MEETING OF THE GENETICS SUBCOMMITTEE OF THE NATIONAL BIOETHICS ADVISORY COMMISSION

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I N D E X

P R O C E E D I N G S

WELCOME AND INTRODUCTION

DR. MURRAY: Well, let me welcome you to this meeting of the Genetic Subcommittee of the National Bioethics Advisory Commission.

Contrary to what some people may have imagined, this meeting will not be entirely devoted to the issue of cloning because we actually have work to do on the topic of our -- our first topic which is human tissue samples not only for medical research but also for other purposes. That is going to be the bulk of the day's deliberations.

We have reserved some time after noon for a discussion of the commission's work and forming a response to the President's request, as well as some time to talk about future issues.

There is time at the end at 12:45 for public testimony and if anyone has public testimony and has not so notified us, would you please -- Patricia? Pat? Patricia Norris. Would you please notify Patricia Norris if you desire to do so?

DR. HYATT-KNORR: Could everyone please pull the microphones a little bit closer to themselves so that the transcriber can hear you? Thank you very much.

DR. MURRAY: Is there any other member of the

commission who wants to say anything by way of introduction or brief introduction? Perhaps the commissioners, if I could ask the commissioners to please very quickly introduce themselves. I will start.

I am Tom Murray. I am with Case Western Reserve University, Center for Biomedical Ethics.

MR. HOLTZMAN: I am Steve Holtzman. I am with Millennium Pharmaceuticals in Cambridge, Massachusetts.

DR. COX: I am David Cox, Stanford University School of Medicine.

DR. EMANUEL: Zeke Emanuel, Dana-Farber Cancer Institute, Harvard Medical School.

DR. LO: Bernard Lo, University of California, San Francisco, Medical Center.

DR. GREIDER: Carol Greider, Cold Spring Harbor Laboratory.

PROF. BACKLAR: Patrician Backlar, Center for Ethics in Health Care, Oregon Health Sciences University.

MS. KRAMER: I am Bette Kramer, Richmond Bioethics Consortium, Richmond, Virginia.

DR. MURRAY: We have asked some guests also to help us in our conversations today. I think we will save introductions of them until we call on them.

The first item, the first substantive item on the agenda, is a discussion of the ethical and normative

issues concerning tissue samples, and Zeke Emanuel has graciously agreed to help lead our conversation on this first item of this day.

ETHICAL AND NORMATIVE ISSUES CONCERNING TISSUE SAMPLES

DR. EMANUEL: I am not sure this is a full informed consent but so be it.

(Slide.)

Tom asked me to talk about the issue of the normative standards for the genetic tests on stored tissue and I want to cover -- I am sorry if I am standing in front of it, I am trying to both get the microphone and use the overhead.

I want to cover these four issues and I want to begin with the position statements which people may have thought should be the end part because they set the frame. There are four of them I am going to look at and try to compare and contrast them. I am going to try to distinguish what the differences are, talk about how they appear to justify their positions, what I can glean about the ethical justification from their own articulations, and then try to raise a few thoughts about some cases.

And here I have to admit that I do not think I zeroed in on the exact cases and how the people who are closer to the actual issues of using stored tissue, like Steve and David, will probably have better cases.

What I am trying to do is to provoke ways in

which we might try to balance the values.

(Slide.)

Those commissioners -- I believe all of these overheads are in a handout that I prepared and I hope it is clear, and I hope these overheads are helpful for everyone else. I have looked at the four statements listed. They are the American College of Medical Genetics, American Society of Human Genetics, the College of American Pathologists, and the ELSI working group. I did not use the OTA because it really does not focus in on this issue in the proper way.

What I have done or tried to do here is to break down the recommendations for samples that currently exist, recommendations for how to handle future samples, and then put them into three categories. Currently anonymous, those which can be anonymizable or anonymized or anonymizable, and then those which need to be used in a link or identified fashion.

To some degree this closely parallels a very clear discussion, although not one with a lot of ethical justification, the American Society of Human Genetics. What this tries to do is to -- as best I can, and again one of the problems is not everyone is talking in the same language, people are unclear about where the references are, to break down what the recommendations are. So, just briefly, because I do think it is

important and I will readily admit I have had to interpret these statements because they are not always clear at various points.

The American College of Medical Genetics just lists a bunch of concerns at the end and does not really come down one way or another about current tissues. Without being disparaging, it was not that helpful on the current issue. On the anonymous issue, on the future use ones, on the anonymous they suggest that consent for use of clinical and research samples, providing information on things like duration of storage, future access to investigators, et cetera. Very similar stuff on anonymizable. On linked and stored they said consent for use in clinical research, communication of the results to the patients of new tests and test results.

This statement is quite close to the ELSI group working statement because they consulted many of the people who were on the ELSI working group statement to formulate their own. So in some ways it is not all that independent.

The American Society of Human Genetics is probably the clearest in what it recommends because it has a nice chart which says, yes, you can do it and, no, you cannot but it is a little short, as it were, on the ethical justification. Basically they say for the current ones no informed consent for the anonymous and

anonymized but informed consent except as specified in 45 CFR 46, which I will go through in a second so you do not have to remember it. They basically recommend the same kind of approach for future samples and they, however, do not recommend having a blanket for general consent for unspecified research.

I would say College of American Pathologists -- and we heard from Dean Korn last meeting urging this position. There has been a policy statement that has been endorsed by a lot of groups and I would say the most permissive for scientists. Basically they recommend no informed consent, no IRB approval for the anonymous and anonymized, IRB approval but no contact with patient or family for link to identified existing samples. In the future they recommend -- here they are ambiguous whether you should have general consent or no informed consent for the anonymous and anonymized. And they recommend general consent for research and education for future linked identified samples.

The ELSI working group, interestingly, is probably the most cautious of the four. In the current samples for the anonymous they say that there is no need for informed consent. They do recommend IRB approval for review of scientific validity and they tried to suggest that there was some ambiguity in the federal regulations, in 45 CFR 46. For the anonymized or anonymizable they

say there is no need for informed consent. They recommend IRB consideration and they have five factors that need to be taken into account, whether there are other samples you can use, whether there is going to be enough tissue left over once you use it, et cetera.

For the future, again I think they are the ones with the most requirements, they recommend obtaining informed consent for all samples likely to be used for research in the future, present options to patients in a detailed way, if it is linked whether they want to be recontacted with the results. They recommend people be informed about the risks and benefits, confidentiality requirements, the ability to withdraw. If it is stripped of identifiers they want people to state whether they want to share the samples with other investigators, whether they want them linked or anonymous, whether they want to limit the kinds of studies or diseases for which the samples can be used. So it is quite -- much more extensive than the general consent recommended, for example, by the American College of Pathologists.

Again, I freely admit that I have had to interpret here and not everyone may agree with every one of those boxes.

(Slide.)

Let me highlight three areas of disagreement that I could define among these.

One is the necessity or advisability of IRB review of the use of anonymous or anonymizable samples. There is clearly a difference where the ELSI group recommends IRB approval and the others -- for example, the College of American Pathologists do not.

Second, informing patients about the results of research studies on their samples. Again the ELSI working group recommends it. The College of American Pathologists is strong that it should not happen because research does not necessarily predict for an individual patient and they have a very impassioned discussion.

Third, the details of consent, whether they should be general or specific consent for future research projects and how far they should extend.

I think those are the three main areas of disagreement and I would like to suggest that -- not from an ethical standpoint necessarily, from a regulatory standpoint I think: One, the resolution for one is fairly clear. Two, I am not going to address directly and I am going to try to focus in on three in the subsequent talk.

(Slide.)

Now all the groups -- and I do not want to disparage these because I think they are actually quite well thought out, but there is this problem of ethical justification and sort of appeal to regulations. They

are not the same but frequently what you read here are sort of a mention of some values but then say we are going to rely on 45 CFR 46, the federal regulations, as if that were defining and, therefore, self-justifying.

So then, unfortunately, it puts a burden on me which not -- most philosophers do not like, which is to try to articulate the values that are really there to try to indicate what kind of balancing informs things.

To set the stage for that let me just review what I take to be the two relevant sections of 45 CFR 46 and I feel somewhat -- I am not expert on this and I know that Gary Ellis is in the room who is a much better expert and there are other people here that know much more than I do about this regulation. But there are, I take it, two key passages here.

The first is it says that research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from IRB review and then it lists among the categories this one which says, "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 reported by the investigator in such a manner that subjects cannot be identified directly or through identifiers linked to the subjects." That is relevant

for whether you need IRB approval for currently anonymous or anonymizable. It suggests to me, though I defer to those who know better, that on those two categories you do not need to have IRB review or consent.

The second issue is when you may waive the informed consent for the linked or the identifiable one. That falls under 46.116. "An IRB may approve a consent procedure which does not include or which alters some or all elements of informed consent set forth in this section or waive the requirements to obtain informed consent provided the IRB finds and documents the following four things: Research involves no more than minimal risk to the subjects, a waiver or alteration will not adversely affect the rights and welfare of the subjects, the research is not practical to be carried out without the waiver or alteration, and whenever appropriate the subject will be provided with additional patient pertinent information after participation."

(Slide.)

Now going out further on a limb, maybe to be cut off, I would just give you my interpretation of that because again all of these people rely on it. In the currently anonymous it suggests that, at least to my reading, that it can be these sources, samples can be used without informed consent or IRB approval since it is existing and subjects cannot be identified.

In the anonymizable or those which can be made anonymous I think the appropriate sections indicate that it can be used without informed consent or IRB review since it is existing and information can be recorded by the investigator in a manner that does not identify the subjects. My own reading of the link or identified is that it requires informed consent.

I would suggest to you that the idea of minimal risk and not affecting the welfare or rights of the subjects suggests that under no conditions, it seems to me, could you get a situation where doing genetic tests is never going to affect the welfare or rights of someone or never be minimal risk. I found it hard over the five days, and I cannot exhaust all my cases where you could rationally or reasonably defend that. So that is my reading and again I understand it is open for controversy.

(Slide.)

Now I want to shift to talk about values instead of just regulations because I think ultimately we have to provide some normative framework or normative justification for these regulations or maybe even suggest that they might be modified.

Again I want to state that many of these statements sort of honor or give homage to values but do not indicate how you weigh them or balance them. And

here is just a list of the kinds of values that one reads in these documents, and again the American College of Pathologists and the ELSI working group are the clearest about what they state.

(Slide.)

I want to propose to you, and I guess this was my real charge from Tom, a kind of framework for values for thinking about this and I do not know whether I have done it and I have great trepidation about this, namely because it was done on the short time and I am not -- there could -- there are lots of different ways of doing it.

One is I want to talk about -- I would like to distinguish intrinsic from instrumental value. Where the intrinsic values are the following four: Respect for persons, respect for communities or family units, or intimate human relationships, respect for cultural traditions just because they are there, and then advances in science even without better medical care.

It seems to me there is some intrinsic value just understanding things even if it does not do anything for anybody. I know that is not fashionable these days but it seems to me quite valuable. Then there are a lot of instrumental values. The benefits could be, I think, provided along this continuum, respect from the person to the community or family and then to the society, and they

range from improved self understanding and improved -- and more informed medical decision making, to better community understanding of what is afflicting them, to improved medical care and efficient research and cost savings in the research area.

The harms are things we are familiar with in the genetics area. A certain element of self doubt or self denigration, embarrassment, stigmatization or social isolation, discrimination, frank discrimination in insurance and employment. It seems to be those are consistent among the personal and the community, although by distinguishing that I want to suggest that they may not always flow together.

And then finally there are some social harms that can result from genetic testing. People could be afraid to give medical information so we could have a dearth of accurate medical information in the system. People could become suspicious of research and things like this.

I do not know if this is comprehensive and I think one of the things we have to discuss is whether this is comprehensive and whether this is even helpful to people in a way of thinking about it. I do want to say quite clearly I think it is -- if we do this thing, the instrumental from the intrinsic, it is important for us to keep in mind that because it is an intrinsic value

does not mean it always trumps in instrumental value. It is quite clear that some instrumental values are well trumped or overruled, or will be weighed more heavily than intrinsic values.

The other thing I think that is important for us to consider is how much weight to put on respect for individuals. Is it so important that it trumps all the other -- that every time it comes up we cannot think of a circumstance where respect for a person can be overruled or outweighed by other considerations. I think that is in the end going to be the most important consideration we make here.

(Slide.)

Now the other thing I -- sorry. The other thing I want to stress here, at least in my thinking about this I want to propose is that the conflict which is very pervasive in the literature and actually comes up in several of the statements of the following: People frame it as if what we need to do is to strike a balance -- sorry for the misspelling -- between the desire to increase knowledge and the protection of individual interest or one of the other statements that to discuss balancing support for genetics research with legitimate concerns about protecting the rights and privacy of human subjects.

This idea of it is society on one hand and

individuals on the other hand seems to me to be too stark and inaccurate a polarization. I want to suggest that we try to stay away from it because frequently what we are balancing is not just individual against society but different interests of the individual, different interests of society. They do not all line up on one side or another. I think to reduce it that way to individual versus society is to too frequently suggest that the only way we can do something is to overrun individual rights or society has to always take a back seat to an individual. There is more than just those two polarized rights and frequently I think the individual is going to be on both sides of the ledger and society or community or family is going to be on both sides of the ledger.

Let me conclude by trying to provoke you because I was trying to provoke myself in thinking through some of these cases to see how these values might balance out and to try to articulate or make us think about it.

(Slide.)

Let's talk about an anonymous existing sample and again the background against which I think we need to think about this is the current regulations. On an anonymous existing sample we need no IRB review and no informed consent. So the question -- and that is pretty

consistent among the statements. So the question is are there circumstances in which we might imagine informed consent or IRB review of something would be appropriate even if they are anonymous samples? Or does that anonymity a la the federal regulation sort of require us not to get consent or not to think about it in a more elaborate way?

So the case I tried to imagine as a good philosopher was think about something that is alleged in there and the case is a communally stigmatizing gene that might be reinforce a socially health stereotype. So say we are looking for gene for addictive behaviors or alcoholism to be evaluated in a specified population sample that -- social stereotypes suggest that that group is, you know, more likely to be addictive or more likely to be alcoholic. I do not think it takes a big stretch to figure out other examples that might fit into this category.

So the benefits of not having informed consent here or of doing a study without any more elaborate protections is that it advances scientific knowledge. It might improve self understanding of both the individual and the family. Why are so many people here alcoholic or engaged in what appear to be or might be described as addictive behavior? It might improve good medical care. We might figure out something to do

and it is certainly going to be efficient for research. The harm is there might be communal and personal embarrassment, stigmatization or discrimination.

So how do you balance these? I mean one of the things -- again the regulations would tell you, well, the benefits here outweigh the harms in part because there is not an individual, you cannot link it to a person and you cannot claim respect for persons it seems to me if you cannot link it, that is really the rationale here. And since respect for persons is the key value, if you do not have respect for persons then you weigh your nonefficient resource. That is how I read the regulations. That is how I read the sort of justification for those regulations.

It seems to me this might be a case where people will say, "Look, even if you cannot identify it to a person, you can identify it to a community." You might have communal embarrassment, stigmatization, and maybe even discrimination because you have gone to a communal sample. And that might be, it seems to me, enough to say even if it is anonymous you might need to do something else. You might need to talk to identifiable community leaders, community groups before you can go ahead and do this kind of research which would suggest there needs to be some approval process.

So that seemed to me to be a case where you

could not invoke respect for the individual but you could say going ahead with anonymous or genetic testing on anonymous samples might be something we should look at more seriously and we might need another kind of consent. That is one case.

(Slide.)

Let's go the reverse way. Is there a situation -- and here is where I think I need more help. Is there a situation in which you might have respect for persons in the balance and you might want to overrule that you do not think that is the value which is always going to be controlling or determinative. I think that is an important question.

Now I will readily admit I am a creature of the 20th Century and I find myself -- I find it difficult to try to articulate that kind of example not because I am not sympathetic, anyone who knows my writings knows I am not sympathetic with trying to figure out those examples, but I think we really do have this groove in which we find it hard to overrule that but let's try this example and maybe again Steve, David and others could think of -- we could talk about other situations.

I wanted to look at a linked existing sample. Now imagine there is a gene for a rare cancer or an ailment but you have -- because it is rare -- you have few identified family cohorts that you might be able to

test for them. There is not a stigmatization if it is, you know, something like cancer I do not think. But you also may not have treatment or you may have treatment, or the gene may lead to treatment. Now one of the families -- you have several individuals in the key family who are resistant to testing although you have their samples for some reason. You have collected their samples over time for something else.

Well, what -- how might you think about say are you making the arguments you need to do the test even if those people object. We have their samples. Well, think about the benefits of doing it. There might be respect for families and communities there because maybe the family really wants to do it over and above the individuals. It would advance our knowledge about certain genetic diseases. It would certainly improve familial or communal understanding about their ailments and it would be efficient. We have the sample. We are unlikely to get another family cohort just because of how rare it is.

The harms are -- well, the primary harm is you violate respect for persons. You might induce a certain amount of self-doubt in the family regarding their genetic heritage. You might open them up to insurance discrimination and employment discrimination that we know about, and it might lead if people find out

to a certain kind of suspicion of research that you will not respect their wishes, you might run over their wishes.

Well, how do you balance this? Are there times where say advances in knowledge improve community understanding and respect for the family overweighs or balances heavier than violating persons. I mean it seems to me part of it might depend upon how devastating the ailment is to those families, whether the fact finding and genetic solution might provide you some therapy. I throw this out as a thought provoking situation because I think the standard view is if the person in a linked sample does not consent you cannot, period, do it. I want to challenge us to think through whether there are cases we might say that is not the only or sole controlling value. Every time it lines up on one side or the other it decides things.

(Slide.)

Let me conclude -- I do not do genetic research but the issues here -- it seems to me one of the virtues of what we are doing is that the issues here are not linked or limited as it were to genetics. This kind of research extends way beyond. So while we may end up focusing in only on genetics I think what we are going to say will have ramifications beyond.

I may in some of my hats worry about health

services research using big databases, hospital records and other such, and it seems to me these are other areas where you have anonymous or anonymizable, or potentially linked data sources where what we say will have implication or where the values we articulate could extend.

Okay. I hope this has been worthwhile. Thank you for putting up with this.

DR. MURRAY: Thank you, Zeke.

DR. LO: Zeke, I want to thank you for sort of putting this together and getting this started. I think this will be very useful.

I had two main reactions to what you have said. One is that I think in -- I like very much the way you sort of started by looking at the existing position statements to sort of see what is there and what are the issues that are raised.

I think one thing I would like to ask us to do is in addition to looking at the issues that were either raised or implicit in the position statement, what are the ethical or value issues that should have been part of the deliberations or weighing that were not there?

It seems to me two of the issues that I would be concerned about are this notion of implied prior consent. If I sign this blanket thing in a hospital

saying, you know, anything removed from me can go for teaching or research, do I really understand what I am signing up for with regard to genetic testing, DNA testing?

Secondly, it seems to me having been involved in some of these projects one of the key problems with unlinking and making databases anonymized is how you actually do that and how solid is the protection of confidentiality? Because just to say we are going to make it anonymous, there are different ways of doing it some of which are riskier to breaches than others. And I would argue that may be one reason why you might want to have some sort of external review, whether it is an IRB or something else.

And my second comment had to do with your cases but, you know, I am always willing and sort of like to think how this works out in actual practice. I like sort of what you did to sort of get us started.

I was particularly intrigued by your case of linked existing samples for sort of a rare disease with new kindred cohorts. It struck me that there is a clinical analogy to a family that needs organ transplant and one member of the family does not want to be tissue typed for -- these would be solid tissue transplants, liver or kidney. And in clinical practice we sort of let that -- not only do we let that people opt out, the

medical sort of system protects that person so if the person says, "I cannot face the rest of the family if I dare say I am not going to do it, I am selfish." They sort of say, "Well, you know, it did not work out."

This, I guess, was an analogy to what you said in your book, Tom. Would it make sense to have different standards in the clinical setting than in a research setting? But in the clinical setting where the possibility of good it seems to me is much stronger than actually save someone's life or prevent serious ability for transplant, we are willing to give so much weight to the family members' refusal to participate in this enterprise. How can we reconcile that with what you were trying to do, which I think it is a very good question?

Can we construct a situation in a research setting where the potential benefits it seems to me are much more speculative? How would we justify overriding the individual refusal in a research setting if we are not willing to do it in a clinical setting?

Tom, it seems to me it is analogous to your argument that you do not want to put more responsibilities on a woman -- a pregnant woman carrying a fetus than you would put on the parents of a born child? So I think, you know, we need to sort of make sure our intuitions here correspond to what we consider

acceptable in a clinical arena but I do think your point is very well taken. How do we balance these different considerations?

DR. EMANUEL: Your first set of points, I did not emphasize enough although it is on the chart that the College of American Pathologists strongly states, and I think this is useful, that their physician assumes a written confidentiality policy approved by the IRB for anonymous and anonymized samples, that they do not rely just on researcher to researcher or the head of the pathology department being a good guy, that you have to have a written confidentiality policy and that has to be sort of background against which not having informed consent and not having IRB approval for each study occurs.

I think that does go somewhat to your question of how firm is the confidentiality safeguards may be a controlling factor. I agree and I think that they have brought it out and I apologize for not stressing that. As regards the sort of general consent I think that is another issue as to how much information people actually need.

The last case I think it might be fair, Bernie, to turn it on its head and ask, "Well, is our standards in the clinic all that right?" Should the presumption be that someone in the family can first say

no and then get the medical system to protect them by somewhat, if not outright lying, then sort of hiding the facts? Or should there be more pressure on someone to do something for familial and community good? I mean, just because we do it in the clinical setting does not suggest to me that we should automatically assume that is right.

Again I think what reins in the clinical setting is the sense of, you know, individual informed consent and respect for persons takes precedent over every other value. I think, you know, maybe you are right. The implications of what we are going to decide here not just to accept other kinds of research except in clinical practice and I think we need to think hard.

I mean, it may be that in the end what we say is there are no circumstances under which we would override individual willingness or individual consent. I guess part of my challenge to you, is that true? Is that really the way you want to come out? Is that the way I want to come out? Is that the way the committee wants to come out?

DR. HOLTZMAN: Can I -- while you are on the last case then can I ask you a question? You have constructed it such that there is a refusal to consent as opposed to no consent meaning the absence of consent. I am just wondering if that makes a difference.

DR. EMANUEL: Well, I take it that the

absence of consent would mean you had not asked.

DR. HOLTZMAN: Correct.

DR. EMANUEL: And you just went ahead and used the sample.

DR. HOLTZMAN: Right.

DR. EMANUEL: So I think even though it -- well, I mean I think that could make a difference but then you would have to defend why you think not getting consent when you could link it and could identify the person.

DR. HOLTZMAN: Right. Well, for example, the pathologists. I am going to call them no consent relying on just the thin general consent essentially. So there is no consent for this particular study.

DR. EMANUEL: It seems to me on those conditions you are weighing respect for persons less. You might not be override. I mean, it might be less of a violation but it is still not putting much weight on that value.

DR. MURRAY: David?

DR. COX: Yes. I had a couple of comments. The first is you make the point, Zeke, that this very strict dichotomy between societal/communal rights versus individual rights may be not a useful way of looking at things. I would like to say that I think that similarly the strict dichotomy between research and clinical

practice may not be a very useful way of looking at things particularly in the context of genetic information. It has been historically but I would like to say that I think that is much less of a clear line now and we have had discussions about that at this group before.

The second point I would like to make, you alluded to this but I would like to make it even stronger, is that we have a whole variety of different position statements but it is a very small number of people who have written these statements and they cross across all of them. Those people, like all of us, are stakeholders but they are stakeholders in a very specific way. They are stakeholders in the context of research or stakeholders in the context of what they would have to do different compared to what they do now.

None of these statements reflect people who are out there on sort of the consumer end of it. So I think that this -- if we focus purely on these statements, okay, then we are losing a large fraction of the people that would be concerned with stored tissue samples.

The final point I want to make has to do again with this last case. First of all, the first case that you showed I think is really right on the mark in terms of a scenario where the present statute, okay, that

basically says you do not need any informed consent may be inadequate in the present world. So it shows that things may be fine but just like research -- the kind of research and clinical practice may have changed. I think that this interest in communities, which again we have talked a lot about on the NBAC, puts it in a different world than maybe when the statute was written.

The same thing goes for the second case. So sort of in one way Steve was right but it is not so much whether it is the -- again this strict dichotomy between society and individuals, you may end up coming down on it but it is the process by which, okay, you get the informed consent. Steve raised the issue of, well, you know, the subject is not approached at all, right. You do not raise the issue of giving consent. The other way is that the person says, "I will not give you consent in the family." But how does that work in clinical practice?

I mean, you know and I know the way it works is that there is what goes on within the family and with the person, and it depends very much on what that family structure is so that the family treads very gently, okay, with the person if the person is not integrally involved in the family structure.

On the other hand if the person is integrally involved and there is really strong family ties then

there is very open discussion with this and -- but the end result, okay, comes after that kind of a process. So it is not only whether the person gives consent or does not give consent, it is the process by which that is adjudicated within the group. So I think that -- but again that is not a straight forward thing either.

So it is not only figuring out, okay, what you are going to respect, either the family wishes or the individual's, but the process by which you came to the conclusion. I think clinically that is very important and I think that whether it is research or clinical, that is the same issue. So those are just comments on a variety of different areas.

DR. EMANUEL: Well, I heartily endorse it.

DR. HOLTZMAN: A few comments and questions. Something I struggle with that I do not see necessarily reflected in these except implicitly in terms of how people come at it are the conditions under which the samples were collected.

For example, if you are going into a prospective genetic study, and that is your paradigm case, and I am thinking that downstream I might like to do additional studies. It only seems right that I should get a very thick consent from the person that says, "I want to use them downstream and I want them anonymized in all different kinds of studies."

But the biologists on the other hand come from a very different paradigm of the conditions under which the tissue is collected. One of the points Korn was making. If someone is in here for a medical procedure I am not going to take them through this extensive laundry list of different consent conditions. I do not know what difference that makes but it may make a difference in terms of how we have to think about this. So that is one that would be interesting to hear people's thoughts.

The second is -- and I may be the only one who suffers from a feeling of ambiguity in the concepts or interpretation of anonymous or anonymized. If you look at the ELSI -- if you look at what the statute says, the information is recorded by the investigator in such a manner that it cannot be traced. I always took it that if I am sitting with a sample, I am a pathologist, and I can say the sample ties to this person, you, investigator, want to write a paper, I can give you the sample to do research on, I cannot -- I will not give you the name or the link so you can write your paper and the community cannot get from your paper who it was.

If you look at the ELSI statement on the other hand their interpretation of this is that if there is any logically possible way that the sample can be traced whatsoever, all right, to the person then it does

not fulfill the condition. At least I think. I would be interested in hearing whether you agree if that is what they say. It is not clear to me that that is necessarily the right reading of the reg.

DR. EMANUEL: I think it is quite clear that they are trying to over read the reg.

DR. HOLTZMAN: Okay. They want to have the reg say something it does not say. Okay. I think the reg is pretty clear that your first example is acceptable. They want it to be -- to over read it. I mean, the reg says if the investigator records it in a way that cannot be linked that is enough. Okay.

DR. COX: As a member of the ELSI working group I will tell you it was exactly for the kind of scenario that you laid out, Zeke. I had to smile because it was exactly for these communal things, okay, that the ELSI working group said this could develop but times have changed.

DR. HOLTZMAN: Okay. So again as we look at -- so I take it you -- in your conceptual scheme you were using it in the sense of which it --

DR. EMANUEL: Right.

DR. HOLTZMAN: -- an ordinary language reading --

DR. EMANUEL: Yes.

DR. HOLTZMAN: -- would suggest. Okay.

A third issue is we appeal to 46.116 in OPRR in saying that genetic studies cannot be construed to be minimal risk. This is a position certainly my company takes and that is why you need an appropriate perspective on it but we have had a lot of discussion and certainly this is an issue the pathologists raise, is how broad is the net of a genetic study? Again I can think of paradigmatic genetic studies but there are all sorts of investigation which in all relevant senses leads to the kinds of information which leads one to worry about or not worry about depending on the case what you can get from the DNA test.

So when you say in the way you said it we will need this for these genetic settings because they will fall under 45-46.116, the question then resurges is that going to be true for all research, which again was the pathologists concern.

And then one just quick last point. Your first case, what I thought was maybe a different way at it, and I think it is an interesting case, and we struggle with this, was not so much attacking it from consent although maybe it ends up there, is re-asking what it means to be anonymous. It may be anonymous with respect to the individual but if it is not anonymous with respect to a group then that tells you that that -- that way you do not have to change your issues of consent

change. Maybe all the same considerations are just there.

DR. EMANUEL: Well, let's talk about the last one first because it seems to me that the intention of the anonymous clause was that you would have basic information, sex, basic sociodemographics, but not a particular individual. So it did -- I mean, again if they -- that may be a historical reading of it but that, as I understood it, was the thrust of it. It is on that reading of the regulation that people like myself go into big databases, erase the name but get all sorts of other, you know, zip codes, all sorts of other information, link hospital use, you know, what they were admitted for, sex, religion, you know all sorts of information.

So I do take it that it was tying you to the individual, not to reinterpret what anonymous means. That may -- to include not being able to identify what social group you are from. That seems to me would probably erase the possibility of doing this kind of research to be perfectly honest because that is essential for that kind of research in lots of other areas.

As we are talking here I want to -- to your second point and I think this goes somewhat back to what Bernie said. The background or the conditions under which you are doing this research in my view, how strong confidentiality requirements are, how much discrimination

you might effect, what really is minimal risk or not.

Really the way I incorporate them and this may be idiosyncratic, just to tell you how these values are weighed. If the information really is potent, it is a dominant genetic disorder that you are after, that seems to me to raise the stakes of the possibility of stigmatization, discrimination.

If it is a more vague genetic information you may say that it seems to me the way that gets incorporated into this is to say, "Well, those risks, those harms are lessened and, you know, where it is minimal is obviously a judgment call." But that is how I understand it.

Similarly with the issue of how secure are the confidentiality protections. Well, if the confidentiality protections are not secure what that tells me, or not as strong as you want, then the possibility of discrimination and stigmatization goes up. You weigh them more heavily. So that is how I incorporate that stuff. When you have strong confidentiality requirements you can say this is an important value but we do not weigh it so much because it is being taken care of in this way.

Anyway that is how I would try to go at the sort of background social conditions where they affect the values by indicating the kinds of weight you would

apply to them.

DR. MURRAY: Thanks. Bernie?

DR. LO: I want to follow up on a theme that you originally raised, Zeke, and I think Steve picked up on. That is sort of the notion of consent. It seems to me that the consent we are talking about is a rather sort of thin notion of consent. That is sort of getting consent at one point in time usually when the sample is collected. And it seems to me that there is a lot of possibilities between that consent and saying you have to get specific consent every time you want to use a sample for DNA testing that was not contemplated in the original consent.

Part of it just comes from the pathological sample example and I think, Steve, you are right that in the clinical setting when you are doing a tissue biopsy you are really getting consent for the medical procedure and the risks and benefits. Frankly, I think a lot of times the research things are in fine print and it is -- you know, you do not really talk about it.

First let me suggest that if you -- and it may not be appropriate at the time you are doing a clinical therapeutic or diagnostic procedure to sort of have a long discussion about a potential future research project. But it seems to me after you have sort of gotten the clinical value and you still have the patient

you could then have a pathologist go and say, "Now we did this study originally for clinical reasons but now I would like to talk to you about putting it in a tissue bank where it can be used for certain types of research." It seems to me there are other ways of having this discussion with the patient other than when they are about to undergo a liver biopsy.

The other point I want to pick up, Zeke, is something you alluded to. I know it fits in with your sort of thinking about community values. I think there is a real role for community consultation in designing these types of studies and again this goes back to my experience with doing HIV testing from previous assembled serum databanks which were assembled for all kinds of other purposes.

One of the questions was since these were all going in perspective studies where they wanted to get ten year and fifteen year follow-up for cardiac risk factors, the real concern it seems to me about potentially at least someone in the community volunteering to be part of a study of cardiac risk factors in young adults or even sort of sociodemographic populated populations, but also in reading the newspaper that in this study the HIV prevalence was 12 percent or one percent, or .01 percent. It seems to me if you -- there is a sort of real danger that people will not want to enroll in perspective

studies if they think that the materials are being used for something very different and that is procedurally different than the original sort of purpose and design of the study.

Again it is often posed as a dilemma where you have got the samples and you cannot sort of go out and find everyone necessarily. It seems to me you could do community consultation. And often it seems to me if it is really worthwhile research project and it is sound in design. One of the problems is a lot of these tissue bank studies are very poorly designed. There is no control group. You do not have information about a lot of the variables you want. But if it is really an important study you should be able to convince a representative group of the subjects that it is worthwhile doing.

I understand what you say, you often get tremendous ideas on how to start these studies. So scientists also often pose this as, well, is this going to make my life complicated, I will not be able to do the study and science will suffer, and humanity will be, you know, deprived of this knowledge.

In fact, it is much more of a -- it can be a very collaborative thing where you go to the community and say we have a real dilemma. We have collected these samples for one purpose and we have the opportunity now

to use them for a very different purpose but there are some risks particularly with regard to confidentiality, stigma and discrimination, can we talk to you about how we might try and balance these values? I actually think that may be a way of, you know, striking a balance.

DR. EMANUEL: I think it is a great case actually, Bernie, but I am not sure how it cuts. Let's just think it through, for example. Are you really going to the community to go to the community to get community consent or are you going to the community as a proxy for all the persons and really as a way of respecting persons. And here is how it would -- how I think, say you go to some representative sample and you have got people there and there is a person who says, "Either I was on the study or I know someone who was on the study and I object," but everyone thinks it is a good idea.

I mean, again it seems to me you have -- that is not an unreasonable or unheard of kind of situation where there is someone who for whatever reason they went into the study and now are worried about their disease or object to it on say religious grounds. They do want someone looking at alcoholism, et cetera.

So what do you -- what is to -- I mean, who do you respect there?

DR. LO: Well, let me just say it would be different if 10 percent or 50 percent or 90 percent

objected. I could see that the balancing you would do would be much tougher if the vast majority of the people say this is a bad study, we would never have agreed to it, we think it has much more potential for harm than just one or two people saying it. And I do not know what the threshold is but it seems to me it is important to know whether it is more like one percent, 10 or 50, or none. But you are right, it will -- at the bottom line how do you balance these is a very --

DR. EMANUEL: Well, actually I like your answer because I agree with the answer. It does depend upon what proportion. But it does seem to me that if some objective, you are still willing to go ahead with that kind of study, suggests that this sort of respect for persons, especially if that one person said, "I was in that study and I object," that that is not a determinative judgment. I mean, I think that is an important --

DR. LO: Well, again it may not -- you may not settle it there but you may say there are enough concerns raised that we want to have some sort of opt out process. So we try our best to contact people and say, "We are going to go ahead and do this unless you object" as opposed to saying, "We are not going to do something unless you consent." So again it seems to me there is -- it is -- consent is a process. We tend to view it in

this research setting of a one shot all or none affair. I think as in clinical medicine consent is always a process.

DR. COX: Actually for my money, Bernie is right on to the button issue about all of this because it is -- we have to adjudicate one way or another, and that is what you are saying. But the -- there is no process right now. So it is sort of like the distinction between do you believe in democracy or do you believe in enlightened despotism. And the way we deal with informed consent right now --

(Simultaneous discussion.)

DR. COX: -- is it like despotism? All right. Because -- and in some ways some of the statements are that way, is trust an issue? You know, we have always taken care of you before. In fact, research subjects are not part of the process at all. And largely they are not part of the process because it does not really relate to them directly as individuals and so they -- you know, we need their samples but we do not need their input.

Now what we are talking about in terms of some of this genetic information, and I think it cuts across many different things, is maybe it is not so bad to get people's input because as Bernie points out is that what that will do is help us to in different

situations adjudicate between these conflicting values. That is what I think is the most utility. But even from a pure scientific point of view, do a better study because our subjects are not, you know, total idiots and they often times have great insight into the process or study the process because it affects them.

So I think this in particular is a single key point that I think this whole discussion about stored tissue samples revolves around. It is the process by which these values are adjudicated and how much the research subjects are brought into the process. That is a separate issue, I think, than how you adjudicate it.

And I again think it is artificial to say that we will always either go for the individual or we will go for the group. But in some cases it can be one way and some another way, and it makes all the difference in the world to me what that process is just as I was describing before with the individual families.

So, Bernie, I think to me this is -- is the process of how much or how much we do not involve people. That cuts across these different statements because the whole basis of these statements if you look at it you can take the statements and you can put them in one camp or the other absolutely.

DR. EMANUEL: Well, I think we are in heated agreement. I think the only thing I was challenging

Bernie on was the issue of how you might weigh these things and whether the individual would always trump.

DR. COX: Yes.

DR. EMANUEL: And I think -- I mean, I agree with you. I think it is a process and that having a community about with the researchers may be a way of having a public evaluation of the risks and benefits at the time.

DR. COX: So we may be in agreement, okay, but I think that there is certainly not agreement out there in the world in terms of whether there should be a process or not. In fact, that is where there is the disagreement. And what I do not have any feeling for is whether the research subjects want to be involved in the process or not. Some do, okay, some do not. What is the general view of that? Certainly a large block of individuals do not want the researchers or the research subjects involved in the process any more than they are now for practical reasons. I do not think not ethical reasons but practical reasons.

So the -- are changes in some of the ethics changing with the practicality of this. Secondly, you know, what do the general -- what are the issues from the point of view of the research subject? Again I will say I think that is where I would like to get a lot more information because I am clueless about that.

DR. MURRAY: Trish, did you have your hand up just then?

PROF. BACKLAR: No.

DR. MURRAY: No? That was an involuntary reflex?

PROF. BACKLAR: I am sorry.

DR. MURRAY: That is all right.

Actually, Zeke, I wanted to compliment you. I listened to your analysis, your initial presentation, and the more the conversation has proceeded the more useful it is becoming to me in sort of figuring out just what is --

(Simultaneous discussion.)

DR. MURRAY: No. That is a compliment.

DR. EMANUEL: I thought that the presentation was vague.

DR. MURRAY: No, the presentation was fine but the way you -- the things you identified and the questions you raised I think really do drive to the heart of the matter and I find myself using some of your concepts just trying to sort out of some of the conversation that has taken place since then. I want to make two points.

First that in this conversation about say community consultation for a project with even anonymized or anonymous samples what is intriguing about that is

that it protects certain -- it does, in fact, protect certain values and interests. Now it does not -- you know, if you really think the whole story is protecting the individual's right to consent or not to be involved in a trial then it does not help.

But if that is not the whole or even the major part of the story for certain kinds of research, say you are -- we will call these just ethnic -- the boozers. Okay. If the boozers -- if you -- but if you consult a, you know, sort of fairly representative group of boozers and they say, "Well, we think this is actually pretty important," you do a couple of things. You get a sense that you are protecting something about the community.

You are also protecting something, I think, I suspect everybody in this room cares about, and that is the future of scientific research because if you did these studies in ways that people found grossly offensive you would -- your research population would dry up. And that is not in the interest of the community or the society, or certainly not in science. So I think that is -- it seems parsing out, pulling out the different interests at stake and saying that, you know, a sort of simple minded view does not really help here as very viable.

The second point I want to make is about the

second case and we will call them the Addams' Family. There I want to make the distinction between what people would be morally right to do or what people would be morally obliged to do, and what our public policy should say. It is pretty clear to me that if there is valuable research that can help my family, my relatives, et cetera, that I ought to consent to permit the research as is my moral duty as an individual.

But if, you know, we run into somebody who is ornery and just says, "I do not want to do it," what policy should we have and the policy might be, you know, if somebody really does not want to do it, they refuse, we should respect that refusal even though we think they ought to do the right thing. And then we leave it to family jawboning, and the other kinds of, as David was saying, those sorts of pressures I think you put on people informally. So the public policy becomes --

DR. COX: Quite effective pressure.

DR. MURRAY: Yes. The public policy becomes, you know, we do not coercive -- the study of science, et cetera, does not coerce you to do this but we certainly do not protect people against their own family's pressures. Does that help with the Addams' Family?

DR. EMANUEL: Well -- I mean, it seems to me to have resolved it in the traditional way and I -- I mean, part of what I -- what the example was trying to

suggest is are we always happy with that resolution or are there times when we actually think we ought to be coercive or more coercive. That orneriness is not a sufficient defense against other goods, including goods of the family. I mean, when do we come to the -- as the state to defending the family against some of its other members? And, you know, we may end up with our -- with the analysis you have just provided. I do not know.

I want to say -- I want to just challenge us to think about cases in which we might not find that an acceptable answer. I mean, in part, I think it depends on how serious the illness is, how likely we are to get therapeutics from this test, you know, the other background conditions that Bernie had alluded to that we need to consider.

DR. MURRAY: This time it is not an involuntary trick.

PROF. BACKLAR: No.

I just want to bring in what we talked about last night and the issue of the kind of case in which you have genetic linkage studies in psychiatric --

THE REPORTER: Excuse me. Would you use your mike?

PROF. BACKLAR: I am sorry.

THE REPORTER: Thank you.

PROF. BACKLAR: -- the kinds of cases where

you might have genetic linkage studies with psychiatric disorders. I think that in many ways we are moving over to the informed consent discussions, I am thinking of our subcommittee and with a lot of relationship between the things we are thinking about there and the things that we are thinking about here.

So if you could sort of explore perhaps for a few minutes such a case in which such research and the differences that might -- you might -- difficulties you might come up with that might be different from your --

DR. EMANUEL: Well, in the case -- why would it be that different? Let me ask that question. I mean, here you have a case which -- where the harms are embarrassment, stigmatization and discrimination, it seems to me very much prevalent in psychiatric disorders.

PROF. BACKLAR: Right. You also have issues of capacity.

DR. EMANUEL: Right.

PROF. BACKLAR: Which you have not addressed -- we have not addressed at all in this discussion and how you would deal with that, and would you deal with it differently, or would you deal with it as you would with -- in a clinical situation where you would get a surrogate and say, for instance --

DR. EMANUEL: I know why I am not a pediatrician because I cannot understand those issues.

Well, I guess in that case the problem is -- well --

PROF. BACKLAR: And you also, for instance, could have a case in which you have certain family members in which it would be -- I mean all the same kinds of issues -- terribly important. They want to know if there are other family members who it would ruin their lives.

DR. EMANUEL: I am sorry. On one foot with sleep deprivation I am not sure I can do it although I think the example is extremely important because it does -- I mean, I think you are right. I am just -- I am sorry -- on one foot at a loss to figure out how we are going to get capacity but it does seem to me to strike many of the same issues especially regarding self-understanding and the sort of self-doubt and self-denigration that really can result from this.

PROF. BACKLAR: I think the reason I wanted to bring it up, see, is because I think it is very important that we do not leave it out and I think we need to think more about this. This is a whole sort of issue that so far we have just sort of ignored.

DR. EMANUEL: Right.

PROF. BACKLAR: And it goes back again also to the issue that Bernie and Steve brought up of the thin or thick consent and how you do this. I am just thinking of Paul Appelbaum's studies and the MacArthur studies,

capacity studies of which it might be useful for us to look at in how one deals with informed consent with groups of people who do not have as much capacity as others and may have their capacity impaired.

DR. COX: I would argue that this is a variation on the same issue of whether you involved the subjects in the discussion or not. It is -- and it falls under the same category as at least -- or taking an extreme view as some researchers do, is that can we afford to involve the subjects in the discussion because if we were implicit -- I mean, no one would be concerned about this, okay, if there was not the possibility that people would actually say, "No, they do not want to do it." So, I think that this is not a hidden issue, a real concern of most researchers who really do not want to rock the boat on this informed consent stuff because the concern is that people may not actually want to do the research and then the researcher would not want to be in business any more.

So -- and this is just to me, okay, the same issue but on a continuum, Trish.

PROF. BACKLAR: I do not disagree but I just did not want to leave it unmentioned.

DR. COX: Yes. But this sort of unspoken concern of the risk that you will actually be able to do your study if you involve the people in the discussion I

think is one that we should not make an unspoken concern. We should make it very spoken and say is that acceptable or not, okay. And -- but that is something I do not think has come up yet formally but it falls into this is where I think this issue of how involved the subjects are in the process is such a key one.

DR. MURRAY: Bernie has been waiting.

DR. LO: I just want to make two quick comments. One is a follow-up on the discussion of capacity. It comes up in a lot of other areas as well. I think of Alzheimer's, you are going to have people with Huntington's, you are going to have people who may already have the disease. It would be very key it seems to get testing of kindred who may no longer have the capacity to consent. Similarly for adolescents and children, do you allow family, parents or surrogates to consent for them?

I want to go back to this other question about the refusal by someone in a family kindred. Tom, I like your distinction between what that individual's moral obligation is and what we will leave to sort of discussions with the family and doctor as opposed to sort of regulating as a matter of public policy. But I just wanted to point out that there are other reasons for not consenting that are not just sort of being stubborn or ornery, or not connected to their family.

You have people who actually are genetically part of a family whose paternity has been misattributed, and maybe have very good reasons for not wanting to consent and not wanting to raise that in public. So I think intention or motive, whatever, becomes important. If it were just an ornery person I would say to the person talk to them some more and twist their arm until they, you know, surrender. But, in fact, there may be other harms that may or may not be sort of unexplicit.

DR. MURRAY: That is good. I should note that geneticists tell me that although misattributed paternity is, of course, an issue and so occasionally but less often is misattributed maternity. That is for another commission.

(Laughter.)

DR. MURRAY: Steve?

DR. HOLTZMAN: I always try to keep my industry hat off when I am sitting here so now I am going to put on my industry hat for a second, all right, which is to say we would like clarity so we can get on with the work. So let me give you three examples of studies we are undertaking, all right. One is a study of bipolar affective disorder. It is a prospective genetic trial in a Third World country, all right, with a very homogeneous population in community, all right.

We work very, very closely with the

physicians who are the caretakers of those people and involve the people who are the leaders of that community in the engaging of what this meant in terms of being able to then provide care back, et cetera, et cetera. I think anything -- and probably not the ideal but trying to do the kind of thing that we have talked about.

Another study involves a Province in Canada again with a homogeneous population but it is for -- it is not for a psychological disorder, it is for a bowel disorder where there are not all of the same kinds of emotional and stigmatization issues. We nevertheless involve the people but we do not have the same kinds of concerns about consent in the same way that you are reflecting appropriately. What does it mean to get consent? But we do have community issues so we involve the people who are heads of the community.

The last is one where we are looking for markers of colon cancer. Very simply we are going into tissue banks or we would like to go into tissue banks. It is part of the reason we want resolution here. Get anonymous samples and conduct association studies. For the nonscientists in the room, including myself, that means it is not a matter of family linkages or homogeneous populations. You are just getting a large number of these things and you are throwing your technology at it, in this case looking for somatic

changes in DNA to ask is there a marker that is indicative of susceptibility or predisposition to colon cancer. Totally anonymous samples, very difficult to do here in the United States just because precisely why we have been convened.

In Sweden no issue. You could even do the epidemiological follow-up because there are patient identifier numbers which carry out through their life and you can say it is a small enough country, it is not completely computerized, but you can say, "Okay, what happened? What is the outcome of that person?" And you can find it. No harm other than questions about autonomy harms or respect for person harms. Okay.

As we -- I do not know if this is useful to just say there is -- every case is different. If you want to be good and do right, do the right thing, you will take into account the differences in the situation but we are really hung up right now with getting on with the work, and we can sit and talk as we are about these different weighings and whatnot but at some point it comes down to some sort of defined process to getting to an answer so you can know what you can and cannot do.

I am not complaining. I mean how do we get there?

PROF. BACKLAR: I think there is a very important and interesting point of what you are talking

about. Each of the cases that you have talked about may have some enormous importance to some member of this population in this room and we forget about the advantages coming back to that very much larger community of which we all are. So, yes, it is extremely important to find ways to do this without the harm.

DR. LO: It sort of links to your comment and what David said earlier, I really feel that there is a perception on the part of many researchers that trying to "do the right thing" will put them out of business. That it would be so difficult to do community consultation and get truly informed consent from identifiable subjects that they will not be able to do the research that they and others believe will have enormous benefits.

I think the implication I draw from what you said, and it certainly is the impression I have from a lot of researchers I respect, is that there is no conflict, that good researchers would be very happy to live under rules that require something more than the very minimal consent or waiver of consent that apparently is either advocated or interpreted into existing rules.

I think we need to address that concern and say that we do not believe that is true. Good scientists say it is not true. In fact, we believe the contrary that if you really do it honestly and with a lot of persistence it does take more time but you get a much

better study out of it and I think it is really the choice between a quick and dirty study versus a more complicated but ultimately more productive study that also gives you the basis to do future studies.

DR. HOLTZMAN: I may agree with you. I am not entirely sure. I had distributed to the commission a research paper that Bill Riley and I did that was in Nature Genetics and that is very thick informed consent I think is articulated there. Because -- this is where I do agree with you -- our basic position was it has not -- does not get in the way of conducting these prospective paradigmatically genetic studies, why not get all of that information? There is no harm. You do not have to take this imperialistic view at all. Just do not provide a very thick opportunity for consent.

But it is very different when I think about going to the stored tissue samples. It is a very different case and they are anonymized. All right. I cannot -- I just -- it is not possible or practically possible to go and get that kind of thick consent.

DR. LO: From individuals.

DR. HOLTZMAN: Right. And, in fact, you know, this idea of maintaining the confidentiality of the information, part of that is to keep you away from getting back to those individuals.

DR. LO: Right. But then you think of

alternatives like the very neat kind of community consultation that you did as part of your Canadian study.

DR. HOLTZMAN: If there is a community.

DR. LO: If there is a -- but you can see that you are doing the best you can. There is always a community of people that just -- it depends on how broadly or narrow you confine it.

DR. EMANUEL: Well, one of the things this discussion suggests to me is that -- well, first I do agree with Steve. I think one of the things we need are a clear articulation of the rules. And I hope that this is not a diversion away from that process and I hope it is part of the necessary process that we just do not sit there with 45 CFR 46 and try to come up with rules.

But it does suggest -- I mean, the last few comments, Trisha's comment about psychological and psychiatric diseases, some of the examples you, Steve -- to suggest that this grid that has been used by everyone else, and I probably should have -- it is not a -- it is not necessarily the be all and end all. It seems to me a long column down.

I mean, anonymous in part -- you know, if you are looking at colon cancer there is no community you are going to identify. None of this stuff that we are talking about is really relevant I agree. But if you are looking at psychiatric disease which does, you know, may

very well track, and what you are looking at is not susceptibility to a gene but a dominant or a series of genes, there may be a different standard. Or if you are looking at one that necessarily tracks with an ethnic group again you may be looking at a different kind of standard.

So we may need to break down under anonymous several sort of paradigmatic categories. The rules may be different. It may be that when there is no identifiable community we say just go ahead and use the samples, right. We do not need consent and we do not need an IRB review in that way.

On the other hand if there is an identifiable community and it can be tracked to some ethnic group then a process as articulated here by Bernie and David is the appropriate forum and you cannot go forward until you have that kind of forum. And, you know, similarly there may be other -- I mean stigmatizing is the natural one which comes up but I am not sure it is the only one. I mean there may be diseases which are not stigmatizing but you still travel in communities that you would say, you know, we need to go into that community and talk to them.

DR. HOLTZMAN: Yes, and I agree with you.

DR. EMANUEL: Maybe the point that I think that the last series of discussions are going is that just to divide it up anonymous and anonymizable linked is

too crude and that what we need is a more subtle matrix.

DR. HOLTZMAN: And that is why my earlier comment was maybe obscured, is that in your first case the relevant sense of anonymous had changed and to bring in an old stalking horse here is that whatever we are dealing with here is not a function of whether it is a genetic test where we are getting genetic information, HIV status is the classic other example that it is -- in one sense your underlying moral considerations are where it really plays out and it is when you try to operationalize it using concepts which are effectively anachronistic genetic information versus nongenetic information.

Anonymous when one has a paradigm of anonymous means of that individual where we are starting to get forms of information which can impugn communities or free communities. It is important to remember that as well.

PROF. BACKLAR: That is right.

DR. HOLTZMAN: Okay. So I think the deep work is to try to get past a bunch of concepts which either have lost their traction in the modern world both scientifically and also in terms of reconstructions and the notion of the self in terms of community.

DR. EMANUEL: Right. So maybe we do need to try to figure out what those other kinds of categories

are in terms of, you know, an identifiable community or genetically linked but not necessarily culturally linked community and things like that. I mean it seems to me that -- I mean, at least as I read it that has not been done but I am no expert.

DR. MURRAY: David?

DR. COX: Yes. So the -- I really like what Steve is doing because I think we are -- we have got a good broad foundation here that you laid out for us, Zeke, that we have been discussing. So let's get on with it and in terms of a very specific example to discuss this which when we have not sort of laid it out this way is tissue samples that are already collected versus those that are not collected. In fact, most people in most of these statements have planned it on the subjects already collected. A lot of these discussions have been about if we are going to do it in the future and that is really what our discussions have been about.

So what are the issues of the stuff that has already been collected. All right. And let's take it in the class anonymized. Okay. Anonymized in the sense that you do not have individual identifiers but you still may have group identifiers. So in those kinds of samples where they have been anonymized where they have already been collected what are the considerations for discussions?

Well, one of the discussions is those people, okay, may or may not have been, you know, given an option to use those samples in research. And are you ever going to go back and redo those samples? The answer is that is not feasible. Okay. You cannot go back. You cannot even find the people sometimes. So this is one of the points for discussion. Okay. Should those samples be thrown away or should they be used anyway? Okay. This is a very important sort of practical issue with those samples.

The second issue on that comes are there additional issues besides -- if they are really truly anonymized are there different issues besides the one of community that we need to be considering? Because if not then we have got just one very specific example of already collected samples that are anonymized, okay, and that if we can get passed the issue of what do we do if people were not really, you know, informed in the way that we would like to see now, what do we do with that sample?

DR. MURRAY: Let's start with Bette.

DR. KRAMER: Today my understanding is that even in the very general consent form there has always been language giving consent for research, it is just that the understanding of the word "research" at that point did not embrace what it embraces now. So I guess

one thing that we might consider is what are the obligations in terms of the new meanings of the word "research?"

I, too, like what Steve said and it seems to me that one of the things that you said, Steve, that there is a linkage back to the point that Trish was making, and that is that the potential for the loss or the removal of stigmatization, particularly that comes from psychological or psychiatric disorders when the research indicates or is finally able to prove that there is a genetic endpoint.

It does -- it shifts the whole way in which both the individuals and the families, and society it seems to me thinks about people who have these afflictions, and I think it is perfectly legitimate to bear that in mind at the risk of being paternalistic, and I would not want to do that but I think that is an important consideration.

DR. MURRAY: Steve, Bernie, and I want to give Zeke the penultimate for this session.

Steve?

DR. HOLTZMAN: Your point where you were going would be extant samples.

DR. COX: Yes.

DR. HOLTZMAN: I am not sure that they have always gotten thin research consent.

DR. COX: It is so thin that it is invisible.

DR. HOLTZMAN: So -- but there may be samples that predate a certain date with no consent whatsoever which are in the repository, okay, and then ones where let's assume with just the thin consent operationally.

I guess what I am recommending is with respect to those samples, okay, that first off we should not be looking at is it this or that type of research, namely genetic versus another kind of research, but asking what is the nature of the research in terms of if it were to be conducted and the result resulted, how would it play out against the issues we care about, stigmatization, et cetera, et cetera, et cetera? That is where -- and that may -- I do not know what the mechanism is, all right, for review of the research to ask that question but that if confidentiality is maintained and there is not going to be any of these harms it passes those tests that you can go ahead with it.

DR. COX: Yes.

DR. HOLTZMAN: Okay. Now -- and then how that would play in the issue of community if you will there or maybe some other concepts I have not thought about yet is that even though anonymous with respect to being able to identify the particular individual person it is not anonymous with respect to other classes of information whose disclosure could result in the harms to

some persons whether by group or whatever and try to come up with an intellectual construct along those lines. Okay.

DR. COX: I completely agree.

DR. MURRAY: Bernie?

DR. LO: Well, again to follow up, I think it is a very fruitful line of discussion.

First, Steve, I would suggest that the implication of what you are saying is that there should be some sort of review other than just the investigator saying I am going to do it. So whether it is IRB review or not, what you are suggesting is we would imply that some sort of oversight or review would be desirable.

DR. HOLTZMAN: Not necessarily. All right. What I am saying is -- okay. What I am saying is what effectively we are asking the reviewer to -- the individual right now is to review and see does it meet certain criteria. I am just changing the nature of the criteria. How you determine whether the criteria are met and whether that is a regulatory body or whether that is an IRB, and whether we say --

DR. LO: Or peer review.

DR. HOLTZMAN: Peer review or there is black cases and white cases, and get review from someone else where we have got the gray cases.

DR. LO: The issue is whether we are willing

to say that -- the presumption is you do not need consent from anyone other than the principal investigator and the researcher.

The second comment I had has to do with what does it mean to be anonymous? In fact, there are very few tissue samples at tissue banks that are really anonymous. All the path stuff I know about comes with a identifiable number to which I can link the medical records right away so that what you are really talking about is anonymizable studies where what tends to happen is you get the tissue, your research assistant goes and review the chart, pulls out all the other data, because the path sample does not -- it is just a sample. It does not even have, you know, demographics, let alone clinical course.

And it seems to me how you do that sort of -- sending the material from another source and then sort of putting it together and then anonymizing it is where I think most of the potential for breach of confidentiality occur.

DR. HOLTZMAN: And that is what I think is so right in Korn's approach which is to focus a lot of energy on what are the structures for maintaining confidentiality.

DR. LO: But I would say -- I would argue that it is sort of the details of how you actually do it

as opposed to -- I am not sure I am willing to accept an institutional policy as being a sufficient guarantee.

And finally to pick up on David's point about you cannot go back and get consent once you have got the tissue. It seems to me that it depends on sort of the type of study you are doing. If it is a very rare disease and you only have 25 samples and 24 of them are dead you cannot. It is a very common disease. Your example to colon cancer, it is a very common disease.

It seems to me if you felt it was so important to get something more than the general consent at the time of biopsy you could, for example, consider trying to contact people who were still active patients in your system, sending out a letter and saying we plan to do this. If you seriously object we will not use your sample. Let us know in the following way.

If the study is of such a preliminary nature that you do not really need sort of a high degree of -- another word is adherent -- I mean you do not have to get all the samples of all the potential subjects enrolled.

It may not undermine your scientific validity. It may make it a little more difficult but it is hard for me to imagine sending out a letter and waiting a month to get post cards back and taking the post cards that say, "No, do not do it to my sample," is such an insurmountable obstacle.

So again it seems to me if the study were such where you had particular concerns about these kind of values at stake, it seems to me there are other things -- there are always minimal approaches than saying we either have to get full thick consent of every individual or we cannot get any consent at all. I just think that is a really false dichotomy.

In fact, we do that all the time. You know, what I would tend to do if I were doing a study is go to the clinicians taking care of cancer patients and say, "Not only can we use your subjects but maybe we can actually get a little more information from the subjects to match up with the samples and make it a better study."

DR. MURRAY: Thanks, Bernie.

Zeke?

DR. EMANUEL: Let me make a proposal along the lines. First -- and it has got four parts. The first is let's collapse the anonymous and anonymizable or anonymized into one category and let's not maintain that distinction and treat them the same. So we really have two categories, anonymous -- anonymizable and linked and identified.

Then suggest that our recommendations need to fall into -- or be sensitive to the types of research being conducted. Not genetic but for lack of a better word stigmatizing or identified types of research. So

even in the anonymized group it seems -- I am going to take a first crack and I do not want this to go down as gold because it seems to me whoever -- we need to think it through and there is no identifiable group in your colon cancer model. No identifiable group or community or family. I would recommend in that kind of research you have IRB review, and I will say why I think that is relevant, but no informed consent, no community to go to, and you just go get the samples and do it.

Second, there is an identifiable ethnic community but the research is not necessarily stigmatizing. For example, it might be cancer research within an identifiable group. It might be some other genetic disorder. That is not in our notion stigmatizing. There it seems to me you need to go to the community and somehow have a process where they approve even if you are using anonymizable samples.

The third group is that some socially stigmatizing condition, a psychiatric condition, the alcohol condition I mentioned, something else that just at the moment may be hot or might carry big down sides even if it is not currently socially stigmatizing. There you need to go to the group and you need to get a consent and there the consent might have to be broader.

The third element -- and I am not sure that those are all the gradations. They are obviously not

regulatory language but I think we need to think about making that kind of division of the kinds of research done. And again whether it should be genetic or not genetic.

Third, there needs to be IRB review to decide which category the research goes into and it should be administrative review in the sense of the researcher proposes it is a no identifiable group and I just want to go ahead. What the IRB does is says, "Yes, we agree that is it," or the administrator says, "We agree that is it. We do not need to review it," or "No, we really think that there is an identifiable ethnic community here, you need to go talk to them."

DR. HOLTZMAN: So the IRB is not commenting on the quality of the science. It is administrative which box does this fall.

DR. EMANUEL: Which box does it fall or we need to take it to the whole IRB because it is a gray kind of research.

DR. HOLTZMAN: You are effectively proposing a three-dimensional matrix here, right?

DR. EMANUEL: Right. Right.

DR. HOLTZMAN: Okay.

DR. EMANUEL: And that we in our report -- I mean one of the things the College of American Pathologists says is that all of this is assumed you have

a background of confidentiality privacy set of rules and regulations, and processes. We need in our report to say what the optimal ideal kind of confidentiality policy against which this kind of process we would feel comfortable with because we cannot leave it to each IRB to invent the wheel themselves, that would be a mistake, and again that would mean that the rules, you know, how many IRBs are there? Thousands? The rules -- there would be a thousand different rules.

We should have one rule. We are going to stick to this policy and that would make it a level playing field. It would be practical I think because you would get administrative decision about the boxes. Once you know which box you are in you know what process you would have to go through.

And I think that would handle the existing samples. How we would handle the future -- it would also handle the concern about particularly sensitive or stigmatizing data, data that is related to a community and data that is just unrelated but still relevant. It would still leave the issue of thick or thin consent for us to further hash out.

Anyway -- it is obviously again not in any -- I should have thought about this before but I guess one of the values of presenting is that more brains are better than one.

DR. MURRAY: Steve?

DR. HOLTZMAN: I just want to say I really like where you are going because what is troubling in all these discussions is the focus has been on these operational things which are not really where the issue is and now you are trying to get at what really concerns us, the kind of issues that have raised things about this community or this kind of trait, you know.

You know, we are looking at -- genetic determinates, and dermal ridge and finger printing patterns, it is hard to get an ethical concern going, right, even though it is genetic. It is highly determinate. But where it touches us humanly are the issues of stigma. What touches us humanly is how we conceive of ourselves. The discrimination issue. Again that goes away if we have universal health care.

(Simultaneous discussion.)

DR. EMANUEL: I mean it seems to me that the way we divide up these types of research depends upon the values that we are highlighting that we are concerned about and I am not sure that, you know, to the extent that we may not have articulated the values completely correctly these groups need to -- will need to be changed or modified, or expanded even. I just do not have a good grasp for all the kinds of research we need to think about.

DR. MURRAY: We have eaten into our break. Can you keep it brief?

PROF. BACKLAR: Yes, very brief. But one of the important things that we have to always keep remembering is what stigmatizing now perhaps with research will become less stigmatizing and it is a very important issue to tie that together.

DR. MURRAY: A good reminder.

Well, Zeke accepted a difficult assignment on relatively short notice and I thought he executed it brilliantly when he began us this morning but he has finished even stronger.

So, please from me accept my thanks. I suspect the rest of the commission feels the same way.

Thank you, Zeke.

DR. EMANUEL: Thank you.

DR. MURRAY: We are going to -- there is actually -- Steve Holtzman has given us a nice segue into the next session. One thing that we -- that the commissioners can themselves reflect at least sort of in an effort to reflect more honestly but can only do it partially is what really matters to people about tissue sample confidentiality, research on their genetics from these samples that either have been held in the past or might be gathered in the future.

So at ten after 9:00, in about twenty

minutes, we will reconvene and we then seek the help of Dorothy Wertz and Chuck Denk giving us advice about what possible ways there might be to find out what really matters to people about this.

Thank you very much.

(Whereupon, a brief coffee break was taken from 8:50 a.m. until 9:18 a.m.)

DR. MURRAY: Before we begin the official business of this session, which is to look at ways in which we can learn what the public thinks about tissue samples, I have two loose threads from the last session. Two pieces of unfinished business that we would like to pick up and take care of.

Trish Backlar had one piece. Trish?

PROF. BACKLAR: I just wanted to make the remark that the word "psychological disorder" is really an inaccurate term. It should be "neuropsychiatric" because it is a somatic disorder.

DR. MURRAY: Thank you.

The second piece, Mark Sobel is here. Mark, could I ask you to introduce yourself and explain or clarify the point that you had made at the break?

DR. SOBEL: Is this on?

I am Mark Sobel. I am the Chief of Molecular Pathology at the Laboratory of Pathology at the National Cancer Institute. I am here today actually representing

the College of American Pathologists' position statement of which I am one of the organizers.

I wanted to clarify the paradigm that you just finished your discussion with which in general I applaud, especially in terms of using a stigmatization paradigm instead of a genetic and a nongenetic paradigm. But I think if you collapse the categories of anonymous and anonymized and identifiable and identified, we have to be very clear on what the definitions are. The CAP statement is working on the basis of the current OPRR interpretation of those definitions which are very different from the definitions you are using around your table.

Anonymized means there is absolutely no link to the sample in any way, manner or form. If I have 20 samples and I recode them, I put the code, the new code and the old code in my filing cabinet, I send the samples with the new code 6,000 miles away to another institution, and they use the samples, even if I promise not to break that code that is not an anonymized sample. That is an identifiable, linkable sample.

So I think if you collapse identifiable and identified you are going to make it very difficult to do some of the things you think you can do with that collapse and I think if you want to recommend a reinterpretation of those regulations that would help

clarify the issue but we are responsible now for educating researchers to say that such an example is not anonymized. That falls into the identifiable category and that is why CAP has pushed many of those examples into the general consent category as long as there is IRB review.

I want to stress that is a big part of the proposal that there has to be a third party review of the researcher's proposal and all confidentiality procedures have to be approved by the local review board to make sure that all those securities are in place.

DR. MURRAY: Thank you, Mark.

If the College or even yourself would like to even submit a brief statement to sort of recount that so it can be part also of the written record that would be -- I would appreciate that.

DR. HOLTZMAN: And I think as a follow-up if OPRR is the right way if we can get a clear definition of -- not right now, but how you guys define these different categories that are being used, anonymous, anonymized, linkable, nonlinkable, that would be very helpful.

DR. SOBEL: It is actually in your books. It is in there.

DR. HOLTZMAN: Okay. But it is unclear from the --

DR. ELLIS: Gary Ellis, OPRR. Anonymous and

anonymized, those are not terms of reference in 45 CFR 46. So the definitions are whatever you might make them.

DR. MURRAY: At the break one of the people attending this meeting, who was just in England, handed me a copy of the Times, the front page of the Times of London, Wednesday, February 19, 1997. This is the headline, which reads, "Life Insurers Demand Gene Test Results." So I just thought I would let you know that that is making news in London these days.

We have two guests to help us. We thought we needed to rely on some outside assistance here. Our two guests are Dr. Wertz and Chuck Denk. And if I could ask each of them to introduce themselves now and then we will ask Dorothy to make -- to open the conversation.

Dorothy?

DR. WERTZ: We are going to have our introductions and then --

DR. MURRAY: Yes. I would like you each to introduce yourselves so everyone knows who you are.

DR. WERTZ: All right. I am Dorothy Wertz. I am from the Shriver Center for Mental Retardation in Waltham, Mass. For those of you who do not know the Shriver Center is an independent institution that studies mental retardation and developmental disabilities. They have a Social Science, Ethics and Law Division, of which I am a part.

I am a sociologist and ethicist. By background I have training at the Harvard Divinity school in religion and society as well as in sociology. And for the past 15 years I have been looking at ethical and social issues in genetics. First working with Jim Sorenson and then with John Fletcher.

In 1985 we did a study of geneticists in 19 nations looking at their ethical views. In 1994 and '95 we repeated the survey in 37 nations, 2,900 geneticists. Almost 500 patients in the United States were surveyed before and after genetic counseling with regard to their own ethical views. These are mostly working class patients by the way, not college educated and sophisticated people. And we also surveyed 500 primary care physicians.

Unfortunately, the issue of stored samples had not come up at the time. It is not on any of these surveys. Nobody was concerned about this a couple of years ago. We also surveyed a 1,000 members of the general public with regard to some of the same questions and that is why I am here.

DR. MURRAY: Chuck?

DR. DENK: Hi. I am Chuck Denk. I am currently a survey researcher specializing in health care research at Mathematica Policy Research in Princeton. I was formally on the faculty at the University of Virginia

and jointly in the Department of Health Evaluation and Sciences, and at the Center for Survey Research. I have a PhD in sociology and I am not an expert in genetic research or in bioethics but I have conducted several studies examining public opinion in various aspects of ethics and bioethics particularly in end-of-life planning and end-of-life decision making. Most of my research now is on managed care.

DR. MURRAY: Thanks.

Dorothy, would you begin our conversation, please?

WAYS IN WHICH WE CAN LEARN WHAT THE PUBLIC THINKS ABOUT TISSUE SAMPLES

DR. WERTZ: Okay. First of all I am just going to talk for a few minutes and then we will have discussion.

First of all, why do we do opinion research? We are not really polling people to find out what is right. We are not doing ethics by majority vote. But one task of ethics, according to my colleague, John Fletcher, is information. We have to find out what all the parties involved think about the issue and as Bernie and David just pointed out the consumers are not really here in any force.

Now my own suspicion is that most of the public really does not care much about this issue. They

would say let's get on with it. Just find us some therapy for heaven's sake. But on the basis of going to a number of conferences at which minority groups were present I would also suspect that among many minority groups, particularly there is a great suspicion of genetic research and a feeling that nothing good is going to come out of it for them. The benefits are all going to go to rich people and they are going to be the guinea pigs. So we really need to find out what people's concerns are in order to draft a decent line item consent.

Now those of you on the committee should have received a great big packet which shows you what you get out of a public opinion survey of 20 questions for $25,000, a thousand people. It does not have this cover on it but those of you who had a chance to look at it will see the entire survey questionnaire in the back.

This was actually handed out door-to-door in booklet form rather than having the interviewer run through everything partly because there were some very extensive questions in here asking people under what conditions they would have an abortion and 988 out of 1,000 answered this.

I had Henrietta circulate this to show you how your data comes back to you and for $500 more you can get a data tape and play around with it and do cross tabs

and find out exactly who was saying what. Though, frankly, a lot of this is in the data report because it is broken down by race, economic group, geographical region, gender and so forth.

Then I hope everybody received this called "Issues in Survey Research, Draft Survey Questionnaire for NBAC." Did anyone not get this? It should have been handed out either by me last night or today.

This is something I wrote up in rather a hurry to show the kinds of questions that you might ask of people and since this is a very complex issue it needs a lot of up front explanation. This is wordier than a survey would ordinarily be. But page one tries to explain what research is all -- what this is all about. Whether names may or may not be on your sample. Who gets the name. The researchers may not get your name but it is somewhere in this traditional locked filing cabinet somewhere or it is on the original paraffin block in the pathology lab. The library's original copy but they do not send it out on the slices they take off the paraffin block.

And then we ask -- turning over to the next page -- we ask if it is all right to use this sample and under what conditions. And they have the option of none of the above. And, you know, this can all be moved around. You can put none of the items below up top if

you want to really emphasize the I do not want to be in research.

Then you would want to say I do not want my sample used in research and list some controversial things like abortion, AIDS, violence, prenatal diagnosis, something that would benefit another ethnic group. Then you want to ask is it all right to share my sample with researchers at commercial organizations or government organizations. You know, it is going to go beyond the original hospital perhaps. Is that all right?

This is not an informed consent form. It is simply to find out what people think about these complex issues.

The next page we ask if people want to be told if researchers found out something about their sample that is life threatening or perhaps it is not now treatable or preventable, that it is treatable and preventable if found early, et cetera. What do they want to know? Do they want a short summary of the research in simple English even if the result has nothing to do with them? Some researchers in social science send out a very simple overview of what happened out of this project that people participated in and that sometimes makes people feel good simply to know that something came out of it. Maybe nothing came out of it.

The next question, profit sharing. And we

have to point out that most individual samples do not result in profits but occasionally maybe something does and would you like to receive a share of the profits depending on the size of your check. Is it going to be 26 cents or is it going to be $500?

The next question, access for others. Your spouse or partner, siblings, children, other blood relatives, and then employers, health insurers, family doctor, life insurer, et cetera. We know from our patient survey what people are going to say about employers and insurers, and the answer is no. Virtually 100 percent. But some of them think spouses should have access to your sample. Again this is telling you what might go on in line item consent form, what items are people concerned about that should go on there.

The next question is about using your sample for future research that was not anticipated. Do you want to be recontacted and we use the -- I use the example here of a study with 160,000 people in it. I am thinking of the Women's Health Initiative which I just volunteered for. And what they are telling the people is we are going to take your blood and store it for eight years, and it is all going to be aggregated and people will get the idea of some sort of great vat or tank kind of where all the blood is poured into.

(Laughter.)

DR. WERTZ: I am sitting there at this general meeting and finally, you know, I brought this up and then they said, "Well, no, we are not really going to put it in a tank. It is going to sit there with your name on it." But they would not have said that. And people start waking up and saying, "You mean you are going to do some genetic testing and you are not going to tell me that I have a genetic disease," and then they said, "Well, we really do not know what we are going to test for and we do not know what we are going to tell you." They are heading for trouble and that is a big extensive project.

And so if someone rules in the meantime that you have now got to go and recontact people, and mind you they are enrolling women up to 79 years of age, eight years from now some of them will not be around, you really have to look out for this.

So we have asked people under what condition -- you know, would they really like to be recontacted every time the sample is used. And pointing out that this is going to cost money. Would I like to be recontacted no matter what it costs? Would I like to be recontacted only if it costs less than a dollar to do this? I would like to be notified and given a chance to withdraw but if they cannot find me it is all right to go ahead, and so forth.

Now again, you know, the committee will have ideas about some of these questions. But it is the kind of thing you ought to ask.

The next question is should my sample be kept indefinitely, destroy it after five years, destroy it after ten years. After my death what should happen to my sample.

And then finally we get to totally anonymous samples where they have taken your name off even the library's original and you will be totally assured of privacy. How do you feel about this? Would you permit research on this or on this only if it were totally anonymous or would you prefer to have your name somewhere in the library because you want to know the results? It might be useful to your family or you might get paid.

And then we end up with two questions on their feelings about genetic research in general. Listing some popular beliefs about genetic research. Is it going to do more harm than good? Are the benefits going to go to wealthy people? Is it going to change the meaning of humanity? Is it going to increase our intelligence and improve our behavior? Are poor people serving as guinea pigs? Is it going to lead to prenatal treatment? And then finally what are people's concerns?

And then some of these we use a five point scale from strongly agree to strongly disagree. My

sample will fall into wrong hands. I will lose my health insurance. My marriage will be affected. My sample will be used for purposes I disapprove of and so forth.

So this is just giving you some idea of kinds of questions that could be asked. And the committee, of course, would be the ones to say what they want asked. A survey organization ordinarily field tests something like this at least briefly to see how long it takes to administer it.

When we went and got essentially bids for our survey that was funded by the National Institute of Child Health, Mental Retardation Branch, we went to Gallop, Harris, National Opinion Research Center, and West Stat, and also Roper, and most of these organizations gave us bids of about $75,000.

Some were more than that because they construct your own sampling frame. They do the survey just for you. That takes time and ORC said it would be at least a year, maybe two, before we could get on their list. Of course, they do beautiful work but we did not have a year or two to wait. And the contracting agency said we are not going to put $75,000 into this.

Roper will do it for $25,000. The fee may have gone up a bit since then. Adding your survey to other surveys that they have going on and they mount one of these surveys every two months or so and they tack our

survey on to it and that is why it is cheaper. It is what they call a quota sample rather than a proportional sample.

The Office of Management and Budget, which this has to go through, ordinarily does not like quota samples but Roper provided us with information showing that their results and results done the other way were similar. This is highly statistical material that they provided. We did not hear a peep out of OMB. Once it reached OMB it got through in three months. It has to be advertised in the Federal Register but it went right through with absolutely no changes.

Our problem was in getting there. It was in going through the Public Health Service to get there. And that took two years because it kept sitting on people's desks and no one will ever admit whose desk it was that it just sat on. Probably several different people's.

The committee I think will not have to go through the Public Health Service route. I think you could go much more directly to OMB than I did. So it is possible.

Now we were also asked to mention focus groups. I have done some focus groups. We did five of them for the New England Regional Genetics Group and this document, which some of you have received, is a Consumer

Provider Consortium on Genetic Services. It covers just about everything except the stored samples issue which again was of no interest to anyone in the group. This is really about services anyway. It is not about research.

But we did the five focus groups for about $10,000 and I have the actual budget estimate with me. That included paying the project director $5,000 and it included payment of $50 to people for coming in to the different focus groups. Focus groups are usually useful before you put a survey together. So focus groups could be done in order to finalize questions for a public survey. Or you could just go ahead without the focus groups.

Now I think Charles is going to add his comments to this.

DR. DENK: Thanks. I just want to make a couple of comments to add to what Dorothy said to tell you a little bit about some opportunities that I have turned up on your behalf.

First of all, I did a quick search of the Roper Center's public opinion archive, a big collection of surveys that have been done, questions and answers, and got by no means a total of response but I did find out that in the '90s there have been several surveys done on the issue of genetic testing. Not the issues in front of this committee right now but on sort of value of

genetic testing.

And from a survey taker's point of view the first question is not how do they feel but is this even a feasible endeavor and it turns out that the public is willing to express opinions on these matters. They are willing to consider specific questions posed by researchers and specifically they seem to be generally approving of genetic testing.

For example, 66 percent of people in a 1990 Gallop poll said that genetic screening would probably do more good than harm. 69 percent in the same survey said that they would undergo prenatal testing for some conditions if that was relevant to them.

In another poll, another survey called the General Social Survey, which is a biannual project funded by NSF and it is sort of the gold standard for looking at trends in sort of four public opinion areas, 60 percent also said that they thought genetic testing would produce more good than harm. These results are generally in line with every survey that asks people about their faith in medical research and in the medical community, trust in physicians and so on. This trust does not extend to health insurance entities or employers by a long shot but so far the medical community still enjoys a high level of trust.

Now these surveys also determine that the

public is -- the public's knowledge of these things and their opinions are fairly superficial. They are naive and overly optimistic about what can be delivered by genetic research and genetic testing. For example, the same Gallop survey found a majority of people thought genetic screening can predict who would have a heart attack and they also thought genetic screening could actually correct genetic defects. Now these are a slim majority of the people. You cannot statistically rule out the fact that they are just guessing but it clearly shows a low level of information.

Two-thirds of people in these -- in a variety of surveys said that they had read or know little or nothing about genetic research and genetic screening and related topics.

So the problem here is that, as Dorothy pointed out, is that survey questions have to be very, very carefully tested because you are really asking people about something they do not really have very firmly grounded opinions or very strong opinions. They are willing to share what some pollsters call nonopinions with you. They will react to whatever it is that you tell them. So questions like that have to be very, very carefully tested and I will come back to the implications of that in a minute.

Some issues are harder than others in my

experience. If the real issue of the survey such as this was about developments in cloning that would be a lot easier. I think I would just ask people whether they felt they would sleep easier knowing that the technology to clone perfect sheep was now available or follow-up by asking what attributes of those cloned sheep would be most conducive to sleep.

(Laughter.)

DR. DENK: And so on. Okay.

Now one other general remark. The purpose of gathering polling information is important to consider. I have often had to remind people who want to do polls on public issues that polls are -- or surveys in general are very -- are largely inappropriate for asking the public's permission to do anything. Okay. And in the case of stored samples I would bet a lot of people are tempted to think that they can do a survey to get sort of citizenry to consent for everyone. And that is just not a very realistic idea and there are several implications of that or motivations for that.

One is what -- a purely statistical issue, what statistical level of approval would constitute, you know, sort of ability to go forward on any particular policy issue. Would it be a bare majority, a super majority, would we want to factor in -- we would certainly want to factor in statistical uncertainties in

a poll and so on. You might also ask the question of whether all subgroups of the population should have to be -- should be consenting or whether sort of just the majority rule should apply.

A second is already stated many times, a common theme in ethics is that what is popular is not necessarily ethical. And, you know, given the superficial nature of what people approve of and disapprove of in areas like this I would be loathe to think of that approval as deeply grounded in anything, particularly if we are going to move to discriminate against people with mental illnesses, you know, people might quite overwhelmingly endorse genetic testing for some groups like that involuntary without any consent at all.

A third implication, which I think is most important for thinking about what a poll or a survey should try to do is that it should not be modeled on the informed consent procedure that you put research subjects through. Okay. You do not want to ask the public for their permission in the sense that you ask an individual for their permission.

The two processes are very different. In informed consent you are trying to get -- using abstractly generic language to get people to consent to a very concrete thing at a very fixed point in time. In

surveys what we want to do is ask very specific questions in order to understand general attitudes. So, in fact, those are probably as about as opposite as you can get.

Viable survey approaches are ones that instead of asking permission generally try to assess or map what public opinion looks like and what public values look like. That is the usual and most positive thing you could do. First of all, map what are -- what the public considers to be problematic and nonproblematic areas. What their fears are and what kind of institutions they trust and do not trust. You will get if you ask a variety -- the appropriate variety of questions about the appropriate variety of acts and actors you will find that they are skeptical about some things and very supportive of other things.

Also you will find out about group differences. Very important from the perspective that I have heard today. Those are the things you can achieve. So sort of a more theoretical look at what the public is -- sort of values rather than what the public approves.

The keys to that are to personalize all the issues as Dorothy was describing and ask people would they want to consent to research, would they want to be a donor of tissues or blood, or something. Present them with concrete situations, concrete risks, concrete benefits and ask them, you know, through a variety of

comparisons and contrasts, try to figure out what things they are approving of and what things they are skeptical about.

Okay. Logistics. The usual thing when trying to do something in a hurry as this commission is at least considering, okay, to do some kind of a survey which would be included in the October report or whenever that fall report is, would be as Dorothy describes, formulate some questions that could be added to a poll that is already being done, or a survey. I use those terms interchangeably and I probably should not.

There are a variety of polls that are going on all the time. Many of them sell you space, you know, like condominium time shares. Some of them are more appropriate vehicles for these kinds of things than others. The University of Maryland, for example, is doing a poll or survey this spring that has some health topics already and could include some others.

All of the professional polling organizations run something like this and there are no doubt others that could be found. Perfect timing, relatively related topics and so forth. They range in cost -- the way I would budget this if I were doing this and this is not a bid, okay, is that I would probably want to spend $10 and $20,000 just to develop the questions and also to prepare a report at the end. The data collection could be

anywhere from $650 a question, which is what the University of Maryland charges, to much larger charges for other surveys probably averaging around $12,000 to get a sample of 1,000 people.

DR. WERTZ: That is now per -- what is a question?

DR. DENK: That is certainly negotiable but I think we are talking about -- a question -- okay. You can do about ten questions in five minutes or not -- you know, 20 questions in about five minutes. That probably would cover sort of the range. So you are getting five minutes worth of information per 20 --

DR. WERTZ: Because when I sent this out, I mean this is -- there are 20 questions and many of them have multiple parts. So you get an awful lot for 20 questions. If somebody says, "$650 a question," I mean I do not know whether that is one part of a question which might have six parts and somebody else might count as one. It is kind of hard to say there.

DR. DENK: It is negotiable. I think that planning on the realm of like $12 to $25,000 is probably right for buying a piece of someone else's survey.

DR. WERTZ: Yes.

DR. DENK: The big logistical problem here is that all surveys funded by federal funds have to pass through the Office of Management and Budget. This is not

-- I am not -- I do not have direct experience with this in my own professional life but I have polled my colleagues at Mathematica.

This process takes four to six months. It is very hard to expedite past that. There is a period where it has to be -- that the actual -- once the questions are developed everything has to appear in the Federal Register for two months for public comment. Then it goes through OMB reviews having to do with cost effectiveness, duplication of effort across other agencies, and so on.

DR. WERTZ: Well, it takes -- it takes three months after it gets there.

DR. DENK: It used to take three months.

DR. WERTZ: They cannot move it up -- oh, that has changed?

DR. DENK: It does not take three months anymore.

DR. WERTZ: Okay.

DR. DENK: Okay.

DR. WERTZ: Because they could not hold it up more than three months by law back in '94.

DR. DENK: As a practical matter it takes more than three months these days. Okay.

The alternative to this is to find private funding for such a survey and one suggestion I can make to the commission is to solicit a private foundation or

other kind of private sponsor to put up the money for this. That way you sort of beat the OMB review procedure and can proceed on this basis of trying to get something by October. Otherwise there is just no way.

I am not sure by the way that I recommend this strategy anyway and so the last thing I want to do is share with you some other opportunities there are around. Maybe what you would rather do is instead of rushing something to judgment instead commission or influence the content of something that will go into the field in the near future instead and not be a product of this commission but be a more thorough going product.

And one possibility here is that the General Social Survey is planning in 1998 what they call a bioethics module, that is some proportion of the respondents will get a whole section of questions on a variety of topics in bioethics. I know that physician assisted suicide will be one of the topics in that module.

I talked to the organizer of that project and she was very excited about including something along these lines also. Genetic testing is something that they would like to also consider. It is timely. They have asked questions before about that having to do with genetic screening. Genetic research is another obvious kind of thing.

They will collect data in '98 and have data available in very early 1999. And that is as I said before sort of a gold standard for these kinds of public opinion kinds of things.

DR. WERTZ: You are talking about the National Opinion Research Center?

DR. DENK: Yes. NORC's General Social Survey. It is the one I mentioned before. It is an NSF core funding project. So that is a possibility for the future.

I did turn up one possibility in the present which I think that you should be aware of. Professor Alan Weston of Columbia and Director of the Center for Social and Legal Research is about to put a survey in the field dedicated to this issue of genetic privacy and some of the ramifications to be considered here. He is going to do this survey in April. Okay.

It is in collaboration with Harris and it is privately funded. A lot of the issues that are related to this issue and a lot of things about the risks of genetic information falling into the wrong hands will be the core topics here. So there is a lot of background information and issues about the knowledge that respondents have about these issues.

It would be a wonderful place to insert just one more set of questions perhaps on the stored tissue

consent and safeguards kind of issue. Okay. He has -- he said that it was okay if I mentioned his project specifically here and invites you to make some kind of contact.

However, the same thing about OMB applies. Okay. A privately funded survey that you sort of buy a piece of, your piece still needs to go through OMB clearance unless it is -- you manage to fund it through a foundation which, you know, looks kindly upon the activities of this commission. You would have to move very fast now. But he has got a very good thing in order already and is very sympathetic to the issues that you are considering and there is some negotiation that can happen here.

That is what I managed to find out and now I guess we will have questions. Right?

DR. MURRAY: Thank you very much.

One of the first things I learned when I entered this field of bioethics was it is important to distinguish between when you have disagreements about moral principles, ethical issues, et cetera, and when you have disagreements about facts. So one of the facts about which there is disagreement is could we do a survey sort of on the time line that we think it is possible and could we, you know, get government funding on a fast track basis or could we as a government body fund on a

fast track basis. That is a fact disagreement.

By the way it turns out that fact disagreements are sometimes more tenacious than the moral disagreements so that I do not mean to say that one is easy and one is hard. This one may be hard or it may be easy. I do not know. But Bill Raub is here and I think can give us a perspective from within the government as to how it -- whether or not it might be possible.

DR. RAUB: There is nothing I can say that would nay say Chuck's point about the difficulties associated with the clearance process. On the other hand, it would be a sad commentary on reinventing government if there were something critically important in the view of this commission that somehow were stymied by our own administrative processes. So I, for one, am willing to pull out my sword on a few windmills as necessary if the proper way to do it would be to have something under the imprimatur of the commission with funding from the federal agencies.

I have been able to walk things through on other occasions. I have also been stymied in attempting to walk things through on other occasions. So on a case by case basis I think the cautions ought to be weighed seriously but also the commission should not be deterred from its fundamental purpose if you identify something that should proceed in the way of an OMB cleared survey

we will pursue it.

DR. MURRAY: Open for all the commissioners. Zeke?

DR. EMANUEL: I just raise three points. The first is a practical point. It seems to me with a little bit of experience of this OMB clearance process being under my belt now that there is no way for October. I just think that would be impossible and it would require so much more of our time that could be more valuably spent on cloning and all sorts of other things. I just think Chuck is right in reading the tea leaves.

Second, I think there is a principle issue here and it is not clear to me that we are going to get that much value added for doing the survey here. I do not think the issue -- and in part it is a matter of things that Chuck and Dorothy both said. There is a huge amount of ignorance out there.

I think what we are going to get is a lot of gut reactions that have no depth to them at all and it is not going to be helpful. I think part of what our report is about is to educate people. I am not sure that the key issues we need to decide are -- that this information is valuable.

That leads me to the third thing which is if we look down the road it seems to me a survey may be valuable on a whole range of issues that this

subcommittee is -- that we could take a more thoughtful couple of years to work on to talk about the future things we are looking at, gene patenting, confidentiality.

I do not know the content of the survey but there may be something that we can add. We could talk about stored tissue. We could talk about cloning. And we might, therefore, think about a survey in terms of all the issues we are going to be addressing and as it were, you know, I do not know whether it qualifies as a separate report but a more thoughtful process of -- Bernie has done here -- and has done a lot of surveys, too.

But a lot of my research is surveys and it just seems to me throwing something together to get it by October and do all this other bureaucratic maneuvering is probably not going to be good for the questions. It is going to take a lot of time and I do not think it is going to be from a practical standpoint that much value added. That would be my own gut reaction. Not that this is not interesting, just I just think we have other things to do.

DR. MURRAY: Carol?

DR. GREIDER: I would just like to second everything that Zeke said and I raised my hand before you started saying that. The question was I wanted to have

some articulation from the other members of the commission as to why it is that we really want to do this survey now. It was not clear to me from our last meeting that we really had definitely said we were going to do a survey now and hearing this discussion raises my question again about that.

So if somebody can refresh my memory as to what specifically we want for this stored tissue topic and why a survey, that would be helpful.

DR. MURRAY: David?

DR. COX: I am happy to try because I think I was one of the advocates of this. I think Dorothy said it really well. It is, you know, not to have people vote but to find out what some of the other issues and considerations are that we might not have on our table.

Now I also agree that this is like, you know, like taking a cold shower. This is reality here. I wonder, okay, I think I could answer this but I will ask anyway, so I think a survey is out. Okay. But are focus groups a possibility? Or is there -- what other mechanism? Is there any mechanism by October where we could get a reasonable -- a sampling of additional information or, if not, we cannot do it, well okay, then we should not do it at all.

But I do not think -- I just feel uncomfortable given the fact that we do not have a lot of

representation of the public. Maybe the answer is that they do not care very much. But I would like to know that somehow.

DR. MURRAY: Bernie?

DR. WERTZ: But some people may.

DR. MURRAY: Excuse me for a second, Dorothy. I am going to ask Bernie to speak and then I will ask for a response.

Bernie?

DR. LO: I was not at the last meeting. By nature I tend to, as Zeke said, you know, think that there is value in empirical research on ethical issues. But I am struggling to sort of try and focus on sort of what it is we will get out of empirical research here.

It seems to me the questions that Dorothy proposed are very interesting because what we would get out of it, it seems to me, is what percentage of people would consent to various sorts of things that are contemplated in a consent form. I am not sure that is quite what we are looking for.

In our discussion earlier today we sort of identified what we thought were some important value conflicts and identified scenarios in which we thought might be sort of counterintuitive conclusions reached or at least we need to reexamine traditional balancing of conflicts. We proposed some sort of steps towards

guidelines or a framework or approach.

Now it seems to me I would be very interested in checking out somehow with the broader public have we missed any concerns? Are there other values that we can throw in? Have we sort of focused on these cases? Are these the paradigmatic cases that you worry about? Sort of the point Zeke raised in his presentation. Is the kind of approach we are sort of starting to articulate something that kind of makes sense to the public in terms of does this seem like a reasonable approach to address things? That is the kind of information I would like to get back.

Now I do not know what the mechanism for getting that feedback is and maybe a survey is not the way to go about doing it. But I think if we tried to look at what it is we are trying to get back from the public then we can look at sort of the technique of how we are going to do it later.

But also to say I am a little concerned about going to a public -- a sort of representative sample of the public, most of whom will probably never donate or never be asked to donate. I mean, is it really we want to look at people who are potentially in categories where people might want to do research so that people with -- Steve, your example -- colon cancer or manic depressive illness who might be asked to sort of bank tissue, or

people in the Women's Health Study. Are there ways of sort of addressing people who are likely to face a decision about having their stored tissue used in these uncontemplated ways as opposed to the general public for whom this may be a real --

DR. HOLTZMAN: One of the big epi studies.

DR. LO: Yes.

DR. HOLTZMAN: Framingham, Nurse's Health.

DR. LO: Nurse's Health is one.

DR. EMANUEL: There is one point of information here. The great loophole in the OMB regs is survey patients. You can not -- you do not have to go through OMB if you survey patients. However you describe patients. A patient can be someone in a study already. A patient can be someone receiving medical care. This was a discovery to me two weeks ago. But it is true. And a patient can be someone in the Women's Health Study. A patient can be a doctor in the Physician's Health Study. So if we tailor it we can avoid the OMB problem. That means we are tailoring our sample which may be fine.

I would nevertheless say one thing, which is given my experience, and I am sure your experience, developing the right questions, pretesting them, all of that stuff is not something we can do in two months even if we got a full-time good staff. I mean, I just think this is such a complicated area. That is my own feeling.

Having -- you know, I generally -- I do not know what your -- I generally spend six to eight months developing a survey and it is not on anything this relatively obscure to the public.

DR. MURRAY: Dorothy and Chuck both have something to say. So let me pull them back in and then we will see where --

DR. WERTZ: Yes, well, Zeke said one thing I was going to say -- actually two loopholes in OMB. One is that if you have fewer -- nine or fewer people you could do a focus group of nine people on one question, a focus group of nine people on another question, and just keep going and cover the waterfront that way, and it would be legal. I do not think that is the way to go. There are too few people covering too few issues. I think the clinical exemption that Zeke suggested is the best.

I got a clinical exemption for my own patient study. I was told very clearly by Charles McKay of OPRR, however, that these had to be people in there for treatment. Now maybe the rules have changed. And that it had to do with the efficacy of treatment. As long as you could prove that this had something to do with treatment, efficacy and so forth. So people's general -- what was going on in a genetic counseling session impact on the ethical issues and we just had the ethical issues.

I think you have got them. But I think it could be worked so that it could be done in some sort of clinical setting.

But I disagree with you that getting this together. For one thing you are not really, you know, asking sensitive questions. You are not saying what would you do with a handicapped newborn or would you have an abortion for spina bifida. I do not think we have to worry about asking things tactfully that way. The issues are generally removed from people's honest feelings.

And I think it would be possible to get it together in a much, much briefer time than you are projecting, you know, because something could be put together in a couple of months easily and field tested, revised, field tested, and then you could start putting it into a hospital or clinical setting if somebody would, you know, volunteer, and you get around the whole OMB thing. You do not have your three months waiting period. It does not go into the Federal Register or anything like that.

DR. MURRAY: Sometimes it is useful to state the obvious. I think what I am about to do is state the obvious. That is that I hear three kinds of questions. I just want us to be clear which we are addressing at each point.

The first question is what do we want to know

relative to the report? We have probably spent the least amount of time talking about that.

Two, what methodology or methodologies is or are likely to provide this information?

And, three, can we do it well in a timely manner under the federal rules? Those are the three questions that we have heard.

We have been hopping around and I just want to be sure that we do not fail to address the first thoroughly and the connection between the first and the second.

Chuck?

DR. DENK: I wanted to go back to Dr. Emanuel's comment about the value added here. I think that is an excellent way to think about things. And I am sorry if I presented a very discouraging view. I did not mean to say that the public does not think anything worth knowing and I do not think you did either.

What I did want to say is that it calls for a very careful development and a very careful consideration of what people are competent to talk about and what they are not competent to talk about. My little remark about sheep and sleeping just sort of illustrates that you have got to ask people what they know about and if that is what they know about, sheep, that is what you have got to ask them.

However, I have also -- I have always found in doing survey work that half the time I manage to confirm the common sense view of what the public probably thought, you know, before even going into it and half the time I find the totally counterintuitive results about what the public thought from what I would have expected. If I could predict which was going to happen in which study I could save some of my clients a lot of money but I cannot and that is the general thing about the social sciences. We do not know how often we will confirm or totally contradict common sense.

In terms of sort of thinking about what areas -- I would think that one of the things you might want to do is try to find out as you have raised issues about what should the public be concerned about and what kind of safeguards should they demand, we might want to confirm, well, what are they concerned about, and what risks do they consider irrelevant. Okay.

A lot of people expected that because of the linkage to abortion with genetic screening and prenatal screening would be a subject which would get no good positive response and it does. I mean, lots of people -- first of all, the majority of people are in favor of abortion under some circumstances.

And a majority of people are in favor of -- well, in one interesting poll in '92 a lot of people said

that they would consider terminating a pregnancy if genetic screening produced results of certain kinds but not other kinds. You know, the child would die in a year, okay, a lot of people would consider terminating a pregnancy and that is a reasonable question.

People are also -- it turns out that even in some of these earlier things people are very -- they have differential responses to screening for treatable versus untreatable diseases. Okay. You might also find that people are just totally resistant to any kind of genetic research that has to do with identifying a homosexual gene or the alcoholism gene, and so on. Okay. And these are questions you can ask the public, what do they support and what do they clearly put into a different realm of no, no, no, no, you know, we do not support this.

One other issue I would really strongly urge you to consider is that in the materials I read prior to coming here apparently currently IRBs have or are being proposed to have an awful lot of responsibility as the guardian of the public trust here in terms of determining what is appropriately anonymized and so on. You might want to get the public's opinion about whether or not -- how they feel about IRB's. Of course, you cannot say that.

DR. WERTZ: Yes.

DR. DENK: But you can ask them, you know, the academic community. You know, do you trust the academic community to protect your interests? Do you trust the medical community to protect your interests? Do you trust the government to protect your interests in these kinds of things? You might get some very interesting results I think along race lines, bias lines and so on of the kind Dorothy pointed out.

One other point on the value added, I am sorry I am going on so long, is that it would be true that it would be impossible to start from scratch today and get anything done by October. But there are a lot of researchers who are not starting from scratch, who have been working for a long time, who have been preparing proposals on exactly this and related topics for a number of years now who have not gotten funding because -- and I heard this story as I was talking to people -- because public opinion research about genetic research falls into a very awful crack to them.

They go -- their proposals always get forwarded to genetic research committees and always get low priorities because it is not genetic research, it is public opinion research.

One of the things that this commission might do is give those people a little leverage so that they can actually get a hearing in the right places to get

their research funded.

The other point was that you can take advantage of the fact that they have these proposals, probably by merit and I brought with me a couple of resumes which I gave to the chairman of people who are actively engaged in this, including Alan Weston, who could assemble the right kind of stuff in a short time if the funding hurdles were cleared.

DR. MURRAY: Thank you, Chuck.

Steve?

DR. HOLTZMAN: Can I come to your first question which is what is it we would want to know?

DR. MURRAY: Yes.

DR. HOLTZMAN: And this is something I -- a version of something I have said probably in every commission meeting. And that is my concern about these surveys about genetic research and genetic testing, et cetera, et cetera, is that we are in a rapidly changing landscape in terms of our concepts of what it is to be genetic information. What it is for something to be a genetic disease.

And that what we might learn from a survey that uses these concepts, and many of these concepts, for example, relevant to here is what people believe, fear, whatever given their concept and it might be an outmoded concept.

For example, if it has as its paradigm the highly penetrant monogenic disorder which translates into a concept of genetic determinism 100 percent certain, okay, where the paradigm case in mind is a test performed in the context of a marriage or a reproductive decision, how my opinions about information arising from such a test I can tell you are a heck of a lot different than if it is a genetic test which is in a polygenic, multifactorial, which gives me another piece of information not a whole heck of a lot different than an HDL test.

Actually what I find myself most interested in learning, because I just made a bunch of statements about what I think is going on out there, the empirical knowledge that would be interesting to me is to find out -- to ascertain how people change in terms of their view on the hot button issues if they have a change in their understanding about what is a genetic disease and genetic test, et cetera. And that may be impossible to get at.

PROF. BACKLAR: Impossible with one survey.

DR. MURRAY: It leads me to think that Zeke may be on to the track here by saying that rather than -- certainly if we are talking about a survey as the methodology to be used, rather than trying to get a sort of short survey that is just very strictly tailored to the point of this report that we might be -- the country

might be better served if we find a more carefully constructed survey to get at a variety of public attitudes, interests and values about genetics. That is one lesson I am perhaps taking from -- is that a legitimate inference from your comment?

DR. HOLTZMAN: Yes.

DR. MURRAY: David?

DR. COX: I think that is true if we are trying to find out about genetics but as I said to come back to something Steve said before because I think it is real important, do we want to find out about genetics, do we want to find out about research on tissue samples in general. But I think that one could have these questions be really quite fairly broad in terms of research and not necessarily so focused on genetics. The danger in broad questions like that is that you get not very useful answers.

But I really like this idea that Bernie said which is getting direct responses to something that we are putting out there. It is sort of -- we have a proposal and we are asking does this apply at all. It is not, you know, looking for expert opinion on it but basically we are either getting -- you know, it is an applause meter. People either understand what this is about, okay, or this is something that they do not get. You know, it just does not make any sense. To me that

would be very useful to know, you know, if we are even talking in the same ball park here.

DR. MURRAY: Let me ask a somewhat naive question since I do neither survey research or focus groups. If I understand -- here is a draft -- my quick draft of what it is we want to know, what it is we hope to get out of this kind of information, and that is to sort of flush in the sorts of interests and values at issue that Zeke began to outline earlier today.

But rather than have it flushed in by professionals who do the research or by ethicists who think about the research, by people who perhaps are representing at least some reasonable diversity of American population say, and explaining to them in a setting just what this means, what good comes out of it, the scientific research that might be done, what kinds of uses to which it might be put, the privacy protections that either are in place or might be in place or might not be in place, and then getting them to say what are your concerns and what matters to you.

What are the values implicated in this sort of set of possibilities? Now is that what we are after and, if so, what methodology can we use?

DR. COX: We are but I think that not it is not in a vacuum, okay, so that I am not looking at a totally unbiased thing but in a given structure, okay, we

sat down here this morning and came up with, okay, as a basis of -- to start with. Because I mean we got stuck with a basis to start with, too, and we are probably in better shape. I mean, that is why we are here touching it up but does it really make sense. That is --

DR. MURRAY: I want to try and clarify that, David. Do you mean sort of the values that we were able to identify? Do we want to see if they, in fact, resonate?

DR. COX: Yes.

DR. MURRAY: Whether people understand them?

DR. COX: Yes.

DR. MURRAY: Yes. I also say are there things we have not thought of that they would think of.

DR. LO: See then the question is -- if that is our goal, and I would agree that I think that is the direction we would like to head for the specific topic of stored tissue samples, is a closed answer survey the best way to get that? Or is something more qualitative where people -- it is not just a show of hands, that 80 percent think we are on target or 20 percent think we are on target. Or someone says, you know, I do not really understand what you mean by that.

DR. MURRAY: Yes.

DR. LO: Or what you seem to be talking about when you talk about autonomy is not what I mean.

DR. MURRAY: Yes.

DR. LO: So I think we may want more qualitative sort of feedback asking people to try and articulate what concerns them, not just the fact they are not sympathetic or unsympathetic for what our position is, is working out to be.

DR. MURRAY: Chuck and Dorothy, are we talking about what you call focus groups rather than opinion polls if this is what we are saying?

DR. WERTZ: I think --

DR. MURRAY: Wait. Zeke had his hand up.

DR. EMANUEL: No, no, that is all right.

DR. WERTZ: I think what Bernie is talking about are interviews done with what you call an interview schedule which is an outline. But it is open ended and you draw out more information per individual then and you find out what they really think and what they really know. And that is the great advantage of it. Yes, you can get at things which are not in a survey such as I put here.

The disadvantage is that you get fewer people. This is labor intensive. You could do this in a clinical setting if you could -- you would have to go through somebody's IRB but, you know, that would not take that long. And you could interview patients or patients'

parents. You would have to have -- you know, well, you would have to hire some staff to do this.

You will get a lot of information and people would -- you know, they could go on and on about what they said -- what they thought. And you could include minority groups. I mean, you could make this quite representative. You could have Spanish interviewers. There are great advantages to it if you want to go that way and if you have the funds.

I think it has to be personalized. I mean I have seen some of these surveys that ask about genetic engineering. Do you approve of genetic engineering? And I do not think they are too useful if you ask these great big broad questions. You have to say you had some blood drawn today, what do you think is going to happen to that blood now that it has been drawn after they have taken the test? Do you have any idea what has happened to it? What would you like to happen to it? Do you have any idea of the kinds of research that are being done? What kinds of research will you find acceptable and so forth? It could be done very nicely by interview.

DR. MURRAY: Zeke and Bernie.

DR. EMANUEL: Chuck had his hand up.

DR. MURRAY: Okay. Chuck?

DR. DENK: Just one little point about the focus groups. Complex topics are not -- I disagree with

the notion that you have to do complex topics in focus groups and easy topics in a telephone survey. That is probably not what you meant.

Focus groups are used most effectively not in opinion research but in advertising for message testing. Okay. And that is a good, I think, way to think about it. You spend two hours with somebody. You talk about what they know. You fill in the gaps of what they know. At the end you ask -- you know, or throughout you probe their feelings about what they have just learned. Okay.

The reason -- all right. And that -- that would be a very useful thing to say, how do we communicate with the public if that is what you want to do. If you want to design some public service announcements here. However, if what you really want to know is what people think, you know, we also say in election polls that if the election were held today this is how things would break.

The peril of the focus groups would be if we could get everybody and sit them down for two hours and really explain it to them what their opinions come out to be but that is not -- I mean, that is not general -- to generalize it that way is meaningless because you will not ever do that.

DR. EMANUEL: I guess my -- if we think that there is something valuable here that we could get out of

the polls, additional values, reaction to the kind of proposals we want to make, gaps in understanding that really need to be attended to, it seems to me that we do have two competing views. One is to try to do it issue by issue and to try to imagine our reports as having some part that has a public survey part. Or I think at the end of several of these reports trying to have a comprehensive view. I am skeptical about having a section in an October report.

The other problem is that we only can address cloning that way. It seems -- again I would urge the idea of thinking about a separate report that would look at the general public's reaction to all -- to several of the things we are looking at. It will allow us a more thoughtful way of going about this and a more -- I do not want to say leisurely but being able to do it in a bit more systematic way.

I think, you know, one of the down sides of these long interviews with open ended questions is you have got to code them afterwards to know what people do, and that is time. And then in the end you are imposing a grid on it. So it is time and money and in the end I just -- I propose a long term perspective since Dr. Shapiro has assured us we are going to be around for a few more years.

DR. MURRAY: At least the commission will be

around for a few more years if not the commissioners.

DR. EMANUEL: Well, yes, that is right.

(Laughter.)

DR. EMANUEL: You would not guarantee that I will be around for a few more years.

(Laughter.)

DR. MURRAY: I am sure that is true. Bernie is next but if I may, Bernie, make a quick response. I both like and I am uncomfortable with your suggestion. I think a kind of -- I think there really could be a contribution the commission could make by a technical report as it were sort of on public views about a whole variety of issues on genetics. I think that is a terrific idea and we should keep that one in mind and maybe identify that as a priority although that would be two to three years or so to do it well.

The other thing I would not want to give is the message that, well, there is the public's view and then there is the commission's view, and they are really not influenced by them. I do not want to send that even as a subliminal message. So I do want to --

DR. EMANUEL: Fair enough.

DR. MURRAY: -- incorporate it as much as possible in what we say even if it not be a section of each report.

Bernie?

DR. LO: Let me try to address sort of the second level question you raised, Tom. I think we -- I think we have some agreement on the kinds of issues or topics on which we would like some sort of sense of what the public feels on things. We have certainly talked a lot about the sort of practicalities of how to do this on a time table.

But I guess my question is what is the best way for us to sort of float some trial balloons of ideas we are thinking about? Because I think if that is what we need I think that is something that would be very helpful as we write this report for October.

Rather than restricting ourselves to close end surveys, you know, open ended, or using focus groups, I mean how do people in other walks of life sort of test out preliminary ideas with people who will be directly affected by them? I think it would be important for us to try and do that. I do not know of a way of doing it. I am not sure public testimony always works.

But I would like to try and think of a way of getting at that because, you know, Zeke led us through a discussion which had, I felt, some very, very promising and good ideas. But I would like to get a sense of whether, you know, people in my clinic who are about to have their tissue samples drawn think we are totally off target or we are missing certain things rather than come

out with a recommendation without some value, you left out X, Y and Z and, you know, you are way off base on A, B and T.

DR. MURRAY: Three commissioners have indicated a desire to speak. I want to ask Bette, Trish and David, in that order.

DR. KRAMER: I would like to remind us that going back to the very first time that we discussed this issue we made the point that the only stakeholders that we have not heard from are the public. I mean, the very people whose tissues we are proposing the use of. And so I think we need to bear that in mind.

I am intrigued by something Dorothy said and that is that although she has not specifically polled on this particular question, but she has the impression that they really do not care. Now if, in fact, we are able to come up with some, through whatever technique we end up using, we were able to come up with information that bore that out, how would that affect, how would that impact what we had talked about earlier at the conclusion of the proposals that you outlined at the conclusion of your presentation this morning?

DR. EMANUEL: I am not sure but it would -- I think that --

DR. KRAMER: I mean, it is really rhetorical.

DR. EMANUEL: Right, but I think in part it

would suggest that we need to meet again, this report is always going to need a public education component because it is not palpable and immediately obvious to people why it is a big concern for them. And even in our polling, you know, even to confirm or disconfirm it, it seems to me we still have that job.

DR. MURRAY: Thanks. Trish.

PROF. BACKLAR: Which really leads into what I wanted to say. I am beginning to hear that this cannot be done adequately and quickly. It sounds as though if we want to get people's values we also have to spend some time educating.

And I could see some kind of patient survey questionnaire which would do both, something of the kind of thing that Dorothy started to describe to us just a few minutes ago when you have a patient there and they are having a blood test or there is something wrong with them, and you explain this to them and you lead them along the way. But I cannot see that being done. I agree with Zeke and Bernie. That cannot be done for an October report. I think we would have an October massacre.

And the difficulty exactly as Bette pointed out, what if all these values are so different, how do we integrate, and if people do not know enough, if you are not educating along when you are getting these values

there may be a terrific discrepancy between what is really going on and what the public understands.

DR. MURRAY: David?

DR. COX: Okay. So I am going to do something here where I am at great risk for doing but I am going to do it anyway. This is not this hard. Okay. We are sitting here talking about an issue that we -- actually Bernie brought it up. Okay. Is that how do we find out about this stuff when we want to learn about it in common sense? So I go up and I ask people, right. And so they say, "Well, I do not know what you are talking about." So you say, "Well, let me give you some specific examples because here is, you know, how I framed it." And then they say, "Oh, well, in those examples here is what I think about that."

So then in my view of this commission that is public testimony but not in Washington. I do not want to hear about this in Washington. I want to hear about it some place else.

So I think that we do not have to go on the road, you know, and do a rock tour but we could go a few places and just ask some people some questions, you know. And we can sit here amongst ourselves and say, "Well, you know, we have been sitting around this table and here are some of the things we are talking about," and there is a completely blank stare and nobody says anything, right.

But that is a really short evening. But at a minimum, okay, I would like to do that, okay, because I think that it is -- you know, in between the stuff we are talking about.

But I do not think that it is impossible to -- we cannot tell people what it is we are concerned about and thinking about in common English, in common language, and get a response from people, you know, who are just like normal people then I do not know what we are talking about. Now that is an extreme statement so I would like to see --

PROF. BACKLAR: Are you --

DR. MURRAY: Trish?

PROF. BACKLAR: Are you talking about focus -- again I do not know where you are going with that.

DR. COX: I am talking in the context of a town meeting. We would go and we would make an announcement that NBAC is dealing with these issues.

PROF. BACKLAR: I would like to respond to that because I come from a state in which there were many focus groups about the Oregon Health Plan and the problem with that is twofold. One is who comes to those meetings and you will find the people who come to this meeting already know and the people who you want to reach do not get there. And so it becomes a very inbred discussion. I am very concerned about that.

DR. COX: Okay. That is the risk. Okay. Certainly, okay, by going outside of Washington we try and reduce that risk but what you are saying is that you cannot reduce it enough. If you cannot reduce it enough and you are only talking to people who already are stakeholders with well defined views then we do not learn anything more. I quite agree.

PROF. BACKLAR: Which is why I like Dorothy's idea of going to patients who have some experience and something going on and something is at stake because they are the real stakeholders. They are already in there.

DR. MURRAY: Bernie and Carol, you had your hand up a minute ago. Do you still -- Bernie and Carol?

DR. LO: I have talked a lot.

DR. GREIDER: Go ahead.

DR. LO: I think there may be a way of combining what Dave is suggesting and what Dorothy said, and that is to sort of invite a random selection or a weighted sample of patients who are either patients or research subjects or have stored something in a serum bank or a tissue bank, and invite them, you know.

Not just say here is a public announcement where it becomes common but sort of say we are interested in your view because you have donated tissue that is the sort of tissue that people might want to use for research. And then you, you know, as David said, sort of

present it and say now what do you guys think about this.

Maybe, you know, we could do it locally and I am not sure we all need to go in the same room but, you know, we could maybe get into one --

DR. COX: We could do something. I mean, I know it gets frustrating.

DR. MURRAY: Well, since David mentioned rock and roll, need I remind you all that the Rock and Roll Hall of Fame Museum is in Cleveland and there are real people in Washington but there are also real people in Cleveland.

Carol?

DR. GREIDER: It seems to me like, having heard the discussion, I wanted to get back to something that Zeke said earlier when we were considering the whole opinion poll and that is that if we were going to do something as intensive as that we might want to consider a lot of the other issues that this committee is going to be dealing with down the line in terms of the genetic privacy and discrimination, and those sorts of things.

So it sounds like what we are talking about is two different things. One is the short term approach of what are we going to do now for the stored tissue issue and how are we going to quickly get a sense of what the public thinks about that. And then to keep in mind considering doing some sort of a polling or sampling for

the larger issues that we are dealing with and accept those only two sort of long-term and short-term categories.

DR. MURRAY: Thanks, Carol.

Other commissioners? Could I ask Dorothy and Chuck -- oh, Rachel, I am sorry. Yes?

DR. LEVINSON: I was not sure if I was going to add this in but it is too interesting to pass up. The idea of testing possible messages or thoughts with the public and not trying to go for a representative sample, but assuming that you are accepting up front that you are going to get only people who have particular concerns or interests in that particular issue, I have in my hand an example of a survey that AOL is running right now that just happens to be on the subject of cloning human beings.

But it is interesting in that they have got 15,000 responses as of last night. 56 percent of AOL members. So they are sampling AOL members who want to log on and look at this. But it is broken down and it is analyzed on a regular, meaning hourly basis, with very simple questions and it is just an interesting way of getting a quick look at very, very narrow issues. This we can get on line.

(Simultaneous discussion.)

DR. LEVINSON: That is what I am saying, it

is very, very highly self-selected but you get a large number of hits and they can come back and give you their ideas, their postings on specific points of it. So if you wanted to look and say have we missed something, it is a way of getting a lot of ideas of things that you might not have thought about.

DR. MURRAY: You do not get many instances or prevalence but you get a sense of at least what are some of the concerns some people are thinking about.

DR. LEVINSON: And Henrietta just pointed out there is an NBAC home page. We could use that for going outside of AOL.

DR. _____: If you can get into it.

DR. MURRAY: It is a home page but we keep the doors locked.

(Laughter.)

DR. MURRAY: Only the commissioners.

We are at about the end of the time we had allotted for this session. If I can summarize what I think I have heard emerge here, it is that we are proposing kind of two tracks.

Track one being some kind of effort to solicit public input, qualitative input about whether we have sort of mapped the terrain accurately or not, and are there other things that people care about, and are there things that we identified that we thought people

cared about but no one seems to have given it two thoughts and even when it is going out to them they do not think it is important.

That is sort of -- and to do that probably by some sort of public hearings which would not simply be the announced anybody wants to come hearing but rather to go perhaps to the community and say, you know, ask to have a few patients identified, a few people who may have given tissue samples, or a few research subjects, and actually ask them to come and say, now, what do you think and feel about this.

What is important to you? Am I correct? Is that the proposal that is being floated? I characterized it as well as I can. That is one track. We could do that I presume in sufficient time to have that input for this report.

The second track is a much more ambitious one, much more methodological sound in the sense of some sort of effort to get a grasp of public opinion, values, et cetera, on a variety of issues in genetics. It was Zeke's proposal but not to try to do that quick and dirty but rather to say, "Well, let's do it right," and it may take two or three years to get that result.

Is that -- first of all, have I clearly stated what I think seems to have emerged?

Bette?

DR. KRAMER: Can I ask you a question and point of information?

DR. MURRAY: Yes.

DR. KRAMER: With regard to the first how would you envision that being done? You said we could do. We could go to the community. We could talk to patients who have given samples.

DR. MURRAY: I was going to get you to do it.

DR. KRAMER: Sure.

DR. MURRAY: A lot of details to work out. I think it could be done. I mean, I think we could go -- we could come to Virginia for example or at least a subset of the subcommittee could come and could set up a -- borrow a room from perhaps the university or a local hospital or something, approach local researchers and ask if they could, you know, identify a few subjects, people who had donated tissue, people who are participating in research projects, maybe a patient or two that did not know -- or may or may not have known that their tissue would be used for research, and half dozen or so people.

I am making these numbers up obviously as we go along. Have a half dozen or so people come and have a conversation with us about this. What do they care about? What are they concerned with? And then we might go to Virginia, we might go to San Francisco, we might go to Cleveland, or Cold Spring Harbor.

Carol?

DR. GREIDER: I was just -- I would like to get the opinion of the people who do these kinds of public polls about how feasible this mini-poll thing that we talking about is.

DR. MURRAY: Well, I would not call it a poll. It is just a --

DR. GREIDER: Yes. Okay. But we are making something up here and I just want to find out what their reactions are.

DR. MURRAY: Yes. That was the next step. I just want to be sure I could even characterize it correctly. We have done that. We are just going over time now but if I could ask Dorothy and Chuck for their quick responses.

DR. WERTZ: Okay. Well, I think it may be better than nothing. I think there is a real danger in going ahead to meet this deadline at all costs in an information vacuum as regards the general public. I mean, one -- if you can -- absolutely cannot postpone the deadline in order to get information, this is one way to do it. It is sloppy, however. I just -- I think if you are going to do it you -- to get the OMB exemption they would have to be patients.

They would have to be randomly selected. Not just the people who self select as so often happens.

They must be randomly selected. They probably are going to have to be paid to go to these sessions. You do not take a couple of hours of people's time and really expect to get a random sample which is what you need. You are going to have to over sample minority groups to make absolutely sure they get in there. Another reason for paying everybody. And then you are going to have to write down, you know, some sort of outline as would be done for focus groups just to make sure that issues are covered if people do not think of them.

Now as I say this is sort of sloppy but it is better than nothing. But I am concerned you do something other than simply letting people know we are going to have a public hearing because then you will simply get all the people with axes to grind rather than hearing --

DR. MURRAY: Just for the record, that is very clearly not what we are talking about in top one track. We had the same experience in Cleveland as Trish reports. If you just open the meeting and say to people, you know, let's come talk about X or Y, you get PLU, people like us, come to the same meetings and we end up talking to people who start out with views very similar to our own and that is not -- we would not want to just replicate that.

DR. LO: Could I ask an information point, Dorothy. When you said these must be patients, do you

mean people who are receiving clinical services as opposed to being research subjects?

DR. WERTZ: Well, it is -- whatever the latest definition is and Zeke says it now includes people in research. That is to get around OMB.

DR. MURRAY: Although we are not doing -- this is not a study. This is a hearing that we are proposing. I do not believe it would fall under those usual rules. It is not research. It is a public hearing where we invite people that we wish to testify.

DR. WERTZ: If you are taking people at random from a list and inviting them, is that --

DR. MURRAY: I do not know, Dorothy. I am not going to get -- I do not want to debate that. But I do not -- as we conceive and certainly as I conceive it, it is not a research project. It is an effort to get some representation -- some range of public opinion. It is not a research project.

Steve and then Chuck, and I think we are going to -- and Trish, and then we are going to have to break.

Steve?

DR. HOLTZMAN: I should have thought of this earlier. I am just tossing it out as something maybe we can come back to. If we try to focus narrowly on this issue of how do people feel about the use of their tissue

samples there are people right now in the hospital who entered the hospital yesterday and the day before, whatever, and signed a consent, right, but that it had that general and your stuff can be used for research.

I personally might find it interesting if you could set up a bunch of exit interviews with those folks as they were leaving the hospital, right, to get out --

DR. WERTZ: And find out if they remembered it.

DR. HOLTZMAN: -- right, and just find out by the way this is what you did, let's talk about a number of things that might now having your consent happen with the sample, how do you feel about these different things, and if you think -- structure those questions well you might start to elicit where the values play out. And it seems to me that logistically -- again there is an issue of getting your questions right, but logistically that could be pretty straight forward to do. Why do I say that? There are lots of hospitals with NIH funding and ways of tagging on -- I do not know. No, forget it.

DR. MURRAY: Trish?

PROF. BACKLAR: There is a lot in here that really worries me. Who are the gatekeepers to this before we get to the interview? How do these identifications go on? I see a lot of problems in here. I do not mean to make things more difficult but this is

not just a straight forward kind of work we are envisioning. Maybe I worry too much about these things but I think that is part of our responsibility is to worry about how we are going to identify who the gatekeepers will be and so forth.

DR. WERTZ: You would have to go through IRB's.

DR. MURRAY: Excuse me. If it is research it would have to go through IRB's. If it is a hearing we do not have to go through IRB's.

DR. EMANUEL: Even -- it is possible to do -- many IRB's have exemptions for small preliminary focus group kind of things. I mean, at least the ones -- I have just been through 42 and I think I could get through every one of them in a week. I do not think that is a big barrier if you like this approach.

DR. MURRAY: Could I ask your reflections on what you have heard?

DR. DENK: Actually I think Steve's suggestion would be an excellent research study. But all those proposals that I have heard that are not research, I mean I just -- my professional bias is to say they are really not research. Okay. They are -- they are going to be like testimony and they are not going to be at all like a survey. And that is -- you know, if that is what you want I think that is okay.

Can I just comment about another issue and that is that the surveys that I described that are either happening or going to happen are going to happen anyway and I would like to suggest that perhaps instead of having your own surveys you could try to articulate why public opinion should matter to these issues to give those surveys a better chance to get the right kind of resources and to focus on the right kind of issues. Because I think the biggest question that has been discussed here, and quite an important one, is where does public opinion articulate with this whole set of ethical issues and the policies that must result from such deliberation, and I think everybody is in agreement that that is not very well worked out but that could be a product of this commission I suggest as a citizen.

DR. MURRAY: Thank you, Chuck.

It is almost ten of so we are ten minutes into our thirty minute break.

Are there any final comments by the commissioners?

David?

DR. COX: Very fast. Two. The first is that we had a meeting of NBAC, okay, in San Francisco at the International Ethics Meeting and it was very instructive because we had people from all over the world. I think there was one message that came from that, is that as

difficult as it to assess what public opinion is, if any commission is worth its salt it better pay attention to that. So that is one thing that just sticks in my mind.

The second thing is that we should not confuse research with testimony but if given our time line testimony is all we can do then we should do it.

DR. MURRAY: Thanks, David.

We will reconvene at ten minutes past 11:00.

Thank you, Dorothy, and thank you, Chuck, very much. We would love to have you stay around for the rest of the hearing if you can.

(Whereupon, a coffee break was taken from 10:50 a.m. until 11:19 a.m.)

DR. MURRAY: Ron Cole-Turner has been generous enough to join us for this session.

Ron, would you please introduce yourself and do not be bashful and explain why you are here?

RELIGIOUS PERSPECTIVES ON TISSUE SAMPLES

DR. COLE-TURNER: All right. My name is Ron Cole-Turner. I am an associate professor at Pittsburgh Theological Seminary in a position that relates theology and ethics to science and technology. I am a member of the clergy ordained in the United Church of Christ and, in fact, in that denomination I have chaired a succession of three panels having to do with genetics. The third is working right now. In fact, our next meeting will occur

late in May.

I am also at the moment involved in a Presbyterian Church U.S.A. study of genetics. I also work with an even wider group of church bodies that attempt to address the relationship between the churches and science and technology generally.

As I understand it, I have been invited today to discuss with you -- to consider with you how the subcommittee would be best served in consideration of religious perspectives on tissue samples. I am going to raise really a bewildering list of possibilities and ask for your help in sorting out where the fruitful areas might be and then leave for your consideration where future work might lie.

So let me begin this rather long list. Essentially it is in two parts. The first has to do with more technical sorts of questions. In your exploration of the question of human tissues, human tissue sampling, do you intend to include a discussion of a patenting issue? And, if so, you need to be aware that in May of 1995 a very broad coalition of religious leaders of some 200 individuals representing, I believe, eighty different faith groups signed a statement in opposition to patenting of really I think anything biological. The statement was a bit vague. For that reason and for a host of others some of us were adamantly opposed to the

statement in the way it was written and the way it was developed.

There has been an ongoing conversation hosted by the American Association for the Advancement of Science that has attempted to broker some of those relationships and clarify the misunderstandings. That is an ongoing process mostly focused on genes. Are genes patentable, should they be patentable, and religious perspectives one way or the other? But it obviously should include a broader range of biological issues than just genes. In fact, the original statement, the May '95 statement does not say genes. It refers to body parts and some other again rather vague language.

Related to patenting but not identified with it, of course, is the issue of profit.

The second issue I want to identify is what do you perceive to be the relationship between your work here and the Human Genetic Diversity Project? This is not well known among the religious communities but potentially is a subject of some concern in that it involves the rights of indigenous populations and the question of collective consent.

Now in all honesty religious communities, particularly Christian religious communities, have not been among the first to defend the cultural rights of indigenous populations and, in fact, the view

historically has often been to convert them to Christianity well encumbered by western culture and western values. At the same time I think it is accurate to say that there is serious rethinking of that kind of policy at least in mainstream Protestantism and in Roman Catholicism and probably across the board in the contemporary understanding of the relationship between Christianity and other cultures.

So there is more emphasis on respect and less emphasis on conversion, but sorting out those issues is particularly difficult. So just how the question of indigenous cultures would play in religious communities would be a bit difficult to predict.

The third issue would be to what extent do you want to include fetal tissue for therapeutic uses and again you know well the way in which the various religious communities have already addressed some of those issues.

Next I want to -- this will be the longer portion obviously of what I want to say -- I want to talk about -- I want to briefly identify religious attitudes toward a number of factors. Again this is a very long list with the idea that by laying out as much as possible on the table initially we can winnow this down to something a little bit more manageable and meaningful.

But religious attitudes toward, and I have

six different ways of completing that sentence. Religious attitudes toward the human body. Religious attitudes toward families and other collectivities, toward health, toward stigmatization, toward research and medicine, and finally toward public institutions.

But first, and this will be the largest of these, religious attitudes toward the human body. If you consider religions generally, the attitude toward the human body and toward the natural world generally, is incredibly diverse and complex. You have diversity over time, individual traditions will change their point of view over time and to a large extent reflect prevailing cultural and scientific views that are in their surrounding milieu.

But there are different traditions, different faith traditions. My examples will be largely from Christianity but there are other faith traditions that hold obviously quite different views.

In fact, I cannot think of an issue over which there is greater difference between Christianity and other traditions than the question of the human body because after all traditional Christianity has made the absolutely astounding claim that the divine is incarnate in the human body. And that has been the most pronounced difference between Christianity and the other faith traditions.

But even within Christianity you see bewildering and complex ways in which that central claim can be articulated and carried through. As I will illustrate in a minute, this is not just differences between communities, Christian communities that you might ordinarily put at different ends of the spectrum in terms of their ecclesiology or their origins.

But even denominations, some traditions within Christianity are closely related in the promise of reformation as the Lutheran church and the Reformed churches, which in the U.S. would include Presbyterianism, have a rather significantly different take on the modality of divine presence in the human body.

Incarnation, I have already used that word. That is obviously the central claim, the claim that God is incarnate in a human body. But the attention to the human body does not end there with that -- in Christianity it does not end there with that claim.

It extends obviously to the central ritual of virtually all Christian communities, the sacrament, the Eucharist, Holy Communion, and again on this issue there is a wide array of opinions as to the way in which one thinks about the presence of Christ, of the divine in the physical. And as you well know, some claims are incredibly realistic about the mode of presence while

other claims of other traditions are quite a lot less realistic about that.

There in particular is where one sees a difference between Lutheranism and reform. With Lutheranism suggesting a doctrine of the ubiquity or the omnipresence of the body of Christ.

So in Lutheran thought and Lutheran piety there is a greater recognition that Christ's body, the body of the divine is everywhere, and this body is by virtue of that ubiquitousness is part of the divine body.

In Reform traditions, for instance, that is -- the mode of divine presence is understood not to be through Christ but through the Spirit, the Holy Spirit, the third portion of the traditional doctrine of the Trinity.

And, in fact, you will find affirmed almost without exception across Christianity the belief that is first asserted by the Apostle Paul in the Biblical text that the body, the human body is the temple of the Spirit, the Spirit of God, the temple of the Holy Spirit.

Now you say, well, who would give consent to giving away tissue samples of the temple of the Holy Spirit for research? Does this mean that with such a high view of the dignity, even a sacrality of the human body, that tissue sample research is going to be highly problematic?

Well, not so fast and this is where I want to suggest that there are incredible complexities even here. Again this gets us to a belief that is very idiosyncratic to Christianity and, in fact, treads on an issue that has divided Christianity from its closest counterpart within the array of religions, namely Judaism.

There is within Christianity the conviction that there is something saving and healing about the shed blood of the one who dies on the cross and that to some extent Christians are supposed to offer themselves as well not to die literally in that way but in sacrifice for one another, even for strangers. So giving away one's body is not the worst thing. In fact, it is the best thing at least if you develop the notion out of that line of thinking. But conversely one could develop a notion out of that other previous line of thinking, namely that the body is indwelt by the Holy Spirit and articulate a highly conservative view of the question of tissue donation.

All of that of course comes together again in a view that Christianity probably has emphasized as much as anyone although I think in different ways it is shared by other traditions, and that is belief in the resurrection. And if anything, Christianity has emphasized here I think the bodily nature of the resurrection even to the point in some Communion, some

sub-traditions within Christianity for making it sound like a resuscitation.

To the extent that it is a resuscitation we obviously have a problem. To the extent that it is a transfiguration of the physical body so that it becomes a new body and to the extent that one enters into that by giving away what one is now we should not have a problem. But again there are complexities within Christianity as to how these terms are spelled out and what they might mean in this kind of situation.

One particular source of -- one particular difference, which is not historically very strong but has obviously come to the forefront as a result of recent debate, is the question of the status of the human fertilized egg and the pre-embryo. And as you -- I assume everybody is aware there is again quite a divergence -- quite a range of opinion within Christian churches on this. And again I am presuming an equally diverse array of opinions in other faith traditions.

But what is the theological and the moral status of the fertilized egg and of the pre-embryo? And I think we need to imagine here how some of these scenarios might play out in the next few weeks, the next year or two. To what extent does cloning blur the line between tissue and embryo, pre-embryo? And will there be those who are so opposed to pre-embryo research that they

are driven to a very strong opposition to tissue samples, not just to a cloning of human pre-embryos but to tissue samples for the fear that somebody might then take those tissue samples. Now there are obviously technological developments that would have to occur down the stretch but to what extent will that become a new concern about the question of collection of the tissue samples?

I suggested a moment ago that the traditions, religious traditions, change over time and let me give an example of a change that is occurring in Christianity, I think in Judaism, probably in some other traditions as well, and that is a greater concern for on the one hand feminist and on the second hand -- additionally in the second place environmental concerns. Often these are linked but not always.

Christianity is undergoing that kind of internal critique and renewal some would say. Others would say degradation. But that is occurring within Christianity. I know it is occurring within Judaism and perhaps elsewhere.

The phrase that is sometimes associated now with this as it relates to the question of the human body is this phrase: The post patriarchal theology of embodiment. If you look at very recent literature you run into that. To give you an idea of how recent this is, at a theology meeting back at where I teach my

colleague, about the same age as I, proposed a theology of embodiment elective. She put forward that proposal. My two senior colleagues looked totally bewildered and I said, "Well, what a great idea? That is obviously a topic of contemporary interest," for which she was greatly appreciative after the meeting.

There is a bit of a generational issue that is going on here but I think those changes are very much in place. Now you might say, "Oh, well, very good, they are now increasing theological resources to address the question of the human body." Well, one of the characteristics of this post-patriarchal theology of embodiment is that it is quite suspicious of science, of technology, of medicine. I mean that is the post-patriarchal notion there that science and medicine have been patriarchal forms of domination over the human body and that we need to get beyond that.

I said that I had six issues now that I wanted to address under the broader category of religious attitudes toward, and that was the first one and by far the most complex. Let me pause with a little aside and I will come back and briefly go through the rest of the list.

The pause here is to raise an issue that I think might be worth discussing. Do you want breadth or do you want depth in thinking about religious things?

Well, obviously you do not want one to the exclusion of the other but what kind of balance is appropriate as this commission goes forward with its work?

Secondly, going now back to the outline, religious attitudes toward families and other collectivities. This is a new trend within Christianity and again I think probably within other traditions as well and that is to develop a theology of the family. Christianity is undergoing its own internal self-criticism for falling into too much individualism in its thinking and to recognize that collectivities or relationships are equally important although in different ways to understanding what it means to be human. So a shift away from the individual alone.

A related question, not so much theological as sociological but I think important for this commission is what does one do, what do health care providers do, what does informed consent look like when family members are of different faiths? Different faith traditions or at least members of different expressions of Christianity or most likely have widely varying levels of participation?

Maybe the coercion that sometimes researchers count on is complicated. If somebody breaks camp with the family on a basic moral question, have they also broken camp over religious issues, and to what extent you

may respect their new religion if that is, indeed, what it is or their repudiation of religion? Questions to which I do not know the answer but I think that those are important.

The third point, religious attitudes toward health. This is front page kind of stuff. You have seen Time magazine, Spirituality and Health, Christian churches themselves are not very far behind in recovering the supposed health benefits of going to church and observing the rituals. In fact, there are programs with little bits of money to stimulate programs to encourage churches to recover health ministry.

I note that simply to say that there is a larger matrix in which this work will occur but also to suggest that religious communities might be useful, not simply obstacles to steer around as we form public policy but might actually be useful as centers or communities that can both motivate and educate people in regard to the whole host of matters here. But I would note that this is an area in which I think it is safe to say that there is rapid change in how the religious institutions themselves are perceiving a religious attitude toward physical health.

Fourth, religious attitude towards stigmatization. What is stigmatizing? Early on I think I got the notion that it was pretty clear what is

stigmatizing. Is it, in fact, clear what is stigmatizing? Somebody suggested down there that it changes over time with developments in scientific research. That is probably true but I am not sure that research alone governs this. I mean is succumbing to a virus stigmatizing or not? I think it depends on the name of the virus. What is stigmatizing is really a distressing question.

Again religions must plead guilty for adding to stigma in some cases. At the same time I think religious communities can deconstruct stigma and again I would point to one resource within Christianity, our greatest saints, indeed our -- the prototype here, namely Jesus, sought out those who were most stigmatized. Mother Theresa today, St. Francis sought out the lepers. So what is stigmatizing is almost a magnet to the greatest saints. Not to most Christians but to the great saints. So stigma is a very interesting notion I think as one plays around in religious communities.

Fifth, religious attitudes toward research, from scientific research toward fundamental advances that lead to developments in medicine. There is hostility in some camps in religious communities. Particularly I think more among academic theologians, less so I think in the rank and file of the churches. And I suspect the same is true in other faith communions. But I think

that is an important question to ponder.

How valuable are fundamental breakthroughs in research? Do the religious communities want to attach a religious value to those breakthroughs? I tried to argue in some of my work that that should be the case. This is valuable. It expands the capacity to help and to heal, and that is a religious value and we ought to recognize it as such. But I think that is an important theme in all of this.

Finally religious attitudes toward public institutions. Do we trust public institutions? You asked me to sign a consent form. Why should I trust you a religious person might ask or anybody might ask. Why should I trust you to abide by the limits that are specified in that consent form?

Now particular communities have histories of misuse as communities at the hands of government and of science. You all need to be very conscious of those histories. But in addition to that, in addition just to remembering the history, there has been a theological point here, a caution about human moral purity, human moral intentions.

I do not want to confuse this with cynicism by which all accounts is in good supply in the present environment. This is not cynicism about human nature but it is at least within Christianity is articulate in the

notion of the fallenness or the sinfulness of human beings. It is not cynicism in the sense that cynicism has often applied to everybody else but me.

The notion of fallenness or sinfulness means everyone equally even our best. Especially our best people as it were. Our most incredible. Our most responsible people will fail us. They will disappoint us. Again Christianity and to some extent other religious traditions presume that as a way of looking at the world.

There are variations here. Some will take such a gloomy outlook that they think that one had best withdraw from public institutions. They are irredeemable, unregulable, simply withdraw from them. My own expression of Christianity sees them as redeemable and indeed as vehicles of good works in the world. And so sees them as skeptically on the one hand but not so skeptically as to say that they are beyond repair.

So the question of regulation, drawing up codes and forming regulation, is absolutely critical to -- I think to the sensibilities of the religious communities. Expect that people will misuse power and will abuse trust, and so we have to design those systems that will permit that to the greatest extent possible.

DR. MURRAY: Thank you, Ron.

There are no questions?

Let me begin by -- this is a question about scope in two ways. Scope -- first of all you listed six major themes. Would it make sense to try to ask someone to help us understand religious points of views represented in America on all six of those themes or should we concentrate our efforts on what may be a key one to some subset of that?

The second question about scope is you have spoken mainly on your own sort of broadly speaking religious tradition, Christianity. There are, in fact, other traditions that are important in the United States. I mean, they are all important but I mean there are some that are -- that have significant numbers of members in the U.S. To what extent should we and to what extent is it at all plausible for us to attempt to increase our scope to cover other traditions? I do not know if you have answers now or not.

DR. COLE-TURNER: Not really. I do not -- I certainly did not come in assuming that all six of those items would translate into separate research projects. I am not sure that that would be necessary. I think some clustering of some -- certainly some reorganizing with some clustering would be in order. To what extent do you need to attend to a variety of religious traditions? Well, I guess obviously so, I think that needs to be factored in. Where does one stop might be the more

relevant question.

And an additional question would be how do you actually structure the multiplicity of perspectives? How do you structure the research into them? Do you ask one person who may be of one tradition to speak for other traditions obviously drawing on their text or do you need representatives to speak or is there some medium ground between those two possibilities? But I think that raises some very difficult organizational questions.

DR. MURRAY: Bernie, did you have a question?

DR. LO: Yes, but you had a second question too.

DR. MURRAY: That was it. Scope in both ways is the two things I wanted to ask.

DR. LO: Let me follow up on the theme of scope. We have a relatively -- we were talking about a relatively narrow topic this morning, use of stored tissue samples for genetic testing. And then there are obviously much bigger issues and to what extent is it possible to sort of think about the limited issue at hand of stored tissue samples without also trying to understand the much larger question that you raised knowing full well that in terms of what is probably the public's level of concern and awareness is not our specific topic this morning of tissue samples but the cloning and sort of allocating what does it mean to be

human and what are the limits that mankind should be doing?

So any advice you can give us on sort of tapping both the limited question and the following question.

DR. COLE-TURNER: Well, again you have got some tricky factors to weigh there. I guess the only advice I would give would be if you really want to draw in religious opinions you will need to allow those individuals or text that articulate those opinions to define scope. I mean to -- I do not think it would be too useful to ask highly narrow questions of religious leaders or religious experts and tell them they can only address those questions. I do not know that that would be very useful to you. I think you need to see the broader context.

I mean if you do not understand, for instance -- I mean, have available for you in digest form the ways in which attitudes toward the human pre-embryo are articulated in some traditions and articulated differently in other traditions, I think you would be missing something. Even though again the linkage between tissue samples and pre-embryos is a bit tenuous at the moment but not in the minds of the religious people. That is the point I am trying to make here.

You need -- if you really want the religious

opinions articulated you need to allow them to say what it is these issues raise for them. Now at the same time you do not want to give them carte blanche. So at least some confining of the topic.

DR. MURRAY: I have been somewhat neglectful in my duties as chair in not greeting Jim Childress who is a member of the commission and chair of the Human Subjects Research Subcommittee and conveniently also an expert on religious ethics. Jim, I hope you will free not only free to join this conversation but to please help as you can.

There were a couple of questions. I think David and Steve.

DR. COX: I just wanted to make an observation, again sort of something to rebut or refute or correct. But I find your analysis of these six points really fascinating but what I took from it is that there is no simple way you can talk about what the religious views of stored tissue samples are even in a single, okay, religion or even subset of religion. So for me what that means is that maybe religious views are not a useful way to classify these problems. But that does not mean you do not take religious views into account but there are many different ways we can slice and dice it. We could have many testimonies and many different viewpoints so I am very interested in your comments to

that sort of statement.

DR. COLE-TURNER: Well, it is tough to even define religion or know what to include within the definition. I mean the definitions are usually generated out of the framework of the major western religions and so Christianity on the notion of religion then asks, "Well, do other people have a religion?" Well, maybe they do and maybe they do not by our definition. Well, to the extent that they do not by our definition, is there still something there that needs to be taken into account? So again it is incredibly complex.

For every -- for practically every religious assertion that can be made regarding tissue samples you can probably find somebody who would articulate its antithesis. Does that mean then that religion is negated? No. And I really would hope that you would not draw that conclusion.

But I guess an additional point to make in all of this is that one has to think of religious communities as -- it is quite volatile and in some respects manipulable. I think the thing that we have in common here is a worry that there may be some manipulation of religious opinion in a way that is detrimental to legitimate science research or legitimate uses in medicine.

I certainly have that motivation in trying to

address these issues is to undercut the misuse of religious themes. But none of us control, I mean none of us in the field of religion control how those things will be used. I mean it is -- I mean I can give examples if you like about misuse in the past. What I am more worried about is how some of these themes might be put together in unpredictable and probably irrational or unfair ways but ways that catch on in popular culture in religious communities but also beyond that have political consequences.

So to the extent that we can anticipate those together I think we will be better off.

DR. COX: I hear you loud and clear.

DR. COLE-TURNER: Okay.

DR. MURRAY: Steve?

DR. HOLTZMAN: I do not know if the following project is do-able but we have an enormous number of different practices with respect to different body parts, tissues, et cetera. Some of which have raised issues where there has been legislation or regulation, organ transplantation comes immediately to mind where that probably are established positions and views. All right. Some of which probably have not raised -- for example, having your hair cut and having your hair cuttings just thrown away. Okay.

But I almost want to say that could one

assemble in some fashion this range of different practices with respect to a bunch of different tissues and have major religious or whatever, okay, how they view these things because then if one goes to the question of the use of tissue in research I think what you will find is that it is not a function of -- there is not attitude that is inimical with respect to the use of tissue in research.

The attitude bears on issues like which tissues, with reproductive tissue probably having a very special status for most as opposed to others -- for others Jehovah's Witness comes to mind. Blood might have a different kind of status.

And that just as this morning where we started trying to get at a different cut at what are the relevant concepts we might be able to contextualize it. Is that a do-able project?

DR. COLE-TURNER: That is probably do-able. Whether it is worth doing is another question. And it probably would be. It probably would be worth doing.

The apprehension I have there is religion is not understood nor in my view would the commission be well served with a simple catalogue of yes/no answers. Yes, Jehovah's Witness would permit the tissues to be used or, no, they do not, or whatever. I have actually seen such things and I think -- I mean such digests of

views.

What is more interesting, I think, is again the question of depth as opposed to the question of breadth. What is more interesting is how are various communities likely to extrapolate now to this question of tissue and subsequent research use.

DR. HOLTZMAN: I want to make clear the depth to me arises exactly because giving a wide enough range of cases is what shows the depth about the whole? How do you take apart the concepts and apply them to the new cases?

DR. COLE-TURNER: Yes. Surveying the breadths can give you an idea of where to dig down for the depth.

DR. MURRAY: Jim?

DR. CHILDRESS: Let me build on the two previous questions. I very much appreciate your comments. You tended to emphasize the general perspectives and how they might well work out in relation to specific kinds of cases but the example would seem to focus on fetal tissue, fertilized egg and so forth. Examples where religious traditions have raised the tissue to a level of great significance in the way they thought about these matters. You also emphasize the volatility with traditions in the way which they can change over time.

I guess that I think these kinds of questions that have been raised suggest that it may well be important not simply to look at the general perspectives and see ways which they have worked out in certain areas to give significance to some tissue but also to consider the whole range and to ask the questions whether in terms of belief or practice, or both as to why certain tissues would receive a lot of attention perhaps leading to strong evidence against their use or their use in certain ways, or their sale, et cetera.

So I think that the variety might well be important in part because I am not convinced that each tradition will in every case connect those general views to this specific tissue. I think there would be a lot of variation and practices that may well simply not direct very directly to the large perspective.

And, in part, I would emphasize something my colleague at the University of Virginia, James Hunter, emphasizes and that is as you look across traditions you may well find that people -- let's use a simplified language -- liberals in one tradition may be a lot closer to liberals in another tradition than to their immediate colleagues. So those very different perspectives may not work out terribly clearly on a matter like stored tissue.

DR. MURRAY: Zeke?

DR. EMANUEL: Maybe I can try Steve's

question a different way. At the end of this morning we were talking about trying to distinguish different types of research as a good way of thinking about policy recommendations and rules, and ethical guidelines.

Would it be possible on that scale or spectrum to get some useful articulation of religious views so that we might be able to establish, if not quite a consensus, at least know what certain major traditions feel about these kinds of research that would be helpful for us? Because -- here is the sort of logic of the thought: If we are going down that line, if we are going to distinguish the rules along different kinds of research and whether they are anonymous or identifiable. It seems to me that the input we should get from the religious community should be along the spectrum we are going to -- we think might be helpful for policy.

So instead of looking at different tissue types or different religious communities could we look along the spectrum of the axis we are actually going to -- I mean, I do not want to jump the gun because I do not want to say we are definitely focusing in on it but at least at the end of this morning seems to be a useful axis.

DR. COLE-TURNER: Practically speaking I am not sure what you would be suggesting there. I mean would we be convening spokespersons for a fairly wide

range of traditions?

DR. EMANUEL: I am not sure. I mean --

DR. COLE-TURNER: I mean -- let me add to that. If you are asking what is already on the books the answer would be practically nothing. Frankly, I think what would happen is if you issued an invitation to a large number of religious communities, denominations, et cetera, the response would be, "Well, we do not know what to do with it. We do not know to whom to refer to this. We have nothing on the books on which they can speak authoritatively."

So there are all kinds of problems one can imagine there. At the same time I think you could identify individuals that would be very interesting to talk with representing a reasonable array of religious communities that are present in the U.S. But the latter is what you have in mind I take it.

DR. EMANUEL: I would think so.

DR. COLE-TURNER: Yes, I can imagine that kind of research process.

THE PRESIDENT'S REQUEST FOR ADVICE ON CLONING

DR. MURRAY: We have two kinds of time constraints. One is the hearing on Capitol Hearing today and the other is the constraint about how quickly we have to do a report on this and in the longer term what we are doing.

I will tell you what our parameters are. We must leave this room, the commissioners must leave this room at 12:45 in order to meet the taxis which will be leaving no later than 1:00 p.m. in order to get to Capitol Hill. So that is one constraint. We have one public testimony which we need to allow at least five minutes for. If we do that at 12:40 that will be just right. So we have a bit under 40 minutes to accomplish the rest of the agenda.

But stay here, please, Ron, because we may be addressing questions to you.

The other time constraint is getting the report out. We had initially set ourselves the target of having a report within -- at the first anniversary of the first meeting so October of this year. We have been given this urgent job of responding to the President's request for some advice and clarification on human cloning and we have been given 90 days for that.

I would like to ask the people here who are helping the commission how should we think about this?

Does this -- does the cloning request influence our -- the deadline we had set for our human tissue report?

DR. RAUB: I think in the broadest sense it could in that it would be within your discretion to tailor the rest of the time table for the commission as necessary to accommodate the 90 day window with respect to the cloning task. I do not think the request from the President went beyond what it says in terms of the cloning issue and I think the unstated expectation was if it were possible for the commission to sustain everything else it was going to do anyway that would be wonderful.

Some of us would need to do some additional fund raising. But to the extent that it is not practical to do that, that some other relevant activities is practical then it would be the discretion of the commission to carry it out.

DR. MURRAY: One of the reasons we picked the October date for this report is we had at least -- I do not know if we still have -- no guarantee that we would be in existence beyond October of '97. I do not know if there is any enlightenment to be had on that question.

DR. RAUB: Do you want to speak to that?

DR. LEVINSON: Sure. The extension of the termination date which was October 3rd, 1997, is an administrative issue. It is being addressed. It does not seem to be one that is particularly controversial.

But beyond that I cannot say that it is actually being done.

DR. MURRAY: Rachel, your best advice to us without committing anything that you cannot commit to, your best advice to us is that odds are that we would if we wanted to set the date of the tissue report back a couple of months that would be -- that would not be a crazy strategy if we thought that the cloning work was going to occupy us for three months.

DR. EMANUEL: I want to say two things. First, I think the October deadline was real in the sense of we wanted to be sure we actually did something --

DR. MURRAY: Right.

DR. EMANUEL: -- real in the first year. Now we have a guarantee, you know. In less than 90 days we are going to have said something real. So I do not think that the October deadline has that same reality.

On the other hand we have set for our subcommittee here a somewhat ambitious agenda. Not just for this year, assuming we actually persist for a while, we have at least two other issues that we think need to come up. The confidentiality and the gene patenting one. If we put the screening issue -- I mean, the samples issue too far along we are going to be getting -- just overwhelming ourselves towards the end.

Having said that it seems to me before we

decide whether we want to push the October deadline back we should think about -- I mean, one of the problems I am having at the moment, I am speaking personally, is what is the chapter outlines of the report. Because if we had a handle on how extensive the report is going to look like and maybe at the end of this meeting we have actually settled some of the details or the direction we think some of those chapters should go, it might not look so daunting to us. We could begin parsing out some of that work in a more coherent manageable light.

So maybe the deadline issue needs to come back to the -- you know, might we in the next few minutes talk about a consensus about the structure or the dimensions of the report. Anyway that is my suggestion.

DR. MURRAY: Speaking personally I would not be in favor of letting things slide very much. I think that is a bad habit to get into. That is why I have mentioned a couple of months. I mean, if we actually did devote all of our energies over the next three months to the cloning issue I would not want to see the tissue report slide by that much, maybe by 45 days or two months at the most, and maybe not at all. But you are right, we need to think about specifics and what we need to accomplish and when.

Quite frankly, some of the work that would go on in the preparation of the tissue sample report will

probably be done by people we contract with and not us. Although we will have work in helping to specify what we ask them to do, interact with them, help shape the report, et cetera.

My guess is the bulk of our really intense attention is going to happen after we get some of these contractor drafts and that probably would not be happening until about the time we have to deliver our response on cloning. So conceivably if you are feeling really heroic and self punitive we could try to do everything on schedule. That is a possibility.

David?

DR. COX: I am going to say in the context of this morning because although, you know, it is far from a done deal, I can see light at the end of the tunnel of a possible framework. And so I am in favor of walking and chewing gum at the same time here.

(Laughter.)

DR. MURRAY: You can get in trouble that way.

DR. COX: I understand.

DR. MURRAY: Yes. Maybe we can pull it off.

Bernie?

DR. LO: This reminds me an awful lot of what it was like to be an intern when you thought you had everything scheduled and prioritized, and all of a sudden you got a horrendous emergency that is going to take up

all the time you have for a short period of time. I think we need to set priorities. I think as important as this topic is, and I think Steve was very eloquent this morning about how some clarity of this is needed just so the work can continue.

I think it is also true that what the President and the country are looking for is some good thoughts on the issue of cloning and sort of -- as I try to reconstruct our warning to sort of justify or prove our worthiness, in part I think at the end of a year we want to have a tangible product and say, "Look, you know, we actually did something that was useful." So it seems to me that the opportunity is presented for us to do something useful at a time of -- I do not know if crisis is the right word, but a lot of much greater concern than I think necessarily attends to the stored tissue samples.

I am in favor of walking and chewing gum except I think we are asked to run now and I would make sure we do the running first, and if we can do the chewing gum, fine, but that should be the sort of priority. I think we did a lot of good work this morning. If there is some way of sustaining that -- sort of pushing further along with the lines that, you know, Zeke led us through, I think that can be very useful. On the other hand I think that we have not even begun to address, you know, as a group issues relating to cloning.

That is really what our first priorities ought to be.

DR. MURRAY: If I may just -- one thing. I want to do two things, Bernie. One is to say the evidence is already there that we are going to be putting more energy as a commission at least in our group sessions to cloning than -- and less energy to the various -- to the subcommittee projects. That is already the case because Dr. Shapiro has decided to devote roughly, I think, three-quarters of the meeting, full commission meeting which will take place at the end of next week, to talking about cloning.

So on that you are right. But can I pin you down? If you had to pick a number, if we were to reschedule our deliverable date on the human tissue report, what would you set it at? If it was October, I am going to say October 4, what is it now?

DR. LO: Probably January 1, 1998.

DR. MURRAY: Okay. Thanks.

Carol?

DR. GREIDER: What about if we think about if we do the walking and get someone else to chew the gum for us in the same sense of sort of reiterating what you said. A lot of these things that we want to do are papers that we are going to commission and have people doing analysis. If we could at least get past that point and have the things that we want to be worked on being

worked on, if we then do not get to actually deliberate on the results from those commission papers and we have to put that off that would be good. But I think it would be a shame to put off the actual setting in motion all of these things that we want to get information for us.

DR. MURRAY: That is exactly right, Carol. I would not -- I was not for a moment thinking of postponing commissioning papers. I think we should commission those papers and we should commission them as soon as we can. I think we already have some potential candidates that we have identified. There is no reason to delay that. It does take some time to talk with the contractors and to interact with the contractors.

And each of you has accepted already an assignment to work with a particular paper for which I am very grateful. I nailed you by E-mail I think and we would ask you to do that even as you are thinking about cloning. But I do not think that is an unreasonable request or burden to accept. So we can start that. It is just that what we will not have is the time to devote to deliberation prior to May, the end of May, when we would presumably finish the cloning report.

Bernie?

DR. LO: Yes. I am great for trying to delegate things to other people and I always try to get my fourth year medical students to do all my intern work.

But it seems to me that what I am taking with the meeting up to now is a lot of excitement and enthusiasm about the 7:00 o'clock presentation and it is discouraging about the 9:00 o'clock and 11:00 o'clock presentations.

I think where we are going to make progress is trying to push ahead along the lines that Zeke led us through and we were discussing. From the 9:00 o'clock discussion and from Dr. Wertz and Dr. Denk I sort of came away thinking this is (a) very tough to do given the constraints; and (b), you know, if we really want to focus on the tissue sample issue as opposed to the genetics in general it is going to be a hard fit.

And then what, you know, Dr. Cole-Turner actually pointed out that this was important but that it is very complex. Things are changing. It is going to again be very hard. We are not going to get a definitive -- I mean if we were looking for a definitive sort of explication of what different religious traditions think about unconsented to anonymous testing which has been approved by an IRB, it is not going to be in the cards.

So it seems to me what we -- I think we can commission the papers and we should do that. But my own take is that the real progress is going to be the kind of, you know, sort of clone Zeke and let him work with this.

DR. EMANUEL: You do not want any more than

one. There are many people who would prefer their own.

DR. LO: But the discussion we were having, I think, is getting close to at least some preliminary ideas on approach, and classification, and a way of thinking about an approach. I think we are a lot further along now than I would have thought, you know, at 6:00 o'clock this morning. But that momentum is going to be hard to sustain because it is not something we can delegate all, it is something we need to do and I think we should try and do it but the constraint is there.

DR. MURRAY: Bill?

DR. RAUB: I have a question for Dr. Cole-Turner that relates to the interaction of the last two topics. You were very clear and I think persuasive in a sense of instilling belief that one could lay out a description of the complexity around these issues.

If one thinks back to the earlier discussion about how to understand public opinion, to what extent would people who view themselves as practicing members of a particular faith necessarily be able to articulate or in some sense recognize how the teachings of a particular tradition get articulated in this forum and does it, therefore, complicate the two things?

DR. COLE-TURNER: Very much. That is a problem that I think is -- it is a problem for the faith communities themselves. It is not a problem for public

policy formation but it is a problem for the faith communities themselves. I would like to think that that is improving. We are in a period in history in which the faith communities are challenging themselves to be able to articulate better for their own membership the public policy implications, the world view implications, the attitudes towards the state and towards politics and towards regulation. I think I see that happening but it is a long way to go.

But back to Bernie's comment for just a second. I think you may be right that there might be easily -- well, not easily, but readily achievable success at one level in clarifying a proposal.

I guess the concern that you would want to weigh against that is have you gone out and created a clarity and coherence among experts that without taking the pulse of the rumblings deep beneath -- you know, below the surface, deep within the Earth that may suddenly change things. And that is the volatility factor that I was pointing to earlier and I cannot make any predictions. I mean nobody is good at predicting earthquakes. I think we have learned enough to know that earthquakes do happen.

DR. MURRAY: Zeke?

DR. EMANUEL: Let me try a proposal. We have a week before we have to turn our full attention to

cloning and we also have to render a report actually at that meeting in the morning. Between now and then I do not think it is impossible to suggest the following:

A sort of outline of the chapters of the report and a highlight of three or four of the major areas where we need to get further clarity. I think maybe even before we need to commission papers. Or maybe if we have outlined them enough we can begin commissioning. Here would be my suggestion: You are looking strained.

DR. MURRAY: No, I am just listening.

(Laughter.)

DR. MURRAY: Distressed.

(Laughter.)

DR. EMANUEL: All right. If we follow this morning's conclusion then it would seem to me a sort of framework or structure is -- we need to be clear about that. We need to sort of outline the kinds of research we want to articulate and why we want to make that division. We need to talk about the value and be sure that we have that in a coherent way. That is the second one.

Third, we need some optimal confidentiality background suggested policy that we would -- and then we need to confirm or settle on some mechanism for public input, religious input, et cetera. Those seem to me four

manageable areas. Some of them I think might be things we could actually ask people to do and come back with a reasonable suggestion to us while we are working on the cloning issue.

Some of them require I think a little more work by us to powwow about before we can even commission a paper, and here would be my cut at that: We maybe could ask Dorothy or Chuck, or someone to tell us within the constraints that we have how we are going to sample people in a reasonable way that is not going to discredit us but is going to get us some useful information within the constraints of time, money, the Federal Government, et cetera.

And I -- you know, Chuck has made informally some suggestions. I believe he mentioned Dr. Henrietta. I am sure Dorothy has similar or, if not, complimentary ideas. That seems to me to go on, you know, while we are talking about cloning we could have a proposal and render -- begin with real terming.

Similarly something about the confidentiality policy might be able to be something we could ask someone to do, focus in on this issue, what are the background, you know, policies that IRBs should adopt on this?

I think the other problems of -- particularly in different types of research we still need to think through as a committee before we can go forward and -- so

my proposal is there are things that will not distract us by cloning. I do agree with Bernie the number one thing is we will have a product, we will justify our existence, and we can put this if not quite on the back burner, at least some of the things can be cooking in this period and we can have an outline for the report that we would be comfortable with on, you know, next week and, you know, in some ways put it aside but have it there so that we could go.

DR. MURRAY: Bernie?

DR. LO: I think it is very useful and if I could sort of comment on that and try and extend it. First, I think one issue that we talked about before our last break and I think we need to address for the religious perspective is how are we going to get meaningful feedback from either the public or segments of the public, or religious leaders or religious communities as we begin to develop this approach and propose sort of a framework and guidelines.

And one of the things that we might want to do to sort of take Zeke's idea a little further is to actually ask four or five different people from the public opinion perspective or public response perspective and the religious perspective to just give us some ideas on how we might elicit that kind of feedback on I guess particularly the narrow topic with the time constraints

that we have got. But also I think we want this more generally as well.

I am not sure I have a clarity of what the different options are. We have them all on the table. How feasible are some of the things that we talked about? But I think we can say this is what we would like to accomplish. Can you find experts that we can commission sort of a mini-paper or mini-proposal as to how we might do that?

With regard to Zeke's question about confidentiality, I think that is very important because, you know, it is sort of kind of the hidden dimension of your matrix when, you know, the IRB has approved a sort of confidentiality sort of approach. What should that look like? I am wondering if we need to talk about that some as a group because we have not really discussed it among ourselves before we go out and have other people -- I mean I think there is a lot of expertise out there but I would like to sort of get our thoughts on that.

So I think there are some things that we can try and get others to help us with but then I think there are some things that we need to as a group try and deal with. I actually thought that the discussion the first thing this morning was very positive in that, you know, I thought we got a fair amount done and if we can somehow sustain that as we also do the cloning, my sense is that

is where a lot of the progress is going to be.

DR. MURRAY: I want to try to put together what we -- sort of the plan we have gone into this meeting with. That is we had planned to commission a certain set of kinds of papers and/or projects and I just want to go over them again because in my initial thinking about this report in a way to shape the report, we -- I want you to tell me if we should drop any of these, if these overlay the things that have come up just now, if they should replace or modify the ethical components.

The first is a descriptive paper. What are these tissue samples? What are they used for? How are they stored? Where do they come from? What is the scientific -- what are the kinds of science that one can do with them? I still think that is important and probably ought to be the beginning of the report. Is that still a consensus? Okay.

A second component was the discussion of the normative or ethical issues. And that is what Zeke led us I think through very well this morning. Now is that still sort of one chapter of the report or do we want to split that? When you talk about the privacy and confidentiality piece are you talking about that in normative terms or more how IRBs should be handled?

DR. EMANUEL: The latter. That is my view.

DR. MURRAY: Okay. So that -- so is the

second piece still the second piece?

DR. LO: I think this is huge. This is the meat of the report. I thought that Zeke also put out, which I think is very useful, is sort of the cases that really push us to think through what we are doing. It seems to me that may or may not be separated from sort of the description of the normative -- the norms and sort of how you might weigh them. I mean the cases are going to be very important to work through and I think that we are just starting to get to them.

And then the third part is actually the framework of a model that was started to be proposed. Each of those I almost see as a little chapter on its own.

DR. MURRAY: Yes. Now I am being dense. Let's go through it. Chapter one is -- it is sort of description. Chapter is now what?

DR. LO: Normative values, you know, at stake. Chapter three is cases that really challenge us to think through how we are going to reconcile these sometimes conflicting values. And four is our proposed framework. Now it may be a much lower number but --

DR. MURRAY Proposed framework would be policy framework?

DR. LO: I would put it in the policy framework.

DR. MURRAY: Normative.

DR. EMANUEL: I actually think -- I think the framework has to be both policy and normative. You are using the framework. And I would suggest actually moving it up because it is going to determine some of your comments about values and things like that. But --

DR. HOLTZMAN: Well, if we are talking framework what we were evolving to this morning on matrix.

DR. EMANUEL: Right.

DR. HOLTZMAN: In one sense isn't the way you get there by starting with the old framework and showing that it is not dealing with the cases well. There is a counter intuitive sense in this very notion that we have got anomalies. Okay. And that leads us to a new framework.

DR. EMANUEL: Well, that may be how we get there. I am not sure in the report we need to say that. I mean it is a --

DR. HOLTZMAN: I think that was not --

DR. EMANUEL: Right.

DR. HOLTZMAN: -- but that would be -- I think it is important in terms of the descriptive part is that we do have a number of organizations who have come out with positions.

DR. EMANUEL: Yes, definitely.

DR. HOLTZMAN: And articulating and describing them and working the cases and seeing what may not work.

DR. MURRAY: Okay. David?

DR. COX: I mean the second part of the second chapter is sort of what we did this morning, you know, in an hour. That is what it is. It was complicated. It was talking about what these other positions have been. It was a discussion of -- it was a normative analysis. It was an example of some cases and it led to a framework for further discussion.

Now that framework played out in many different ways. But the second chapter I would see as exactly what we did this morning and that does not mean it is finished, right, or even that it does not get expanded in that context. But then you go from there. Exactly where we go from there, I mean we have not talked about.

There is a variety of points we can touch. I mean, one of them -- this is what I hear you saying, Zeke, is the issue about, you know, the protection of confidentiality. So that is one wing that comes out of that. But I see that coming out of the second thing and not part of it. But I would not like to see the second one be too narrow, you know, just normative and then case studies. I mean that is -- what we did this morning I

think was extremely useful to put as a package.

DR. EMANUEL: I think all I heard is that they were taking that package and dividing it into sort of a digestible chunk but not chapters.

DR. COX: Yes. Well, but I am not sure that you want to digest it up too much because what may be useful was the fact that all those things were slammed together to me at least.

DR. MURRAY: We have been speaking of other pieces that we felt might ultimately become part of the report. In fact, four other pieces. A quick study of international comparisons. What are other countries thinking and doing about this? Do we still want to go ahead with that? I do. Is there a sentiment that that is still something that we ought to do?

PROF. BACKLAR: Yes. We could get somebody to do that for us.

DR. MURRAY: Yes. Well, that is a contractor.

Then we have the two things that comprised the second two sessions today. We had some effort to find out what all this means and matters to the American public more broadly. And in particular if certain faith traditions in the U.S. found this to be particularly vitally important and had views about it. Those are two pieces.

The last piece that as I sit here with my notes in front of me about this, the last piece I remember was we were going to commission a paper on policy options which may -- which probably would not be in the report as such but it was more an effort to feed back to us, well, here are the major sort of choices that you face as a commission. Can you -- is there one that seems obviously right to you that you wish to pick and defend, and propose?

DR. COX: I just had a thought, Tom, when you were saying -- it is that maybe what happened this morning in this normative analysis discussion should go first because all these other things -- what you kept saying, I think, over and over which always rang true to me is that we had these other things. There are so many different ways you can slice and dice them. Let's look at them in the context of the format we have already laid out.

So that is certainly true, Tom, in the context of what kind of tissue samples are out there. That is what I have been thinking about a lot and it makes it much easier instead of just going and making a collection of them, okay, grouping them according to this framework that we have talked about. That is true for public opinion and it is true for religious, and all these different aspects. So I mean we can make that --

we were not thinking about that framework of being our first one but then all the other ones are how they relate to that.

DR. MURRAY: Are these the pieces that we want to see taken care of? Now let me see if I understand. We can -- what we can sort of ask others to do at least the groundwork for us if not the draft, the descriptive piece we can farm out. A piece on the normative issues and the key values that Zeke has begun this morning, we had talked about asking a contractor to do that and we may want to revisit that possibly. And cases that would challenge us.

DR. EMANUEL: I think that could go into the descriptive piece, frankly.

DR. MURRAY: The descriptive piece.

DR. EMANUEL: That is part of it because really what -- you know, what is the culmination of the descriptive piece, but we have got these hard cases, here they are, five or six of them, seven or eight of them, whatever the number is.

DR. MURRAY: Who will provide those cases?

DR. EMANUEL: Well, I think Steve has provided some, researchers may be able to help us, people at the Genome Project may be able to help us.

DR. MURRAY: So we should solicit.

DR. COX: When we describe what these sources

of samples are I can guarantee you there is going to be a case that can go in each one.

DR. MURRAY: Okay. That is fine.

DR. EMANUEL: It would be helpful, however, to have those cases link up somehow with our framework so that they are illustrative in some way.

DR. MURRAY: We have some development of "what we call our framework." I think that is the job we need to do.

DR. COX: Right.

DR. EMANUEL: Exactly.

DR. MURRAY: That is not something we can farm out.

DR. COX: We cannot farm that out.

DR. MURRAY: We still have to deal with this problem of public views and we have got, you know, some encouragement and some discouragement this morning. Trish has --

PROF. BACKLAR: Talking with David, yes. Do you want to discuss that quickly?

DR. MURRAY: Well, we have got not much time to but it would basically be an idea where each of us might in our own local settings try to get some information. I also at the break was told by some people at the Genome Institute that there are families, if I remember correctly about 100 families with severe

combined immune deficiency in the families, is that right, who are gathering here in April voluntarily and, you know, one or more of us could come and talk to -- just talk with those families and get a sense of how they -- what they are thinking about in terms of genetic tissue, tissue samples and research of those samples, et cetera.

So it is possible to get at least some ideas about what people might be thinking about. It does not seem possible to get certainly a full opinion survey done. We have been I think steered away from focus groups if I understood you correctly. Although Steve had this intriguing suggestion about maybe even a real research study of sort of exit interview study on hospital patients and we have to think about that.

DR. HOLTZMAN: The ones that exit.

DR. MURRAY: The ones that exit.

(Laughter.)

DR. MURRAY: Right. Not final -- not making a final exit, just exiting.

So we have more conversation to have about that and we do a piece of that perhaps. We need to talk about it. Some of it we might ask someone else to do.

DR. EMANUEL: We might ask Chuck or Dorothy I think to give us a brief five-page recommendation about -- I mean, some of the things that they were saying is

there is some literature out there about some of this, that they could draw in already that we may not be aware of.

There may be -- of the various different ways we proposed some -- again now they are fully aware of all our constraints and our ideas, that they can propose to us to do it and I think we could contract with them to deliver that quickly because we do not want a big long effort. We just want suggestions that will be useful for us and will give us useful information. It seems to me that is a way to go.

DR. MURRAY: Okay. I am going to mention the international perspectives next because that is relatively easily encapsulated. We will ask a contractor to do that for us. Which leaves us with the religious views and the policy options. The religious -- I mean, Ron has not made our life any simpler but he has been I think very honest and very helpful to us.

I would think it a great loss were we not able to get some -- a decent representation of how religious views that are significant in American culture might influence or ought to influence our report and I would look to Jim for help if you have any suggestions as to where we really might go here. You do not have to answer on the spot.

DR. CHILDRESS: I think you have to resolve

that tension between the general and the specific recognizing as the discussion emphasized that there may not always be a connection between those, that is the general kinds of perspectives. The particular views through the public survey focused on the religious groups, those would require more in-depth work and it may not have meant as much to the judgments religious people make in this particular area.

DR. MURRAY: I am a little sorry to say that I have a pretty clear instinct on where to go with this and I am -- it does not make me completely happy with my instinct. My instinct is to try to ask for -- rather than the deep exploration of these really fundamental issues, is to ask a relevant question but may not have the intellectual or theological depth. And the relevant question being how do these traditions -- you know, what will they say about the use of human tissues, the storage of human tissue and the use of it in research, and I think you have given us, Ron, a rich picture of how the apparently superficial questions like that really connect to deep issues.

I would love to do that if we could. I do not think we will have the ability to have all that. Do you think there would be any usefulness in public dialogue to ask for sort of questions -- to ask whether than going into the full depth to say how do you feel

about that.

Bernie has a --

DR. LO: Yes. I think that to use your analogy -- to use Ron's analogy it is sort of looking for earthquakes. I mean I would rather know earlier rather than later that some religious communities --

DR. MURRAY: Big faults.

DR. LO: -- were totally going in their own direction and we would miss the major issue and our proposed outline is worst than the present state by an order of magnitude. I would like to sort of find that out earlier than later.

DR. MURRAY: We have three minutes by the way. So go ahead.

DR. HOLTZMAN: Would it be feasible without getting into what the various groups think and why about each of these to ask a question of a form of what do you think are the relevant considerations? Would that be useful?

DR. COLE-TURNER: Well, again if you simply put that out through the mail you will get zip as an answer and it would be a waste of time. What I guess I would suggest is -- there is just nobody there to answer that question.

DR. HOLTZMAN: Okay.

DR. COLE-TURNER: What I would suggest is

that the commission work very carefully through religious communities to identify six, eight, ten, twelve people, and convene them, give them the requisite scientific, technical, ethical briefings and give them an unpacking of some of the religious motifs that may be suggested by this, and then you can give the largest block of time to their response, and then perhaps develop that into some sort of a background paper but give each of those persons a chance to respond to the paper and maybe issue a minority report.

DR. MURRAY: I think that is a splendid idea. How does the rest of the commission feel about this? That is terrific. Thank you, Ron.

And the last piece is the policy options paper. Do we want to have such a paper? This I take it is somewhat different from our sort of framework analysis. It says, "Look, given this is what we have desired we think it would be good, what are the -- you know, in terms of federal policy, what actually can we do and ought we do to approach what we see as the good?" It still makes sense to me to ask such.

DR. GREIDER: Doesn't it have to come after our framework has been worked out though?

DR. MURRAY: Yes. I think it can be developed along the way and it probably would not be a bad idea to have someone who will ultimately do that for

us being present early on in our conversation so that they understand really what our concerns are given our imperfections at articulating them at times. But, yes, I think in the end it will have to await these other steps.

I believe we have -- if not -- come to the conclusions on the substance of everything and we have identified a process for everything, and we have identified a full set. I am impressed. Good work. Good work. And we still have -- we are on time for our -- for Dr. Mark Sobel of the National Cancer Institute.

Mark, thank you for your patience. We have five minutes.

COMMENTS BY THE PUBLIC

DR. SOBEL: Thank you. I know it is a very hectic time for you so I will be extremely short.

I wanted to say for the public record that unfortunately the College of American Pathologists position that has been outlined and that was presented in the overhead that I saw from back here is completely wrong and inaccurate and I hope that that is not distributed to anybody because we would like to send a clarification immediately. It has been completely misread.

In specific, we as well as every other group that I know of in no way would recommend anything other than informed consent for identified samples. I think

part of the confusion is the lumping again of linkable and identified which I think confuses the issue considerably.

The position that many researchers in 17 societies have now signed on to that position has in part been outlined by Dr. Korn to you previously. But it is really based on a realization as you have come to a conclusion this morning that artificial distinctions between genetic and nongenetic tests will not quite do in this scenario and that there are many protections that must be provided to all human subjects no matter what the kind of test. And what we need to do is to have some practical solutions to some of these problems given the current regulations and scenarios.

One of those is to define what is a medically useful test such as one that would wind up in the medical record and what would be a research test. Those are very difficult lines to cross. But we do have some ways around that. For example, there are federal clear regulations that state what is a clinically regulated laboratory and it is only those tests that are medically useful, and those are -- we could make some distinctions starting with some of those scenarios.

I also would like to stress that we think that the big loopholes that we find researchers and the public, and from what I can tell from this morning this

pane does not understand is what are the practical ways that you can really secure and keep information confidential.

And, in fact, the College of American Pathologists and other groups are right now setting up model confidentiality proposals that, for example, would include not just the principal investigator but to increase sensitivity and education, would include anybody that would ever handle tissue, technicians, students, post-doctoral fellows, occasional visitors to the laboratory. That would increase the educational level of everybody involved in the use of human tissue.

So I think if we begin to explore those sorts of solutions to the problem it might not be as complicated as it can sometimes be. So we would like to send a clarification of some of the positions and stress the correct definitions of some of the designations to help you with your matrix form.

DR. MURRAY: Bernie?

DR. LO: Yes. I would also encourage you to send us what you are working on in terms of confidentiality.

DR. SOBEL: Yes. That is really in not even a written draft stage yet but we realize the importance of that and we are stressing it in our agenda.

DR. MURRAY: David?

DR. EMANUEL: I mean, the number nine suggestion here is where identity can be determined, research using specimens should be permitted under general consent procedures for IRB approved confidentiality and security --

DR. SOBEL: Yes, but that is in the context of what goes before that which stresses that that is not for identified samples.

(Simultaneous discussion.)

DR. SOBEL: Identifiable. That means identifiable. That is why we are going to send a clarification in case there has been any misinterpretation of what has been written. And it is also within the context of that, that is for retrospectively obtained tissue that is human residual material that is in the context of the entire document. So we will clarify that because we see that that could have been misleading.

DR. MURRAY: David?

DR. COX: Dr. Sobel, something that I would find particularly useful is the distinction between -- in the case of identifiable sample with a very broad base consent versus a more specific consent because certainly that is an issue that I think is going to be a point of extensive consideration with respect to your group's position.

DR. SOBEL: I think that is a very difficult issue to delineate and it was alluded to this morning. What is the education of the public in terms of what exactly is specific informed consent and how understandable is it and how can it be obtained.

DR. COX: There is a second area that I asked Dr. Korn about and I will not ask it but I would just like to state it again. This very sharp dividing line between what is research and what is medical practice is a foundation basis for the position of this statement. I question how clear that dividing line really is in the present stage. So I just make that as a statement.

DR. SOBEL: I think we are all aware of that and that is why we need to find specific solutions and regulations that will define when these broad sweeping recommendations apply.

DR. MURRAY: Mark, thank you. I genuinely look forward to your clarifications.

DISCUSSION ON FUTURE ISSUES AND MEETINGS

DR. MURRAY: We have a minute. Bette Kramer has gently reminded me that we were supposed to talk about future meetings as well as future issues. I hope you will accept my apologies. We are going to see each other again at the end of next week and I think we may just -- if it is all right with you we will talk about future subcommittee meetings in the context of our

subcommittee report next week.

For the commissioners taxis will be waiting downstairs at the entrance to the stairway which is I presume where you entered. I will see you all at Capitol Hill.

(Whereupon, the proceedings were adjourned at 12:45 p.m.)

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