing. In my view, Eric, if you followed this process, it wouldn't have changed -- you would have had to go to the consent process, but at three weeks later, after the community has consented, you have changed everything, anyway, right? They wouldn't have objected to it, because it

wasn't stigmatizing then and now it is discovered --

DR. CASSELL: You're absolutely right.

DR. EMMANUEL: While the research is going on, they aren't going to object.

DR. CASSELL: You're absolutely right. And actually, that objection points out, I don't want it to get too complicated. Sometimes, if it is going to get complicated so that you really cover everything, you end up with people not doing what you basically did want to do. You are saying, when you work on a group, you shouldn't work on a group differently than you would work on an individual. You want to get that consent. Or you say, no consent is necessary. If no consent of the individual is necessary, maybe no consent of the group is necessary. But putting in a third category, assent, consent, the researcher part of my past makes me say, Jesus, you're going to drive everybody crazy that way.

DR. EMMANUEL: I guess the reason I thought it might be relevant is to add another level of check to the IRB, making the determination whether it is stigmatizing or not, for either communities that we don't understand, that the IRB may not understand well, or various uses within the community that we may not have fully appreciated.

Since we want to make the classification of stigmatization as objective as possible, I think the second category adds a second check. If the community really thinks

this is stigmatizing, then it can object and we can reconsider, as Bill has suggested, in some kind of process.

DR. CHILDRESS: To pick up Eric's point for a moment, and make this as simple as possible, the only change that would be required if we went to two categories rather than three would be to make community assent community consent. So are the costs so heavy in going in that direction that for purposes of simplifying the procedure and so forth, we shouldn't just go that way? That is, any time you have an identifiable community or group, you get community consent.

DR. EMMANUEL: I think it could be.

DR. CHILDRESS: So if you go that way, then basically we get rid of this middle category.

DR. EMMANUEL: I think it could be.

DR. CHILDRESS: So they could help determine whether there is stigma or not. We could simplify this without heavy cost.

DR. CASSELL: And then if we get a complaint later on from the community, you fooled us, you didn't give us a chance to refuse, when in point of fact, you weren't trying to fool them at all. Things just changed as time went on.

DR. SCOTT-JONES: I have a comment. IRBs should have a community member on them in the first place. Maybe part of this should be that IRBs should do a better job at having community representation.

Then I have a comment about your bigger chart, your four by six. I wanted to ask a question about that one.

DR. EMMANUEL: Your first comment. They may represent a large number of communities, and they may not be able to get the relevant person from any community. So just having a community member on the IRB is no guarantee that the correct -- or the community is necessarily going to be covered. And the other chart?

DR. SCOTT-JONES: The one that is four by six, that has the various reports.

DR. EMMANUEL: Yes.

DR. SCOTT-JONES: The ELSI working group according to this chart recommends that the IRB review proposals for scientific validity. Could you say a little bit about how IRBs could actually review for scientific validity?

DR. EMMANUEL: Whether the study that is being proposed is a good study, whether the statistical power of the study is appropriate for this study. Part of what an IRB is supposed to do is to say whether the research is valid. So that is what they are proposing.

Currently, for example, -- well, not at my institution; at my institution I do have to get IRB approval. But in some institutions, if you want to sift through the medical records of everyone with X disease, you don't need IRB approval. You don't need someone to administratively sign off

on it. They are suggesting, based on the code that I read, they are suggesting that you have to get this before you can go through even anonymous samples.

IRB review at many institutions is not a trivial process.

DR. SHAPIRO: Can you say a few more words about a question that has come up? Let's assume for the moment that you collapse two and three and you'll go with consent instead of assent, just a presumption, which may be unwise. One of us raised the question of, how do you know what that is? When does one know you have community consent? It seems to me that that is a much harder problem to deal with than the issues between two and three.

DR. EMMANUEL: Again, I think in theory it might be harder than in practice. A lot of examples extant already, the example of thalacemia treatment in London when they went to the Greek and Turkish Cypriot communities. Again, it is not a politically organized community, but they do have some leaders, they have organizations that they went to, got their participation. That was prospective, not for stored tissue.

We have many examples with AIDS research, where there are AIDS groups that one goes to, to get assent. With the BRCA-1, as a matter of fact, in different cities we have gotten very different responses. A lot of participation in Washington for doing studies, and complete stonewall in Boston. So there are

ways that the community, while not technically, politically, formally elected or organized, does represent the groups.

DR. SHAPIRO: If that is in practice a fairly easy process, it doesn't seem to me there is a big difference between two and three.

DR. MURRAY: I want to ask you something about that, but Betty and Carol have been waiting, so I'll let them go first.

DR. KRAMER: First of all, I like the way that it is set up. One of the reasons that I do is, I think that just for an IRB taking a look at it, it almost imposes a process of thinking about it, of identifying where the proposed study actually falls. So it is just another way of creating the process or a process that Bill Freeman referred to.

But a lot of the examples were given, going back to the square with the AIDS study. The particular example that you have given was only for the creation of the cell line, so that the samples would exist for doing future research. Whereas, it seems to me that the examples that were cited here at the table in taking a look at that with regard to studies that might be stigmatizing, those particular studies in and of themselves would fall into that third category.

DR. EMMANUEL: Maybe, maybe not.

DR. KRAMER: But those studies will get a different look from this particular example.

DR. EMMANUEL: You may be right. In my view, it depends upon what the research is. One question is whether we should collapse two down or two up. If it is not stigmatizing, why should we have community involvement at all? I don't know, Jim, why you thought it should go down.

Again, going back to reconstructing our discussion, what seemed persuasive in March was, there is an identifiable community and they should have an opportunity to comment. But the climate that is imposed upon the researcher if it doesn't appear to be stigmatizing shouldn't be very severe.

DR. FREEMAN: The reason to go down is that the IRB should not be sure that it knows all of the stigmatizing conditions.

Just one example. There was a newsletter on a large study that involved American Indians. It said, we are looking for the effective gene that causes diabetes. It sent Indian readers ballistic because of the word defective associated with a gene. It gets all that stuff about racial inferiority. It is things we may not appreciate ourselves, who are not members of that community.

DR. GREIDER: I just wanted to revisit this issue of, are we going to collapse up or down, or have three categories or two, as we seem to be discussing, although I was having some trouble exactly sorting out how you distinguish two from three.

I think when I do understand it, that it is a very

useful thing. So I would try and argue to keep the three categories, because I think that with a clearly articulated set of ways to get into category two or three, as Steve pointed out, first, is there a group and then second, is there stigmatization, is a useful way to distinguish them.

DR. EMMANUEL: I don't know that we are going to resolve it all today. Maybe I can move on. There is more.

DR. MURRAY: I think because of the substance here, we are going to go to three with your session. I'm going to take a break out of my hour.

DR. EMMANUEL: I just wanted to add a little more gasoline to the fire here.

DR. BACKLAR: I just want to say one thing. That is, when you have a group that can be stigmatized in any way, if you are going to keep your three categories, you had better put that group into the third category, willy nilly.

DR. EMMANUEL: I think that is for the IRB to decide. I think just because they could be stigmatized, doesn't mean the research at hand is going to lead to stigmatization. I think it is important to keep that.

That was the point of selecting the AIDS group. Maybe I can just --

DR. SCOTT-JONES: Zeke, I want to say one thing. I have had my hand in the air for a long time. I would like to say just one thing that bothers me a little bit about the

overall conceptualization. It seems to have undergirding it researcher versus community, as if researchers themselves will not be of the same community as the participants in research. That bothers me a bit. I think this needs something more than this notion of community as separate and apart from researchers. People who become researchers aren't community-less themselves.

DR. EMMANUEL: No, I agree, but they might not be part of the community they are studying at one time. That is all I'm saying. Right?

DR. SCOTT-JONES: Yes, but -- well, we can talk about it at another time.

DR. EMMANUEL: Let me draw up the other example. In Boston, the people who came to the Ashkenazi Jewish community were Ashkenazi Jews themselves. The community stonewalled, despite the fact that the researchers were part of the community and thought it should go forward, and thought it was good for the community.

The rule shouldn't bias you one way or another. Just because you're a part of the community doesn't necessarily insure against the fact that the community still might have objections.

DR. SCOTT-JONES: Then maybe you should use another word. Use research participants, or use some other word that doesn't include this opposition of researchers and community.

DR. EMMANUEL: Well, but you have to identify roles

here. I'm not sure I understand the --

DR. SCOTT-JONES: Participant is a different word from community. Researcher, participant, those are different words.

DR. EMMANUEL: I feel like the reason we did community in this context is because the results of the research, as Steve was pointing out, could have a taint or a stigmatization or a problem for a community that is identifiable, whether the researcher is part of it or not.

DR. HOLTZMAN: Even before you get to the stigmatization, there is a general theme that has been running through this group since October. That is, that certain kinds of research have as their subject not individuals. But there is the possibility that there is research which in its nature has a group, a collective, a community, take your choice, as its subject. That is all that is at stake here, is the notion that even if you could not -- it was anonymous with respect to an individual, the particular research project and the results of the research project may not be anonymous with respect to a group, a collective, a community, take your choice. That was all that was at stake.

I think that is an important distinction that at least I have been hearing since October, and that is something we need to recognize. So we naturally raised the question. If it is part of a tradition to have conditions of consent under certain kinds of conditions by an individual, because that individual is

paradigmatically the subject of the research, if the subject has changed to a greater social entity, then we need to start to think about the conditions under which we ought to seek consent for something that smells like consent from that entity.

It is that simple. It is nothing more charged than that. That was the first point.

Now, to Eric's point about the simplification, we can ask the question, why is it, when the subject is in community, box one, we are not making distinctions between research whose results could be stigmatizing versus not. Whereas, when we have gone to the community, we seem to be wanting to make that distinction. That is profitable for us to think about, why we reach that conclusion.

DR. MURRAY: Actually, there are a number of things I want to say, but I'm going to hold off and let Zeke finish with what he wants to present, and then we will have until 3 o'clock to come back.

DR. EMMANUEL: All we have been talking about is the stored stuff that already exists. Part of the bigger controversy between the existing report is what should we do from today forward, from when we release our report forward, and what should we do about tissue samples that we are going to collect, say, if we release this December 31 to a resounding silence, what happens to the tissue sample on January 1?

My suggestion -- and this was a bigger leap, because

we really did not get to discussing this much -- is that on the anonymizable research, we probably shouldn't do much different from what we have already done, except down here in the last category, where I think it may be relevant to consider the possibility of a research advance directive or a prospective consent that the ELSI group has suggested.

When you get to the linked or identifiable, I think the requirements for having an informed consent that is specific -- sorry for some of the misspellings -- are higher and I think should be required.

Now, on this sheet of definitions, I have said something about what I understood a research advance directive might include or might not include. I thought that we might have a formal document, and that the consent form should be more than general, not agreeing with the College of American Pathologists.

Here are some of the things I thought we might include. We might specify whether the research could be on a disease different from the one the sample was taken from. It might specify whether the research that is potentially linkable could occur or not, and specify whether the person should be contacted regarding future research.

Now, those of you who see that list will quickly recognize that much of it is borrowed directly from the breast cancer consent form, which upon reflection, -- I have to say, my

initial reaction was negative, but upon reflection I thought was actually quite good.

I think it is a bad idea -- and here I depart from the ELSI working group -- to specify a specific investigator that could do it. What happens if that investigator dies tomorrow? What happens if that investigator leaves? For the duration of the tissue storage sample, if we actually had the duration, soon a lot of the samples we won't be able to use, a lot of the valuable information we get are from very, very old samples. I just don't think that is a very helpful idea. It is not an idea that probably the research participants like to think about, whereas the first three do get to the heart of the issue of stigmatization and protecting someone against stigmatization.

Just one last -- whether we agree or disagree, modify these tables and come to some consensus on whether the tables really capture -- or some modification captures the essence, there are still some things that we need to make some sense of.

One, all of this operates with a background of community notions of confidentiality, which we have said nothing about. They don't usurp, replace, substitute for standards of confidentiality. We have to say something about that.

I haven't said anything about informing patients about the results of linked research. That is a bone of contention. I think we probably have to say something about that. And what do you do in the absence of community consent, or presumed

consent? We have to agree whether that automatically means the research shouldn't go forward from that, and how we handle it if a researcher and a community couldn't come to some agreement.

DR. MURRAY: I've got a couple of things. This is really good. You got us off in a good direction, Zeke. It has got me thinking about, among other issues, we have one of the virtues of a policy, a good public policy. We have heard candidate versions.

Simplicity, I agree with that. The simpler a policy is, the better. You don't want to make it more simple than it need -- you want to make it as simple as you can make it, consistent with the goals.

You want to make it clear. The policy should be clear, so that somebody reading it who hasn't invested their lifetime in becoming an expert in the policy can look at it and say, oh, this is what I should do, and it can be a relatively clear and easy read.

It should protect legitimate interests of the parties involved. Here, we are looking at both the individual's interest, the interest of communities, the interest of researchers.

It should impose the minimal burdens necessary, and no more than the minimal burdens necessary to accomplish legitimate aims.

Maybe we can have some other policy virtues here, but

it struck me that that is a good set of architectural principles from which to work.

Just a couple of directions. I think the idea of collapsing up or down is a good idea, because it would simplify, if it doesn't do violence to what we are out to protect. So I'm not sure whether I am ready to go up or down. I was learning down, but I want to be open-minded about it.

A second thing is, we talked a lot about stigmatization. I was thinking that it was -- the problem was in part, what is stigmatization? How do we know it when we see it? How do we express that in a policy statement, so that people can look at it and know what we are talking about. Sociologists indicate it reads relatively clearly, but I think we are looking for a broader concept.

Without knowing the answer, I would want to push us back to say what interests do we think we protect when we seek to prevent stigmatization.

DR. CASSELL: Because of what was identified, a community is going to find itself dealt with differently medically, let's say, whatever. They are not really stigmatized; they are seen as different in a way that influences what happens to them. In an individual, we would say they were put at risk in some regard.

What you are looking for is a term that has to do with putting a community at risk for something.

DR. MURRAY: It may or may not be a single term. We have been using stigmatization as the umbrella concept to identify whatever it is that we are -- I think Eric is right, and certainly as Zeke has been talking about, the same basic idea that somehow it hurts a community. What do we mean by that, and what interests are we seeking to protect? Can we find a pretty clear, cogent way to express that in a policy recommendation that in the research arena, they know what we mean.

DR. SCOTT-JONES: I would like to try again to say why the idea of community bothers me just a little bit as it is presented here. I suppose it is because I can imagine researchers identifying persons within communities that could give consent, that would be a spokesperson of sorts, and may or may not actually represent the interests of that community.

So it might be, for example, like getting a nurse in Tuskegee, Alabama, who helped with that study. It really bothers me, because it somehow supplants the idea that in an ongoing way, we should make sure that research is -- the results of research are used to the benefit of communities, and you can't do that just by getting the consent of an identified leader in a community. It takes a different kind of process.

It takes a lot of hard work to forge connections between a community of researchers and a community of people who are not researchers. I think the way this is being incorporated

here would lend itself to finding people who would go along with researchers. It doesn't have in it the depth and richness that would be required if you were to genuinely establish good relationships between a research project and a community of participants in a research project.

DR. EMMANUEL: You have to remember, this isn't research on real people. This is research on stored tissue. The people from whom it came may be dead long ago. So it is not exactly the same as saying, here is a community, I want to go in and study them prospectively.

DR. SCOTT-JONES: My point has to do with the relationship between segments of society. I'm not making it very effectively.

DR. HOLTZMAN: I now understood what you are saying. You are articulating an idea. Even if they are dead, Zeke, the fact that you can tie the samples to a community if you are about to undertake this research, you would have some sort of relationship with a community in terms of the value of that research and why it ought to be undertaken.

The question I would then have, having articulated that ideal, is, what does that look like in the context of a consent process or an IRB process, and what are we proposing for a clear policy that says that if an investigator wishes to undertake the research project that comes in the IRB, that would be very interesting, what that would look like, what you are

looking for.

DR. SCOTT-JONES: It would take a lot of thought. It might take the researchers showing some effort to reach out to the community, to inform the community. The IRB tries to do it by having a community representative who represents the kinds of participants who are likely to be included in research at that institution. That is the purpose there.

I'm sure if we really thought about it, we could generate many ways in which the community of researchers could try to have good relationships with a community's participants, or communities that have ties to the tissue samples. It would just take some thought, and I haven't thought it through enough to try to lay that out.

DR. MURRAY: There are some people who want to get in the discussion, but are less likely to grab a microphone than others of us. So let me get Trish and Arturo into the conversation.

PROF. BACKLAR: I just wanted to go back to the issue of stigmatization, and how complex they can be. There may be shame involved. So if you belong to a community of people who have serious mental disorders, there is shame. On the other hand, the other stigmatization which is very common throughout this country is that information may come out in which you lose your health services.

So I wanted to get back to the point of how diverse

these issues of stigmatization may be, and why one must be very careful about possibly giving an identified group like an AIDS community more protection rather than less.

DR. BRITO: I think the division is very good, but I do think we need to go to two categories, whether up or down. I think what bothers me about the way this is done is that, the worst thing with stigmatization is that it is itself a subjective term.

Going back to something Bill touched on earlier, I think it is arrogant for somebody, whether or not they are in that community, because you can be a community leader and not represent most of the people in that community. That was what Diane was talking about. I think it is arrogant for somebody to determine beforehand what could be stigmatizing for a group of people.

So I don't have the answer. I don't know what the answer is, but I think it is very arrogant to be able to divide this in that way, whether this commission, an IRB or somebody determines what is stigmatizing for somebody else, or a group of people, even if they are leaders.

So I think that is what is bothering me about this. I think what the hurdle is going to be is, how do you determine what the community is and who is to represent it.

PROF. BACKLAR: But in fact, that was exactly my point. Some of these things are subjective, but some of them

are objective, like loss of health benefits.

DR. BRITO: Like what? I'm sorry.

PROF. BACKLAR: Loss of health benefits. It is not subjective. So that is why you have to be careful to make the difference between the kinds of stigmatization. That was the point I was trying to make.

DR. BRITO: So maybe that is where we need to go.

DR. EMMANUEL: When we laid this out in March, we had a bunch of values that were at stake, some of which were self identity, some of which were social standings that had nothing to do with economic, and some of which were over discrimination that had economic consequences.

So we haven't recapitulated all those interests that are at stake, but it seems to me it is a very slippery slope for us to say that any subjective sense of (word lost) is sufficient stigmatization. The idea of shame, that in itself, if we recognize it as shame, or we understand that someone could feel shame in the following context, in the following social context, that is very objective. That is not a subjective standard. On the other hand, if someone just claims, I am feeling ashamed and you don't understand that, that is a subjective claim which we wouldn't give credence to.

So I think we should try to make it objective, and shame is no different than discrimination or denial of health insurance, employment, life insurance, et cetera.

DR. MIKE: Whether we move it up from two to one or three is not a question of stigmatization. It is a question to me of whether we value privacy more. If I say regardless of stigmatization, I have a right to my own privacy, I would move two to three. If the stigmatization issue is the primary one, I would move two to one. So it is not a question of the relative stigmatization, it is what you put greater value on.

My second point is really a question to you. In your last slide about future research, would that apply only to tissues being collected for research purposes? Because if we apply it to any tissue collection, it is going to be a mess in terms of the informed consent.

It seems to me that tissues collected incidental to operations, et cetera, can be dealt with in a retroactive manner once that tissue is used. But tissues collected for research purposes, then I can buy into what you propose. So to me, it would make a distinction about what you apply these to.

DR. EMMANUEL: First of all, it is in direction to me. I was just trying to synthesize or distillate what we agreed to in March. My own understanding of the current direction is that those prospective research advance directives would apply to everything collected, including clinical tissues. You have to remember, most of the research that we are talking about are not actually on tissue samples that were collected for research. Most of them are on tissue samples collected for clinical

purposes that are then subsequently used for research.

That is where we have the vast majority of tissue stores, and that in the future is where we are still going to have the vast majority of tissue stores.

DR. MIKE: Then my purpose would have been for a general informed consent rather than these very detailed ones. The important point to me is that, at the time in which those tissues are then proposed to be used for research is when you apply your more rigorous standard.

DR. EMMANUEL: You can't do that. That one you can't do, because many of these people will be dead for whatever reason.

DR. MIKE: No, but by whatever proxy measures we currently would try to deal with existing tissue, is how I would deal with it in the future.

DR. EMMANUEL: I think it may be useful -- unfortunately I didn't reproduce it, but I have it here and could reproduce it for tomorrow, the breast cancer sample. It is a one page item, which is quite straightforward. It is not that cumbersome.

DR. MIKE: But that is a research project, right?

DR. EMMANUEL: No, no, that would be for any woman getting either a lump removal or a mastectomy for clinical care. That is the proposal. We may object to that, and we may follow what you are saying.

DR. MURRAY: We've got a problem, in that we've got lots of people who want to speak, and not enough time.

DR. EMMANUEL: Sorry.

DR. MURRAY: No, it is a tribute, not a criticism. You have raised good issues.

Let me propose the following. I didn't write the list down, but I think I can remember who is on the list, and you can berate me if I have forgotten who is on it. Let's take a 15-minute break now, pick up this conversation for another 15 minutes. I can do what I need to do in 30 minutes, and that would still end our part of the session by four. But let's give everyone a brief break. So we will see you in 15 minutes.

(Brief recess.)

DR. MURRAY: I'm going to start off, because I am here and I have a microphone in front of me, and I have a loud voice today.

One thing I was encouraged to hear Zeke say awhile ago was that there appear to be examples of successful community consultation -- we are not going to call it consent/assent -- where it seems to have worked. That was a question I had actually written down on my way in here; do we have any such examples. You say that there are.

I'm not going to ask you to describe them in detail now, but I think it would be important, if we are going to recommend that there be some process of community whatever we

want to call it, that we have some confidence that it can be done well in a way that is not unduly burdensome, and in a way that is not just a sham, but can actually be authentic, and with reasonable efficiency.

So I will ask Zeke at some point to recommend that we ask to draft that section to look at some places. We might even want to give little profiles, along with whatever analytic or descriptive section is, we might want to have this little profile of a couple of such programs.

DR. EMMANUEL: All I was going to say is that most of those programs I don't think deal with stored tissue. Most of those programs are prospective written future research or future clinical involvement.

DR. MURRAY: Do you think that the processes would be applied, applicable?

DR. EMMANUEL: Yes, because it is, who is the community, who do you identify as the leader.

DR. MURRAY: I was thinking of that, more than the strict rules, more than one that is strictly on the tissue samples.

PROF. BACKLAR: Actually, I really want to talk about research advance directives, but I do think that one can't necessarily classify shame as objective. I think it is an exceedingly subjective feeling.

DR. EMMANUEL: It is objective when you have it. It

is objective when we talk about your shame. In other words, you say I am ashamed; only you can know that. But when you say why you are ashamed, it becomes an object for discussion, it becomes objective.

PROF. BACKLAR: Well, it is objective, in that we know that people in certain communities feel ashamed about being connected to those communities. For them it is exceedingly subjective. So I just wanted to make that point.

In this little piece on research advance directives, you feel that perhaps the consent form should be more than general. You are saying that you feel it should be specific and not general. I am interested to know why you ask for that, because I see it in quite a different way. I think it should be very general. If you would explain to me why you think it should be specific, what is your argument.

DR. EMMANUEL: I think that there are -- we don't have enough of a background understanding to what that general consent would entail, or people could feel secure if we haven't had some of that history.

If you look at some of the things I put here, one wouldn't automatically know if they had been contacted for future research under a general consent. People might generally object if their tissue would be used, and they might not understand that a general consent could include that.

So it is my view that, because we don't have subtle

background understanding, the general consent, which would have to draw on that kind of understanding, would not really be useful or valid.

Let me be frank. Part of what I was trying to do was to say in essence that I think the ELSI suggestions, the ELSI working group suggestions, are wrong. They are way too significant and would be a serious impediment to real good research. These three are the maximum levels of specificity I think we should feel comfortable with.

When that breast cancer (words lost) happened and we looked at it, I have to say, my initial reaction was somewhat skeptical. On the other hand, having thought about it some more, what I would be concerned about, it would seem to be quite reasonable. It is one page, quite understandable.

But look, I'm just making a suggestion. The commission could move in a completely different direction, and I am happy. I think we should discuss them; I don't think we should make that kind of decision standing on one foot.

PROF. BACKLAR: I think maybe I was concerned with your first point, not with your second and third. That would specify whether research could be on a disease different from the one the sample was originally collected for. What I would want is for a much more open agreement about what the tissue could be looked at.

Then I think the second and third points are very

important.

DR. EMMANUEL: I am sympathetic with you.

PROF. BACKLAR: I also think that you are right about -- consent form should not look at the story. I think that should just be general and open; the consent is that it will remain in storage and everything is going to tamper with.

That was the only point that I saw. I see this as very, very different from the research in mastectomy, for instance, in somebody who has cognitive impairments.

DR. EMMANUEL: I was least comfortable with one as well.

PROF. BACKLAR: Okay. That's all.

DR. MURRAY: And that is the one about whether it would --

DR. EMMANUEL: Specifying only one disease. I think that --

PROF. BACKLAR: Right. I would urge that it be just open.

DR. EMMANUEL: I think that could be extremely restrictive, without very much protection to the individual.

DR. MURRAY: You had referred earlier, Zeke, to the AP receipts model form.

DR. EMMANUEL: Right.

DR. MURRAY: It would be useful if the staff could copy that, provide a copy for us.

DR. EMMANUEL: Okay, I'll make sure we have it for tomorrow.

DR. MURRAY: Thanks a lot. Harold, Steve and Carol, all of whom wish to speak.

DR. SHAPIRO: You just made one of the points I wanted to make, and it is very helpful. The other point I want to make is a more general one, namely, that what we are trying to do here, as others have pointed out, is to balance various values and interests at stake here in a way that is helpful overall to the society we serve.

We shouldn't get on to the tackle of trying to avoid any possible harm to anyone under any circumstances. That is not possible. So I just caution us, as we think through this, that that is not our objective. Our objective is to reach a balance which we feel good about and feel others can feel good about.

DR. MURRAY: Steve?

DR. HOLTZMAN: A comment on two distinct issues. The first comment, the conceptual framework and stigmatization. Zeke accosted me during the break and started to point out that these are my ideas, and I'm going to step to the --

(Laughter.)

So I tried to recreate what we did the last time. One was this notion as I said earlier of individual identifiable versus community identifiable. But the other at the time we

were struggling with is, is genetic information special. I think what emerged from it was, rather than genetic versus non-genetic when a community is involved, is whether the nature of the research and the results is benign or not benign.

Hang with me for a second. If we put aside the sense of stigmatization, what we said is, there is clearly kinds of research which is where the results would not be benign examples, such as the one Zeke has here, or studies of alcoholism in certain populations and whatnot.

There, we said even though it is individually anonymized, there could be a stigmatization. It is not a benign result; it could be harm to a group and therefore, some sort of consent community involvement ought to be involved.

So that was where we started in our thinking. That didn't matter whether it was genetic or non-genetic.

Then we said to ourselves, well, what about the stuff that is benign? I think what Zeke was reflecting here was the notion that it shouldn't have behooved us to assume that we know what is not benign -- what is benign. So in a place where it is clearly potentially harmful, get a robust consent, and in those in which you think it is not going to be harmful, you still ought to reach out to the affected community and get some sort of touch on whether or not you are right in that assumption.

Now, it may be that you will end up collapsing and saying, you should always have a robust reach-out and get full-

blown consent. But that was conceptually where we were coming from, if that is helpful.

DR. MURRAY: Let me just clarify something. Would that mean, if we were to promote some policy, that any time you could say of a particular research project that it dealt with an identifiable group or groups, that you have to go through this process of community consent? And is that something that we wish to have be true, and is that desirable?

DR. HOLTZMAN: I think that is what we are struggling with.

DR. MURRAY: It could become a pretty common requirement then.

DR. HOLTZMAN: That's right, and I think that is what leads you to try to get some mid-ground. In a world of blacks, whites and grays, it would seem that what Zeke was trying for was a case of just looking for some kind of cell surface marker, who has ever been stigmatized for just a cell surface marker. That could then have an additional association with something else. But that would mean another research study, so to speak, which could have the potential.

So I'm not saying we have an answer, but I was just trying to clarify what we were thinking.

The second thing I want to make a comment on is, Zeke, your notion of an advance research directive. This ties to a comment that Larry made, which I struggle with. That is, the

distinction between what kind of consent and how robust the consent ought to be when the sample is collected as part of a routine clinical procedure versus one that is being collected as part of a research procedure.

So for example, my company conducts paradigmatic genetic linkage study research. I have distributed to this group an article some of us from my company wrote concerning the very, very robust procedures we go through for consent.

In the studies, we do specify the specific disease we are going to be studying, where we ask for consent to use it in additional studies. We may not specify the specific studies, but we allow the person to say, no, I am only interested in helping this because it affects my family, et cetera.

It seemed to me that the kind of arguments that David Korn makes for the sample that is collected in the context of a clinical procedure and how robust the consent reasonably can be, I find very persuasive in many respects.

So I am asking, Zeke, did you find that what came out of the national breast cancer action coalition was something that could be used in a normal clinical kind of context, which wasn't so -- what is the word, invasive? I think that is what Korn was arguing: when a person was there for a medical procedure, they don't want to go through a 27-page -- you thought it was a good kind of --

DR. EMMANUEL: I thought it was reasonable. I think

it could be modified to be made even more simple, especially if we took out specification one. But I guess I do have some problems personally of just having a general consent, knowing that one of my samples -- say it turned out to be a rare disease. It could be very easily linked to me or to my family, and not having given a consent for that. Or someone out of the blue says, I'd like to do additional research on you or your family, because we found the following.

It seems to me that it is reasonable to ask someone beforehand to look at that. Now, is it going to satisfy the ideal standards of informed consent? Probably not, for lots of reasons that David Korn has raised. They are anxious about surgery, et cetera, et cetera. Is it going to make me feel that we have done a little better than if someone says, you can use my tissue sample for any educational research purpose if that comes up in the future? Yes.

It is literally one page of introduction and one page of three boxes to check. It is not that onerous.

DR. MIKE: But Zeke, you were talking earlier about when someone was concerned about the unusual cases, where you said you can't really address all of these with these general clauses. My question would turn that around. How much of tissues collected in clinical settings actually get used in research projects?

DR. EMMANUEL: I don't know the answer. I don't know

that anyone knows the answer to that question. But it is not unusual at major research hospitals for people to say go back and collect out 200 breast cancer tissues looking for something. That is fairly common. A lot of the Mayo Clinic studies result in having great mathematical records on all sorts of diseases in a community.

So is it simple, easy to use, or is it going to be a big impediment? You may be right. We may say the impediment is too large on a clinical service, where there is no chance it is likely to be used; we don't want to impose this.

DR. SHAPIRO: I have seen that breast cancer proposal, and it is a cinch compared to what you have to fill out in the hospital today when you walk in. This is nothing. What you have got to fill in there today is much more overwhelming than this. But we ought to send that around.

DR. KRAMER: You know, I just had surgery Friday, and as I was sitting there, going through the admitting procedure, I was thinking about all of this. I was thinking about, having just read the material, nobody is really going to pay any attention, you've got other things on your mind, and that part of it.

But I also was thinking about the technical people there in the admitting office who, starting at 6:30 in the morning, they are seeing all these people coming through, lots of families there with young children. They are so diverted. I

don't know how they could possibly administer the passing out and overseeing, the taking of anything that requires any kind of thought, I really don't.

When you think about what goes on -- now, I'm talking about community hospitals. When you think about what goes on in terms of people filling out advance directives, and we all know how poorly that is administered, can you imagine having everybody who is coming into the hospital having to fill out a really specific lengthy consent form? I just don't know how it would apply.

I think when you are talking about the consent form for breast cancer, I think it is excellent. You are talking about a small, specialized community of patients who from the moment they become a candidate for one of these procedures, very, very quickly they have available to them a lot of educational material, a lot of education resources. They quickly become educated. I think it is a highly specialized community. I think it is very different from the everyday person who is coming into the hospital.

DR. MURRAY: We need to acknowledge that our job isn't to create an ideal model that would look good if it could ever be implemented, but never could. That really isn't what I think this commission ought to be about. We ought to be about thinking about what the realities are of the circumstances, the people involved in them, what is on their minds, what would it

mean to someone to fill out the form in this way.

Now, Bette just argued that for most people in the hospital setting, the chaotic circumstances would make for, at best, a kind of minimal, pro forma signing of the consent, whatever. Is that your idea?

DR. KRAMER: Yes. I think that if I were confronted with something like that under those circumstances, and I didn't have a special interest in it, and I didn't have any kind of background in it, I would look at it and say, what the hell is this, and check off no on everything, and be done with it, just because I really wouldn't be able to concentrate on it under those circumstances.

DR. MURRAY: Most people don't, though.

DR. KRAMER: They don't?

DR. CASSELL: They check off yes.

DR. MURRAY: They check off yes, exactly.

DR. KRAMER: It does raise a question as to, whatever you check off, is it informed.

DR. CASSELL: No, but they have a benign view of the institution, or they used to.

DR. DUMAS: They don't always give it to you just before the surgery, either, that some people get beforehand. There are some agencies that do try very hard to get informed consent. They have an orientation for people who are going to have major surgery a few days before they are due to come into

the hospital. They give you those forms to take home, and then you sign them and you bring them back when you come in. There is an opportunity to ask questions.

So I think it varies by region, but there are some trends where there is really a serious effort to inform people.

DR. MURRAY: When a family member just experienced out-patient surgery, I watched very carefully how this was handled, both as a family member but also because of our work on this issue. It wasn't done in the admitting office, which it should not have been done in the admitting office. It was done in fact when the consent for that procedure was being obtained, and it was done as a at least quasi-separate request; would you agree to having your tissue, et cetera. It was still pretty generic, not as detailed as the form that has just been passed out, the model breast cancer form. But there was a chance, if a person were interested, for them to read it and respond, and perhaps respond in a meaningful way. I understand your concern, Bette.

DR. KRAMER: No, I'm not saying that it can't be done, I'm not saying it shouldn't be done. Quite the contrary. I am only saying that it is not a matter of small concern. It is going to be a major imposition.

DR. MURRAY: Carol has been waiting patiently.

DR. GREIDER: I just have one quick point. I know that we are going to come back to this issue of the three

categories that Zeke brought up, and once again come back to this issue of two categories versus three categories.

My understanding of either collapsing up or collapsing down hinges upon the community consent, as it is written here, or presumed consent, either requiring no consent or requiring consent. That is really the crux of whether we collapse up or down, how you go about getting that community assent or community consent.

So what we need to do, what would help me make up my mind about having three categories or two categories, is finding out what the risk-benefit analysis is of that issue. How hard is it really to go out and get presumed consent from a community or to actually get consent from a community.

If we could maybe look at that issue to some degree, that would help determine whether there should be two or three, how onerous is the burden of changing those categories.

DR. MURRAY: It is very important that we decide whether to do it two or three categories. Does that make it a category impairment? Sorry.

Is it being a good or a bad chair when you run into your own time, and leave yourself not much time for discussion of what you had thought to talk about? But I do want to give Zeke a couple of minutes, if you want to say anything further.

DR. EMMANUEL: I think this has been very fruitful. As I said at the -- probably not at the start, but somewhere in

the middle of my own defense, I was trying to summarize what the genetic subcommittee had done last March 5. I think actually, as I recall that meeting, much of the discussion we have had here is really wrestling with this complicated issue, and balancing off a lot of these concerns and interests for people who may be coming to it fresh. So it is in that sense helpful.

I would also suggest that people take it home and think about it, and that probably at our next convened meeting we should make some of the bigger decisions after people have had a reasonable time to reflect and evaluate this, putting it in the back of their minds and thinking about it. But I think we are going to have to make some decisions about this kind of framework, maybe not exactly this one, but something similar, and write the report.

DR. MURRAY: Thank you, Zeke. Thank you for leading us through this discussion.

DR. SHAPIRO: Could I mention a very contested analogy? The words that come to my mind in trying to tussle with this assent versus consent and what it all means and so on, is something which is also contentious, namely, environmental impact statements.

I'm not trying to draw this analogy too closely, but it is a somewhat different model than these. It is more like the assent. It is a way of generating information, and then having people who have the broadest look at it being able to

make decisions. That may be useful as we think about it.

I don't want to press it too far. There are lots of things about it which are not analogous in any way and so on. But it may have some usefulness.

DR. MURRAY: I'm puzzling over that one. What aspects?

DR. SHAPIRO: The question is, where does the decision come in the end? If you go to consent, that means the community involved, however that is defined, has the ultimately veto on this research. It could be that that is exactly what you want, but it is not necessarily what you want. It may be that you would want to say, you really want to know what they think and what impact it is going to have on them from their perspective, but that stops short of saying what you get in any community, whether it is Ashkenazi Jewish women, whoever it is. You stop short of giving them a veto on it, and leave that final decision in view of this information that is lodged somewhere else.

I don't want to press this, because I haven't thought it through. But it seems to me it is a useful thing to think about.

PROF. BACKLAR: But I thought that if you didn't give assent, that if you objected, that stopped it, anyway.

DR. SHAPIRO: That is now how I understand it.

DR. EMMANUEL: I left it ambiguous, and I think that is something we are going to have to decide. One of the things

that we have to remember is that this is stored tissue. You don't need someone to come in and give another sample, as it were, or answer a questionnaire or any of that stuff.

So if they raise some objections, but you didn't find them or the IRB didn't find them persuasive, and you thought the research could go ahead, it is eminently doable to let the research go ahead. So in that sense, I think there is a strong analogy here on the assent part.

PROF. BACKLAR: But I think you have to be very careful on how you define that assent, because it is used in other ways. As Diane pointed out, and as I always understood it, objection meant no.

DR. EMMANUEL: Well, I think Bill's reformulation of my assent of presumed consent is probably the correct formulation of that.

DR. MIKE: Zeke, let me ask you. In Boston, did the study board agree with the objection?

DR. EMMANUEL: But that wasn't merely moderate, mild objection. It has been a major campaign. It was a completely different order of magnitude.

DR. GREIDER: What is the answer, though?

DR. MIKE: What is the answer?

DR. EMMANUEL: Parts of the study are going ahead, parts of the study isn't, and more importantly, we are trying to do a big study to figure out why this community is so different

from every other.

DR. BRITO: What study are you referring to? We missed it.

DR. EMMANUEL: There have been several big attempts to get into large Jewish populations in major American cities, looking at the prevalence of BRCA-1, because it has been reported to be high among Ashkenazi Jewish women. In many American communities, they have been warmly received. In Boston, they were stonewalled, and a lot of effort put into preventing the research from going forward. Some of it is going forward, most of it isn't.

DR. LEVINSON: But don't the studies differ in whether or not they go back and talk to the women about their results? And whether or not it would be --

DR. EMMANUEL: I think that is only part of it. I'm not fully aware of all the details. I was brought in to help with the survey and to try to help figure out what the real concerns were.

#### PROJECTS AND PRIORITIES: A TWO YEAR PLAN

DR. MURRAY: Right. Well, we now have 15 minutes. I have several things I would like to cover. I just have to do it quickly.

I was going to use some of this time to talk not just about our plans for the tissue sample report, but our long-range plans. I think we're just going to have to put that off until

the next meeting; sorry.

I worked out a rough schedule. It is very rough. But if you figure out, work backwards, if you figure out a release date in the first half of January, and you allow roughly a month for the actual printing, vetting, et cetera of the report, is that a reasonable figure to allow, rather than a few days?

(Simultaneous discussion.)

DR. MURRAY: With the holidays, the print shop is closed down, like the other places. That means that you go to NBAC with the following report sometime probably in the first half of December.

Now, I'm not going to deal with all the procedural issues here. I'm not sure we even have a meeting scheduled in December. Maybe we don't need a meeting of the full commission. We don't have a subcommittee report yet. I don't know that. But it would mean that you probably need a meeting in November some time, in which the genetics subcommittee or the full commission would resolve the remaining substantive issues that you would then charge to the staff to incorporate into language for the report.

Moving back from there, the penultimate draft is distributed to the commissioners about two weeks before that meeting. Moving further back, I think means sometime in October, either the subcommittee or the full commission should have all the papers in hand, all the contractors' papers and the

draft of the key substantive parts of the report in their hands prior to the October meeting. At that meeting, they would try to discuss and resolve most of the substantive issues.

Moving back again, that means that the contracted papers and drafts of report sections have got to be distributed to the commissioners by early October, which would also permit us to have a September -- I believe we have a September meeting scheduled, mid-September, where we could hear from staff authors and from contractors, those which have material to present to us, where we could then provide feedback and guidance as to their work.

I am wondering if that strikes people as --

DR. EMMANUEL: We don't have any of the papers commissioned.

DR. MURRAY: I believe we actually do have some things in process. We are working on it, which means we will have to strike immediately when we get all these pieces going.

DR. KRAMER: Tom, what is this? Is the plan for public hearings of the subcommittees --

DR. MURRAY: That is one of the two things I want to talk about we quit today.

Now, that is a pretty ambitious schedule, by my judgment. I am eager to solicit the opinions of other members of this commission or staff who have tried to prepare reports, to see if you think it is doable.

DR. CASSELL: What are the alternatives?

DR. EMMANUEL: Put it off for a month.

DR. MURRAY: I would rather not put it off. I don't see why we can't remain sane and have this report out by the middle of January.

MS. HYATT-KNORR: I think it would be highly preferable to aim for that date, and if there is a last minute glitch, we certainly would -- if there was a serious glitch, we certainly would postpone it by another couple of weeks, or something. But I would not start out by planning on that.

DR. MURRAY: It gives us an urgency of commissioning papers, bringing staff on board to do drafting, et cetera. That has to happen now, within the next few weeks.

DR. SHAPIRO: I think that is exactly right, Tom. I think to make that kind of schedule, one has to define and assign -- two separate issues -- define and assign those initial bits of work quickly. You want to be able to review them on September 18 and 19. That means someone has got to be working on them the month before. If that can be achieved, then I think the January date can be achieved.

So I think that is where it is, and I guess we would know by the time we met on the 19th of September, whether that was the case or not. So maybe one possible approach, if it suits you, is to adopt that kind of schedule, conditional upon being able to define and assign these papers, and if that works,

great. Then we just continue on. If it doesn't, obviously we have another decision to make.

DR. EMMANUEL: I think one of the things that means is from the 18th and 19th, we need to define the major substantive issues and be able to resolve most of them by the 18th and the 19th, whether we are going to have three categories or two, what we are going to mean by various different terms. We have to have a pretty good framework and outline for the report then, substantively, not just, this is what the chapter is going to deal with. That I think means that the 18th and 19th are a pretty intensive meeting.

DR. GREIDER: Is that a full commission meeting, the 18th and 19th?

DR. SHAPIRO: Yes. Well, we have kept those dates. We haven't actually done an agenda for those meetings yet, but those dates we have chosen some time ago.

DR. MURRAY: I expect that we will need to do something in September, and we would do that part of the substance for which we had the appropriate background papers. But we have time in October as well.

DR. MIKE: Why don't we decide now that in the September 18 and 19 meetings, the subcommittee meet for two days? I don't know whether you want to meet then, but it seems to me that one day won't be enough. So I would rather the subcommittees meets on those two days and reach a conclusion for

all this.

DR. CHILDRESS: I think there would be some advantage to at least having some period to bring the whole commission together and talk about some of the issues. We will have some things we will want to run by the whole commission at that point in order to get a feel of deadlines of the agency report.

DR. SHAPIRO: Well, we will certainly be here the 18th and 19th. That is what we are planning on. It is only a question of what we schedule here today and so on. There is also an issue which I will bring up shortly, public hearings and so on, but let's come to that after.

DR. MURRAY: In response to Harold's challenge, I think we have -- I know we had laid out even back in March a tentative set of projects for the report. I'll tell you what they were. We may wish to advise them, based on discussions today and everything else.

I'm going to name them, and then I'm going to go back and revisit a couple of them and ask other people to help me. This is the organization/tentative outline of the report.

First is a description. By description, we meant what are these tissue samples, where do they come from, what form are they stored, what kind of science are they used for, what happened if we were to make it more difficult to do that kind of research, what would happen if we made a very liberal interpretation of who made it, what would scientifically be of

interest. This ought to be a piece of the report -- I feel very strongly about this -- that some member of the public could read and say, that is what the process is about. That is why it is important that we resolve this. So here are the concerns that people have, here is the science that will be done. That is number one.

Carol had a very interesting proposal to make about how to accomplish number one. We'll come to that.

Second will be an analysis of the ethical issues.

DR. GREIDER: I'm sorry, could you say that again?

DR. MURRAY: An analysis of the ethical issues. That is two. Three would be -- this is not necessarily in this order in the report. Three would be something about the views of the public on tissue samples. We have talked about this a couple of different ways.

Three would be religious perspectives.

DR. GREIDER: Four.

DR. MURRAY: Four, right. This is the new math. Five would be international perspectives. Six I think Zeke had proposed, that we come up with a framework that we intend to employ. We sit down, not just analyze, but say this is what we think the kind of balancing framework one ought to employ. And seventh and last would be the recommendations for policy. And there will probably be an introductory chapter before all this. The introduction you write at the end, in this case. Just

chronologically you write that toward the end of the project, and likewise the policy chapter.

Those are the pieces. Now, do they still make sense as pieces? Do you want to drop any out? Do you want to add any?

DR. EMMANUEL: I think if we were going to talk about the examples of where community consultation works, we might want -- I don't know if a whole chapter on that, but giving the mechanics via some substantive and rich examples.

DR. MURRAY: That might -- we could actually take that and use it in two different places. We could use it in the public views and say, this is a way of getting public views. We are going to report what we have learned about the public's views about tissue samples, but B, we are going to talk about a mechanism for getting public views on protocols, and then also work the specifics into our framework and our policy recommendations. Does that make sense to you?

DR. EMMANUEL: That is certainly a possibility.

DR. MIKE: Two things. One is that what is missing is how things are handled in a regulatory or ethical manner or consent matter or whatever you want to define that currently. Some of that was covered by Sheri in terms of the applicator things. I think that should be a distinct piece.

I haven't heard anything about whether religious aspects should be a separate chapter from the overall ethical

side, because that is how I started when we went to the cloning issue, remember, but then it turned out that religious perspectives were a really critical issue on the cloning issue. I haven't heard anything that tells me that in the tissue sample issue, it is all equal -- so important that it had to be separated out from the ethical discussion.

DR. MURRAY: You really make two different points, both important things. One is, you're right, we didn't list the current policy, and we need to have that piece, whether it is a separate chapter or folded. I think that is right. Can we get agreement on that? We need to have that piece. So that is without question.

The religious use, I haven't heard distinctive religious perspectives on tissue samples that seemed to have quite the independent status that they have in cloning, for example. So might we have one chapter which dealt with both ethical and religious perspectives? Yes. We might well have to ask different people to help us do those two pieces. We just may not find the same expertise in one of those. But they could be made into a single chapter.

Does that make sense? So we know we need to assign tasks, those two different tasks, even if we fold.

DR. FREEMAN: Religion in the broad sense, including religious of culturally different groups, have distinct concerns about specimens. Some body tissues are sacred to some Indian

groups, like the placenta, vocal cord and vocal cord blood.

In fact, Bob Beach reports an IRB was wrestling with a hospital whether to allow use of placental tissue, anonymous placental tissue research, and someone raised the point, gee, shouldn't you ask the woman, whether they would want to consent or not. So they did a survey, and the pregnant women at the hospital who had just delivered postpartum said, yes, that is special to me. So it is not just funny Indians, said facetiously, it is mainstream Americans. Some tissues are more important than others. As a matter of fact, we heard that this morning.

So something about culture and culture that is religion as opposed to theological, might be relevant.

DR. MURRAY: I don't remember if you were there at the early meetings when we began to address this, but we used the metaphor of a lake, the average depth of which might be 18 inches. So if you did a public opinion pool, a national probability sample, you mightn't find a whole lot, but there might be regions of the lake which are very deep. For certain people, certain cultures, certain religious groups, it might in fact be very important.

I would like, whatever we do about public use, to show that we acknowledge that possibility, and to the extent that we can identify deep areas of the lake, that we ought to try to do so.

PROF. BACKLAR: Which leads me to the point that it might be far better to do our religious analysis connected into the public issues, rather than put it into the ethics chapter, because that is what it is beginning to sound like. We might want to be very careful, a little bit more careful, about how we are going to go out to do our interviews in the public arena in order to capture some of that.

DR. MURRAY: We were talking about whether we have the right pieces. Any other pieces, or anything we want to drop out, or anything we think is important to have? Steve?

DR. HOLTZMAN: In this instance, there are a number of professional societies who have come forward with statements already. Do we cede that in an analysis of the different positions and whatever position NBAC comes up with reflects, disagrees? I take it that is a large part of what Zeke has been doing.

DR. HOLTZMAN: Right, but in terms of what you laid out, wherever that goes, it didn't seem it was the view of the public, so I wasn't sure it went.

DR. MURRAY: I guess I see it both ethical analysis and as policy recommendation, and I wouldn't see us getting in both of those pieces. But if anybody has a different view, --

DR. SHAPIRO: One possibility, Tom, just for discussion is that the first chapter really brings a set of initial conditions; this is how we got here, this is where all

this stuff comes from, here is where we are, here are the practices, and here are what people are saying regarding the future. One possibility is there, but I think it is equally possible to do what you suggested.

(Simultaneous discussion.)

DR. MURRAY: Then you look more carefully at the arguments they propose. That would work just fine.

I am over time. Can I have a couple more minutes?

DR. SHAPIRO: You can have more minutes.

DR. MURRAY: Carol had I thought a very fine idea about how to get into the description chapter. Carol?

DR. GREIDER: This is getting at the issue of what is out there, what kinds of institutions, what kinds of tissues, what are the issues that are raised regarding these tissues. One way that we might go about doing that is similar to how we dealt with the use of scientific societies for the clothing chapter. That is, if we could come up with a set of questions that we want to ask and identify a fairly large number of different kinds of institutions that have tissue banks, and send them this set of questions, maybe 10, defining what the areas are, and then follow up with some phone interviews or in-person interviews to ask questions about their responses to this questionnaire, and then write a report that summarizes what all these issues are, and professional societies that might have tissues in stored banks.

But even within the types of institutions, we even have that today on Sheri's outline. She had somewhere in her outline a list of some of the kinds of institutions, research institutions, large university hospitals, community hospitals, some government agencies, breaking it down like that, because it might be different issues for those different agencies.

We had a report that was written on the cloning for the views of the scientific societies, which very nicely synthesized a lot of the issues that came back on this self reported information coming back to us. I think that sort of a model might work well again in this instance.

MS. HYATT-KNORR: When we did this for the cloning report, the feedback that we got was really that there wasn't enough time to answer this adequately anyway, considering that we had a 90-day mandate by the President. Now, we don't have a 90-day mandate in this case, so if we do this at all, we would have to define what that is going to be really very quickly, like, immediately, because it is just not fair to present organizations with these questions over and over again without getting some adequate time to answer it.

DR. MURRAY: But we need to do it right away. We would not need an answer from them quite yesterday. Another distinction is that they have thought about this, where they probably haven't thought much about cloning. So they can draw on -- rather than having to create a position, they can actually

draw on experience. I think it would be in some ways easier for them to respond to.

DR. MIKE: That is what I was going to say. We're not going to be asking them policy loaded questions or evaluating questions. We are going to be asking them what are we talking about, this kind of nuts and bolts kinds of things are what you're getting at, right?

DR. HOLTZMAN: Tom, what are we thinking of in terms of the collections that we are interested in? There is the paradigm pathology tissue samples. Then there's the blood spots which are collected from every child at birth and then stored. Then there are lots and lots of repositories of tissues, fluids, et cetera, et cetera.

From personal discussion, when we take only one example, we tend to think in different ways than you might than if you start to cast the net widely about how we relate to various kinds of body parts. You find yourself starting to try to draft regulations with one case in mind, and lo and behold, it doesn't really make a lot of sense when you think about dropping hair on the barber's floor.

DR. MURRAY: One of the elements of genius in Carol's suggestion is that we would gather a much fuller portrait of the kinds of collections that are out there.

DR. HOLTZMAN: And what they are used for.

DR. MURRAY: What they are used for, what kind of

science they make possible, not just basic research obviously, but it would also be useful to say to potential patients, these tissue banks and our ability to use them led to X, led to this therapy. That kind of information is important, I think, in helping us to understand the significance of the question. So I don't have an answer.

DR. HOLTZMAN: Then a recommendation. I want us to cast the net widely, things that aren't obvious, what does the Red Cross do with outdated blood.

MS. HYATT-KNORR: The other thing we have to consider is that we don't really want to create a survey here, either. So we have to be very cautious.

DR. MURRAY: Right. We need the sort of expertise that we had do a similar job for us on the cloning report. That was Carol's recommendation.

DR. PITLICK: Excuse me. We might not want to overlook education, how samples are used in education. That is somewhat peripheral, but it is still very important as part of what we are gaining informed consent for.

DR. MURRAY: Thank you. Bill?

DR. FREEMAN: The Department of Justice doesn't consider specimens as specimens that they collect if they are urine. So you might want to include the Department of Justice and what they do with those specimens that they collect.

DR. MIKE: Can I say this? We are now ranging way

beyond our original focus on genetic research.

DR. GREIDER: Tissue is genetic.

DR. MIKE: I know, but -- so you have my leg in the hospital. You also have my blood. Which would you use for genetic research, my leg?

DR. GREIDER: Both.

DR. MIKE: But what I am saying though is --

(Simultaneous discussion.)

DR. MIKE: I understand that, but let's remember that we are trying to get focused on something. I don't want at the last minute for us to expand way beyond what -- we can do that later on. I think the only thing we need to be concerned about is that whatever we do in this area is consistent with what we explore and continue to move on in the future.

DR. GREIDER: But the point was about information. The issue isn't necessarily about the tissue, but it might have to do with the information inherent in the tissue.

DR. MIKE: But only in terms of what we are talking about, about the genetic information contained in that tissue. Otherwise, why are we worried about collectivities and all of those other kinds of issues?

DR. GREIDER: Right, genetic information. But just because your leg is sitting in formaldehyde somewhere because of some reason that we don't know why it was there today, it could be used for genetic information. So a leg is not irrelevant.

DR. MIKE: Right, but only if my leg was collected for some ideas for which there is enough information around.

DR. GREIDER: Any piece of tissue has DNA in it, so it is irrelevant.

DR. MIKE: I understand that, Carol. But what I am saying is, let's not forget that our purpose over here is about genetically based research.

DR. MURRAY: We are going to leave Larry's leg behind for a minute here. One other thing we really only have time to mention, and that is that we have been flirting with a plan to hold some public mini-hearings to get some input from people. I think we focused on what one might call somewhat interested publics. That is, not experts, not just scientists, not researchers, not the M.D., but say people who have had recent experience with being asked to provide different tissues because of biopsy or surgery or some such thing, or participation in a research project, I suppose, and having mini-hearings in different regions of the United States to get some -- to have a structure to them, but in order to provide us with some information about what the views are among interest public about tissue samples.

Trish and Bette have both been interested in this. I don't mean to lay it on their shoulders, but we have been given a handout which I trust you all have planned for public hearings for the genetic subcommittee. I don't think we have time to

talk about that in detail today, but I would urge you all please to read it and provide feedback. You can do it by e-mail probably best, to Henrietta, because if we are going to do it, we need to move on it immediately.

MS. HYATT-KNORR: Could I suggest you provide me feedback within the week?

DR. MURRAY: Within a week, that is the challenge. Thanks very much.

Any other business related to tissue samples that we must cover? Harold, thank you.

#### COMMISSION BUSINESS

DR. SHAPIRO: Thank you very much, Tom, and thank you for all the leadership you have given to this committee.

I just want to use -- I won't use all our remaining time today, but I just want to bring the commission up to date on certain logistic and business matters, just so you all will know where we are.

First of all, probably the most important item is dates of future meetings. We have circulated you all, and we have received responses from a majority of you but not everyone regarding dates which are available.

For the remainder of this year, probably the most important question I have to ask is whether commission members are willing to meet on a Sunday or not, because for the obvious reasons: no one chooses to meet on a Sunday. But could I have

some expression?

Let me put it this way. Particularly in October and November, if we cannot schedule other dates, would you be willing to come on a Sunday?

(Simultaneous discussion.)

DR. SHAPIRO: We don't know if we will have one or two day meetings yet, but Sunday will certainly be part of it. So you are willing if there are no other reasonable alternatives.

DR. HOLTZMAN: And Sunday is preferable to Saturday?

DR. SHAPIRO: Yes. There is a larger number of commissioners available. We will probably schedule at least one day meetings in October, November and December, just judging from -- I had a talk with Jim, and of course he will be talking with his committee tomorrow. Judging from their needs, which are going to be very intense during this period, and of course with the issues we have just finished discussing, it seems to me that although some committees may have to meet at additional times, that we ought at least try to get the commission available at least at three different moments. We are going to be meeting in September, and then we will schedule something October, November, December.

We will try to get dates to you later this week, actual dates later this week. Maybe even tomorrow we can get some of it done, but we will try to do it tomorrow if we can. If not, this week.

We will also schedule meetings for January, February, March, May, June and July. We may or may not use all those new meetings, but we have information from you all, so we can try to put those on our calendars. If we need them, we will use them, if we don't, we may release a day here and there if those aren't necessary. So we will try to get as much of it settled tomorrow as we can, for those of you that are going to be here tomorrow, and we will certainly be in touch by e-mail and other ways some time this week.

Now, the meetings on the 18th and 19th, I need some guidance both from Jim and Tom and others on the commission regarding the agenda. It is highly desirable for us to allow some time for public hearing from people, interested parties who we can identify and invite to speak to us, as we did do in the cloning case. We could use some of the time on the 18th and 19th for that.

But let me first of all turn to you, Jim, and see if you think from the point of view of your committee, there are groups that you would really like to hear from on the 19th. It may be almost the last time you have a chance to do that before we go into the intensive report writing stage.

DR. CHILDRESS: We will know better after the session tomorrow morning, but given our need to try to bring to closure a report on conduct in impaired subjects, and the fact that we really need to hear from a number of patients and patient

families and representatives in that area, I think we could usefully spend a big portion of a half a day perhaps on this kind of hearing. Do others agree on that?

So that can certainly be a portion of what we do on the 18th and 19th.

DR. SHAPIRO: How about you, Tom? Do you think that is an appropriate time, or would you rather do this later on or at some other time regarding your committee? Would you like to use some of the 18th or 19th here, just to hear from groups that you feel may be important from the commission to hear directly from?

DR. MURRAY: Yes, that would be fine with me. I don't think the issue we are dealing with has galvanized the kind of general public response the way Jim's subcommittee has, so I don't think there will be that much.

DR. SHAPIRO: I think that is probably true for the general public. It may be the opposite is true for some of the professional groups who are really focused on this.

DR. MURRAY: Many of them have had a pass at this already, and we will --

DR. SHAPIRO: So it is not a high priority item for you in September?

DR. MURRAY: No.

DR. SHAPIRO: That is very helpful. We will certainly make an opportunity, Jim, for you during the 18th and 19th, and

we will see whether time allows regarding the genetic information subcommittee.

With respect to other business, I will just bring you up to date on the cloning report. Probably I expect to approve within a week or two what are very modest -- typographical errors and so on -- changes in our report, plus putting the appendices together and publishing them together as a volume also. We are hoping to get that out of the way in the next couple of weeks, so that we will have this in the final printed format.

What we are thinking of right now is having the executive summary and the report as it stands, which includes of course the executive summary, in one document, extra copies of the executive summary for those that just want that, and then the appendices together, all the papers put together in a separate volume which will accompany that. That will help in coming up with the next -- we should be through with it in the next week or so. So that is coming along fine.

We still have an adequate supply of the second version copies you got, which of course are just bound somewhat differently. If any of you need more copies of that, you can certainly request them.

Let me also remind all members of the commission that the e-mail that you send through the lists you have, that is, messages you send to everybody, through the Listserv, are public

documents. The e-mail we have has been requested by the media, and they will receive them in some number of days now, receive copies of all the things that came through there. I just want to remind you about that.

So if you want to communicate something to one individual, not to the whole committee, but to one individual which you don't want to be treated in that way, then don't use that Listserv, use some other ways of communicating with them.

DR. HOLTZMAN: On a similar point, when someone sends something to everyone on the commission, and then individuals want to respond to that person and you just hit reply, we all get it. If we can avoid that, and put the address in, --

DR. SHAPIRO: Yes, type in the address. That's fine.

Again, just on some logistical issues, we have moved the offices. We have somewhat more space now in the NBAC offices. I myself have not visited them all, I hope to do so later this afternoon and report more back to you tomorrow. With respect to reports, we of course have a report on cloning that is out. We have the annual report of this certainly, which is due by legislation sometime before the end of this calendar year, and then we have the reports that will come from our subcommittee.

The current schedule as I see it is that we will have by the end of this calendar year, in addition to the report that is already out, our annual report, which will try to give both some

logistics and supplement it somehow to give it some meaning and some oomph, so to speak, but a largely straightforward report, that will be done by the end of December. I will be working on that.

We also will have the reports I believe by January 1 or before from Jim's subcommittee. Jim and I talked about that, and we will have more on that tomorrow, but that may amount to something like two or three separate reports, which we hope to issue sometime in December. Hopefully before the dreaded December 15 date which Tom highlighted before, but in any case, I think that would be quite a significant accomplishment, followed by the report in Tom's committee which will hopefully come out January 15 or thereabouts, or if for some reason it is a little bit later than that, then certainly that is manageable. Now, we also are going to begin something a little new, which responds to a question that Steve raised earlier today. That is, we are going to provide every six weeks or so something which I am calling a legislative update, just to keep the commission members informed of what legislation that might be of some concern to us is coursing its way through Congress, in case any of us have any ideas, or we might be asked to appear at hearings and so on, just to make sure that we are all updated on what information relates to topics of concern to us is going on in Congress. We hope to have the first one sometime beginning of September, and then every four to six weeks after that, just

update that, so we won't all have to do it on our own.

Of course, other matters -- we are now in a position of course to look for an executive director, since we have both the budget and the authorization to last beyond October of '97. We will now last until October '99, at least that long. Therefore, we are in a position -- and I will begin a notice. We put out a notice of this some months ago, but I will begin addressing that, and I will probably ask two or three members of the committee to review possibilities with me, so that we hopefully can get a full-time executive director in place hopefully in the next couple of months.

DR. EMMANUEL: Do you think by our next meeting? It is potential.

DR. SHAPIRO: Potential, yes, potential. If we can identify a person and that person is available that soon, yes, we will be ready. But whether we can identify and get that person here is something I'm not sure about.

So those are all by way of the simple logistics. I don't know if any of you have any other additional questions regarding the business of the commission.

DR. BRITO: Beginning October last year, we talked about holding meetings in different areas of the country. For me personally, it is easier to make the trip here, but in terms of public visibility and for other areas of the country to be able to be involved in public comments, et cetera, I think it is a good

idea. I don't know if we can still work that in there.

DR. SHAPIRO: Yes, thank you for raising that. We were about to make some decisions in that regard when the cloning issue came up, but we just put it aside because we couldn't move quickly enough. But that is a very good suggestion. I'm glad you brought it up. We will revisit that. There are a number of places that have invited us, or asked us to come. If you have any ideas, let me know, because we could do that at least for two or three of our meetings if we wanted to. Thank you very much. That had just slipped my mind.

For those of you that are interested in two unlikely issues, that is, one, modification, which came up as you may recall in some of our discussions regarding cloning, and secondly how economists deal with this issue, two unlikely events, there is an excellent article by Kenneth Arrow in this current issue of the Journal of Economic Literature.

It is in the form of reviewing Reagan's book. Some of you know her, and I think she may have been at the San Francisco meeting, although I was not there. That is the form it takes. So for those of you that are interested in that subject, I thought you might be interested in looking at it.

I don't have any other business items. Anybody else have any business items that come before us?

PROF. BACKLAR: Rachel said that you went to England right after the cloning report. I would like to know what went on in your

discussions there.

DR. SHAPIRO: I met in England with Colin Campbell, who is the head -- I keep forgetting what the committee is, but it is the NBAC-like committee. It has got some human genetics in its title somehow, I think. But in any case, it has the same function we have here, advising the British government. They are in the process of looking at the cloning issue, and they were very anxious to review our report, which I went over with them earlier last month.

Some of you may remember a woman who spoke to us in San Francisco, announcing the creation of this commission in Britain. She is a key staff person there. I met with her, and Colin Campbell.

They were very pleased with our report, in the sense that it parallels what their own thinking was, as far as I can tell. They thought that we were about as wise as they were, and that seemed to make them feel good, whether justifiably or not. But the general reaction in England, I found, amongst those people working with this commission, was that on reflection, the issue of cloning will turn out to be much less important than many other issues because of the advances in biotechnology. I think most people -- that is not an unusual opinion; lots of people feel that way.

So they are already trying to look ahead. They would very much like to have all our materials that we have produced, and they

have agreed to send us theirs.

Colin Campbell I had not met before. She is the vice chancellor of the University of Nottingham, a constitutional lawyer by training. I enjoyed a lot and learned a lot by listening to him. A very thoughtful person. Also, I promised to give him the dates of our meetings this next year, since he comes to this country quite often. I thought he might like to come to one of our meetings, and we could have a joint conversation with him regarding their interests, and so on.

Any other issues, questions, concerns? Okay, we are adjourned until tomorrow morning at 8 o'clock, I think the same place, Building 31C.

(The meeting adjourned at 4:30 p.m., to reconvene Tuesday, July 15, 1997.)