NATIONAL BIOETHICS ADVISORY COMMISSION

Thursday, January 9, 1997
8:13 a.m.

The Madison Hotel
Washington, D.C.

EBERLIN REPORTING SERVICE
14208 Piccadilly Road
Silver Spring, Maryland 20906

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I N D E X

P R O C E E D I N G S

CALL TO ORDER AND OPENING REMARKS

DR. SHAPIRO: I would like to call our meeting to order. Is this microphone working? Thank you very much.

We still have a number of members of the commission who are expected today that are not here yet. We all can tell by a brief look outside the weather is not exactly propitious but we expect that they will be joining us very shortly.

First of all, let me welcome the commissioners back to what is our third meeting and to once again express my own debt of gratitude to all the NBAC commissioners who are giving their time to the work of the commission.

I think -- let me introduce myself also for those members of the audience who may be attending their first meeting here. I am Harold Shapiro, Chairman of NBAC.

Now this is, as I said a moment ago, NBAC's third meeting. Our first and so sweet inaugural meeting was in October. I think it was October 4th. It was held here in Washington. We had a second meeting in San Francisco. I believe the date there was November 21st. That was a very special meeting in a number of respects. Most importantly because the meeting we put together was an international summit in which NBAC welcomed to the meeting members of various similar commissions from around the world so that we could learn from their experience and ideas that they had on similar subjects which we were addressing, similar to which we were hoping to address.

At least from my perspective that was a very successful meeting held one day in advance of the --

PROF. CAPRON: Third World.

DR. SHAPIRO: -- Third World Conference on Bioethics which was held in San Francisco this year and I want to thank not only the staff but Alex for his work in mobilizing that meeting. It was at least in my judgment successful even beyond what I had anticipated.

Of course the two subcommittees of NBAC, both the Human Subject Protection Committee and what I am thinking of as Genetic Information Committee, the first, the former headed by James Childress and the latter by Tom Murray, met in December.

I believe, Jim, your committee met on the 13th.

DR. CHILDRESS: 16th.

DR. SHAPIRO: 16th. And Tom's met on the 13th. That was on the 13th of December. Of course, a good deal of today's agenda will focus on reports from those committees. Indeed when those committees report I will ask the chair of the committee to come up and join us -- join me here perhaps just to my left to just help in the discussion when we get to those committees.

I want to take just a moment here to express my gratitude to the support staff who have really worked extremely hard. This committee has just gotten under way. If you include the subcommittee meetings which include together really all the members of NBAC, that is five meetings put together in a very short period of time and I particularly want to thank Margaret Quinlan, of course Randy Hall and Mary Ann Rapp (?) for the work that they have done to enable us to

meet quite so effectively during this very short period of time. I also extend my thanks, of course, to Bill sitting to my right here for his work in mobilizing that staff.

Now as I have already said, the bulk of our agenda today really focuses on reports and future plans for our two subcommittees, the Protection of Human Subjects and the Management of Genetic Information. Those were the two subjects which we were asked under the Executive Order establishing the commission to address as our first priority. So we have responded to that and indeed have proceeded along those lines.

Let me say a word about what I hope the outcome of today's and tomorrow's meetings will be, at least some of the things that I hope will be an outcome of these meetings. We need for certain to be able to identify quite specifically our plan of work over the next months so that we can provide to each of the subcommittees a staff that is necessary to achieve their objectives.

I think we really cannot allow ourselves to leave Washington this time without having really a pretty good idea of what the priority tasks are for each of the subcommittees so that we can very shortly just mobilize the staff resources and other resources necessary to enable the committees to achieve their work. That is in my view the most important outcome I am hoping for from this meeting.

We will also, of course, be discussing future agenda items beyond those of the two subcommittees. That will come principally tomorrow where we will have further discussion about further activities of the committee and in particular how we want to organize our March

meeting, what we expect to be done by that time and other aspects of the meeting which we will have in March.

Now the March meeting is scheduled here in Washington. I will probably at least discuss the possibility of meeting in the summer, which is our July meeting, somewhere other than Washington. I think it is important for the committee to meet elsewhere around the country.

We have a number of possibilities and we will be discussing them tomorrow as to where we might meet. There has already been some discussion amongst us informally and we have received some invitations and indications of other invitations would be forthcoming if we indicate an interest in meeting elsewhere. We ought to discuss that before we leave also.

I will also report later on today or tomorrow on two issues which are obviously important to everyone who is giving their time to this commission, namely what our budget situation looks like and whether -- what the time horizon of this committee is. I can -- we will report on that either later today or tomorrow.

So that is our objective for these meetings. Obviously other things will come up as we discuss things together.

Are there any questions on these issues or prospects for today's meeting?

Okay. In that case let's just proceed and go to the first item on our agenda which is to hear from Jim and his committee.

Jim, do you want to just join me up here?

I will really let Jim run this part of the meeting just as he sees fit.

DISCUSSION OF THE ACTIVITIES OF THE NBAC HUMAN SUBJECTS SUBCOMMITTEE

DR. CHILDRESS: Thanks, Harold.

The Human Subjects Subcommittee, sometimes I will refer to it as HSSC as it is appearing in our e-mail exchanges, had a very productive meeting on December the 16th. At least members of NBAC probably already have a fairly good idea about the direction of that particular meeting from reviewing the transcript. But I think the transcript itself fails to convey fully the progress of the Human Subjects Subcommittee made as a deliberative body, a deliberative community.

We went through a very valuable process. A process that helped our subcommittee form its identity and its mode of operation, and helped us as individuals to get to know and to appreciate each other's prospectives and approaches.

We regret that two members of the subcommittee could not attend the meeting because of prior irrevocable commitments but we brought them up-to-date through e-mail exchanges and through discussion last night, and through their review of the transcript. We look forward to their participation in the discussion today and also in subsequent meetings.

I think the meeting on the 16th generated some useful, some interesting and perhaps even important ideas for directions for our work, and ways to get there, and we will come back to some of those later this morning.

A few other -- one other preliminary point before turning to the first task, our mandated task. We are continuing to formulate our

strategy as a subcommittee for the next year in view of the chair's request for a draft report and for NBAC to issue a report by the early fall of 1997. At this point we have to formulate two versions or two tracks of the strategy depending on our level of funding and our life expectancy.

One strategy assumes adequate funding and long life expectancy. The other modest funding with at best a low quality of life and early termination of life support.

(Laughter.)

And more about these strategies later.

We do have for NBAC as a whole and then for the Human Subjects Subcommittee one mandated task. A task our volunteer staff has already started. That task is a study of the adherence of federal agencies and departments to the Common Rule. We would like to spend a few minutes at the outset this morning on this task as Chairman Shapiro requested before turning to the other task we discussed at our December the 16th meeting and move into the general conceptual, normative, and empirical kinds of questions we have to address as a group.

But rather than -- we heard a preliminary report on this study of this mandated task at our subcommittee meeting and obviously with the holiday season not too much has happened since then. But rather than summarizing this report I will turn to Bill Dommel, who is directing this for the staff with Joel Mangel and Emily Feinstein working on that, and we will get a brief report of just where those matters stand.

DR. DOMMEL: Thank you, Jim.

Indeed, as Jim mentioned, this effort is being carried out

primarily by volunteer staff, Joel Mangel, retired Deputy General Counsel of the Public Health Service as a volunteer, and Emily Feinstein as a volunteer. We are bringing on some paid staff this month to work with them in their effort as they move outside of the written reports.

Joel, you can just bring us up-to-date on what you have done so far and what you have been doing with the site visiting of the agency.

DR. MANGEL: Sure. Can I be heard?

I gave a fuller report earlier so what I would propose doing now is kind of getting a summarization and then be available for questions.

As required by the Executive Order the federal agencies have now submitted their reports. We have reviewed them and I would characterize them in general as uneven, some of the agencies, as you might have guessed. Some of the agencies' reports are quite fulsome and some of them are merely assertions of compliance with all applicable rules.

But in any event even where they are fulsome there are a number of questions which come to mind and it is my belief that what is going to be necessary is meetings with the agencies, perhaps a series of meetings to follow up on some questions which quite naturally arose out of the reports.

Some of the questions that occurred just to give you some sense of what we encountered, it was not always clear whether -- and just how assiduously agencies were getting assurances from those regulated and supported activities, and I think that that is a question

that would need to be pursued.

There was a lot of question in my mind just how the agencies were determining whether or not human subject research was going on in the agencies and in some cases it seemed like there might not be complete communication within an agency and in some cases agencies would assert that they were not doing any human research, but if one read the Washington Post one would see announcements of grants which would lead someone to believe that perhaps there was not complete coordination within the agency. One of the advantages of living in Washington and reading the Washington Post.

Another thing that was troubling and I hasten to add that at no point am I asserting that there is any evidence of noncompliance. What I am doing is pointing out that some questions come to mind as one read the report. The uses of some of the exceptions to the Common Rule were sometimes -- sometimes gave rise to questions, particularly the survey research and research like that which do provide some rather significant exceptions to the applicability of the general rule. It seemed to me in some cases were not understood or maybe thought to be broader than they really were. Then monitoring. It is not clear the extent to which monitoring is going on and just how assiduously that is being done.

So those are kinds of examples of the questions that have been raised.

Now we have not made a good deal of progress since our last meeting because we are still attempting to find someone to head up this individual project who would be the lead person. We are hopeful

that we have located someone but I have been hopeful twice before and each time it has not come to eventuation. So that is essentially where we are now and I would be glad to entertain any questions.

DR. CHILDRESS: Thank you, Joel. Are there any questions or comments at this point from the subcommittee or NBAC members?

DR. MANGEL: Jim, let me make one more point. I think I -- in looking at the Executive Order and trying to figure out just what our task was, it did seem to me that there were two parts to what this task should be. I think it might be important. It is not simply to assess whether there is compliance, but I think what you have got are a number of agencies that have now had a five-year track record and could be helpful in providing advice to us as to what they thought the weaknesses were, the problems, and how those problems could be solved. So it does seem to me there is a twofold goal here.

DR. CHILDRESS: I think that is right. One might also add that in addition to finding out where the agencies are in their compliance or adherence the order also asked us to consider their plans for enhancement in subjects protection so there is also a future forward looking aspect to this.

Alex?

PROF. CAPRON: Well, Joel, you have just responded to the two questions I was going to ask, which was how they have identified the measures that they propose to implement to enhance protections.

What I was wondering was at this point as preliminary as it is whether you have any kind of a, as it were, a grid or a matrix that

you are going to be using in following up. You have mentioned a number of kinds of questions. Some of these I would suppose from a few of the agencies or departments are probably addressed explicitly in their own reports. I would certainly expect that the HHS related agencies, which are very familiar with this task and carry it out, have given you quite complete reports and probably talk about what monitoring they, themselves, are doing, what problems they have found, how they have addressed those problems, perhaps HUD or some of the others that may not think that they are doing much until you read about their programs in the Washington Post may have been less so.

But have you developed anything that you would be in a position to share with us on the commission as to the different categories that you are looking at and the extent to which the staff going out will be directing questions in particular directions to these agencies? Is that organized in some fashion yet?

DR. MANGEL: Well, I -- the -- I guess the most complete answer is no. We have been waiting to get someone to come in and head it up, and I have not been anxious to make too many decisions before that person comes in, in deference to what -- the way they may want to proceed.

I have in my own mind some suggestions that I would make to whoever comes in and heads this task up. Of course, I did try to run through the things that struck me as being questions that should be asked. But those were things that kind of jumped out at me from having just worked in the area.

I think it sounded to me like you must have read some of

these reports because your identification of the agencies was right on. But my question --

PROF. CAPRON: Just a lucky guess.

DR. MANGEL: Well, maybe not too lucky.

But my proposal would be -- there are going to be a lot of resources that are available to us. My proposal would be to set up a series of meetings and the critical thing being making sure we are speaking to the right people in each agency and not people who are necessarily identified as running programs, but the people actually involved in the programs. And then sitting down with each report and going over it and preparing a list of questions that is going to be geared to each of the agencies because it is going to be very different and the reports really are very disparate. So it is going to be very different. But beyond that I have got nothing --

DR. DOMMEL: Alex, one -- just to expand just a little bit that Chairman Shapiro and I looked at sort of an expansion of a grid very early on in the commission's life, an expansion of what is like a grid coming from the radiation group's report and with a focus on resources and kinds of resources, full-time equivalents versus people who do that as a part of a lot of other activities, and we think that is an important area of focus. But again we will turn that over to whoever is the eventual --

DR. CHILDRESS: I might also add that some subcommittee members would be interested in actually getting copies of the reports if staff could make those available so that at least the subcommittee and maybe some other members in the audience too

would like to have copies of the reports fairly early so that we can participate more effectively in the process.

Alta?

PROF. CHARO: That was exactly what I was going to ask for.

DR. CHILDRESS: Okay. Other questions or comments?

DR. SHAPIRO: I would just like to make a comment. I have read all the reports and I support what has been said so far in characterizing them. We did have to -- I think it is also fair to say that we had to prod some people into generating a report whereas others were obviously prepared to do something like this all along. So there is a lot to learn and you should recall, as I guess some people have, that the Executive Order itself refers back to the -- well, there was an Advisory Committee on Human Radiation experiments. I have the name right? And asks us specifically in this context to take their recommendations into account and they say some very specific things that are well focused. Some of this evaluation regarding various -- so I think here at least from my perspective we have a pretty good idea of what to do next. Undoubtedly we will learn as we go along and I am very pleased with the work being done so far preliminary as it is.

But I think the idea that we would expect to come out of this not simply an evaluation of just what it is that each or a criticism or evaluation of what it is that each of these agencies are doing, but I hope, Jim, some recommendations regarding what is needed. I am sure we will discuss more of that as we get to the other subjects we are reviewing today.

PROF. CAPRON: Just one other question about the operation of the Common Rule itself. It is a two part question. Is there now a mechanism which actually does meet and coordinate on a federal level on a periodic basis and, if so, what is the period of the agencies using the Common Rule and is there any way in which -- I do not recall under the Common Rule -- is there any way in which deviations from the rule -- conscious deviations from the rule are recorded and reported to anyone on an ongoing basis if an agency decides that it just cannot live with something and wants an ad hoc exception for a particular project?

DR. MANGEL: There is an interagency advisory group that is chaired by the Office of Protection from Research Risk that meets periodically and exchanges information.

PROF. CAPRON: Do you know what that period is?

DR. MANGEL: Gary?

DR. _____: Every six or eight weeks.

DR. MANGEL: Every six or eight weeks I am told. The Common Rule itself contains mechanisms for granting exceptions. Now whether or not there is a place where that is all reported I do not know. I would assume that the interagency committee is aware of those but I cannot tell you. Agency heads through a process of publishing in the Federal Register may declare exemptions for certain activities and then of course there are the exceptions within the rule itself.

PROF. CAPRON: Yes. Within the rule, yes.

DR. MANGEL: Yes.

DR. DOMMEL: Dr. Ellis, would you like to come to the microphone and comment? Dr. Ellis, Director of OPRR, who chairs the --

DR. ELLIS: In this capacity the chair of the Subcommittee on Human Subjects Research of the Committee on Health, Safety and Food of the National Science and Technology Council, which is the coordinating committee that Alex inquired about. We met in December. We meet again on February 20th, every six or eight weeks, as months go by.

I just want to correct a misimpression in the second answer. Remember that the Common Rule is actually six to fifteen separate parallel and identical rules. So the rule says to each department there must be an assurance satisfactory to the secretary or agency head and there is no authority anywhere for me as chairman or for the committee to exercise any real governance with any teeth over another agency. So it truly is a coordinating committee. We try and have a uniformed implementation of the Common Rule. But when push comes to shove there is neither a reporting requirement or any authority for one agency to tell another agency you are out of line.

PROF. CAPRON: Yes. I was not asking for an enforcement. I was asking whether it was known in any reported fashion even for information purposes that the Defense Department has decided that although it is in the Common Rule and does not have a standing exception to X, Y, Z provision of the Common Rule, it has in this circumstance decided that it will conduct or sponsor research that deviates, in a way that deviates from the Common Rule.

Since we are sitting here in the interagency coordinating committee we are letting the rest of you know that we are doing this. Does that happen? Do you keep records of it? In other words, as Joel

and whoever becomes the permanent staff person involved in this area goes around, will they have a dossier which would allow them to know what you and your ongoing six to eight week meetings have found out and done?

DR. ELLIS: Well, Section 101(I) of the rule requires that any time all or part of a clause of the rule is waived by the department or agency head notice is to be given to OPRR and to be published in the Federal Register. I can speak for the Department of Health and Human Services there have been three such waivers in history published in the Federal Register.

I am not aware of any waivers and Bill might correct me. I am not aware of any waivers under Section 101(I) of any other department or agency. So the dossier would contain, I think, just three such waivers historically. All from HHS.

DR. CHILDRESS: Are there other questions or comments?

Well, thank you very much for the work that has already been done and we will look forward to getting copies of the reports at least for the Human Subjects Subcommittee and other members of NBAC should mention to Bill or to Margaret if you would like to receive those as well.

All right. The procedure for the next period will involve the following: I will offer brief summaries of some of the topics and themes we dealt with in three or four different sections and then invite members of the subcommittee to elaborate those, to alter or modify those, to suggest problems that we have as a subcommittee or that

NBAC might well have with those as we proceed. So I will simply provide the skeleton and the subcommittee members will flush out the topics and themes that we dealt with and some of the directions we hope to take.

The way I will proceed will be to work as the subcommittee did and that is with the assumption of adequate funding and of the longer life expectancy that is that particular strategy and we can come back later and talk about how we might have to provide a truncated version of what we propose.

As we think about a possible report from NBAC in the fall the subcommittee felt that it would be appropriate to begin with several of the changes that have occurred in the area of research involving human subjects since the work of the National Commission in the mid 1970's, over about a 20 year period.

Several changes have occurred in the area of research involving human subjects including the size of the research enterprise and the particular research projects, the locations and sites of those studies, and sources of funding for that research. For example, from a typical single investigator with few subjects to teams of investigators at many sites with large numbers of subjects, and an increased role for private nongovernmental funding, particularly with pharmaceutical and other companies playing a major role.

The shifts also include alterations in the public's perception of the benefits and burdens of research to participants. For instance, many now view participation in clinical research as beneficial rather than burdensome and want to be included in that research rather

than protected from it. Several commentators described this as a shift from protectionism -- from a protectionist to an inclusionist paradigm.

Well, if we start with and try to describe and understand those changes the changes at least I think indicate a need to reexamine the substantive principles and guidelines, and the procedures and structures that have been employed over the last 20 years to protect human subjects. And in this reexamination we will have to work on several levels. We will have to pay attention to important conceptual matters. We will have to pay attention to important normative concerns including fundamental principles or values and substantive guidelines and we will have to pay attention to a number of empirical issues, and we will spend some time in our report today talking about some of the areas we need to conduct additional empirical research into.

In terms of the substantive principles or fundamental values the subcommittee will look carefully at the formulations and interpretations and the interpretations that have evolved over time, the Belmont principles of beneficence, of respect to persons, and of justice. At the last or at the first NBAC meeting Zeke Emanuel proposed that we attend to the role of the value or concern for community in the way we think about research involving human subjects and in different ways the subject -- the Human Subjects Subcommittee at its meeting on December 16th thought about the importance of community in interpretations and reinterpretations of Belmont principles. For example, focus on community would require that we attend to persons in their particularity which will include their particular communities, their relationships to others, or in terms of interpreting the principle of

justice.

Attention to community would require us to look at the way in which community participation may be very important in formulating research protocols and also in trying to interpret risk benefit and other ways to protect human subjects. Or the way in which community understood as the common good plays a role in the way we interpret the principle of beneficence and so forth. This is just one example. The Human Subjects Subcommittee went through other discussions as well and the way in which it might be possible to broaden or to enrich or to deepen the interpretation of the Belmont principles. Certainly this is one important aspect of our task over the next year.

Now in approaching not only the fundamental principles and values, but also the substantive guidelines, the subcommittee focused on one particular concept as a possible way to illuminate the whole area of research involving human subjects. I want to say just a bit about that and then open it to a discussion from the subcommittee for elaboration and clarification.

Particularly as a result of some suggestions from Arturo Brito and other members of the subcommittee we propose to take a distinctive approach at least to see if it will work and how well it might work by examining the concept of vulnerability. Now all potential research subjects are vulnerable to some degree and the critical question is the degree to which different groups of potential research subjects are vulnerable and the kinds of protection or inclusion that are required.

Rather than simply listing vulnerable populations or

groups or trying to single out some for particular attention as we do intend to do we thought it was also important to develop a more general concept of vulnerability that applies to all but obviously with important differences and distinctions.

Now the formulation of vulnerability, I will ask the subcommittee to help elaborate, that we came up with is very tentative at this point and obviously requires a great deal more work again to determine whether it really will be illuminating and just how illuminating it will be.

But I would say that it generated considerable enthusiasm on the part of the subcommittee, though not without reservations, and it could become our key for approaching ethical guidelines and considerations in the whole area of research involving human subjects. It could lead us for example to develop some additional guidelines for example regarding cognitively impaired subjects and this is an area that we will attend to tomorrow in our subcommittee discussion with help from Bob Levine and Rebecca Dresser in getting at the fundamental issues that arise as a result of the huge gap in existing guidelines regarding the cognitively impaired. A gap that then requires IRBs to do a lot of work with considerable variability. So that is one area that we could certainly focus on.

Approaching matters through the concept of vulnerability could also lead us to try to improve some guidelines, perhaps to get greater clarification and specificity, and thinking about minimal risk and more than minimal risk in the guidelines involving the use of children in research. And our concern for vulnerability could also lead us to argue

to extend the Common Rule, as Gary Ellis argued so eloquently at the first NBAC meeting, to others including those outside federally funded or supported research.

Someone commented at the subcommittee meeting, I think it was Alta, that this may be the most vulnerable population of all. Furthermore, vulnerability as the subcommittee thought about it would include risk of exclusion from research as well as risk of inclusion. So one might state it in the following way: The concept of vulnerability would basically lead us to recognize rights of access to research and to the benefits of research as well as rights in research.

Now the concept of vulnerability as we approach it will obviously encounter a number of philosophical and rhetorical issues. It is probably not possible to spell out necessary and sufficient conditions for vulnerability. Probably the concept that is better understood is the family resemblance concept with several relevant features, not all of which have to be present to have a vulnerable subject, and we are going to be looking at degrees of vulnerability.

But our basic concern here would be to try to see what is common and then to see what is different and distinctive. Now again whether this will work or not is, I think, an open question. But it did for the subcommittee seem to be an interesting and potentially fruitful way to explore this whole area. So this would be on the conceptual level but it would also have obviously important ramifications for the way we think about normative guidelines.

Let me stop there and I will do this for two or three other blocks as well. Let me stop there and get the members of the

subcommittee to offer their further reflections since this is simply a brief introduction to what we spent considerable time discussing and then also to get reactions from NBACers as a group because we want to see for each of these topics each of these directions we are proposing whether that makes sense to NBAC and what kinds of suggestions all of you might offer to the subcommittee as we continue to work on this.

Alta?

PROF. CHARO: In some ways I would simply like to add some emphasis to some of the things that you mentioned, Jim, because I do not differ from you on any point especially in light of the uncertainties about the extent of the work that we will be capable of doing within the financial and time constraints that we have. It seems to me that there are some things that are highest on the priority list in the collection.

The first is that regardless of the strengths and weaknesses of the current system by which we monitor and enforce protection of human subjects, all of which is subjected -- could be subjected of course and regardless of that it is essential that we reaffirm most of the basic principles of the Belmont Report. In other words we reaffirm the notion that based on human rights and human dignity there is an entitlement to be free of unwanted or unknown medical experimentation.

And that based on that that we make the strongest possible statement about people that are currently uncovered by any system in the United States of protection for research subjects. I am talking now about a moral entitlement based on human rights, human

rights documents, as well as just human rights as discussed more generally.

The questions about how one might implement such a thing for the populations currently uncovered is a separate question and one that might be complicated enough that deserves attention only if we have a longer tenure. But I think it is important that there be discussion and I am personally hoping some consensus on the notion that uncovered populations indeed are the most vulnerable because we do not know anything about them.

And that that in turn leads to the next point which is that we need to be learning more about them and that within voluntary systems of reporting that do not raise questions about monetary constraints, legal constraints, that we need to get beyond the current noninformation, nonreporting, nonregistration status that plagues the field of human subjects regulation, the human subjects protection, and that we look to things like the animal experimentation area for some models. We look to the kind of voluntary reporting that now goes on with regard to many scientific journals that ask for authors to submit some kind of evidence of compliance with local rules as a condition of publication of the article as ways to encourage the professional societies and journals, et cetera, move toward better understanding of the empirical situation with regard to uncovered subjects.

And next that in terms of looking at flushing out notions of the Belmont Report the only thing I might add to your list is something that I thought about as a result of some comments made last night at dinner by Trish Backlar about her frustration with the lack of

universal access to health services in the United States.

That notions of community and notions of justice will never be fully flushed out until people both have the opportunity to be research subjects and patients within the same health care system, and that talking about justice and community is a little difficult when there will be populations of people who will now be eligible for research even encouraged to become subjects of research but who will never be able to most directly benefit from its results. This also goes back to a comment made by somebody in one of the things we read for the last meeting. An African American woman who said that nobody has ever been all that interested in having her as a patient and she finds it kind of ironic that they are so desperate now to get her as a research subject, and that comment has stuck with me for weeks.

But given that we do not have that kind of system and against that back drop looking to flush out notions of community particularly with regard again to the issue of power that underlies the notion of vulnerability, to understand the degree to which research subjects may want or need to be better informed about the progress of the research and the outcome of the research is to take seriously the notion that they are participants and not merely fungible data points.

Finally, on the notion of vulnerability, a word that many of us find uncomfortable because of its connotations of an intrinsic weakness of the subject as opposed to a situational problem of power imbalance that Arturo was trying to discuss, I am in some ways the last person to be saying that the problems of exclusion ought to be ignored having written specifically on the problem of exclusion of women from

clinical research and having a particular interest in the problem of pregnant women being the unwitting subjects of experimentation without any oversight because of the number of things that they have to take without any knowledge of their operation and their bodies.

I nonetheless think that since this problem of access occurs most frequently closer up to the therapeutic end of the research scale, an end that is characterized most frequently by drugs and devices, i.e. characterized most frequently by things that are already being regulated in terms of research by the FDA where there has been very significant movement over the last ten years on the question of enhanced access to investigational drugs and devices, I would urge that we focus first on filling the gaps as best we can on the protection of people who are currently not being protected against abuse of research practices and then move our focus to access. I say this as somebody who cares deeply about that problem like I said, but nonetheless just in terms of priorities and personal inclination on priorities. I think that abuse of research is more significant a concern in terms of public confidence in the research endeavor.

DR. CHILDRESS: Arturo, would you like to add anything this morning?

DR. BRITO: I agree with most of what Alta is saying but the only problem I have is the last comment about focusing strictly on the problems of inclusion in research. The reason I say that is because I am concerned that we are really dealing, even though it seems like we are not, we are really dealing with the same problem because once again problems of inclusion in research, those that are most vulnerable to

abuses in that area are also most vulnerable to the problems of exclusion. I agree we need to start somewhere and I think starting with that. But I just do not want us to forget the problems of exclusion and that is all I will say right now.

DR. CHILDRESS: Before opening it to other members of NBAC let me just see if any of the other subcommittee members, Laurie and Diane, would like to add anything.

MS. FLYNN: Just very briefly. I certainly appreciate the comments we have heard. Of particular importance I think to underline is, as I think you mentioned in your remarks, we know very little about the variability and the experience out there with the IRBs as they attempt to work with protection of human subjects. I think that that is an information gap that is critical for us as we look to ways to strengthen protections and deal particularly with the issues of vulnerability. It has been surprising to me just how little information about the operation, about the implementation of the guidance that we do have seems to be functioning out in the IRBs.

DR. CHILDRESS: All right. Let's open it more broadly. Zeke, I think I saw your hand up.

DR. EMANUEL: I was interested in your review of how research has changed basically in terms of you said the size, the sites, the sources and the perceptions. One of the things that strikes me looking forward, and the only reason I raise it is because I think it does bear on what we might call uncovered research, is the change in the nature of research. While over the last, you know, since World War II the focus has been on drugs and devices, I think I can say pretty

uncontroversially that over the next few years certainly in medicine it is going to be a lot more health services research about access and changing the structures of things rather than different kind of drugs.

And that -- since much of this is going to be done by private companies now for profit as well as not for profits that does raise a lot of issues. And since also much of it can be incorporated under the rubric of quality assessment which standardly do not go through IRBs, it seems to me the change in the nature of the type of research we are doing is something if we are going to look at recommendations that are going to have impact is very much important. Just because you can call it a quality improvement does not seem to me it should be exempt from the kinds of scrutiny.

It does not mean that it is wrong, unethical or violates the guidelines. It just seems to me we need a consistent standard and here we should not be blinkered by the concerns that were operative 20 years ago. I commend the enhancement. I just wanted to add this one other item because I think as we look to the future it is more than new drugs and devices that will be much more important.

DR. SHAPIRO: I did want to ask a question to make sure I understood the comment you made. Is it that research projects designed to assess the quality and treatment over 10,000 cases for ovarian cancer or some other type of research like that should be IRB reviewed just as if -- well, let me just leave it there without giving you an example. Was that the point you were making?

DR. EMANUEL: Partly the point I am making. Part of -- partly there is going to be a lot of research now that is done inside of

organizations like managed care organizations and others that is related to their quality of delivery that they may not have to adhere to the Common Rule. Second, there is this other situation which I and other researchers in the room I am sure have confronted, which is that if it falls under the rubric of enhancing the quality of services provided to your clientele, it is a quality improvement or CQI type thing that does not -- is not considered research. Nevertheless, those results look very much like research the way they are published if they ever get to publication.

Just to give you an example: There was an effort that one of the managed care organizations I know to improve the quality of care for asthmatics and they surveyed all their asthmatic patients. Well, who you identify, how you identify them, whether you are keeping this confidential or not, what you are going to ask them looks like research but if it is under quality enhancement it does not have to go through the IRB process.

DR. CHILDRESS: Thank you, Bill.

DR. DOMMEL: And just to add to that there is a rather broad exemption in the Human Subjects Protection regulations even today that even when you meet the definition of research, however if the objective of your activity is to assess whether you will improve services by decreasing benefits, for example, because there will be less demand and therefore quality improvement that you may reduce those services and do that under a research mechanism and be exempt from the regulation.

DR. CHILDRESS: Trish and then David. David?

DR. COX: That was -- actually Zeke's comment was very

interesting to me because I am going to make a comment on the flip side of it but let me just say that it all pertains to this distinction between research and medical practice. All right. Zeke was talking about medical practice that may in fact be research that is being called medical practice. A lot of the sort of laying out of the playing field is saying, well, if stuff is research then it, you know, does not go into medical records and it really does not pertain to medical practice. I think that that may have been true in the past but I think it is far less true now.

If we are unconcerned about it in the context of vulnerability that was brought up, people that are being vulnerable because information is being found out about them in the context of research, but if it is solely as research, it is never going into the medical records it can never be used to help them. So this murky area between what is research and useful to people versus what is medical practice I think is right now a very slippery slope but yet there are short lines being used to try and have a quick fix to this problem by simply saying, well, it is just research so we do not have to put it in the medical records.

I think this is the flip side to what you were talking about, Zeke, and they come together by trying to -- also nicely with vulnerability of trying to say what is really research versus medical practice, and maybe they are not the same definitions that they were 20 years ago, which is I think what Zeke is talking about.

DR. CHILDRESS: I think that is one very important conceptual area that really is going to need a lot of attention.

Alex?

PROF. CAPRON: Well, this may be a somewhat unfair interjection at this point but I have the hardest time understanding how we can have this discussion without some sense of what kinds of things are going to be possible for the commission because the comments that have arisen have gone -- with which I agree across the board with the other commissioner's comments -- have gone from pointing out that we do not as a society really have a very good picture of what is going on in research with human subjects. We can tell you more about what animals, what primates are being used in research and what is being done to them than we can human beings. I mean that just is the case right now.

Now we could conclude that that is a perfectly fine state of affairs but it would be at least helpful to make clear to the public that that is the case, that most of this is being done on some kind of a general sense that researchers have enough guidance and have enough understanding of what the rules are that we do not really need much of a mechanism and that what we have is not much of a mechanism.

For this commission to study that and actually to find out should that -- should we feel a sense of public confidence or are we going to wait for another Jewish chronic disease hospital case, another Tuskegee, another radiation, set of radiation cases, which will suddenly shake up the research community, shake up the federal structure, and respond in a crisis vote. Are we going to have the resources to actually give some answers to people and say we have done enough. The mechanisms for sampling are sufficiently sophisticated and detailed and probing enough so that not just at the federal level which Joel has

already described where some people in the departments are filing reports who do not know what is going on in their very department, but at the local level that that same kind of miscommunication and lack of reporting is not prevalent.

And then we hear that there is this whole other area which does not fit the model of 20 years ago where most research was either biomedical or behavioral and was, therefore, probably tied into the federal government in some way with the institutions doing it even if every dollar for the research did not come, so much of their money came from the federal government that they complied voluntarily with the notion that when Merck comes in and says test a drug, well we will run it through the same process, we will review it the same way.

But when one of these managed care companies decides that they are going to get all their doctors or half their doctors to behave differently for a while and see if they can save money and give -- but without hurting the quality of care that is not part -- that does not fit the model that we have. What is our response to that?

Well, part of my response to that would be is anyone being hurt by that? Is overall that something to worry about if we are charged with reporting to the public and to the president and whatever about this? I am not clear that that is our charge. If we are just supposed to say to the federal agencies, hey, you are doing an okay job, you filed some reports, they look like you know what the rules are, this agency better spend a little more time in internal education, but you have got the rules, then we do not need to have very many resources. But the rest of this discussion which is the basic stuff I cannot tell if we

should be having this discussion because I have no idea. You are talking about a multi-year project that to be done well would require a large number of people.

DR. CHILDRESS: Several people want to respond.

PROF. CAPRON: Okay.

DR. CHILDRESS: Let me just offer one point from the way in which I think the subcommittee proceeded because this does raise a question of the two type strategy. Our discussion proceeded and what have we done so far today has proceeded on the assumption that there would be adequate resources and adequate time.

If we move to a version where we do not have adequate resources and adequate time basically it seems to me from the subcommittee's work that we felt there were certain things we could do on the conceptual normative level that could be useful. Some of that we have already talked about today. But obviously for this to be persuasive in the context of policy we really need to know a lot more about what is going on or what we are saying on the level on the conceptual and normative levels really will not have that much impact.

So basically we thought there were some things we could do and the members of the subcommittee, several of us actually will have to spend a lot of time and energy over the next year working on this to make a draft report under the guidance of and for the consideration of NBAC. So we think some things could be done even in a very limited budget and limited time frame on the conceptually normative.

Obviously what we need to do on the empirical level, and there is a lot, and there is also a lot we have not even talked about yet

that we will come to later today, but we need to know a lot more before these recommendations could be at all persuasive. That is really going to depend on the resources.

PROF. CAPRON: Right. If I can just follow up. I was provoked by the new attention to the word "vulnerability." Vulnerability includes a notion of harm it seems to me. I mean vulnerable and suffering is not vulnerable to benefit here. It is vulnerable to harm that we are talking about. Do we have any indication that the research enterprise actually makes people vulnerable to harm? Years ago Bill Dommel wrote an article in the New England Journal, I believe, that looked at a lot of research that had gone on and concluded that people in research were no worse off than people in ordinary medical care and there was a lot of sort of intuitive attractiveness to that because the kind of research we were talking about meant you were getting your medical attention in the context of the first class university medical centers where you were of great concern to the researcher and the researcher was paying particular attention to every aspect of your well-being versus going to see your GP who maybe was not up on all the latest stuff and just overall medical care in those settings was just as good even though there was research attached to it made even better than ordinary medical care.

So that whole notion of the risks of every day life being more or less the same as the risk with research, to me that does not talk about vulnerability. I mean, then you could say within that there is the question of vulnerability in a Kantian sense to being used without realizing you are in research, without really giving consent to the

research. But when you come down to it I do not think the American public, maybe they should be more concerned about that, but I do not think that the American public has been concerned about research in an apathetic way because of that as much as they have the sense that people have been injured or are at real risk of injury. I do not know whether that is true or not.

DR. CHILDRESS: Except that we heard at the subcommittee meeting that most of the complaints actually center on the consent process and consent form.

PROF. CAPRON: Well, I know I have not read it. We have this document from the Breast Cancer. But do we even know that -- if that is the case then change that to the harm. That is fine. Do we know whether a lot of research is going on without consent?

DR. CHILDRESS: Sure.

PROF. CAPRON: However you put it, if you come back, if you elaborate a notion of vulnerability, do we have any notion whether this once elaborated applies? I am not disagreeing, Jim.

DR. CHILDRESS: I agree with you. No, I agree that it is going to be important --

PROF. CAPRON: But I think it is central to -- if we are going to have more than an article in the Journal of Bioethics about a flushing out the notion of vulnerability.

DR. CHILDRESS: If it does more than simply provide a lens through which to view this and that is certainly one way one could think about what we propose so far if we do not have the resources to do the serious work that you are talking about. I agree.

DR. DUMAS: I have a concern about having the problem of resources constrain our thinking. I would like to suggest that at least carve out the work that the commission is going to do and the subgroups will take responsibility for, that we deal with the concerns about the conceptual issues and those that about the operational separately. I think we should think about and formulate ideas in regards to the problems that need to be addressed as broadly and comprehensively as is possible without concern about resources. And then in thinking about how to implement what we would believe is needed we would take into consideration the matter of resources so that we would have a report that would say what we believe needs to be done and attended to and whether or not this is feasible within certain resource constraints is another separate issue.

DR. CHILDRESS: There are two issues there in terms of the resources and part of what Alex is raising is whether we would have enough resources to be able to do the kind of important thinking we need since that thinking would involve not only conceptual and normative matters but also the actual context in which this research could involve and whether people are really at risk of harm or at risk of not giving consent. And then there is the second issue of resources that was also raised at the subcommittee meeting and that is we have to attend to the cost in a broad sense of trying to implement some of the kinds of things that we might well propose.

So we have to attend to both of those at least. But your argument is that at least with regarding the second we ought to go ahead and formulate what we think would be ethically significant and

then --

DR. DUMAS: Absolutely and in either case I think the --

DR. CHILDRESS: -- and see what happens.

DR. DUMAS: Yes.

DR. CHILDRESS: Thanks.

PROF. CHARO: I know that you want to go into the strategy possibilities a little bit later but indeed, Alex, what I was trying to do before was to outline what could be done on the assumption we do not have any resources. Not because I do not want to think about the larger question but because I wanted to get on the record what might be do-able. And those are a subset of the things that are bigger and they come out of the subcommittee meeting.

DR. DUMAS: If you do not think they are do-able you are not going to -- if you decide a priori that they are not do-able because of resources then we are going to eliminate that whole area of concern and thinking?

PROF. CHARO: No. What I was suggesting is that there would be a discussion and a statement about the full range of things that we think should be done.

DR. DUMAS: Right.

PROF. CHARO: And that within that that we set a list of priorities.

DR. DUMAS: Okay.

PROF. CHARO: And the priorities do respond to financial realities or time constraints.

DR. DUMAS: Absolutely.

PROF. CHARO: Okay. Now within those I think, number one to answer Alex's challenge about harm, I think that number one it is true that we do not have a good thorough documentation of that phenomenon and I would love to have it. I would put that on my list of things that would go on strategy B, the longer term strategy. But I do think we have enough evidence of real harm other than just the dignitary harms that you were referring to. We do have adverse event reporting so OPRR does have files. We do have periodic newspaper scandals. You will find that if there are scandals they involve physical harm to patients, that there has been a particularly strong pattern of scandals regarding the difficulties in the area of psychiatric research and physical harm or psychological harm to patients having to do with the patterns by which drugs are either reduced or increased, or withdrawn completely in the process of having various kinds of tests for new kinds of psychiatric medication which dovetails I think very reasonably then with the fact that the cognitively impaired have been high on everybody's hit list for a long time for appropriate regulatory attention.

As well as financial harm and that complicated area of private sector, innovative medical care that is sold to patients even though under some people's definitions you might more accurately classify it as research and therefore inappropriate for sale to patients. And then the dignitary harms I think go more generally to the credibility of the medical industry in the United States, particularly at a time in which the credibility is being stretched by virtue of changes and service pattern.

I think that realistically what we are capable of doing

without much by way of staff or money or time is to recognize where we fit within the governmental system. We are a bioethics commission that supposedly gives advice to the President. In fact, what we do is we give advice to the President's science advisor who sits on top of OSDP, which sits on top of NSCC, which sits on top of the Interagency Task Force that Gary Ellis was talking about, which means we can make recommendations to that task force to number one look for opportunities to by any means possible gather whatever empirical data you can.

But more importantly number two as they work through in their six to eight week cycles where they are going to be trying to come up with regulatory suggestions that will be adopted across agencies because that is what the interagency group does that we think their priorities ought to be X, Y, Z and it might be cognitively impaired followed by children, whatever.

And that we think that that should then be followed by an explicit consideration by the Interagency Task Force of the problem of exclusion in non-FDA settings since FDA is working along the way on that. And this I agree is going to be very important not only in terms of health services research but I think the whole area of genetics is exactly the one that is not going to fall conveniently under drugs or devices except to the extent that genetic test kits are considered devices.

So with regard to the whole area of research that is going to be about attitudes and services on genetics that is the kind of thing where the Interagency Task Force might turn some attention and it is exactly also where the community issues come up very, very strongly.

By making those kinds of recommendations we do not

need a lot of staff. We are saying, in fact, in those recommendations we need staff. You guys are the ones who actually have the expertise in law and in regulatory drafting, et cetera. And in the absence of us having duplicative resources in order to make specific recommendations on our own, all we can do is make recommendations about what you ought to attack and the directions from which you ought to attack it. But I do think that that is not an insignificant function for a group of people that are going to meet a total of maybe 12 times over their lifetime.

DR. DOMMEL: Jim?

DR. CHILDRESS: Yes.

DR. DOMMEL: Just to add, we also have a responsibility to report to appropriate congressional committees.

DR. CHILDRESS: And I had planned to bring this up later as a larger topic but let me go ahead and do that now because questions have been raised about what kinds of empirical studies we might need. So let me just pull together some the subcommittee talked about and some that have already emerged to date and think about those and also about the ways in which we are able to get some information in those areas.

IRB's, what is going on there? What kinds of problems have emerged, et cetera? Charles McKay's study apparently is going to be delayed long enough that it may not be able to provide the kind of information that we would need at least within the first year of our work. But how does one deal with the interpretation of the problems that we hear reported anecdotally and in articles such as the one that appeared in JAMA that was circulated to the -- at least to the subcommittee.

Are we to focus on IRB's as burdened with bureaucratic requirements in an effort to make them accountable or are we to focus on the other side and that is the problem of variability and the results from IRB's?

And you never push in two different directions. Well, obviously we need to know a lot more about IRB's. That is one area that has already been identified today as well as in the subcommittee meeting.

Second, we need to know more about subject's experiences. Not only subjects in research but also those who decline research. Why? There are certain things that would be important to know in that area. It would also be important to have more empirical research on informed consent and there are two NIH grant programs I understand. But again the results would not be available within the year for our results.

We need to know more about researcher's perspectives, investigator's perspectives, and the kinds of problems they are experiencing.

Now one of the things we plan to do and I am sure you will list in just a moment some additional areas where we need more information. The National Reference Center for Bioethics Literature is making its resources available to us to help us draw together the literature in these areas so that at least we are up to date on what is available in the literature reporting on these particular areas and others.

Furthermore, at the subcommittee meeting several individuals volunteered information in particular areas. Obviously those

two fall short of what we need if we are going to have the full range of information in these areas and others. But at any rate there are some things we can do and we can report on that at a later meeting of NBAC of what we have been able to draw together and find out and see more clearly where the gaps are in empirical information.

Let me raise this for the group as a whole, but also let me mention this side of the room is probably not getting enough attention from me. In part, because I am up here on the left and I am left handed and I lean this way and so forth. For all those reasons those on the right will need to be more vigorous in waving hands to get my attention.

(Laughter.)

DR. CHILDRESS: Larry?

DR. MIIKE: Actually you -- the last two comments partially began to address what I think is what we need to devote a meeting to. That is where in the analysis and the application and recommendations, where do we stop, at what level? We could be a constitution drafter and say all men are created equal and that is enough or we could be a Supreme Court or we could be an Executive Branch agency that applies it.

I think that is the -- we need to address that directly because that is the only way we are going to be able to see at what level we are going to be effective for which audiences and which will answer Gladys' question about I want to be able to do this without being constraining my thinking about the resources that we will use.

We spent a lot of time in our subcommittee meeting because so much of what you have started to touch on about empirical

research has a time line longer than my life on this commission and maybe even longer than the life of the commission itself. So I think we need to spend explicitly time addressing directly that issue.

DR. CHILDRESS: Any response to that or any response to the list of areas where we need additional information and could be helped in those areas if we had additional resources or commitment of resources? Any comments?

PROF. CHARO: I think one of the things that came up at the subcommittee meeting, and just for the record for this one as well, is that the IRB system itself has been plagued by lots of problems because of its decentralized nature, because of its lack of -- speaking of lack of resources, the lack of resources at the federal level to permit it to do more nuanced oversight and to vary the paperwork requirements perhaps in direct proportion to the credibility of the committees at the time. Right? The committees that are working well and have adequate resources probably do not need to be quite as burdened as the ones that are clearly subpar and there is no capacity to handle that kind of problem.

In an ideal world we would have a much better handle on exactly what is going on in those committees, the degree of conflict of interest, the degree of under staffing, the rate at which research proposals are increasing, the rate at which private sector research that has to do more with marketing than it does with actual knowledge generation has increased a number of things that need to be reviewed and the way in which that is taking its toll on the IRB system.

So that in an idealized world, yes, we would be able to

have empirical research that would go into both the OPRR and the IRB level of understanding, how it functions and where it could be improved.

DR. CHILDRESS: Okay. Other comments at this point on the issues that we have raised? Rachel?

DR. LEVINSON: Maybe at this point I can offer some clarification or suggestions about two of the issues that have come up repeatedly this morning. One of them has to do with the charge to the commission, the basic charge that is laid out in the Executive Order, but more fully in the charter, and the other is the issue of resources and for that I would like to offer thanks to Alta actually for giving a positive view of the rather lengthy reporting chain that NBAC has going down through the President, Jack Gibbons, OSTP, the NSTC, and Gary's committee.

On the issue of resources, both financial and in terms of support, that committee and other agency groups or individual agencies I am sure would be very willing to provide help, to provide some of the research that you are talking about, information and maybe where they are not so willing or have not been made aware of the need for such information your simply asking for it could start a very useful chain of events.

PROF. CHARO: I am sorry, Rachel. But I have got to intercede here because I am completely confused now. I thought that those agencies had signed on with actual dollars and all that had to happen was that they be asked for that money. But as far as I know, I know that you said you were going to say something about this, Dr. Shapiro, we have not received that yet so we do not know what our budget is. We do not know how much money we are going to have or

when it will come in so we do not know whom we can hire or whom we cannot hire, and where it is that we need to ask for things otherwise we could just get.

Second, because we do not know that we are really going to be reauthorized in October, asking other people to do work which is going to have a time line may be unrealistic because it is not going to come in, in time, for us to do anything at all. Finally, the one single real task that we actually have totally mandated has to do with the review of those agency reports for which we have got people who are volunteering their time so that you cannot expect them to turn their lives over to this.

But, you know, it has been since October 3rd, the first meeting. I would love to see those damn reports. I have never seen them. I do not know if it is possible or not, but I think it is not entirely impossible to think that the subcommittee could read those reports, come to some conclusions, and make some statements even before the volunteers have had a chance to do the proper kind of review, and I am so frustrated at not understanding what is holding everything up.

DR. SHAPIRO: I cannot say a lot to relieve your frustration but just to in some sense, in part to express my own, there is a lot of issues which remain unresolved and despite a lot of effort we have been unable to completely resolve them. But let me say a couple of things about this.

I think the committee is going to go on for quite some time. Despite the fact that I cannot guarantee that to the committee is beyond my power, beyond my authority, beyond anything I can muster to guarantee that, I do not think I would have had the nerve to call a

meeting or to ask or to encourage people to attend meetings if I thought we had a one year existence. But I cannot do more than say that. That is just my strong belief. I would not be spending my time here if I thought we had one year I assure you.

So I could be wrong. I cannot relieve your frustration on that.

I also think that we are going to have adequate resources to do important things. That is what I believe. I think we have two kinds of resources here. We have intellectual resources of the members of this committee which need to be mobilized properly and used. So we are going to be asking members of the committee to do that and many have already.

Second, we are going to have additional financial resources which I think will be perhaps not everything we would like to do, but that is probably true. That is probably a truism. We probably -- our aspirations will exceed probably any level of resources we could reasonably expect. But I think we will have adequate resources to do important things. At this moment it is very frustrating because mainly what it interferes with is our planning process and our capacity to bring on the kind of staff we need to support the committee's work.

Therefore, it seems to me that the strategy that we ought to follow was really very well articulated yourself just a few moments ago so I will not bother repeating it. But it is to use the intellectual capital we have in the committee together with the staff resources we have now to outline a map for us and say this is what a committee should be doing. Now then we will say, as you articulated just a moment ago, the

real hard question. All right. That is the map. Now where can we go?

I think that was behind Jim's suggestion which came out of the subcommittee that you are that they have two strategies. But I do not think it is at all appropriate for us to -- and frustrating as it is -- to get side lined now into saying, well, what kind of compromises we have to make and so on and so forth. We will reach that point very soon if these issues are not resolved.

But I think we still have a little time maybe between now and the next month or two to mobilize our map and get our best ideas down, and see how we can articulate them. I have heard many very thoughtful ideas here today and some that came out of the subcommittee. It would be an enormous if that is all we did although that is nowhere near what my aspirations are.

So I think that is the situation we find ourselves in as I understand it. So, in part, I cannot relieve the frustration you feel or that I feel also. But in part I am quite confident we are going to have a path through here and even if we do not, if everything just does not go, I think there is something quite important we can say here and we ought to say it.

PROF. CHARO: Right.

DR. SHAPIRO: Even if what we do is say it and get out of town, we ought to do it because no one else has that chance right now. But I do not believe that is going to be the case here. So that is where we are. It is frustrating to deal with.

DR. MIIKE: Two follow-up comments. Can we start with coffee as a resource?

(Laughter.)

DR. SHAPIRO: I will have to speak to my physician. I do not know.

(Laughter.)

DR. MIIKE: Water is kind of hard to take the first thing in the morning.

Second, the second point I think from my side is that since we really have to focus ourselves even at the most detailed level at institutional responses, I would hope that this committee addresses in its lifetime of work the IRB's and the informed consent processes that is currently done.

DR. CHILDRESS: I might just add before turning to Rachel in response to your earlier question about the level we might address, one of the things that came out of the subcommittee as those of you know who have had a chance to review the discussion as reported in the transcript is that a great deal of attention to education of investigators and IRB's. So apart from the issues of legislation and so forth, a great deal of attention to how we might proceed on the level of education of IRB's and investigators.

Rachel?

DR. LEVINSON: Okay. To go back to Alta's point and perhaps to give you a little further information about particularly agency's involvement and an interest in the establishment of NBAC. This is a ground breaking committee in the sense that it was a number of agencies that came together, came to OSTP and made the suggestion initially that NBAC be established. Those agencies made commitments

of resources, including dollars and intellectual resources in order to see that it would happen.

It happens that Congress does not agree that agencies should be able to come together and commit financial resources, especially prospectively to advisory committees that operate under the Federal Advisory Committee Act. There is a statutory prohibition against that happening unless Congress specifically authorizes such activity.

In the case of NBAC for fiscal year 1997 we were given that express statutory authority for one year. It is attached to an appropriations bill so that authority expires at the end of this fiscal year. Which is why even if the policy decision is made to extend the charter for NBAC we have to go back to Congress again and seek an additional change in that authority, which they can do multiyear if they choose to.

PROF. CHARO: But, Rachel, that authority was -- that authorization for an exemption was passed in September just before our first meeting and that means that the agencies that had agreed to contribute to NBAC could have been giving us money as of the first moment that there was an account number assigned for their transfers to take place.

And I do not know of any report that we have heard yet that that has taken place, that the agencies have gotten together, have been called together to be told how much each one is being asked for particularly, and that the money has been deposited which is necessary in order to start thinking about staffing.

I am just confused as to what the obstacle is after -- well, how long? Four months? I do not even know how much time it is to

accomplishing that. It is because I am not a bureaucrat that I do not understand the obstacles. It is not that I do not believe there are not some, but it is frustrating when you do not know what they are and you cannot imagine what they might be.

DR. CHILDRESS: We will take one more -- a couple more responses to Alta's confusion and frustration, but we need to get on to some of the issues that the subcommittee wants to address in order to get more feedback from NBAC about how to proceed.

DR. _____: At least at the moment of not being constrained intellectually by the resources for reasons that have been said and that is if we look at the Radiation Commission they had a lot of limitations, but one of the consequences is that they did stir the NIH to begin looking at informed consent and establishing resources there for empirical work.

One of the things we might find is that we could lay out sort of an intellectual and conceptual framework, indicate what kind of research should occur, would be needed to occur, how that research would affect the implementation of this institutionally, even if we cannot do it. And that might be taken up. It might not be taken up but it might be taken up by the agencies that are interested in what we are doing and in particularly the NIH and the HHS.

It seems to me that rather than spend much more time on these resources and what there are you said three or four other things you needed to tell us about? I would love to hear what they were.

DR. CHILDRESS: Okay. All right. Moving from the notion of vulnerability and we talked about Belmont. We also talked about

some of the areas where we need more empirical information. But moving from the notion of vulnerability into particular vulnerable populations I have already mentioned that the subcommittee would be giving immediate priority just because of the gap that exists to cognitively impaired subjects and that would be what we will focus on tomorrow.

I will also mention that we will attend to children as a vulnerable population and see what kinds of changes might need to be made in the guidelines. We have talked about other vulnerable groups as well. Those who are institutionalized, the military, prisoners, perhaps those who are involved in transnational research and so forth. So those are some of the groups that some of the subcommittee have felt we ought to attend to. I am not sure we reached a full consensus on the whole range and we might well have a debate about priorities, but it seemed wise to move into focus on the cognitively impaired subjects in view of the gap that is present there.

But is there any response to -- not only to this list of vulnerable groups we would like to attend to in a special way but also the larger model we are proposing because I am moving sort of to the end of covering the major topics we dealt with. One of the important things again is to see whether NBAC feels comfortable with this as a direction for our work and then more specifically what kind of guidance you would offer to us beyond the points that have already been made.

Yes, David?

DR. COX: In a direct response to that I was really struck by Alta's plea to enter some priorities if I heard it right, is to focus on the

groups that are not protected at all and particularly those that are not protected under federal mandates. I think that that is a pretty broad vulnerable group that that would -- I like that idea as being a very important priority.

It fits in with the concept of, you know, the whole concept of research changing too. So it fits those together.

DR. CHILDRESS: Steve?

MR. HOLTZMAN: I was very struck in reading the minutes from your subcommittee to watch this intellectual crystallization on this concept of vulnerability just watching it happen. I felt very engaged by it myself. But later as I think about it I am a little worried about it. I mean, we have heard some concern here from Alta about it and then Arturo came back and said, "Well, it is the same populations."

When you think about children as an example, are you really more concerned about children being included and potentially harmed or issues of autonomy which they can exert versus the children being excluded from AIDS research for example? You can call it vulnerability in both but I do not know -- I really loved it initially but I do not know how much light it really sheds. I mean, I think you really need to think about it. That is one point.

The second point, I do not know if you are going to come to it. I found the stuff that Laurie talked about just absolutely fascinating and I do not know if you are going to come to it in the next 20 minutes, of the role of the community groups or patient advocacy groups and a whole changing notion of what it means to design your research.

It could perhaps introduce a new paradigm in maybe not all research but many forms of research of how an IRB should function, what it should be thinking about in terms of approval of a design of research, and then it also could be a mechanism addressing issues of informed consent of the subjects. And, lastly, also addressing some of the notions of community in terms of who is the consenter/consentee, whichever.

So I just think that that was a very -- at least to me, and I am very innocent in these matters, but it was very striking what Laurie talked about.

DR. CHILDRESS: Let me speak to the first one. I used the language tentative and so forth in talking about vulnerability because even though the subcommittee was very enthusiastic about it at the time, some problems were recognized then and some have been raised subsequently, and I think it is a matter in part of exploring that to see whether it would work out in an instructive way in the way we think about research involving human subjects. So at this point it is exploratory rather than definitive.

Let me get Larry's comment and see if there is further discussion on the issue of community participation which I simply introduced under the heading of what we think about community injustice but really did not elaborate today.

DR. MIIKE: Steve's second point was the one I was going to comment on.

DR. CHILDRESS: Okay. That is fine. Go ahead. That is fine.

DR. MIIKE: Just in the sense that what Laurie said is true from my experience in Hawaii in the sense that there can be better research design and there can actually be a better acceptance of a research in a particular community when they are involved, and I think it took a long time in some communities in Hawaii but especially from the researcher's side not believing that they could have a really fine protocol if they compromised in the community but they found otherwise.

DR. CHILDRESS: Laurie, would you like to say more about this for those who did not have the benefit of the discussion at the subcommittee meeting?

MS. FLYNN: I am cognitively impaired due to the shortage of coffee.

(Laughter.)

MS. FLYNN: But I appreciate the comments. Just to try to summarize, I was trying to express a concern that certainly in dealing with cognitively impaired subjects, the vulnerable populations, but I think it is a broader -- and it was part my trying to grasp what was meant by this notion of community.

Looking at new power relationships as Arturo would say, looking at ways to engage the subject population in its many forms, including community activists and advocates, in thinking about the research enterprise from the very beginning so that the issues that are reviewed, the subjects that are viewed as urgent, the methodologies and mechanisms that will be used, the sharing of information throughout the process, informing on findings in an early stage as well as participation in communicating those findings if they have general interest or general

relevancy.

All of that speaks to a whole new way of dealing with people that starts at the level of informed consent but really moves to a community partnership with the research enterprise that is I think critical for vulnerable populations, both as individuals and as a larger community but I think has some implications for the changing -- all of the changes that we have discussed early on in the research enterprise and some of the issues that were forecast as being very significant in the future.

DR. CHILDRESS: I would note that in part this discussion came up in relation to the concept of vulnerability. It is not as though this focus on community is separate from that but closely related to it. It is also an effort to address certainly what Zeke raised at the first meeting.

Alex?

PROF. CAPRON: You used the term "family of concepts" when you were talking about vulnerability. I want to invoke that talking about this notion of community. I think that there are some real values to us in pursuing what Laurie has said. But I think we are also at risk of getting some fairly distant cousins confused under one family heading and maybe I am sounding like Steve on the issue of vulnerability.

It seemed to me that in some ways this term "community" is useful if we are talking about how particularly people who work in social science might be helping people who work in the biological sciences to recognize what the people in the social sciences, the anthropologists and sociologists have known in their research for a long

time, whether they are working in the United States or abroad in not marching into a community and pretending you can conduct research in the community and the community may be very dispersed. It may not just be an area of the city. It may be women with breast cancer or something who see themselves as a community and have some interest in being addressed as a group, being involved in the research design, helping to respond to ways of expressing things that make sense to them and so forth.

But that is a level of strategy. It is not an ethical principle as much as it is saying it will not make sense to talk about consent in this area or you will not get data that are useful if you do not attend to these issues. Then there is this notion of community, which I took Zeke to be raising in more of the ethical principle level, and what puzzles me about that and I know that the term "community" is in the context of bioethics. It is the new darling of bioethics because we have forgotten about community. My goodness we have been so focused on the physician/patient diad and now community is being invoked in the futility debates and so forth. And people like Dan Callahan have drawn our attention to it over the last decade.

It was never absent in discussions of research. The whole question of research ethics was to say you have got the weight of the community over here. The community as embodied in the desire to develop generalizable knowledge of benefit to human kind and the community. And that heavy weight is hanging over the head of research subjects who may get crushed in the rush to get that valuable information and that was always there. We do not need to inject

community there. It is there.

Now to some extent the notions of justice or the principle of justice was intended to talk about that. The whole notion of a good proportion between the benefits and risks was intended to convey that. So I am a little worried about our getting swept up with the notion that we have something new to add.

Now that does not mean, and I assume that at some time, this is a general comment, not just on this, it does not mean that I do not agree with Rhetaugh the notion that we ought to scope out everything we should do. And one of the things we could do would be to commission some thoughtful people to explore this idea and not to accept my facile disagreement with the notion that it adds anything. Maybe it adds a lot. I just do not see it yet. I mean, you know, I am perfectly prepared to --

(Laughter.)

PROF. CAPRON: -- but I am very concerned as we go into it that even if we do that, that we be clear that we are talking probably about three or four different things and we are using one term to describe them, and we may -- I would be very interested in hearing from anthropologists and sociologists, and so forth on the question of to what extent this notion of community has played in their research and then from some biological sciences, medical sciences, about how they would use it, and then I would be interested in hearing some philosophers and the like on this question of the principles question.

At some point I want to know when we leave Washington at the end of today or tomorrow are we going to have set out this

research thing? Because I agree with Rhetaugh. We need to do that and we do not need to cut it off at the knees because we do not have funding or we do not have the authorization for interagency cooperation after September 30th.

DR. DUMAS: The chair said we are going to do that before we leave here.

PROF. CAPRON: Are we going to do it?

DR. DUMAS: We are going to do it.

PROF. CAPRON: All right.

DR. CHILDRESS: Let me just respond and then Larry wants to respond as well. This is simply one of the concepts which may also be a normative concern that the committee felt it was quite important to address, but not simply as a supplementary principle to the ones in Belmont but as a way to interpret or reinterpret the principles of Belmont. When you focus on beneficence where it clearly plays a role and I very briefly stated this, and I am just elaborating for a moment, we talked about principle respect for persons. You can give that a very individualistic or also communitarian interpretation.

Eric Cassell who just finally arrived because of probably the storm delays was very eloquent in our discussion in the subcommittee about the way in which it changes your interpretation of the principle of respect for persons with the persons located within their communities. Or the way in which justice along the lines that Laurie was talking about would require community participation and so forth.

So there are ways in which attending to this theme can help us understand the Belmont principles in a better way. At least that

is the direction our discussion was going rather than offering it as something different from or a supplementary principle to. Though it could well function that way also, but our direction was much more along the lines of trying to understand these other principles in this way.

Is that fair, subcommittee members, for the way in which we were thinking about it?

Let's see. Larry?

DR. MIIKE: Yes. On the -- I agree with Alex that we need to tease out what we mean by community. But I also need to say, Alex, you just do not get it yet in terms of community and I think that is what we need to discuss in this commission.

DR. CHILDRESS: Now I have covered most of the topics and themes that have come out of our subcommittee deliberations. It seems to me one of the major things we need to talk about and some points have already been raised along these lines. But some of the things we need to talk about have to do with whether you think the general direction we are proposing to go especially on the conceptual and normative levels, whether those general directions seem appropriate or not.

Again we have a commitment on the part of the subcommittee to work vigorously and we hope creatively in this particular area under your guidance of course. But does this make sense and what kinds of suggestions would you have for us? Obviously how much we are able to do on the level of empirical studies would depend in part on what we determined is actually already available but then also as we have mentioned finally on what we are able to do from a

resource standpoint.

Zeke?

DR. EMANUEL: Yes. Correct me if I am wrong but there are two topics that have been floating around that I did not hear you mention.

DR. CHILDRESS: Okay.

DR. EMANUEL: One was the question of a national IRB for certain kinds of research that was raised by the Radiation Commission and I think has been a concern of people and maybe you guys decided no, maybe you want to put it in a different place. The other one which is of some concern to me as a researcher wearing that hat for the moment is the question of going through multiple IRB's and is there going to be some attention to those kind of -- now there are a little bit more mundane institutional things but nonetheless extremely important and they do, I think, speak to some of the audiences we need to respond to.

DR. CHILDRESS: We did discuss this a bit and let me get subcommittee members to elaborate. We did not come to a particular conclusion in part because it relates in some ways to the issue of exactly what is going on in IRB's, but also what other kinds of mechanisms have emerged and how we have put those mechanisms together with the local IRB's, mechanisms such as the Data and Safety Monitoring Board now which functions in a very significant way but actually does not relate that much to local IRB's in terms of providing information and the like.

Or ad hoc committees being set up to examine things like the clean needle exchange controversy and so forth. Or the RAC and the

Human Gene Therapy Subcommittee to look into particular areas or proposals have emerged to have special national committees to look into xenograft transplants and so forth.

So one might make the arguments on all those levels and the subcommittee considered that area and it is not something we have excluded but rather we are thinking about it as let's think about the IRB's, then what else might be needed in relation to those, or how should those be modified.

So that is certainly part of our concern, too, and I think that you would like -- your argument that this should be a priority one.

DR. EMANUEL: Yes. I guess the only point of re-raising it is to say that if we get out of town in a few years or whatever the time line I would feel that we had not done our job if we had not specifically addressed that especially since some of it was hanging over from the Radiation Commission which in some ways, you know, was a necessary midwife to our birth.

DR. SHAPIRO: Just a few small comments. First of all, just to pick up on what Zeke just said now. Probably if I just look at my mail on the issues that NBAC address and the IRB issue is the most common issue, and opinions at least judging by the mail I get are above it. That is there is a whole group of letters I get from thoughtful people for the most part which say the system is working great and just get rid of some of the unnecessary bureaucracy and everybody will be better off, patients, subjects, mankind and so on.

Another set of observations was run exactly in orthogonal place saying look there are some very serious problems here and

somebody better attend to them or suggest that they be attended to. So I would just make that comment not because that is a systematic survey of any kind, but there are two very different world views out there about the IRBs and we would at least like to consider whether we have something to add in that respect.

Is this about the IRB's?

DR. DUMAS: Yes. The IRB is a mechanism for -- the IRB as I see it is a mechanism for addressing a broader issue. And I think that the subcommittee should address the broader issue and address the concerns, the pros and cons of IRB's within that broader context.

DR. SHAPIRO: Let me just make the second point I was going to make. It is really just elaboration on some of the issues that have been raised by other people around the table. It had to do with this issue of community which I have to confess also I feel very -- it is an important, but I feel uneasy about it every time I try to think about it exactly and carefully as to what it means.

And, therefore -- and I just wanted to offer the following observation: You have community in the sense of community versus the individual, that is community rights versus individual rights. Is the community impressive to the individual or is the reverse true? There is that whole set of philosophical issues about how the rights and expression of the individual relates to the community somehow define if, in fact, it can be defined carefully.

So there is that whole set of issues which I think requires careful articulation so that what we say is understandable in those terms. Then there is the other set of issues which Alex referred to as

perhaps getting some advice and assistance and commentary from social scientists and anthropologists, and others who have studied communities and, therefore, who have got some notion of how it is one approaches communities in an effective way both from the point of the research and from the point of view of the researcher.

That is a whole different set of issues, particularly when the researcher is crossing a cultural divide in order to reach the population who are the subjects. And there as I think many of you around the table know has been a virtual revolution in thinking about how you proceed when you are crossing a cultural divide on the delivery service or to do research. But that is a whole different set of issues. I just encourage the committee to think of perhaps other classifications.

I do not know if I have done it carefully enough here but there are quite different issues and we do not want in our discussion the subcommittee potentially as they may appear in anything that we do to confuse those issues. Those are really quite different and we want to attend to them.

I cannot resist the temptation right now to tell what I thought was a good anecdote because of the expression Alex used when he said, "Oh, my God, we forgot community," and his hand went to his head and it reminded me of a t-shirt I saw coming down Madison Avenue some months ago. On a t-shirt is a whole bunch of men and women, all of which are grabbing their heads and saying, "Oh, my God, we forgot to have children."

(Laughter.)

DR. CHILDRESS: Steve?

MR. HOLTZMAN: Yes. Before I comment, a question. Is it useful to you at this point for having members who are not on your committee say if there is one thing you do I would really like to see you do this?

DR. CHILDRESS: Yes, this is the time.

MR. HOLTZMAN: Okay. It is echoing something Alta said. Let me speak, when I came to my first meeting here, coming from a background in which all of the research I have ever been associated with has been under IRB's, I was literally astonished to learn that there was research taking place in the United States without informed consent. Whether informed consent is good, is as good as it should be, whether the IRBs are as good as they should be, whatever else, I was astonished. And it may not be part of our charter to talk about this. I do not know. But we are a bioethics commission.

I am going to assume there is a reason why there is excluded research that I do not know. My gut tells me it is not a good enough reason. It seems to me without a huge staff one could engage in an inquiry as to why there is excluded research and how do we feel about it and if we conclude that it is beyond the pale, that it is unacceptable to come out as a forceful voice to say that.

DR. CHILDRESS: Bette?

MS. KRAMER: Jim, the presentation of your committee's report was so full and I possibly missed this, but I think that -- and I only know this anecdotally, that as more and more of the research moves out of academic centers or is extended out of academic centers into community settings then I think that the local community IRB's, the

community hospital IRB's, do not necessarily have the same amount of regulation, training, supervision, et cetera. And I think that that is an area that needs to be looked at as well.

DR. CHILDRESS: Thanks. Trish?

PROF. BACKLAR: I just wanted to make a few more comments about the word "community" because we have been talking about it in this rather larger abstract sense and I was hoping, Harold, that you would have gone in your progression of community to -- I am going to use the word "family" and not using it in the Kantian sense that it has been used heretofore. But I think that, Laurie, when I read the transcript, you used a term that I thought was really quite wonderful which was the "community of participants."

And I know that case that you were referring to that OPRR did a report on where there was a drug wash out with a group with schizophrenia. I heard that community of participants being the immediate relationships of the individual which might be family, kind friends, persons who have some invested interest in the research person.

But I also found it very interesting when I read the OPRR report and went back to the Common Rule and this ties in to what everybody and different things that are being said about the IRB is that it seemed to me that Alex had -- we have these things in a sense in place and I was reading what you said about the -- well, we have ways of looking after people already that I see that are in the Common Rule. But the problem is that the IRB may not be reading the Common Rule adequately.

I do not think that we have addressed that quite today

and I wanted to bring that up, which comes back to your -- Eric's concept of education being such an important part of perhaps what we might do as a commission.

DR. CHILDRESS: Eric?

DR. CASSELL: Well, if I am saying what you have already said because I traveled rather further than I meant to today --

PROF. CHARO: Where did you land?

DR. CASSELL: I would rather not talk about it.

(Laughter.)

DR. CASSELL: Maybe not even in private.

But I think that one of the things in the discussion about community was not merely community in the two senses but the fact that the previous understanding of respect for persons was about a person that really does not exist, a freestanding person uninfluenced by others in the sense -- a philosophical sense commonly used for autonomy and that the sense of the broadening out of the interactions of that person with others around them to whom that person is both responsible and who are responsible for, so our sense of community is just exactly that enlarging it up to individual relationships, family and then that larger sense of community. People are responding -- and that Dr. Brito's understanding about vulnerability is very important to understand that you are only vulnerable in relationship to somebody or something.

DR. CHILDRESS: Yes, Tom?

DR. MURRAY: I may have to struggle to express this clearly but I think I see actually an interesting continuity that translates

into a conceptual challenge for your subcommittee. The continuity I think I perceive is between on the one hand Steve Holtzman's concern about might there actually be research for which there is no informed consent obtained. Of course there is lots of subject research on children and other kinds of research. But I presume you have in mind potentially competent adults and on the other hand community.

Here is how I perceive the continuity: However rich the conversation about the ethics of human subjects research has been in practice it often reduces to worrying about the consent form. So we have come to hang a great deal on the particular language of the consent form. Probably more than we hang on the actual process of consent. Consent can be a very rich and vigorous protection of the interest and rights of human subjects, but it can also be routinized, it can be unintelligible to the subject who happens to be reading the form. There are lots of such issues.

Maybe a way to think creatively about the best sorts of protection of the ethics of research and of human subjects is to open things up a bit and see consent as not quite the whole story or not as much of the story as it has occupied. On the one hand there might be instances, certainly some researchers, and others think there are instances where consent is not necessary, at least not in the way we have normally understood it.

On the other hand there is a sense that informed consent might not be sufficient because there are other interests, there are other -- there is a community but not, you know -- not disembodied, but desocialized individuals, autonomous isolated individuals, they may not

be the appropriate model for how to think about the efforts of research, at least not entirely.

So I think on both ends there is a kind of continuity there.

DR. CHILDRESS: Alta?

PROF. CHARO: I would like to add one more thing to this notion and it goes back to the interaction with the word "justice." For those of us that have served on IRB's I think we have all noticed that there are certain kinds of protocols that repeatedly arise and pose certain problems. In Wisconsin, example, we have a number of reservations and we will see proposals for research on topics like alcohol use during pregnancy on Indian reservations. Hot topic. The kind of thing that might get grant funding. This was a few years back around the time the cocaine babies was a very big deal, et cetera.

And it was troublesome to note that a place that is notoriously inadequately served by the health care system in general in a therapeutic sense, something beyond our control because it was controlled by the federal government and not by the state, was nonetheless going to have this sudden influx of people who would come in and often the protocols -- and I saw this on protocols that talked about work in other countries, which was the interesting kind of comparison suddenly. But as long as the researchers are there their health care services are going to be better than they have ever been because they are going to get more attention than they have ever gotten.

But, of course, when the researchers leave that all goes away and again it circles around to that comment that has been plaguing me ever since I heard it about the woman who said, "Nobody wants me

as a patient but they were all excited about having me as a subject." Justice in some ways requires that there be some commonality between the people who are being the subjects of research and the people who are benefiting from its results.

And I do not know what the answer to this is. I do not know because it is almost frightening to say, "Well, should enrollment as a research subject suddenly be a new way into publicly funded health services?" Does enrolling in an experiment give you one year's entitlement to eligibility for public service? I mean, that is scary. That is almost Dickensian although probably would be in the short term better for many people. And yet you do not want to make a condition of research of people who are otherwise unserved by the health care system that you provide services because then you will just reduce research even further in areas that it needs to be done.

I struggle with this. I do not know what the answer is but all I know is that there is a notion about justice that is bound up in the notion of commonality of democratizing research in both its risks and benefits so that each person who approaches it is a policy question of how you want it to run thinks of themselves as a potential beneficiary and a potential victim of it and makes the balance accordingly. What to do with that I do not know but I just wanted to mention it.

DR. CHILDRESS: It also raises for me two issues of compensation we talked about. One is compensation for participation in research. Obviously important if we are thinking about whether particular forms of compensation constitute undue inducements in relation to the consent for research. But also the area that has been

discussed for a couple of decades and not fully resolved, and that is compensation for research related injuries and issues of justice and community that arise in that regard, and those are obviously two areas that are important to think about.

Compensation for research related injuries we could think about in conceptual and normative terms, offer some recommendations.

Obviously there is empirical matters that would be useful to know for trying to recommend any particular proposal and someone recommended we consider what was done at the University of Washington in terms of the self insuring program to see what the experience has been in terms of the number of injuries reported and also the cost involved as a way to help us understand since it will not be possible probably to conduct the kind of larger study that might be useful.

I am not sure how far you want us to go in terms of getting the response at this point from NBAC members about the direction of the subcommittee report and how much you want to reserve for this afternoon.

DR. SHAPIRO: Well, thank you very much. I think that we will reserve the rest of the comments for this afternoon but we still have quite a bit of time to review where we are and where we want to go. And just to state once again to the commission my hope is that in the subcommittee meetings tomorrow morning the word product, if I could use such a word or such a phrase, will in fact be a kind of general outline of where it is that we want to go, what has to be built in, who is going to articulate it, so that we can begin to match resources against needs and

make the priority decisions that a lot of people have talked about here.

So I hope that that will be the work product of tomorrow morning's subcommittee meetings and that the discussion this afternoon, which will circle back at least in part for both this discussion and the discussion that will follow shortly on the management of genetic information will just simply contribute to that. And contribute to some ideas we might have on that.

Given the fact that it is 10:15, which we had scheduled a break, and there is enough -- a number of caffeine deprived members of NBAC, in view of stimulating our further discussion we will take our break right now. Thank you.

(Whereupon, a break was taken from 10:16 a.m. until 10:53 a.m.)

DISCUSSION OF THE ACTIVITIES OF THE NBAC GENETICS SUBCOMMITTEE

DR. SHAPIRO: Thank you. I would like to call our meeting back to order and move directly to our next item of business which is a report and discussion of the activities of the NBAC genetic subcommittee. I will have some other miscellaneous issues which we have to deal with which I will try to get to perhaps just before the lunch break. We will probably have to be a little more innovative in deciding what individually you want to do for lunch today given the storm that is going on outside but I am going to ask Bill to speak to that issue as we head towards 12:30 or so.

But let me now turn to Tom to inform us on how that committee's work is going and to once again express my gratitude to

him for his leadership in the work of this subcommittee. Tom?

DR. MURRAY: Thanks very much, Harold. The Genetics Subcommittee as it is becoming to be called met on the 13th of December. All the members had planned to attend.

Can you not hear? Okay. I will try to speak very close to the microphone. How is that? I mean, rock stars do this, don't they? They get right up to the microphone. I never thought of myself --

(Laughter.)

DR. MURRAY: All but one of us made it. That member was ill.

I do not want to encourage this business of our subcommittee is better than your subcommittee but we did have a very productive meeting.

(Laughter.)

DR. MURRAY: We did have a very good meeting due in significant measure to the members of the subcommittee, to the excellent planning by the NBAC staff, and to some guests who helped us out and I will mention them when I talk about the substantive areas of their concern.

We organized our meeting to talk about initially four topic areas. We identified the four areas based on our charge, on the discussions at the first meeting of the full commission, and on discussions substantive to that first meeting among NBAC members. Here were the four topics:

The first was tissue samples for DNA research, genetic research. The second was genetic privacy and there we had two guests

who were particularly helpful, two invited guests, Robert Gelmann and John Fannon (?). Third was genetic discrimination and our invited guest there was Karen Rothenberg. And fourth was gene patenting. Our invited guest was Rebecca Eisenberg and someone who stepped in at the last minute and did yeoman work of getting us started on the discussion was our very own commission member, Steve Holtzman.

Now we ended up deciding that two and three, that is genetic privacy and genetic discrimination, for our purposes at least were so joined together at the hip that we ought to treat them as a conjoint subject for the purposes of writing a report.

My plan for the time that we have today before lunch is to give a very brief overview of what we discussed at the meeting. That is giving you the four topics. We are going to treat them as three topics combining the middle two. Begin with a brief description of some of the other issues that were proposed at the beginning of our subcommittee meeting as possible subjects for NBAC work, things that were not in the list of four to begin with. Ask you if you have anything, your reactions to those, if you have anything else you would like to add, and then go to a discussion of the now three main topics, and I will enlist the help of my subcommittee -- fellow subcommittee members as well as the other commissioners in that discussion.

One thing we did try to do with -- well, you will judge how much success or lack of it -- was identify specific tasks to be accomplished. Studies to be done, papers to be written and the like. And I will again list the reasons insofar as I can reconstruct it from my notes and the transcript I will list what I took to be the task that we have

identified.

So I will begin with the possible other subjects for NBAC related to genetics not in the list of four. The first was to look at the commercialization of diagnostic genetic tests and/or the clinical availability of diagnostic genetic tests. Second was to look at the notion of group vulnerabilities in genetic research. The third was to consider the significance of the distinction and I am going to do a very crude job of trying to present the distinction between disease, genetic disease on the one hand and genetic defect, predisposition or something else on the other hand, but where you have a gene but you do not have a disease per se.

Another issue was, and this is one that turned out to recur in our conversations on that day, is genetics different? Is genetic information meaningfully and substantially different from other kinds of information or materials?

And lastly it was suggested we might consider the adequacy of the information held by health professionals about genetics. That is what is their ability to interpret, use and so forth, genetic information and genetic tests, et cetera, in their professional practices.

Now those were not on our list going into the meeting. Those are things that are potential candidates to add to the list. I will stop right now and just ask if anyone wishes to comment on any of those or to add to that list?

DR. SHAPIRO: Really not to add to the list but just a point of information. You talked -- apparently considered the distinctiveness of genetic information and so on, and education of health

professionals. Did any of this discussion in your subcommittee also kind of slop over so to speak or reach over to the issue of medical records all together or the confidentiality of medical records? Was that something that was part of that discussion or not?

DR. MURRAY: The answer is yes. It turns out to be a very important observation and when we get to genetic privacy we are going to spend some time thinking about that.

The plan then for today is to give you -- I will give you a quick run down of what I thought the significant points were in each of these subject areas and of the tasks that we had potentially -- we had identified as potential things to be done by NBAC and then just open it up. And I will try to take us through the various subjects by 12:30.

Alex?

PROF. CAPRON: I thought I saw in your transcript something which is I think slightly different than any of the topics you said were added. That is the question if we are talking about genetic information of the effects of genetic information on our understanding of the world and in particular on the effects on policies and practices in the kind of genetics versus environment range of issues which is in some ways an over arching question. The explanation of things in genetic terms.

It is not something for which a regulatory response is likely to be very useful but it is in some ways I think what worries a lot of people both at the gut level, the members of the public, and some of the people who have been articulate critics of certain genetic research and so forth, is the ways in which it rests on and perpetrates the sense that

what matters is genetics. This is happening because. And, of course, the controversy over the Maryland conference on genetics and violence, the whole genetics and intelligence debates.

But beyond that the explanation for people suffering diseases. Well, that is because of their genetic predisposition and sort of the blame the victim issue versus the environmental causes and so forth. I just -- I thought I detected some of that being raised at one point or another and I think it might be worth just as you have genetic disease versus predisposition as a potential topic which focuses on how do you understand an individual in any one stage of their life when they have a gene that has not manifested itself, the larger issue of the geneticity of things these days.

DR. MURRAY: Yes. That is a new one. I have heard geneticization. I have heard a few other --

PROF. CAPRON: Well, I think it --

DR. MURRAY: -- but, yes.

PROF. CAPRON: I use geneticity a long time ago. Susan Wolfe has recently written very interestingly about geneticization and whatever. That whole thrust. Genetic understanding, genetic explanation, genetic reductionism, all those are different words that can be used to describe the topic.

DR. MURRAY: Yes, fair enough. I think it was -- the concern which I think you have correctly identified was so pervasive through the many topics that it did not occur to me to pull it out but we certainly could if the commission should decide that is an appropriate thing to do.

PROF. CAPRON: Thank you.

DR. MURRAY: Let's turn then to the discussion of tissue samples. Well, we will in a moment.

Alta?

PROF. CHARO: This will be brief but I do think that behavioral genetics, I think is in fact having an enormous resurgence. The Violence and Genetics conference is only one example but the literature is now replete with more and more interest in this area. This is on my fantasy list for you. But my fantasy list for you would include focusing attention on the enormous range of settings in which that becomes pertinent in sociobiology, not just in criminal law, but in the development of social policy based upon prediction of people's characteristic behaviors and preferences, and tendencies, as well as a slop over into human subjects research.

DR. MURRAY: Okay. Any other new candidates?

Let's talk about tissue samples. I would invite anyone to read the full transcript of the subcommittee's deliberations because all I am going to give you is a -- I am pulling out a few things that struck me as particularly interesting observations.

One observation is that there are a number of samples and the image that was used was samples in purgatory. That is samples gathered before an increased consciousness about getting really detailed and careful informed consent for subsequent use of these samples but maybe really interesting and useful samples for scientific research. What should we think about those?

The question was raised, is genetic analysis of tissue

samples really all that different from other kinds of analyses of the same tissue. A series of concerns were articulated about possible uses of tissues for genetic research that -- about which people might be concerned. One was the possible use of information obtained from such research to discriminate against individuals.

A second was to do research on differences between groups. Research that the groups themselves might object to or at least significant numbers of the members of such groups might object to.

A third concern, about which I have a more difficult time flushing out but I am concerned that there is something not natural -- unnatural about doing this sort of research in this way.

A theme that also emerged and the metaphor that we used to describe it, I will get to it in a minute, but a theme that emerged was to look at different views among different -- within the larger American scene among different cultures, religious groups, ethnic groups, potentially different views about the meaning of tissue and the meaning of genetic research on human tissue.

The metaphor we used was you can do a public opinion survey and that is sort of taking the average depth of the lake, but there might be parts of the lake that are in fact very deep and you could be in real trouble if you step into that part of the lake depending on the judgment of what the average depth was. It might be useful to find out what the different regions of the lake are in fact like.

A final issue that was problematic even within the subcommittee about whether we should even address it was compensation. If you get tissue samples what, if anything, do you have

to do or should we think about in the way of compensation for the people who provided those tissue samples?

Now among the tasks we identified I have four listed that I think there was some consensus or near consensus that these would be valuable components of any report we might do and two others that are possible candidates that we might include.

Now the four tasks include (1) an analytic paper on these cultural, religious and ethnic differences and their views about tissue samples and genetic research.

A second was a sampling of public opinion in the line of a general or Gallop or Roper poll about tissue samples, informed consent and their use for genetic research.

A third was focus group research. That is rather than kind of measuring the average depth of the lake at least getting some groups together, smaller groups together and asking them in a more detailed and richer way their views about the use of such tissues for genetic research. We subsequently learned that part of this third issue, the focus group issue, some of that has been done and we are going to hear about that tomorrow morning.

The fourth component was a normative analysis, an ethical analysis of the various position statements. We had at our disposal as I recall five different position statements from different organizations and collections of individuals about the use of tissue samples and informed consent for that use.

So we thought it would be helpful to have a careful sort of conceptual mapping of the different views, an identification of what were

seen to be the central and important issues, and a normative analysis of those to see whether, in fact, what the basis of those claims seemed to be and whether they seemed to be valid and legitimate claims.

Now two other items that arose, I do not recall us having a consensus about them, but one is it would be useful to have an international perspective. What are other countries thinking about the same issue either officially in terms of public statements or in terms of the discourse that is going on in those countries.

And lastly, a possible -- one of the things we could do in a product is to look -- do a kind of policy analysis of options. Now from my reading of the transcript I do not think we made a decision whether that was the right way to end up with or not. But that was -- I wanted to mention it because it was raised as a possible product.

Let me invite other members of the subcommittee now to elaborate and I see Larry and I see Zeke.

DR. MIIKE: On the issue of tissue samples I guess there are several considerations. One was that it was a discrete enough topic that it was do-able in a fairly short time frame. However, what our concern -- I guess our concerns were or I should say at least mine were twofold. One was that do we have a framework in which we would make that decision, whatever that decision is. And we spent, I think, a lot of time talking about that. And we will get into that I believe later on as to what our framework would be.

The other part was that do people really care other than the people who are in limbo in purgatory with these tissues and that is how we got into the issue about what is this -- what is the value of this to

the public. And then we got into a discussion about -- then what do we mean by the public and how do we get that information from them? If we do the Gallop type poll that is a very expensive way of going about it. So we are trying to find some practical means about a level of comfortableness in terms of is this an important issue to the public and do we need to -- and what import would we give to the information that we get about what the importance are to the public in our decision making.

I guess we have never really decided, although it was implicit that we should -- let me back up a minute by saying that from my standpoint I think we need to make a decision based upon the collective value of this group and not be -- not say we make a decision because this is what the public wants. But we also -- but on the other hand we wanted to get a sense of, number one, the importance of this issue if they did not know it was an issue out there and then if they do have opinions about it what it is.

DR. MURRAY: Zeke?

DR. EMANUEL: To some degree my comments just echo what Larry said. One of the reasons we did identify the tissue samples is that everyone at least given the position statements is talking the same language and the same conceptual framework which makes a tractable problem simply that is do-able in short order so we can have a report.

But there is this countervailing concern which is it somehow does not seem to rise -- or to address some of the depth of the issues. And there was this concern that this may be a sort of -- to use a phrase, a geek issue for the research scientists and not for the, you

know, many, many other people who are very concerned. And we may have this sort of marginalization of our endeavor in that way. Nevertheless, I think we did conclude that it was of very significant importance for the research endeavor.

DR. COX: So from my personal point of view of this I completely agree with what both Larry and Zeke said but I see this issue as a hook in a way because there is this tremendous volume of reports and we are not a loss of people telling us what to do on this and except from the context of the people whose sample it is. And so whatever that public is, is that this is a hook by basically showing that if we want to consider these issues we want to look at not just the people who are stakeholders in the context of professional societies or other things, but we want to look more broadly at sort of what the national interest is.

So I think that while it is geeky in a way, it demonstrates that there are some stakeholders here who perhaps have not been heard from and then if we can look at all of this then that is a start of going in and of bringing those stakeholders in to the other issues. So I see it sort of as a hook.

DR. SHAPIRO: Just for the benefit of the older generation would someone tell me what "geeky" is supposed to mean here?

PROF. CHARO: What most of your students at Princeton are like.

(Laughter.)

DR. SHAPIRO: I do not know if that is too encouraging.

(Laughter.)

DR. COX: Harold, look at Saturday morning cartoons and

at how scientists are represented. That is the definition.

(Laughter.)

DR. MURRAY: I guess we should be grateful that ethicists have not appeared on Saturday morning cartoons yet. Heaven only knows what we would be represented like.

DR. SHAPIRO: I have just one or two comments or observations on this. That is I did read the material that was sent around and I guess most of you have also on the focus groups which was done on this specific issue although related to a particular area.

What struck me about that is that we are unlikely to find out what they think, whoever they is, simply by doing something which attaches itself to a national survey. People will not know what we are talking about. We will not get at the issue. So it strikes me that from the point of view of trying to get some sense of that that perhaps it is true that this focus group type where one could really explain the problem to an appropriate group of people might really be the best research strategy. That is just something we will have to -- the committee would discuss.

It seems to me, however, there is one other aspect of this in which we could perform a very useful service as part of our report on this -- as to our part of what we have to say on this issue. And that is to clarify for people why this is an important issue. There are real important issues here. It may not be on anybody's top 50 list if you just take a random sample but there are important issues as I understand it in medical science that this issue addresses.

And we could perform, I think, a useful aspect or

educational function and something, Tom, you and your subcommittee might want to think about just by highlighting why it is that the geeks care about this problem and why we believe others might want to care about this.

PROF. BACKLAR: Because the "others" are stakeholders but they do not know it.

DR. MURRAY: Right. Actually I think, Harold, I think for every report this commission issues part of the -- one of the necessary ingredients in that report ought to be an explanation of why this is significant, why it matters, and it also ought to be in as plain an English as possible. I mean, a good model was the Presidential Commission in which I believe Alex was involved some years ago. So I think that is -- we will try to do that and I think it is important.

PROF. CHARO: In my experience on an IRB we periodically had problems that involved going back to stored tissue samples and I suspect many other IRBs have that experience too. So either by surveying IRBs that are known to exist because they are part of the multiple insurance program or by surveying the state labs where many large sample collections exist it might be possible to begin to get a handle on which protocols involve that kind of thing, often going back to people because of new information that made those samples useable in a different fashion and beginning to be able to identify the people you might want to survey. Because I think that that information exists already indirectly.

DR. MURRAY: When you say "that information" --

PROF. CHARO: Larry was saying that it would be -- one of

the tasks is figuring out how to identify which people to talk with in a way that is efficient and I am simply saying that our experience is that there are large numbers of people that already have been in the position of having to deal with how they want to react to people who want to use their stored samples for some other purpose and that they might be a good place to start.

DR. MURRAY: I have the word that Zeke has articulated but we did not call it a "geek" concern in the subcommittee meeting but it is as good a label as any that this would be seen as too much an insider issue. I think that it remains a danger. I think if the subcommittee -- if the commission rather is to take this on we really have to make the case as powerfully as possible that this is -- that there are stakeholders that just do not know it yet but we can explain why they are stakeholders and why it should matter and what difference it makes to them.

I became convinced in the course of our discussions in the subcommittee that this question of what happens with tissue samples, issues of informed consent about those tissue samples really go to the nature of the relationship between on the one hand the scientific community and on the other hand those individuals and everybody else who both supplies the tissues and occasionally their own bodies for the purpose of scientific research.

PROF. BACKLAR: And also the members of the -- the pedigree so to speak. We go back to this whole community discussion. It is more than just those individuals.

DR. MURRAY: Right. Carol?

DR. GREIDER: I would just like to reiterate and underline what David said before. My understanding from our discussion about the tissue sample was that it really encompasses a lot of the other issues. Tissue samples means DNA which gets to the issue of the genetic privacy and genetic discrimination. So I really do not see it as an insider sort of an issue but rather a means to an ends to a lot of the other things that the commission wanted to address. So that is what I understood David to mean as a hook to get at some of these other issues.

DR. MURRAY: Okay. Trish and Zeke?

PROF. BACKLAR: Two things. One is again to emphasize that however we do this we do it in ordinary language and the other piece of it is looking at what Alex said is how will genetics make the way we look at ourselves or will it change the way we see ourselves.

DR. MURRAY: Zeke?

DR. EMANUEL: I think the point of having a report that does educate people as to why this is more than insider interest is key. But the other thing we did mention I believe if my memory is not failing me is that it also depends on the context of the other reports we are going to undertake if this "insider" issue is in the context of other reports that are -- that clearly palpably, intuitively, instantaneously are of concern to people like the next two, the discrimination and privacy. As long as people understand that we are taking their concerns, the ones they can articulate without prompting, then I think this concern is of lesser significance. So I think both of those, how the report is phrased and how it is -- and in what context it appears are key.

DR. MURRAY: Eric had wanted to speak and then David.

DR. CASSELL: I wanted to underline Carol's remarks before. I think that it is an insider concern if it is separated off -- if the problem of tissue samples is separated off from the whole entire problem of genetic determinism. I mean, what gets people upset and worried about it is the idea of almost like earlier in this century of unconscious determinate which renders people powerless. When they begin to understand that the tissue sample is all part of that larger issue and we are perfectly clear about it and elevated away from the issue of genetic reductionism which is a real concern I think people will see that it is not a narrow thing that belongs to scientist. A geek no longer meaning the person who bites off the chicken's head.

DR. MURRAY: Yes, thanks. David and Alex?

DR. COX: I would like to just be very specific about my point of view of how it broadens out in addition to what has already been said by the previous speakers. We talked earlier about this issue of what defines research versus medical practice and what kind of information you use and supply to people to affect their lives as opposed to do not give them information because it is just research.

Stored tissue samples are at the crux of this because, in fact, the way the whole paradigm is being laid down in some views is the stored tissue samples are just for research. So that it is not such a big issue. In fact, I think a lot of people would view stored tissue samples as the vehicle to lots of information on which they would make decisions about their life.

So I think that already this turf is being divided up with

stored tissue samples as the sort of ball in this game of what is research and what should research subjects get vis-a-vis their life and medical practice. So that I think it is a perfect ball to discuss that particular issue which came up in the earlier subcommittee discussion.

DR. MURRAY: Thanks. Alex?

PROF. CAPRON: I think we are probably on this subject at the point of a tactical question eventually which is whether we imbed this particular -- the discussion of this particular topic in a larger report in which it will automatically -- the context that goes beyond the question of stored tissue samples being analyzed to the question of the use of the information, the obligations of researchers for the medical well-being of the people whose information they have now found out through a retrospective analysis of the samples or whatever will come out or whether we issue it as a separate report in which we have to elude to those issues of discrimination and privacy and so forth and say that those are being written about separately.

I would gather it would premature for us to figure that out but I think it is important that we have a discussion and are aware of it.

Obviously in a certain way we could be discussing this issue under Jim's subcommittee. That is to say if the primary question is a difficulty that arises as to the obligations of permission and disclosure to the people from whom the samples come, as a research question -- and I agree, David, it may have nonresearch implications, but if the person is saying we do not know, do we have a useful marker here, how often does it occur in the population, et cetera, et cetera, I need to look at some samples. There are some here. Can I use them? Is a

research issue at that point and if we were to have a very full research report ready by October but we do not have a very full genetics report we might even find this an instance of a difficulty in managing research issues and imbed it there.

I also think that the correct term is "nerd" and not "geek" for what we are talking about.

(Laughter.)

DR. MURRAY: Do we need a report on that or is that --

(Laughter.)

DR. MURRAY: -- list that as a disagreement.

DR. MIIKE: Let me just expand on Alex's comments. I think before we issue any specific report we need to issue a statement by the commission about how we see our charge and how we are going to address it. I think that within that broad context you can explain in a fairly succinct and straight forward manner why we decided to pick up and focus on the topics that we are going to do. I think that -- and that would mean a melding of both the -- both subcommittee reports and it seems to me that is a pretty straight forward task that we can do.

DR. CASSELL: Just as a quick point of information have not there been uses of the large stored serum banks particularly when serologies for syphilis were part of premarital? Was there an obligation at that time to report back to the person what the finding was on their serum?

DR. MIIKE: It is too bad that Bernie is not here but we did discuss that issue around the context of prevalence of HIV infection among stored samples for hepatitis B testing, I believe, and that Bernie

did explain in some detail to us that when that issue came up it did go back to that particular community to get into the issue about consent and the importance of those kinds of things. So there are parallels that go outside the genetic area.

PROF. CAPRON: In a separate comment I wanted to echo what I took to be Harold's concern and several other people with the thought of our conducting at this point in time any public opinion poll. I just do not think that the issue of stored tissue samples has enough salience to people that you are going to get answers that mean anything. And some of you may recall a March of Dimes -- I think it was Gallop, Harris or Gallop, March of Dimes sponsored poll a few years ago that was trumpeted the results that most members of the public were quite sanguine about genetic research and about gene therapy, and 70 to 80 percent said it was a good idea and so forth.

Later in the questionnaire, of course, they were asked if they knew anything about genetics or gene therapy and almost 80 or 90 percent had no idea what the subject was and so forth. You know what do you find out through public opinion polls about? So to the extent that it was raised as a possible avenue of research and that several people have commented I will add my comments to those that say it does not sound like given the great expense that Larry noted would be associated with it, does not sound like a good use of money. I know it does not mean that it does not belong in the list but way down at the bottom.

DR. MURRAY: Alta?

PROF. CHARO: Without suggesting how high a priority it will be, I think actually, Alex, there are subpopulations that have a very

concrete understanding of certain applications and that would be different.

PROF. CAPRON: That is not a public opinion. It would be a panel's opinion. I have no objection to your suggestion.

PROF. CHARO: Right. That is why I am saying I do not think we need to limit our thinking about this to public opinion polls and then say it is impossible to find out what the stakeholders think. There are subpopulations that have been contacted about whether or not they want retesting for more sophisticated markers for CF, for example, and there are -- it is a criminal population and the criminal bar with regard to sampling of evidence that has been stored. There are distinctly different subpopulations. They may be more accessible and more realistic.

DR. MURRAY: Bette?

MS. KRAMER: Well, I think that since every stakeholder except the public has expressed their point of view that we are certainly I think well advised to investigate whether or not the material can be gleaned from any kind of a survey. I think it really would fall to the role of professional survey people to advise us as to could it be done, how could it be done, at what cost, et cetera. It certainly bears looking into.

DR. MURRAY: Let me just make a point about how we have kind of parsed the questions both between subcommittees and certainly within the Genetic Subcommittee. I am not going to defend the proposition that these distinctions are hard, fast and absolute. They are not. In fact, one of the things as has been pointed out that makes the tissue sample question interesting is that it does have tendrils that reach out to the privacy and discrimination. It has other implications as well.

It also has tendrils that reach out to human subjects research.

I think if we take it as an absolute requirement that whenever we write a report on it, it be completely distinguishable from anything else we are interested in, we will not have any boundaries. My sense of the subcommittee's views about this is that the issue of tissue samples was of significant concern immediately, had big enough ripples and ramifications that it was worth the commission's time and effort.

Furthermore, it was relatively definable and something that we probably could not finish our work on within our first year of life. That is how we approached the resource question. We assume we are going to have adequate resources. We just do not know for how long. So we want to do something within the first year to be sure we actually have something done and to show at the end of the first year.

The other two broad areas you are going to hear us talk about now are things we just know we cannot do in a year and so we would -- they are going -- we are going to take them up on the presumption that the commission's life will extend beyond this current year.

What I would like to try to do is move on to the second subject. It is now about 11:30 and this will give us roughly 30 minutes for each of the next two big issues.

Is that all right? Is there any finishing comments on the tissue sample question?

DR. SHAPIRO: Just to say a word about agenda and timing. It is true we have a half hour for each of these. We do have some flexibility this afternoon. So if you feel that you would like to go

longer with any one of these you should feel free to do so. We can pick up the other one later. So just do not be too constrained by the agenda.

DR. MURRAY: Part of me wants to say thank you and part of me wants to say, ooh, it is nice to have limits.

(Laughter.)

DR. MURRAY: We will try to finish them and if we do not and if discussion is really substantive and people care about it we will just thank you for the permission and we will go on.

Well, the next issue we had, as I said privacy as distinguished from discrimination. But one of the conclusions we reached was that at least for our purposes as a commission it probably makes sense to treat the two of them in a single report. But let's -- nonetheless, let's begin with privacy.

We had Bob Gelmann and John Fannon who are two privacy mavins. We had their assistance. Bob Gelmann had a particularly effective way of sort of describing cases or incidences or facts in the world. So I am going to share a couple of them with you. One said -- Bob said, "Well, if you are thinking about privacy, even just medical privacy, think about this case: Someone with Huntington's -- the gene for Huntington's disease who has AIDS who is a drug abuser and who because of all this is depressed." Bob is a -- he is not a legislator. He is a person who writes legislation and regulations I guess.

He said, "That could easily fall into four or five different legislative regimes depending on how we do it." He also said, "You know what is sensitive information to some people may not be so sensitive to others." That he knows lots of people who see psychiatrists. They tell

him all about it. He says he does not know anyone who has ever been to a proctologist.

(Laughter.)

DR. MURRAY: We also heard, I do not remember who we heard this from --

DR. CASSELL: Well, but people do not hold back from telling that they have been to psychiatrists on their employment forms. I mean, you know, about proctologists, but they do about psychiatrists.

DR. MURRAY: So it is not just different sensitivity, it is different sensitivity within different context and for different purposes. It is a good point.

Another observation was made that the amount of medically relevant information about people is multiplying and it is becoming more and more electronic in its form and better organized. For example, apparently as there has been a consolidation in the pharmacy industry, not the drug producers but the retailers, we have computerized pharmaceutical records that may, in fact, be chain wide and in that sense national in scope.

Gelmann's interest is not just medical privacy but is privacy in general. He talks about the growing vast quantities of information available about potentially each of those. Somewhere somebody may know what your favorite pizza toppings are. Certainly people know when you use your credit cards, where you use them and what shops you are buying in.

PROF. CHARO: They know which groceries I buy. The coupons are particular to what I bought that day.

DR. MURRAY: Okay. It was also pointed out to us that much privacy -- privacy law in the U.S. is a fairly scattered affair. Here I will certainly defer to the lawyers around the table. This is what I recall us being told. Particularly with electronic information and particularly with a lot of privacy law being state based. Those state based laws become increasingly ineffective and we were told that it might even be the case that we do not know where physically your records reside.

They may be on a computer server in a state quite a different from the state in which you live, even different from the state in which the organization you are dealing with is because they may contract out the electronic record keeping to another organization.

PROF. CAPRON: There are all kinds of possibilities.

DR. MURRAY: Do you want to say that aloud?

A question that emerged in a couple of different forms was and one of the things that we might look at is why is privacy important? Well, sometimes the simplest sounding questions are the most interesting and profound. I thought that was a pretty interesting question. What values do we see at stake in our concerns about privacy? Here I think we are not limited just to medical privacy but more broadly concerns about privacy. But then specifically within privacy to court, privacy about medical information, and then privacy about genetic information.

DR. CASSELL: May I comment on that?

DR. MURRAY: Please.

DR. CASSELL: One of the interesting things about biology is that any close look at any biological system starting way, way down at

the subcellular level is that every piece is different than every other piece. If you assemble a human being, every human being is really very different than every other human being except when you come to behavior in groups. That just will not do. You cannot have a behavior in groups if everybody really acted differently than everybody else and so when you see everything like from traffic to school patterns and so forth you see conformity to a general rule.

One of the things that happens in medicine particularly is that different behaviors do out -- they do become known and one of the major reasons I believe for the confidentiality rule that is part of every medical oath is the fact that one's difference from the community can become clear in what happens to one medically and what one does and so forth and so on.

In order to keep a society together the conformity is really necessary. In order that people can be who they are differences are really necessary. Privacy preserves -- first of all, it preserves the illusion that we are not so different on the one hand. But it also preserves the ability to remain different and not to live your life as you are. I do not mean just in a democratic society.

I mean in all societies privacy permits that and that is why it is so interesting when you find cultures where privacy is really actively suppressed. There is a culture which interestingly enough shaves pubic hair and it is a culture which suppresses privacy rigorously. So the issue of privacy really strikes at the way people live their lives apart from the social world in which they exist.

DR. MURRAY: Alta?

PROF. CHARO: Leaving what I think would be a fascinating anecdote, but I do want to hear more about it maybe at lunch.

DR. CASSELL: Some other time, Alta.

PROF. CHARO: Yes. I agree the question is fascinating but I would like to ask a different question and that is whether we should start from a different presumption. And that is that there is no privacy and move forward on that basis.

Given the technological difficulties of achieving security across computers as now exists, given the phenomenal number of small pieces of information gathered by myriad different organizations for different purposes that in theory can be put together and on occasion are put together by people who have a will to do so, whether it is credit investigation or it is the FBI background checks, given that medical record privacy is a ludicrous notion considering the sheer number of people who see medical records in the hospital on paper as well as the computerization problem, maybe it is worth at least asking should we start all discussions on the theory that there is no privacy if somebody wants to put it together and there will not be until sometime in the future when we have both the legislative and technological skills to achieve this kind of compartmentalized information storage and then move on from there?

That the real question is, is there somebody who is interested in getting the information? Because actually being a New Yorker my notion of privacy is more anonymity and the lack of interest on the part of other people than it is of being physically hidden or having

data physically not available. It is the confluence that nobody cares. Now that I live in a much smaller town I have discovered how little privacy I actually have because almost everything I do is seen or noted by people who happen to know me and might have at least a passing interest. That has been the distinction.

DR. CASSELL: Put the two comments together that there is an absolute human need to be private and that there is no privacy and then you begin to see how people exercise a need to be private in a world where there is no privacy just as you have changed how you exercise your need to be private in your new small town.

PROF. CHARO: Right. I lie much more often.

DR. CASSELL: Exactly. Exactly.

PROF. CAPRON: I was going to say that there is a --

(Simultaneous discussion.)

PROF. CAPRON: -- that again there is a link to the human subjects field here because there is some literature on the offense that people take at the notion of anthropologists or sociologists studying them in public settings in which you on one level have no expectation of privacy. You are doing something in a group. You are at a demonstration or you are in a crowded theater or whatever. But the notion that in that group someone has chosen to study your particular behavior and then maybe afterwards come up and try to find out some demographic facts from you is bothersome to people.

There is a whole literature going back to what's his name, Lord Humphrey's book on the Tea Room trade in which a researcher was studying sexual interactions in men's rooms and then under the guise of

doing some other social or health survey or something went to the homes of the people to try to get demographic data about them. That, of course, is --

(Simultaneous discussion.)

DR. CASSELL: He is saying --

PROF. CAPRON: It is a very famous -- it is a very, very famous study. But out of that because that was a sensitive subject people then wrote in the literature about the questions of what if they were just watching mothers and children in shoe stores interacting with the children being -- acting as children and seeing how the mothers controlled them in a public setting where they are trying to get them to do something that the kids have very little interest in or something. I mean, a study that on the face of it, I mean do you sit in a shoe store with your kids and you know everybody could watch you but you do not really think about that, but is it different.

So I think Alta is right that there is a question there that again ties in. It is an interesting subject. I think as always anything that challenges assumptions and says we ought to look at it from the other way around, that is to say there is no privacy, and then what do we do about that, is interesting. That is not the normative statement I hope on your part.

PROF. CHARO: That there ought not be a privacy --

PROF. CAPRON: Right.

PROF. CHARO: No. That is simply a statement of my perceived facts.

DR. MURRAY: I am tempted to make a flippant response

which is that could be a very short report. There is no privacy, it is a fiction. Next. Although even the privacy mavens with whom we spoke said that, you know, privacy is not an absolute thing. It is a matter of how difficult you want to make it for someone who really wants to know or how casually available information in an organized form that is accessible to others. So it is a -- you know, it is a matter of -- you do not erect impermeable walls but you make it more and more difficult to get or put together information in certain ways.

PROF. CAPRON: For the record I want to note that if you are interested in the issue of the use of tissue samples you are a geek but if you are interested in privacy you are a maven. Right?

DR. MURRAY: I thought we were nerds.

PROF. CAPRON: No, that is your description.

DR. SHAPIRO: I would just like to say this last issue that came up that I guess Alex brought up that while there is no absolute privacy there is a very big difference between that which I accept as a reality today as Alta has suggested, all you have to do is buy a prescription drug somewhere and you can watch coming up on the screen the person in front of you -- the total prescription record is just right before your eyes if you want to see it. There is a -- I accept that myself as a statement of fact, which is a very big difference between what Alta said which is with those the will and capacity to find it. That is a big step because it does take -- it is just not casually available. That is something that has to be -- I guess a point Alex made.

PROF. CHARO: Well, I have got to say that my point in saying this was simply that in the committee's work on how to handle

questions about information that will be generated, I was simply saying it might be interesting to approach it not from the point of view of how do we preserve the privacy that exists but to start with the notion that there is no privacy and what does that mean about what information you are willing to generate as well as in what form you will store it to make it more or less difficult.

But I will tell you I do not know how much you are a computer geek, maven, nerd, but I am a semi-geek, maven, nerd and I have found out the most extraordinary things when I have got insomnia. And you would be amazed at how easy it is for example to wonder exactly where somebody got the cash advance on their book to be able to finance such a rapid transition from their condo on lower Connecticut to upper Wisconsin within a month of, for example, a change of administration. This is kind of creepy. He has also got an extra half bath.

DR. MURRAY: That is kind of creepy. Does anyone have anything to say about that?

PROF. BACKLAR: Yes.

DR. MURRAY: Trish?

PROF. BACKLAR: I think in the mid-80's Mark Zeigler wrote a paper which is very apt -- the title of which is very apt, Confidentiality is a Decrepid Concept. And I think Alta's suggestion or the way I see it is actually it might be very useful for us and that is knowing that this is so, that there really is no privacy, if you want to get the information it is available, what is it that we value most. What is it that we are going to be the most concerned with about keeping private?

What is it that is the most important for all the stakeholders?

DR. MURRAY: Thanks, Trish. Zeke and Alex?

DR. EMANUEL: Yes. I thought one of the most interesting things about our discussion at the subcommittee meeting was when Bob Gelmann sort of rattled off to us about the policy train and the legislative train that was rushing down the tracks in terms of privacy in the health area. He sort of certainly personally threw me aback in some way saying whatever you do is going to be irrelevant to the legislative train predicting that we were going to have legislation on privacy, you know, either in this session or shortly thereafter, certainly before we could get going. I thought that was relevant in the sense of framing what we would be doing when we looked at the issue of genetic privacy in that we have to choose our targets likely differently.

The impact would not be going down towards legislation and I think evolving out of that discussion was a notion similar to what Alta is articulating here which is we need to take the bigger picture. Why do we value privacy and what areas do we value it? What are the context that make us value it differently in different areas?

So it really was while not be divorced from the legislative problem because no doubt whatever legislation passed would have big gaping holes, will require interpretation, et cetera, it was a -- maybe one step higher that we need -- I thought had agreed we needed to focus. Sort of conceptual normative with important policy implications but ones that may as it were not be immediate for the current Washington context.

So I think that might put -- I mean, these comments that

have recently been made were I think understood in that conversation and clearly are ones that were shared by the subcommittee. It may be in a different -- phrased in a different way.

DR. MURRAY: It is a good reminder, Zeke. In fact, I think we did have a conversation about what sort of flavor of a report that we might do could have and it was much more to be conceptual, a statement about what is important about privacy rather than a detailed recommendation for legislation.

On the other hand, as I remembered what Gelmann and others said the sense was that whatever happened, first of all it may not happen that fast and, second, whatever happens would be only very partial and incomplete and so it will continue to evolve, and we should not see this as a sort of policy train that is about to reach its destination but as just sort of one stop along a very long route and we might, in fact, be issuing our report long before it has reached whatever its end life is.

DR. EMANUEL: Yes. I thought they said in that context that there would be a lot of -- I think their phrase was "weasel" words that would need interpretation and one of the things we could help with was the sort of conceptual background to the interpretation that would be useful.

DR. MURRAY: I have three people in line here and they are Alex, Eric and then Jim.

PROF. CAPRON: Two quick comments. The first is on this issue unlike the previous issue, Bette, I do think that it might be possible to have some useful input on public opinion because it seems to me that this is an issue that has a lot of salience. People do think about

this. It is generally in their lives. Indeed, sometimes those studies can come up with surprising results.

One of the studies that the President's Commission did involved also a public opinion poll on the issue of informed consent and I was surprised, maybe no one else was, but to find out that the public's basic view was that this was just something that doctors use to protect themselves. They did not see it as protective in patients by a strong majority. Not something that had been in the literature before. That was the public's view. That should affect the way we talk about it and we think about policy. The same thing may turn out in this privacy issue.

The second thing is one of the -- the only direct charge to the President's Commission that it did not execute was a report on privacy and confidentiality. We began looking at the issue. We commissioned a couple of studies and in our final report we said that Congress is dealing with this issue and we were -- the reason we did that was we went up -- when we were talking to the people on the Hill they said, "Do not worry about that. We are dealing with it." Bob Gelmann had written a very interesting report. That was 1982.

As far as I know most of the recommendations that Bob was talking about there that were going to be in legislation like this are still not in legislation. I would think that the major issue that we have in this area is asking is there anything about genetic privacy that deserves separate treatment or is our major conclusion that the kinds of concerns that may now be grabbing attention about genetic privacy actually apply more broadly to other medical and scientific and research records, and so forth, and we can have useful things to say about it by insisting that it

not be treated differently.

DR. MURRAY: Eric?

DR. CASSELL: Well, I am struck that here as in other areas there is a -- we have -- privacy is destroyed in part by a conflict of interest. I mean, when that appears on the screen of your local pharmacist there are a strong interest in having that information all in one place. There are often commercial interests. The other is an individual interest. So it is a conflict of individual and larger interest that I do not think we should allow to disappear from view.

I do not think we should treat it as relatively small pieces of a privacy issue, as though it is just genetic and so forth, but we should take the opportunity to grab a part of the larger. We are now in an age in which the constant conflict in a democracy between the interest of individuals and the interest, the corporate interest, however you define conflict, constant tension from the very beginning is now tilted by virtue of an electronic revolution. And that is -- I think we have to keep ourselves against that problem.

PROF. BACKLAR: And also the way we deliver health care at this point causes a lot of that tension.

DR. MURRAY: Jim and Bette?

DR. CHILDRESS: Perhaps one part of the conceptual work that is important is to deal with the distinction and overlap between privacy and confidentiality. Both terms have been used today. Sometimes they have been used interchangeably. But there may be some more distinctions and in some of the legislation that has been proposed sometimes it is on some privacy, sometimes it is on

confidentiality.

I think it is important to attend to the areas of overlap and also the way in which these concepts function distinctively. With privacy being, according at least to one understanding of a state or condition of limited access to a person or information about that person, and confidentiality emerging within a relationship where there is already access to the person or information about the person, but then further limitations are set on additional access, and how those work out in practice I think would be very important.

Another way in which they differ is that medical confidentiality is something you can find in virtually every code of medical ethics cross cultures and time. Whereas privacy, as we understand it in the U.S. at any rate is a much more recent innovation conceptually and the way it functions in both ethical and legal reflection.

I would also note that this is another area of major overlap between the two subcommittees and even though we did not specifically focus on privacy and confidentiality it is really an important part of the whole area of research involving human subjects.

DR. MURRAY: Thanks, Jim. Bette and Steve?

MS. KRAMER: I am rather intrigued by Alta's suggestion that we take a look at the issue and try to get a handle on the issue because we had so much trouble getting a handle on the issue beginning with a statement that there is no privacy and then take a look at what are the evils or the potential evils that ensue and I think that Eric's last comment is appropriate.

I think the comment that was made at the meeting that if

you could fix discrimination then privacy does not become so much of a problem. I think it might be an interesting way to take a look at the problem.

DR. MURRAY: Steve?

MR. HOLTZMAN: One of the things that our subcommittee kept coming back to and you mentioned in the beginning is, is genetics distinctive and should we take that on as a separate topic? And Alex just mentioned in the context of this that maybe the essential issue we should be tackling given our charge to look at genetic information and its management is distinctive.

Maybe it is obvious that we could use that for all of these issues. Instead of taking on abstractly is genetic information special is rather say in this context is it special, in this context is it special, in this context is it special and, if so, why. Just as a way to tie it all together.

DR. MURRAY: Okay. Alta?

PROF. CHARO: Actually in keeping on to the very concrete, I do think that some of these things may fall together again. For example, as I understand it from the presentation at the first meeting, a big dilemma in the area of stored tissue has to do with identifiable versus nonidentifiable sampling techniques. Because identifiable techniques have advantages in terms of being able to improve the quality of the follow up research that will improve the quality of the fundamental epidemiological stuff.

On the other hand if you start with certain kinds of attitudes about the impossibility of real guarantees it gets you a step forward I think in the discussion about whether or not what remains in

terms of potential uses of information is enough to justify a recommendation against identifiable collections at all. I mean, I am not saying that that is where we ought to go but I think it gets you forward because you do not have unrealistic cost benefit balances.

I think, though, it is also important to understand in a very concrete fashion some of the other costs. Eric talked on his e-mail at one point about the way in which medical records are no longer genuine documents of true situations because of the perception that those records are not going to be able to stay local, that they will be transmitted.

I can testify from personal experience in the reproductive area that it is extremely common for physicians to not list whether or not a woman has had an abortion on her medical record. They will say how many pregnancies, how many live births. What is left ambiguous is whether she miscarried accidentally or whether she miscarried deliberately, i.e. had an abortion, in terms of the nonlive births.

Now this has real consequences. I mean today they finally announced the results of a huge study in Denmark on the relationship between abortion and breast cancer which is credible only because there they actually did know which women had abortions. And all the stuff that was done in the United States in which they thought they were finding these kinds of connections had the underlying problem that they did not accurately know whether or not the women who were being reported to have never had an abortion had never had an abortion which was screwing up the data.

There are going to be many, many concrete examples of

this in which we can identify the costs of this kind of failure to accurately make our medical records reflect what is going on which, in turn, I think is about the fact that things are not confidential.

The more that we begin to move towards a rejection of identifiable collections, of identifiable information, and move towards a more population based approach as the best solution in a bad time in which you give up on some of the benefits of very individualized information being widely available for certain purposes and you say we are going to do things on an epidemiological basis and that will feed into insurance patterns that are based on community ratings because there will not be a way to get individual information, et cetera. You may find that you are beginning to move thematically towards a notion that we are not capable at this point of handling individualized information very well.

I am not -- again I am not prejudging and saying that is what I think ought to happen but it may be a way to kind of tie things together.

DR. MURRAY: I am going to complicate our task a little further. When I introduced this session I said that we decided after having talked about genetic privacy and then genetic information that they ought to be treated together. Well, I did not get through my little list of things in genetic privacy and confidentiality. So I am going to try to do that quickly and also just mention the discrimination piece of the pie. It is a massive piece and I do not pretend that we do anything exhaustive with it.

One of the issues of the confidentiality -- we used the rubric privacy, Jim. We were not very precise. The issue of genetic

privacy was behavior genetics. That was thought to be particularly important.

Also something that was mentioned, although I think it was mentioned more than once but I am not sure it is a terribly important issue in the larger context although it is very important for particular research projects, are certificates of confidentiality which can be given to specific research projects. I want to just get that on the record.

Let me list the tasks together. The potential tasks together. In discrimination the discussion was as you might imagine very lively. Just to note a few highlights of it. There obviously has been some research and some scholarship and some reporting, public reporting on the possibility or existence of genetic discrimination. Some of the things that are lesser known include that a number of states, I am not sure of the precise number, it is between 10 and 15 I think, have passed laws recently designed to fight genetic discrimination in one form or another.

Karen Rothenberg had given us an update on that. I cannot -- does anyone here remember the number of state statutes?

PROF. CAPRON: Health insurance?

DR. MURRAY: Well, genetic discrimination --

PROF. CHARO: In health insurance it is probably around 14.

DR. MURRAY: Yes. That sounds about right.

It should also be noted that in -- I know this is true about health insurance. I do not know about other forms of insurance. There

is a federal law, the Employment/Employee Retirement Income Security Act, which says for employers who self insure it preempts state laws. So, in fact, many, many large employers have gone the so-called EERISA route as a way of evading or avoiding jurisdiction of state laws on their insurance programs. So even if you have a state the law the point is if you have a state law it may simply not apply to the great majority of people who are employed in the state and have health insurance through large employers.

PROF. CHARO: Just though because the EERISA stuff is very complicated, so just to nuance that a little bit, okay. The kinds of employers that are likely to be able to self-insure and, therefore, exempt themselves from most state regulatory laws because they are coming under EERISA are going to be large employers. It is not with that exception. So one of the most famous cases having to do with this kind of EERISA problem arose in Texas with a fairly small group employer. It had to do with somebody who was HIV positive whose coverage was severely curtailed. The HNS Music case. But nonetheless by and large it is large employers.

Large employers are also characterized, however, by large groups in which entry is not conditioned upon individualized testing. So the real problem predominates in the population of people who are individually tested because they are coming in looking for coverage outside of large groups. They are not coming in as a state employee, as part of a group of state employees. They are not coming in as an IBM employee, as part of 10,000 employees. And those people tend actually to benefit from some of the protections of state law. But

the state laws themselves are extremely spotty. The enforcement is very poor.

The insurance industry is a captured industry on the state level. I am not poo-pooing the problem but just to kind of keep it all in context. It is a very messy kind of demographic legal regulatory complex there.

DR. MURRAY: Laurie wants to say something.

MS. FLYNN: If I can just add to what Alta is saying. Many of you may be aware that there may be some impact on this problem by the passage of the Kennedy-Kasselbaum Health Legislation which specifically breaches the EERISA wall which is why the business community had such a hard time with it. And most specifically addresses the issues of preexisting conditions as well as affordability of coverage so that it is a timely issue. There is, however, some movement which is helpful and which we might recognize in any of our reports.

DR. MURRAY: Just to make a couple of other general points about discrimination and its relationship -- genetic discrimination and its relation to genetic privacy. Genetic discrimination exists -- can exist potentially in many forms. Certainly with insurance, possibility with employment, but also in such things as adoption cases, custody cases, and even potentially the allocation of scarce medical resources. If one candidate for the heart transplant has a genetic predisposition that the other candidate does not, is that considered or ought that to be considered? So discrimination can range fairly broadly.

We did speak about whether if you took care of privacy, would it take care of discrimination? I think that the tentative conclusion

we reached was not completely. They were intimately connected but they were not exhaustive, mutually exhaustive of one another. And one could still -- you could guarantee privacy to a considerable degree. If you could you would still have certain kinds of genetic discrimination that might still be operative.

Furthermore, if you forbade effectively all forms of genetic discrimination then people still might have concerns for genetic privacy that went above and beyond the discrimination, the danger of discrimination. But we thought they were so intertwined even though they are analytically distinct and even to some extent practically distinct that we ought to treat them together. Now we had some potential tasks. I will have to tell you that our thinking on this was not nearly as complete relatively as it was on the tissue sample. But let me mention some of the tasks we thought might be done.

One task was to have the -- through NBAC staff probably and perhaps through a contract, I do not know what the mechanism would be, to compile and evaluate the arguments about genetic exceptionalism. That is the arguments about the idea that genetics is somehow different. That was one.

A second was there was a real interest among some members of the subcommittee to gather sort of a rich collection of positive and negative examples of the use of genetic information. Now in part that was based on methodological privilege. Some members felt that they really learned a lot from looking at cases and the richness of cases. One metaphor that I think was used was could you immerse yourself in these cases, you could draw better, fuller, more complete

conceptual maps of the terrain, and that would enable us to make better comments, recommend better policies if we are going to recommend policies.

A third task was to have -- this would also look like a paper -- to have someone reflect on why is privacy important. Again the values of privacy.

A fourth task which I really think is a subset of the second was the commissioners were being urged to bring in their own examples of genetic discrimination and genetic cases about breach of genetic privacy.

It was also suggested, and I am not sure how this could be done, but that we somehow use the commission, the commissioner's own resources or through NBAC to begin to develop a conceptual framework to try to bring together genetic discrimination of genetic privacy. Say more precisely how it is that privacy and discrimination in this realm are intertwined and are distinct.

That was our list. We clearly saw this as a project not to be completed within a year but to have a longer time horizon. We did not specify the horizon. But let me just leave it open to you now to talk about those potential tasks for a few minutes and then we will turn to the gene patenting.

PROF. CAPRON: To follow up on what I mentioned before, you had on your list of tasks when we were talking about the tissue this notion of finding out what the public and stakeholders think. You did not mention it here. Was it discussed? I cannot remember looking at your transcript.

Because again to respond to that point that Bette had made about the value of knowing what the public thinks, I think on the question of privacy and discrimination that people do have a better handle on that. You are not asking them a question where they would have no notion about is privacy important to them, is it important that certain people not know certain things, to what extent do they associate with this notion that it is a vehicle for controlling one's life and defining one's self and so forth. The kinds of ideas that we are throwing around here. Does that have any resonance with the public?

If you are looking -- if you are assembling a wide range of possible tasks, some of which we may be able to afford to do, some not, I would not knock it off the list at this point.

DR. MURRAY: David?

DR. COX: So this is not really being responsive to your charge on the list but it is sort of trying to synthesize something that has come to me by hearing this discussion. It really is why is privacy and discrimination an issue with respect to genetics and it comes back to our earlier morning discussion too.

So what this is all about in the context of research at least it seems to me is gathering information in an effort to do good and not do harm and to figure out how you can use that information to do good. And the practical issue from the point of view of genetics when I think of things broader than this discussion of lack of privacy generally, is that it is precluding the collection of information in any way that anyone can use it. Okay. It obfuscates the information and makes it unavailable to use either for good or for bad.

Now in the context of a genetics researcher, which is what I am, is that you cannot use genetic information if it does not exist, if you cannot get your hand on it. And so for me the issue of privacy and discrimination in this context is one of being able to accurately collect information. If we have social or cultural things that keep us from doing that then it is a moot point about the use of genetics.

So this is a framework within which to me it can bring together the information. It can bring together many of the things we have been talking about here towards a very specific goal which is, is it worthwhile collecting this information and, if so, then how can we collect it so the people can actually use it.

PROF. CAPRON: David, I am very sympathetic with the concern you expressed but it seems to me that the whole idea of privacy is exactly responsive to that, which is if you have a regime in which you have confidence that information that is collected about you for one purpose by one person will remain private or will only be used in ways which you are comfortable in having it used, you are then willing to have that information collected. So the privacy is actually protective of the research process and protective of the use of information in ways that is helpful and beneficial.

It is likely that people will hold back information precisely when they do not have confidence. I think the whole reason that we have special laws in many states on AIDS testing, HIV testing, is precisely because people said, "We are going to end up either with people not being tested or being tested anonymously or not giving real names," which is then very destructive of gaining real knowledge because the

public was profoundly suspicious and particularly the communities involved were profoundly suspicious that the ordinary information coming out of ordinary medical tests was not adequately protected."

And we had to -- the only way to address that was to say we are going to erect some real barriers here with real teeth and just by giving it this attention we will say to doctors and labs and everybody, hospitals, do not do with this what you do with all the rest of the medical information. You may not reveal this to anyone without the explicit permission of the person who has been tested. Now people who think they ought to be tested come in and have some confidence in that. So privacy is actually protective of the very concern you have. It is not in opposition to it.

DR. COX: Let me try again. Because that is what I tried to say but it clearly did not come through. My concern right now wearing a hat as a genetics researcher is that unless we can have real safeguards in terms of information in place this information will never be used ever. So the first question is should it be used and I am not addressing that one right now. Just saying -- assuming that yes, you know, it could provide good. It is not going to provide good in the society that we have right now without these kind of safeguards in place.

So that is a general issue about how we handle information in our society. So I think that to focus narrowly on genetics again may be a hook into this but it is a general solution, a general approach to how we deal with information. The medical records just being one part of it. But if we do not as a society deal with this issue we are not going to be able to get any kind of real factual information out of

it because we will not be able to have access to the information.

DR. MURRAY: Let me try to bring this piece of the second piece of the larger puzzle to reach an interim conclusion. I think -- I do not know if I am stating the subcommittee's conclusions accurately. Genetic -- the use of genetic information and the implications for privacy and discrimination are important. They are a part of our charge. We thought they were an appropriate part of our charge and that we ought to try to do something.

We got the beginning of a handle on some of the pieces that we might do that would be useful and not merely a duplication of what has already taken place. But I think we have considerable work to do and that is my impression. We have considerable work yet to do in further refining precisely what we ought to do in terms of our own work.

DR. EMANUEL: I thought that one of the reasons is that in tissue samples we agreed that there was sort of a common framework that everyone was working with and at least there we did not have to reinvent the conceptual wheel.

Whereas the problem of privacy and discrimination is it seemed that the framework was not present and in part it may be that it is just so complicated no one has gotten their arms around it correctly and, therefore, the committee's work would have to be more, if you want to use it, foundational or rudimentary before we could get much beyond that. Therefore, it was going to be a longer time line, time horizon, and much more conceptual work.

DR. MURRAY: In some ways it is paradoxical. I mean there is a lot more written about privacy and discrimination but it is all

over the place where we have a plethora of mavens let's say.

DR. COX: Tom, I could not agree with Zeke more. In fact, he articulated actually what I have been feeling and have not been able to spit out which is that everybody knows something about discrimination and privacy. You can always get their two cents worth. But not in the context of an organized -- a framework that we can move forward on. So I think you have really articulated that well.

PROF. BACKLAR: But there might be a little bit of an overlap with all of these because there is an enormous overlap, not a little bit, going back to the tissues section. So that when if we do a public opinion poll of some kind or a study of focus groups we certainly an look at privacy issues in that context and use it for both areas.

DR. SHAPIRO: I just have to -- I want to ask a question which concerns -- make sure I understand the interchange between David and Alex here. Namely I certainly understand the issue that the provision of reasonable assurances of privacy may encourage the possibility of collecting information which is important, which I think to point out is like using the AIDS or other examples. If I understood David's comment, it was yes, that is true, however the provisions are strict enough and the walls high enough no one will ever see it, and collecting it therefore at least from the research point of view and not the clinical point of view may not be so helpful.

Now are you seeing something like that, David, or I misunderstood you?

DR. COX: No, I was not saying that.

DR. SHAPIRO: That is why I asked the question.

DR. COX: I was not trying to say that and I was really saying exactly what Alex was saying but not very well.

DR. SHAPIRO: Thank you, I appreciate it.

DR. MURRAY: We have nearly 13 minutes left. That ought to be plenty of time to deal with gene patenting.

(Laughter.)

DR. MURRAY: I am not going to go through and reiterate the discussion that we had except to say that it was very substantive. We characterized the patenting issue as a kind of Lazarus issue thinking that it had been died and been buried several times but it keeps seeming to rise from the dead. That itself is an interesting phenomenon and so the question -- the challenge for us becomes what can we do, if anything, about gene patenting which is a part of our charge that would be different and more successful than past efforts. That is, in fact, the challenge.

We have a lot of useful information as I said thanks to Steve and thanks to Rebecca Eisenberg about the context within which this debate arises and several different possible angles into the ethics of gene patenting. I want to just -- I would invite Steve, if he wishes, to add anything about gene patenting or anybody else. I will say that in the end I think we felt that it was worth doing, that we probably could add something to the public debate.

It would have to be different in some respect from what has gone before and would have to involve a very open and inclusive process where spokespersons on both sides, people passionately on both sides, really had a chance to state their best arguments and have

those arguments heard, and have them considered by this commission in an effort to sort through, sift, evaluate and ultimately to come forward with what we think are the best understandings in a report that as much as all the other reports have to be educational and public this one has to be doubly so.

I am going to put you on the hot seat, Steve, our resident expert. Anybody may join in.

DR. DUMAS: Gene patenting?

DR. MURRAY: Yes.

DR. EMANUEL: I thought one of the useful issues that came out of that discussion was this issue of I think phrased as utilitarian concerns versus sort of intrinsic concerns about the genome and one of the benefits we might serve or purposes we might serve is to clarify that kind of conflict. That in some ways this might be a conflict of frameworks in which looking at it one way does not take into concern -- into account the concerns certain people raise looking at it another way, also minimizes or dismisses the concerns of others.

I think there was a general sense and I would reiterate it, that this might be a -- to use David's phrase -- a hook to go into what at least I perceive out there is a very serious unanswered concern of a great majority of Americans which is why is this again exceptional or different. This might be the way we can most effectively address that or at least say we are taking it seriously in an arena that has important economic and regulatory --

DR. MURRAY: Rhetaugh?

DR. DUMAS: It mentions conflict of frameworks and I do

not know how that differs from conflicts of interest. I think that is one of the things that is going to be very important in relation to this, is to address the issue or issues of conflict of interest which someone raised earlier. I hope that will not get lost in this subcommittee's work.

DR. MURRAY: Do you have particular conflicts of interest you are thinking about, Rhetaugh?

DR. DUMAS: No. I think that the whole idea of conflict of interest needs to be addressed. What does it mean and what would be under certain conditions considered to be a conflict of interest?

DR. MURRAY: Thanks. Steve?

MR. HOLTZMAN: In the talk I gave to the subcommittee I noted that this Lazarus issue as many times that it has come up a number of commentators or reports have concluded that it is not really an ethical issue and I made the suggestion that what you cannot avoid is the fact that it is a lightening rod for a series of ethical concerns.

DR. DUMAS: What is the "it" you are referring to?

DR. MURRAY: The issue of gene patenting.

DR. DUMAS: Oh, gene patenting.

DR. MURRAY: All right. And that to simply say it is not an ethical issue does not get you anywhere. We think of ourselves in our educational function here that we could be -- play a very important role in terms of elucidating what are the different kinds of issues getting clarity about what is a patent and what is not. Now that is very difficult. It is a very arcane subject matter.

What is an intellectual property right from how important that is to the public. I wonder how successful we can be in this regard

because you are still going to be left with the rhetoric and the semantics of ownership of life which gets you into very deep issues about what Zeke was pointing to, was our relationship to ourselves as physical beings.

But I think there is a role for the commission. Tom's phrase was this is an issue that has legs and you cannot duck it. I think we can play an educational role and maybe if it has been done before by others maybe that is the nature of education and we can kind of educate ourselves.

David and Alex?

DR. COX: So this one issue that Steve just spoke of which is sort of patenting life forms in general is one point and just to reiterate what you just said is, well, you know, how much are people really getting into this and thinking about it. An alternative aspect, you know, not one or the other, but it is an alternative way, is it is something that people bring up all the time. And that is it is not just in patenting per se but it is patenting human genes and in particular based on human research and that is that they will give certain materials or give up their time sort of as a gift and someone else gets very rich. So this is the issue of fairness and justice.

Now anyone who I have ever heard speak on this from the point of view of patents says do not touch that one. So I always say, well, that is something to look into. But it has been in the context of individual compensation and reimbursement, not in terms of the team of researchers and subjects and everybody else.

So there has been some e-mail going around from Bob Cathegan (?) and others about this. I found it an extremely interesting

discussion because again a way of not looking at it in terms of patenting of life forms per se, but looking at it in the context of a new research paradigm where the subjects are more empowered of a way of giving back to those subjects, not individually but as maybe a community, some resources which definitely is empowering.

So I am very interested in looking into this area -- this aspect of patents because I for one thought the patenting issue was fairly dead. I was not very interested in it but I have become extremely interested in it from this point of view.

DR. MURRAY: Thanks. Alex?

PROF. CAPRON: My bench mark on such matters is always to what extent is Jeremy Rifkin making an issue of it because Jeremy has a very keen eye and ear when it comes to issues that resonate with the public. I think that when one moves to the human genes in particular there is a way in which those issues are stated that grabs the attention of a lot of people and it is not on an economic level and it is not on a technical level. It is an ethical issue in most people's views.

It reminds me of what happened vis-a-vis the gene splicing issue or the genetic engineering issue at the beginning of the '80s when again Rifkin raised that alarm and one of the things that the President's Commission did in addressing the issue was to look to leaders of a broad array of religious faiths. Part of the reason was that Rifkin had marshaled the major organizations for religions as stating that this was a matter of urgent concern and to look at those religious traditions and to say to what extent what is being talked about in human

gene therapy are offensive to those traditions or troublesome to it, and was able to lay to rest those concerns and to place it into a context but not to dismiss them.

So as we begin to think about tasks here I think we need to think in terms not merely of a philosophical or analytical approach but also an approach that talks about what values informed by religious or other views people bring to the subject and how if you then do look at what is actually at stake in a patent are those values really offended or not in some way. And say to people your gut reaction is something we are going to pay attention to and we are going to address, and I do not know what the outcome of this analysis would yet be but it should be part of what we do.

I also want to agree with the comments that were being made about the fairness/justice issue as being another one that grabs people's attention. I thought our chairman was right in some of those exchanges and finally saying that it did not seem as though it was likely to be well addressed in the patent system as such but we do know that there are times when patent rights have been given with certain requirements as to what happens with the information and how it could get used and how even the proceeds could be used without saying we are going to have a special category of patents for human gene patents or something.

Anyway I think those are both issues that deserve attention. We are approaching lunch. Do you have something urgent, Steve?

MR. HOLTZMAN: Can I?

DR. MURRAY: Yes. Go ahead, Steve.

MR. HOLTZMAN: I want to jump on what Alex just said because back in 1989 I had the good fortune of giving a talk at Princeton in the DeKamp lecture series and I took Splicing Life and the way I described it was exactly the way you did. What it did was it took a new practice, gene therapy, and contextualized it. I was able to draw, you know, affinities to organ transplantation. When you transplant an organ you are transplanting 100,000 genes. But you drew the kinds of distinctions which are obvious today but were not then between germ line gene therapy versus somatic gene therapy.

When I look at the patenting issue, and maybe this whole issue of genetic information is being distinct or whatnot, the kind of enterprise you undertook in Splicing Life to me is the paradigm. Things get so confused and jammed together. Patents have nothing to do with compensation, absolutely nothing to do with compensation but they do get jammed together.

The kind of function we can serve is teasing that all apart and say, you know, this is what exercises people, issues of compensation, what is fair, what is just to he or she or community who contributes to genetic research contributes to clinical research. The same kinds of issues come up. How do we tease them apart?

So I can see something there which does not involve Gallup surveys. I do not think you have any Gallup surveys when you wrote Splicing Life, all right. It is going out and hearing the voices around this. It is a philosophical endpoint that is public policy based. It gives you the kind of clarity necessary to then go forward with the public

policy.

DR. MURRAY: Thank you, Steve. Larry has the last word before Harold leads us into lunch.

DR. MIIKE: I just wanted to add my interpretation of what went on in our subcommittee meeting and perhaps it will answer Rhetaugh's question about what is the difference between conflict of interest and what are we talking about, about the conflict of structures. There were two types of discussions going on over there. One was that, which irritated me at that meeting, was that the Supreme Court has ruled a certain way. The patent office does certain things. We do not have anything yet to add to that discussion. It is closed. It is an economic issue. There is historical precedence. The Supreme Court does not. They are not going to listen to us.

I do not care if they do not listen to us but there are obviously words and wisdom outside of that narrow framework. So, for example, as an example outside the genetic area it came as a surprise to me that you could patent AZT treatment, not the AZT itself or a unique way of making AZT, but the actual treatment itself. So that it was a surprise to me that if someone had wanted to patent the use of aspirin for preventing heart attacks one could have done that. But it just happens in the practicalities of it all is that aspirin is out there and can be used for other purposes and you could never really enforce that patent because it is so common out there. But the example that was used was that if AZT was great for polishing your shoes you could do it.

So I think that as an education tool if we can be again in very plain language about what are the values in the patenting system

and why they come out a certain way, and why it may conflict with other values that stand outside the patenting system and the way the Supreme Court has looked at we would provide a valuable service on that side.

The other part that we talked about was what has been raised here already. The Jeremy Rifkin people, the people who say that everything around the human body has a sanctity about it. You should not fool around with it. Versus the side that says there are values to society in what is coming out of genetic information and research and we should do that.

And that we are never going to resolve the difference between the two sides but I think it will be useful for us to say very clearly and explicitly that there are these differences and then we may not have any kind of solution to that but to make it fairly clear about where we are in loggerheads in that and then why we will never reach any satisfactory resolution at any time when we conflict in this area.

DR. SHAPIRO: Larry, thank you very much particularly for those remarks. It is my own view that the most beneficial aspect of everything we do is to think carefully and deeply about a problem, more carefully and more deeply than others, and then articulate it in a way which can communicate them. I quite agree with you we should not think in this case the Supreme Court is any final arbiter of what we think and what we think is appropriate.

An example of that, I think, has come up here this morning just in the last few minutes. That is the patent issue is not just an issue. It is a series of issues, each one of which has its own vitality. One is whether it gets a patent under the meaning of the law here and

another is how the benefits are shared. It is a whole other issue. So it is a series of issues and parsing these issues out carefully for people and can perform a very valuable function. I take it, Steve, that is in part what you did in the lecture that you referred to before and it is certainly an important function that we could develop here.

We also have to have in my view the confidence, kind of the self confidence to identify issues which we think are appropriate because while we certainly want to consult others because we only contain a finite amount of wisdom even amongst all of us put together on a number of different ways, it is not kind of a popularity contest. We are not going to help in that scheme. Of all the great things in people's minds out there in the world which ones are we going to address? That is not our charge.

We have a much more focused set of issues and a lot of competence together to decide what is important and we should have the self confidence to proceed on that basis. But no chairman has the self confidence to proceed right through lunch so that let me -- as the committee members know we have not made any special arrangements for lunch. We have information about it for those of you who want to take advantage of that and decide what you want to do.

Let me turn, Bill, for that before closing. Bill?

DR. DOMMEL: I am informed that as of five minutes ago it was sleeting and the front street is not clear. Therefore, I have abandoned the sheets that describe just a pleasant walk and an entertaining jaunt and only a cheery stroll away, and replaced it with within the hotel we have two restaurants, a formal dining room and

informal, the Retreat is the informal, on the first floor.

Within a couple of blocks of the hotel are restaurants that the concierge could check on a waiting list for you at Georgia Brown's which is two blocks away and Girard's Place two blocks away. Also a couple of others four blocks away and you make your own choice. But check with the concierge if you are interested in those restaurants.

Deli's very close by, Jack's, which is a half block south of here, and the doorman can direct you in which direction. The Washington Post pub also about a block away and the Wall Street deli close by about a block away.

DR. _____: And there is a hot dog stand across the street.

DR. MURRAY: Thank you. When do you want us back?

DR. SHAPIRO: Approximately 1:45. I do not want to start any later than 2:00.

(Whereupon, a luncheon recess was taken from 12:39 p.m. until 2:00 p.m.)

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A F T E R N O O N S E S S I O N

DR. SHAPIRO: Colleagues, could we please assemble?

You may be wondering what it is I am sitting here doing with this large cylinder with some unknown contents in it. The purpose of these cylinders for which one exists for each member of the commission, this one has the Honorable Ezekial J. Emanuel written on it. But there is one -- there is a box of them here. I think you will find one for each commissioner.

If anybody had any doubt whether they belonged on this commission or whether they were appointed to it in very sophisticated calligraphy it is marked here that, in fact, you are a member of this commission and the nature of your appointment and so on.

So you can pass this down to Zeke. He does not have to search. You do not have to search in that box later. But those of you when we break at 3:00 o'clock or any other time if you are inclined to do it even earlier you can retrieve one of these for your collection.

DR. EMANUEL: I feel like I am knighted.

PROF. CAPRON: Right, except you left a "B" off.

CONTINUATION OF MORNING DISCUSSIONS

DR. SHAPIRO: There is probably a way to open it but I am not sure that we want to open all of these. For one reason is all the space they take up when they are opened.

All right. Let's now proceed directly to our agenda and let me just say one or two things by way of clarification of where we are headed and how I anticipate we are going to get to that destination.

It is my intention for NBAC to issue a report in

approximately October. We are, as many of you know, obligated to issue an annual report both through the various congressional committees and the president. That of course can be anything from a rather modest formality of reminding them who the members are, when we held meetings, what we discussed with some modest description of what we are doing. It could be something as modest as that according to the regulations. Or it, in fact, could encompass some substantive assessment of particular issues that we are dealing with.

It has certainly been my intention and continues to be my feeling that we should do the letter so that at least in the first year of our operation we have something substantive to report on an issue of some importance and begin to establish the credibility of this committee and the work that we will be doing.

That does not mean in future years that that will be the model that we take. There may be years when we want to accumulate information and work into bigger and more comprehensive reports. That is certainly to be the case sometimes. But I think in this first year that we should continue to aim at that objective of reporting in October, at least roughly speaking in October, and do so on some substantive issues in addition to the more logistical issues of what we have been doing when we met, so on and so forth. As you heard this morning, I told both Tom and Jim, that is the way they should plan the work of their subcommittees.

Now in that respect what our objectives are today and tomorrow, and they may achieved in sort of somewhat different ways with different committees, is to achieve enough consensus here so that

very quickly after today's meeting what Tom referred to in a conversation I had with him this morning that we can commit to writing a kind of mental map of where it is, how it is the committee understands its subject, what issues it wishes to focus on both short term and long term, and how it expects to go about that so that can be reviewed in writing by all NBAC'ers.

Presumably that will happen before our March meeting. We may review it finally at the March meeting but I would hope for us to have these kind of written proposals before the March meeting so that perhaps some final adjustments may be made at the March meeting but really to have a chance to do that somewhat before the meeting. That will then initiate a period of very active work starting some time between now and the middle of March to follow that agenda out.

In some areas some aspects of the agenda are already very clear. So, for example, the first report you heard this morning on evaluating the status of the adherence to the common rule in the various agencies is going forward, my hope is that most of that will be done pretty early on. It is pretty clear we have a mandate to do that. Whatever else we might think about newer and additional alterations or amendments to the common rule and how it might be enhanced, so on and so forth, all of which are extremely important. But the earlier aspect of this is really quite straight forward and we will proceed to do that almost right away.

So what is really quite essential for us to accomplish I think hopefully in the next hour is to confirm that the two subcommittees at least on their major projects which they are anticipating completing

before, within this calendar, before October, I will put it that way, meet with your consent and agreement. They are -- whatever the long-term issues are and whatever the longer term agenda is that the early focus of their activities is really amenable or agreeable to members of the commission.

So, for example, in the Genetics Committee the first project that the committee wishes to undertake as you know from the report is the tissue sample area. They want to deal with that area and areas that surround it in ways that they believe are important. Other issues which they also want to begin working on if I understood it, Tom, they certainly want to begin before October will not be completed by October. So if you think of the Genetics Subcommittee that is really the issue. It is very important if we feel that is inappropriate or the inappropriate first project that we should say so and discuss it and find -- either disagree or agree or find some substitute for it.

And likewise we will have to look at the initial projects of the Human Subjects Committee. As Jim said this morning they have a short-term and long-term strategy. They have a low resource/high resource strategy and so on. But I think we can be quite clear that there is a number of these first party projects that can be done and should be done by October.

So let me start now since it is probably freshest in our memory with the Genetics Subcommittee and, Tom, if I have laid this out incorrectly please correct me. It seems to me that one thing we have to inform this committee of is whether we think the topic that they are considering for this first number of months for detailed thoughtful work,

the tissue sample one, is appropriate given the various issues that we face.

Now there were many comments this morning on this particular issue which I am sure enrich the understanding of Tom and his colleagues on these issues and we will of course be taking into account I am sure as we proceed. So let's start with that particular subcommittee.

Let me turn first of all, Tom, to you to see if I have not articulated this in a helpful way and if there is other things you want us to focus on as well?

DR. MURRAY: I think you have got it just right. We believed that our instruction was to given the only assurance of one full year of life for the commission that we wanted to have something to show before we went out of business should that happen. We thought the tissue samples was an issue of the size and scope that we could do in a year so that is exactly right. Of course it does have connections with some of the other issues about privacy and the like.

We would certainly mention that in the context I think of our report but we would see -- we see three reports at least, tissue samples to be due a year from October, from last October. We see a report on genetic privacy and discrimination and we see a report on gene patenting. Those with somewhat longer time horizons. We would like to begin work on all three, at least background work on the latter two, but to focus our intensive efforts on the fourth first.

I would like to know whether that, in fact, is the commission's will.

DR. SHAPIRO: Let's deal with that issue so Tom and his colleagues feel that they have our assent or lack of it if that is the case.

Alex?

PROF. CAPRON: I just want to ask Tom and the chairman having said that that is your objective are we now also going to go on and talk about what would be encompassed in that. Secondly, there were a number of other topics, Tom, that you raised before the four that you had as you went into the subcommittee meeting and other topics were raised from the floor. When you say we are going to have three reports, three areas of study, tissue samples, privacy and discrimination, and patenting, what about those other topics? Are they -- I mean where are we as a group now in our discussion of the genetics agenda? I am a little unclear.

DR. MURRAY: We definitely like your okay to proceed with the study on tissue samples.

PROF. CAPRON: My question there was when you say you are okay for that are we then going to discuss what that would consist of?

DR. MURRAY: Sure. Whether that takes place today or whether that takes place in subsequent discussion, including tomorrow morning, we will have two hours to talk about tissue samples substantively tomorrow morning we could do that.

PROF. CAPRON: Yes. My sense was that tomorrow both of the subcommittees were, in effect, going to be working substantively on a piece of their agenda rather than having a talk about the agendas.

DR. MURRAY: Right.

PROF. CAPRON: And if that is the case I would think it would really be today's task to talk about our overall objectives within each of these subfields and not do the work that a staff will eventually have to do of breaking all this down to the point of a paper on this and here are the people who could write that paper and a paper on that. That is not -- I am not talking about that level of detail. That has to be done between now and March by the staff and coordination with you.

DR. MURRAY: Well, I am a little confused, Alex. The second point you wanted to make I certainly understand. That is we had recommended these three reports and indeed we had even raised for ourselves some other possible issues.

PROF. CAPRON: Right.

DR. MURRAY: As has come out also in today's deliberations. Clearly that conversation ought to take place today.

PROF. CAPRON: Right.

DR. MURRAY: But then I thought you were also saying that --

PROF. CAPRON: I was saying as to the first one, the tissue sample one, besides saying, yes, it makes sense to take that on as the first topic, besides saying that are we then going to have any further reflections on some of the things that you raised this morning about how one would go about that, as I say, not at the level of detail of saying that John Jones ought to be asked to write a paper on X, Y, Z. But rather what are the components, what are the issues that we want to make sure are examined under the heading of tissue sample?

DR. MURRAY: I do not see a sharp distinction between

having part of that conversation today and continuing that tomorrow morning. Even as we get into the substance, part of getting into the substance will be, well, what pieces do we need ultimately to ask them?

PROF. CAPRON: Yes, I see that.

DR. SHAPIRO: We are going to have an opportunity do that momentarily.

PROF. CAPRON: Okay.

DR. SHAPIRO: I will spend some time on it but just constrained by again our need to get to the other committee, but we can have an initial conversation on that indeed right now if people are satisfied that this at least as an initial topic does make sense given what you have heard and understand about this issue and of course other alternatives.

DR. SCOTT-JONES: I have a question about how we will handle the overlap once the subcommittees really get involved in their work. In the discussion of your subcommittee this morning there was a lot of mention of topics that overlapped with the other subcommittee. So have you thought about a procedure for making sure that we are not either duplicating our efforts or not keeping each other informed about what we are doing when there is overlap?

DR. MURRAY: We are going to speak in code so you cannot copy what we are doing.

(Laughter.)

DR. MURRAY: You all know the signs. Actually Jim and I very preliminarily we agreed that wherever possible we would like to schedule the meetings of the subcommittees even back to that so that

people who wish to be present at both would, in fact, be able to be present at both. Now that cannot be a hard and fast rule because of people's schedules and there will be times when we need to have a meeting and we just will not be able to find the two days that will be perfect for everybody. So that will be the -- something we will strive to achieve each time.

Plus, I mean I think everyone ought to be in the loop for all communications among -- even within subcommittees. Is that -- would you agree with that, Jim? We did not talk about that.

DR. SHAPIRO: Let me say a word just about that issue. Just looking at e-mail traffic amongst NBAC'ers there is a lot of us who just do -- everything we do we just send everybody. Others probably for lack of even thinking very much about will just send it to A, B or C and then some other communication starts referring to these things and not everybody knows what is going on. So unless there is some specific reason that is helpful for everyone when they use that form to just send it to everybody so that if someone wants to follow through -- you know, nothing I have seen so far is in any way confidential and so on.

DR. BRITO: But it is private.

(Laughter.)

DR. CHILDRESS: Given the overload that many of us experience I would just urge restraint and discipline in the sending of e-mail messages.

PROF. CHARO: Yes, Jim, I will.

(Laughter.)

DR. SHAPIRO: That reminds me of an anecdote that

Howard Baker used to tell when he was in practice with his father as a lawyer down in Tennessee. After presenting his first -- I guess going through his first trial he asked this fellow how well he did and he said, "It would be helpful if you thought before you talked."

(Laughter.)

DR. SHAPIRO: So maybe that should go for our e-mail messages as well.

DR. MIIKE: On the issue of overlap I do not think we should be constraining or assume, or not discuss an issue. Like, for example, the informed consent and confidentiality, they are going to come up everywhere. I think only as the committees progress and we get into written documents that we can -- I think we will be able to easily merger it and we will be meeting as Tom said back to back and we will be getting information from the other committee's work and it will become clear to us which areas we are overlapping on and which we have to reach some commonality. I think we are going to reach that even without having to address commonality explicitly.

DR. SHAPIRO: I think that is right. I want to say I have been very encouraged by how well all members of this commission have worked together so far. I think we will work rather easily together.

Let's return to the topic at hand and I am going to assume unless there is some objection here because I have not heard any indication to the contrary that this is a good initial project that would be aimed for completion in October while other projects will go along at a different pace.

Let's turn to the question Alex raised because we do have

some time for that regarding how that study might be carried on or what kinds of issues people would like specifically addressed to see what kind of advice any of us have for the subcommittee.

Yes, David?

DR. COX: Just to start this off that although as Tom brought it up we were initially considering these samples in purgatory, the previously collected samples. Any discussion of tissue samples, even talking about those types obviously brings up what you do in a prospective fashion of the samples that have not yet been collected. I think that that is going to be a much more difficult process myself. But one that I think we should consider also but I would be very interested in other commissioner's views on that and whether it should -- I think it would be very narrow personally just to do the previously collected samples but I would be interested in people's views on that.

DR. SHAPIRO: Thank you. I have others who want to speak but let's see if there is anyone who has a comment on this particular aspect of things, that is a suggestion that the committee deal not just with those existing banks that are around but how one is going to proceed in the future as I understand what you said, David.

DR. COX: Yes.

DR. SHAPIRO: What kinds of guidelines. What the issues are for future samples that will be taken up?

Alta?

PROF. CHARO: Yes. I am not sure if this is jumping the gun, Tom, but I suspect having not had a chance to read the transcript from that meeting, I apologize, that you noted that there might be

different emotional reactions to stored tissue that represents reproductive tissue, whether sperm, eggs or embryos, and all other tissue. It might be possible to divide the tissues that you are looking at into those that invoke reproductive issues and those that do not.

I think the ones that invoke reproductive issues because they are already subject to a variety of influences and have a whole separate set of concerns might be best left to be dealt with especially separately so that you can work on the much larger set of samples that are out there before delving into what otherwise could be an endless debate.

DR. MURRAY: You would suppose incorrectly because we really did not focus on the reproductive tissues at all. We probably should have been sensitive to that distinction but I do not recall it arising. We had in mind more the kinds of tissue samples, pathological samples.

PROF. CHARO: Which is just what I am suggesting anyway. It would be more productive to work on it, so it does not matter.

DR. SHAPIRO: It is a helpful suggestion. Thank you very much.

Eric?

DR. CASSELL: Well, I am sorry to be retro but in your introduction to your topic you listed four things, commercialization of diagnostic genetics, test group vulnerability, et cetera. So I can tear this piece of paper and throw it away where did that go? I mean, when they --

PROF. CAPRON: That is later.

DR. CASSELL: That is the later after all these are --

PROF. CAPRON: We are now talking just about the tissue samples.

DR. CASSELL: Those were suggestions for other reports and so forth.

PROF. CAPRON: Yes.

DR. CASSELL: Fine. Thank you. Since we are not going to get to that until after October --

(Laughter.)

DR. SHAPIRO: You have a good memory I see.

Alex, did you have your hand up?

PROF. CAPRON: I wanted to underline a couple of suggestions and say that I would very much hope they will be part of the research approach. One is the international perspective. We have to understand that there may be particular reasons why other countries are doing particular things for cultural or historical reasons. But it still would be very informative I think if one of the papers that you commissioned look at position statements or even governmental positions that have been taken in other countries.

The other was I was very taken by Alta's suggestion that we try to find out through IRB's or people who have conducted studies using stored tissue samples a data base of people whom we might approach, I do not mean we directly but somebody on our behalf might approach, for whom this would have been a very salient issue as to their attitudes towards anonymous versus nonanonymous use, what obligations they think are created to them if their tissues are used and

so forth.

Again what's people's views on this are not necessarily determinative out of all of our conclusions of what is ethically required. But it would certainly be that this is a stakeholder group for whom this is an issue that they have had some reason to think about and it would be a study I think worth trying to do.

DR. SHAPIRO: Yes, Bette?

MS. KRAMER: I had more of a procedural question. Do we need -- if the subcommittee decides that it would in fact like to investigate the possibility of doing either a survey or focus groups, do we need the authority of the full commission to do that? Specifically if we should decide to both investigate and then go forward with that, who gives us the authority to spend how much money?

DR. SHAPIRO: One, you do not need the permission of the full committee to do it. The people who will give you the authority to do it and how much money is available is Bill and myself.

MS. KRAMER: Thanks.

DR. SHAPIRO: I am not going to address the issue of which IRB you have to speak to.

Other suggestions?

I have just a -- I am sorry. Excuse me.

DR. MURRAY: Go ahead.

DR. SHAPIRO: I have a really very small question. It is an issue which only I suppose a nonphysician would ask. We keep talking about this as tissue which is a way of talking about material I take it, genetic material. It is just a shortening for that. That is this

includes, for example, blood samples.

DR. MURRAY: Yes.

DR. SHAPIRO: Okay. Thank you very much.

PROF. CAPRON: Blood is an organ.

DR. SHAPIRO: I will not get into that argument.

DR. MURRAY: Blood is an organ.

PROF. CAPRON: Blood is an organ.

DR. SHAPIRO: Okay. Are there other issues you would like to raise or bring before Tom's attention? I know, Tom, you wanted to make some remarks.

DR. MURRAY: Well, just very quickly then. What I am hearing, I want to be sure that I hear correctly, now I think --

DR. SHAPIRO: Yes, that is a good point.

DR. MURRAY: -- the subcommittee will still want to talk about this a bit tomorrow but what I hear is of the things that we probably ought to do as preparation for the report would include Alta's suggestion as restated by Alex of looking at people with some experience as having provided tissue and then also being asked for permission to use it, et cetera. Focus groups, now we may or may not do them ourselves. We may be able to take advantage of research done by other people such as Debbie Saslow who will speak and be with us tomorrow morning. This is prospective tissue donors being asked what they care about and why particularly in the informed consent.

Things that have not been addressed at least not since lunch was the notion of an effort to find out whether there are different cultural, ethnic and religious views about tissue donation particularly for

genetic research. Do we agree that that seems worthwhile?

Normative analysis of the position statements issued by the various groups that have seemed fit. Okay. We agree with that.

And some international --

DR. SHAPIRO: Just to interrupt, I think the latter is extremely important because these are issues that are out there on the public record and are being pursued and believed by various people. I think the latter is really a very important issue.

DR. MURRAY: And we will have a head start on that tomorrow because we will have representatives both from the National Center for Human Genome Research and a very distinguished pathologist coming in and presenting somewhat different points of view about it.

Lastly, the international comparative perspective. I hear those components. Thank you.

PROF. CAPRON: Policy analysis of the options?

DR. MURRAY: Well, it is on my list. I did not mention it because I do not know. That seems to me to have more to do with the format of the report. I suppose we could have a paper that looked at policy options. Yes, we could even if we in the end decided we wanted to make recommendations about a particular policy option.

PROF. CAPRON: Isn't the reason to commission all of these papers to provide fodder both for our discussion and a basis on which whoever writes the report can draw on something that the group has discussed?

DR. MURRAY: So that would --

PROF. CAPRON: Yes. In that same context to follow up on the chair's suggestion, I think it would be very useful for the subcommittee and maybe the whole commission to hear and to have in writing a simple presentation of what we are talking about here. I mean, it is the collection of what are the tissue banks, how do they exist right now, what kinds of research are being talked about when we talk about DNA analysis of this. The genetic tests and so forth. What would be done? What are the purposes and uses?

Obviously many of these would -- the latter particularly would just be illustrative. We cannot -- we are not supposed to be surveying every possible use but just to give a layperson some sense of why is not anyone doing these studies? What comes out of them? What good comes out of them? What kinds of information are produced? A descriptive, a technically descriptive in lay terms paper on that I think would be useful and obviously is going to have to be part of any report. I mean, some boiled down version of it would have to be part of any report that we write.

DR. MURRAY: Yes. That is a good suggestion. I mean I intended all along to make sure that such a description would be part of the report but it makes sense to think even from the beginning about how the commission then gets somebody working on it.

DR. SHAPIRO: Eric, Alta and then David.

DR. CASSELL: Just quickly, I for one would really appreciate early in the process of a brief report to say this is what people are using tissue banks for, this is what is being done, this is what raises our concern. That is a very short -- I mean, it could be a page or two

that says what is going on so that I understand better what you are doing and what the problems are.

DR. SHAPIRO: Alta?

PROF. CHARO: A couple of other things that may or may not be on the list that you did not think needed to be mentioned. One obviously is a literature review because there is stuff out there both on what is being done and proposals for how to do it in the future. I know that there was a piece by Ellen Clayton, et al. that came out of a larger effort that was published in I forget it if it was Science or Nature.

DR. MURRAY: Alta, we have five such statements.

PROF. CHARO: Great. Okay. The second thing in terms of areas that you might want to make sure you touch on has to do with private sector tissue collection, specifically the New York Times story that was distributed about the mortuary business now getting into the process of collecting tissue for storage and why it is that people want to do this. They did not mention it but the potential use from an epidemiological point of view of the public health authorities for such a kind of system of collection struck me as being something where it would be very interesting to understand better what is going on in the minds of those who are offering the service as well as people who are choosing to purchase it.

Then further out on that extreme, of course, there is the collection not just of tissue but of whole parts of bodies then frozen and kept in stasis for endless periods of time. There are more extreme examples. But nonetheless I think the private sector is a very distinctly different area than what I think most of us have in mind which is

collection in the context of surgery and other therapeutic situations.

The Public Health departments that themselves have been doing massive collections, especially neonatal stuff, which then provide data bases of enormous amounts. And then as a closing remark, not everything I think needs to be done by us or the hypothetical staff to go out and do it. I think a lot of these people, entities, institutions might be very responsive to an inquiry as to whether or not they would like to submit in writing or by physical testimony during the public comment section a description of what they are doing.

DR. MURRAY: I cannot resist this because someone in the audience today gave me the printout of the homepage of the organization that was profiled in the New York Times. "Genelink. Protect your family by banking your DNA with Genelink." Let me mention a few of the other items on the same homepage.

The Quarterback Club. Exclusive Quarterback Club hat with players signatures. The something alpha, elude police laser detection, it is a laser license plate cover. The Amazing Wind Float, a revolutionary new fishing system. Body by Nature, herbal weight loss system.

PROF. CHARO: Could you give me the address for that last one?

(Laughter.)

DR. SHAPIRO: Larry?

DR. MIIKE: Just a comment. I thought we were taking on this topic because it is do-able by October. What I hear now is this large expansion of this topic. If we get into all kinds of -- everything related to

tissue storage, of course the military is getting everybody to give up a little piece of their DNA, et cetera. So maybe the only way to address it is to explain the broad picture or describe briefly the broad picture but say why we are particularly focused on it. I am just getting worried now after hearing all these comments that we end up with a non-do-able project.

DR. SHAPIRO: I have every confidence that Tom will sit and make judgments as will his subcommittee on doing something that is do-able and I think these suggestions are helpful because they stimulate the discussion. But I think you are quite, Larry, we will not be able to do all these things. I think you are quite right it will not get done.

Alta?

PROF. CHARO: I am sorry to the extent that I added to that mess but I would like to emphasize one thing. Over and over in the area of genetics as Tom knows better than anybody else, private sector goes much faster than the academic sector in implementation of all of the possible uses of various pieces of information or techniques and so over and over I think that academics tend to forget to focus on the private sector, see where they are going, and really pay attention to it to become a little closer to on the curve. Forget about ahead of the curve. That is the only area that I would emphasize as being really worthy and I think it is very isolated. So it is probably manageable.

PROF. BACKLAR: I guess of course the rush to market.

DR. SHAPIRO: Well, as advertised it seems to be the rush to immortality as far as I can tell from the material that we received. Are there any other -- yes, I am sorry, David. I did see your hand before. I

apologize.

DR. COX: So actually Larry was the only one that really possibly alluded to this. I would ask Tom directly about this point about just whether we focus on already stored samples or whether we look at other samples. My concern is exactly Larry's. It does not mean that we cannot bring it up but the -- what is your pleasure, Tom?

DR. MURRAY: That is a subcommittee decision, not individual. My inclination is that we probably need to do both.

DR. SHAPIRO: I think perhaps it is -- I frankly do not think that people will take us seriously if we do not do both. That is my own assessment. We will see what the subcommittee thinks.

DR. COX: But that is my own personal view too, but I really share Larry's concern with doing both by October and doing them in-depth. It is going to be hard. So I just -- I raise this not because I think it is not -- you know, we cannot adjudicate it, but it is an issue that I would really like to see very clearly spelled out in terms of how we spend our time vis-a-vis the product that we are going to have in October.

DR. MURRAY: David, I think much of the analysis would be the same. I mean when you are looking at sort of the moral considerations weighing on protection of human subjects and tissues, et cetera, you are going to have a similar analysis and where you are going to end up a little bit different is in the balancing of the --

DR. COX: Okay. And that is why you are not worried. Okay. I got it.

DR. MURRAY: Yes.

DR. SHAPIRO: Other comments for Tom and his colleagues? Yes, Steve?

MR. HOLTZMAN: I guess reflecting on Alta's comment about this crazy mortuary business.

PROF. CHARO: Not so crazy.

MR. HOLTZMAN: I think our issue here is the use and the research of stored tissue samples and the conditions under which one can access them and the nature of the use. I think that is very different than getting into a discussion of where our culture is at and this hang up in the DNA. There are companies out there right now, send them a blood sample of their PCR and send you back an amulet with your DNA in there. I do not think that is part of what we are looking at right now.

PROF. CHARO: The reason why I was emphasizing private sector stuff is that regardless of what one's predilection is about the best economic system for the United States, it is true that if there is money there will be somebody who finds a way to use something. That then generates a something. In this case it will generate large collections of samples. Right? The fact that the samples come from people who are dead means that although the issues regarding family and relatives remain, the most affected individual is no longer around to raise objections or to have feelings about what might or might not be done.

So you have got private sector collection of stuff. You have got somebody else who approaches them and says this is an interesting data base and because it is characterized by X, Y, Z, you know a certain class of people that will pay this much for a funeral or

whatever, we have got some demographics about it, we would like to test it for something.

I can see this becoming an easier source of tissues than in some cases public sources either through hospitals or through state labs where it is going to be both a political and legal confusion -- there will be political and legal confusion about the status of those samples.

That is why I say it is not crazy necessarily to take advantage of this phenomenon to follow what is happening, how likely is it that this is going to expand to understand what usable purposes the stuff could be put to besides the purposes for which people are buying the service just to anticipate it. It may turn out to be nothing and it may turn out to be farsighted. I do not have a clue. Since it is their subcommittee why do I have to worry?

MR. HOLTZMAN: To the extent that you are focusing on it as this will be another collection of tissue so what are the conditions of access --

PROF. CHARO: That is right.

MR. HOLTZMAN: Okay. I completely agree with that. So I would tend to be much more worried about there are newborn -- every newborn in this country I think just about has a blood spot taken from them. They are collected on cards.

DR. EMANUEL: But it also seems to me that part of this issue goes to what system of accountability do we think is going to be appropriate? What are the accesses? To the extent that we do devise rules which are generalizable applying them to the context of either the academic research on stored samples, the prospective or the private, I

think is something that we can handle and think through at that stage. It does seem to me that our biggest bang for the buck is going to be trying to look at the big picture which if we are not -- again we should be able to encompass all these issues. That we raise them and bring our attention to them is useful. It would be a mistake to single them out too much.

DR. SHAPIRO: Thank you. Any further comments?

All right. Tom, I hope that you feel and certainly I feel that you have gotten both some advice but more important or equally important to advice the idea that this is a good first project. We all understand that the committee will be pursuing other issues on a somewhat different time scale, many of which were covered this morning and I am not going to go back to deal with those now since we do not really have the time to do that effectively.

Let's turn then to the Human Subjects Protection Committee. Jim, perhaps it would be better for you rather than me to articulate what it is analogously that you would like us to think about.

DR. CHILDRESS: Thanks. Alex's suggestion regarding a board and I will ask someone who can actually write legibly to put stuff on the board if there is a volunteer for that purpose.

First, after general points, in talking about strategy and tactics in the area of research involving human subjects, the work of the subcommittee and NBAC in this area, I think there are some important differences between this area and the genetics area in terms of the longer tradition of reflection on some of the ethical and policy issues surrounding research involving human subjects and the number of

standards in place in laws and in practice.

Part of what we will be doing, for instance, in thinking about the common rule which is dealing with something already in place is ask where there are gaps, ask where there are areas that might need to be revised, but to a great extent will be affirming at least our previous discussion which suggests we will be affirming much that is present there.

Now I would like to distinguish in terms of our proposal which we discussed loosely this morning a general direction and several specific directions. First the general direction. We were interested in exploring a general approach that would look again at the Belmont Principles and think about them particularly in relation to notions like community. We were interested in the second place in rethinking the area of research involving human subjects by looking at the concept of vulnerability. So those are the two major aspects of what I would call our general approach.

Then there are several specific areas and in thinking about these areas I would note that our subcommittee did not vote on these. We rather had a fairly general consensus that we should paint with a broad brush and cover as much as possible. And yet in trying to rank these I am drawing on our discussion and also our discussion today, as well as thinking about where and when we can tie in with other studies that are currently under way or other projects that are being discussed and proposed.

If we go down through a list of specifics the first one which is our mandated task is federal adherence to the common rule.

That is underway and we had a preliminary report on that this morning.

A second area that we discussed and we have had some very strong statements about is the extension of the common rule and I understand that there will be a proposal, a Senate proposal, from Senator Glenn and others to extend the common rule to groups currently uncovered. We can think about both extension within the Federal Government but also extension outside to uncovered populations.

Then a third area where there has been a lot of discussion over time and something that is do-able if we do not have to think about the cost involved in implementing it would be compensation for research related injuries.

And then there are several vulnerable populations and among these vulnerable populations are first of all the cognitively impaired subjects. That is a huge gap in the rules that are currently used by IRBs in making decisions. There is a lot of discussion of this and we will tend to that tomorrow. There are also some very concrete proposals. For example, you had in your packet the proposal of draft legislation in Maryland. So this is an area that we propose to look at and we starting to look at. And one that we think is probably do-able as well as certainly needed.

Then there are other groups as well. Children, the institutionalized, prisoners, the military. Some of those are probably groups we will have to look at assuming a second or third year of existence. But at any rate part of the task is to see how far we can get particularly with the cognitively impaired and then see how we might extend to other groups.

Then there are two other specific areas that we have discussed and areas that are also being worked on by other groups. I mentioned for each of these there is other work going on because part of the timing question has to do in part I think with tying in, you know, with reports that may be coming from other groups that we can build on rather than simply having to do everything ourselves or simply contracting everything ourselves.

One of those areas would be informed consent. You have got a draft in your packet of the Pennsylvania Center for Bioethics' work and that is a preliminary draft. I think the final version will not be ready until March but obviously that is something to build on. As well as perhaps if we send along the results from the different NIH grants that are being offered in this area.

In this area as in others as I mentioned this morning we are doing as much as possible in terms of literature review with help from the National Reference Center for Bioethics Literature. The next area and the last one I will mention is the whole area of IRBs and I found out over break this morning from Dana Miller at the Office of Inspector General and the Office of Evaluation and Inspection that there will probably be a study coming out I think developed in that area regarding IRBs. Well that is important to know and may well have an impact on the timing of our approach to these different topics.

PROF. CAPRON: The HHS office?

DR. CHILDRESS: I am sorry?

PROF. CAPRON: The HHS Inspector General?

DR. CHILDRESS: Yes. I have to check that. Right. Yes.

So again we did not vote on this ranking. I think it grows in part out of the consensus that was present at our subcommittee meeting and part of our discussion today, and in part in thinking and offering a proposal relative to where and when we might be able to tie in with other programs and projects.

DR. SHAPIRO: Zeke?

DR. EMANUEL: I was just a little unclear, Jim, what you thought the relationship between the general and the specifics are. If, for example, you were to pursue the vulnerable population and the cognitively impaired, would you first address the general direction and then apply it to the --

DR. CHILDRESS: Thanks. I had planned to mention that area of research. Thank you. Basically as I understood the way our group reflected on these matters at the subcommittee meeting we see a movement back and forth between these when we work on the general and on some of the specifics simultaneously.

Is that true, subcommittee members?

So this did kind of let the movement back and forward between the two. We had hoped for a final report, that is not a final report but the report in the fall, we hope for reports after that, however the report in the fall to be able to say something on the general level but also several of these specific areas that we mentioned and identified.

DR. EMANUEL: Several other specific areas?

DR. CHILDRESS: Well --

DR. EMANUEL: I only --

DR. CHILDRESS: Everyone adheres to the common rule,

extension of the common rule, compensation for research related injuries and at least one of the vulnerable populations.

DR. SHAPIRO: Microphone?

MS. FLYNN: I would hope that we would be able to at least begin to look at the issues of informed consent for these populations were we to take that approach which I think you are accurate, Jim, in describing what the committee expected.

DR. CHILDRESS: I have suggesting informed consent and IRBs lower on the list was simply to say we probably would start on those as part of the whole process but given the number of items on our table probably would not get to those during -- or at least not thoroughly during this year.

DR. EMANUEL: I guess I raised my eyes in some skepticism not because what you have outlined is unattractive. It just seems to me the first four topics seem to be way too much for the next nine months.

DR. CHILDRESS: On the specific?

DR. EMANUEL: Yes. That may be just one, you know, voice. I can understand that you think it is possible to do the evaluation of the government adherence to the common rule. The question --

DR. CHILDRESS: Part of the issue it seems to me is what you think is needed before the others and if you feel that we have to have, and this will depend on NBAC's judgment, that a recommendation of extension of the common rule to uncovered groups is going to require say major empirical studies versus a strong argument that this ought to be extended then obviously there will be two different projects there.

Our view was that this is something that we thought at least in the subcommittee that we could get pretty strong agreement on pretty quickly and then try to make the case for it without knowing a lot about the universe involved.

Alex, you are --

PROF. CAPRON: No. Now I am just maybe a little confused about what you thought the specific directions were. If the specific direction in the issue of extension of the common rule which I completely agree, a statement about the extension of the common rule is not conceptual problematic or practical --

DR. CHILDRESS: I know it is really difficult to --

PROF. CAPRON: Right. If that is what you mean, yes, by October that seems quite reasonable to do. I guess I have a different understanding of what you were proposing there.

DR. CHILDRESS: These were set out in part in terms of do-ability and the same with compensation of research related injuries focusing on the medical compensation. Again if we wanted to conduct empirical studies really to find out exactly what would be at stake and what the costs would be beyond say checking with the University of Washington or something like that then obviously there would be a lot more than we could do in a given year. However, we want to look over the arguments again that have been mounting in this direction and consider their possibilities and limitations then that is something that could well be do-able.

PROF. CAPRON: I do not want to dominate but it seems to me that these first three -- the first one is a sort of assessment of the

reports we have got, not conceptually difficult, easily do-able. The next two are really declarative statements, position statements that are not going to involve a lot of conceptual work or research. So it is really only the next one that I guess in my mind and it is a sort of new report kind of where we are going to break some ground.

DR. CHILDRESS: Right. And it may well be that we have to draw the line here in terms of being able to cover these very thoroughly. I do not know. But that is -- we probably will not know until we really get into this.

PROF. CAPRON: I guess I am in partial agreement with the way you have sketched this out but I see the project slightly differently. As to some -- just take what is up there now since I asked to have things in writing so we could all focus and understand. I think it has been helpful for me.

When we get to the vulnerable groups and you have cognitively impaired children and institutionalized persons, for example, those are all at least as to the institutionalized as mentally infirmed as opposed to the prisoners, those are all groups for whom past commissions have reached recommendations, not all of which have been implemented.

And in some ways one thing we might be doing there and on the compensation of research subjects is looking carefully at those past reports asking why it is that their recommendations were not implemented. Both were there problems that we as analysts see with their recommendations or are there institutional impediments in addressing those? That is certainly something we can do between now

and October. It does not involve new research.

It does involve some work and familiarizing ourselves with those recommendations and I would think that that is a very important topic because the only way if we come to any strong conclusions on those the change will occur is if we say it early and often and monitor and get the people who are responsible before us to say why hasn't this happened and why is my microphone breaking up?

(Laughter.)

PROF. CAPRON: Somebody who knew what I was talking about has a remote control over there on that side.

Then you have other topics which I am not clear as to what is encompassed in them and that is what I would like to end with a question. If you flip back to the first page that you have there -- no, excuse me, this is fine right here. The extension of the common rule to uncovered subjects. Within that it seems to me there are three distinct groups.

One are those that might be on the previous list, that is to say they are people in a grouping like the mentally impaired where there has been no agreement to have the rule apply because there has been debate about what the effects would be.

Second are those people whose research is conducted privately and where the extension, just the application of the common rule or any set of IRB procedures to them raises two sets of issues. One, do we know that they are particularly at risk? Is there a reason for the Federal Government marching in and saying you have to do this?

And secondly then there is the legal or legal authority

question by what right does the Federal Government command this? In the case of drugs it is you cannot get your drug approved unless you have gone through this process first. In the case of federal money you cannot get the money unless you have done this. If I am doing something as a private company that does not go through one of those channels what is the federal hook? There is some conception or whatever you want to call it, work to be done there.

And then there is a topic that is related to that which is those people who are involved in activities which to some people as Zeke pointed out to us are not necessarily conceived of as research and to others would look very much like research. And there, there is also a question of is it obvious that we would extend to them if they are in an HMO that is doing work looking at a different delivery mechanism because it is supposed to be more efficient, or a managed care plan or whatever, again important stuff to do. Is that what you mean by the extension of the rule to uncovered subjects? So it is all three of these groups and, if so, do you intend in that first go at it to get to all of that?

DR. CHILDRESS: Well, I have to ask the other subcommittee members to address this. My impression was we were actually going to try to hit all of those in one form or the other.

Alta? Eric?

DR. CASSELL: I think if you see the task as occurring on more than one level. Looking at the extension of the common rule, for example, or the extension to uncovered subjects what we would like to be able to do is to make a case for, in part, actually doing it in some areas, for uncovering the problem in other areas, recognizing that when

we are finished we do not have the last word, we have made an argument in some places for action and in other -- I mean, for further rules and then in other places for further action by us or others.

I think also this is easier to understand if you recognize in here -- I want to make sure I am speaking -- I am not misspeaking. But I think part of our consensual task is to try to understand the word "subject" again, to begin to go look at what do we mean by the word "subject" which takes on some of the issues that you want.

So when we talk about vulnerable populations in a way that is a way of going at the whole issue of who, in fact, is a subject and what makes them a subject, and why do they need to be protected, which may unprotect if you wish some, and on the other hand bring other populations under coverage.

So as I heard at our meeting and Jim's elegant way of making things come together it is being able to do those two things. One a conceptual question and the other is a multi-level attack at each one of these subproblems.

DR. SHAPIRO: Alta?

PROF. CHARO: And, in fact, following directly on that and to make it really concrete so, Zeke, it will not sound so daunting, we will work this out tomorrow. But the image I was --

DR. CASSELL: We will give you the details at the end of the day about it.

PROF. CHARO: Yes. But the image I was beginning to develop is one very similar to the one I am developing with regard to the endless renovation that is my house. It is the first time I have ever had a

house. It has been an adventure. The kitchen started with a paint job the day I moved in. To me that is the simple discussion about whether or not some form of protection is a basic human right that transcends questions of how you would achieve it, how you would enforce it, how, da, da, da.

And then somewhere down the line I finally saved enough money and I replaced the counters and I had the floors resanded and I put in some cheap shelving inside the cabinets that existed, and to me that is a lot about the empirical stuff on who is there, what is their situation, what do they need, what are the kinds of harms they are experiencing. Basic functional stuff which we may or may not be able to get to. It depends. Or if we do get to it we will get to it later because we will be working on paint jobs not only in the kitchen but every other room that he has outlined there.

Then the last which is the data I am still waiting for and it is as much of a fantasy as everything having to do with this commission having a lifetime of 25 years and a budget equal to that of HHS has to do with actually getting some new appliances and some cabinetry both of which in my house date back to the '30s. Actually work through in every level of detail what you would need in order to actually have a regulation issued. All the stuff that goes into what is politically workable, what is administratively workable, what would actually make the investigator's lives better and the subject's most protected.

So it is an iterative process. What we will probably be doing once over lightly is trying to make sure that we have to have some reference to the bigger conceptual issues that will go all the way to the

end so that you know what to do even on the once over lightly. But you do the once over lightly and then you return to each subject and try to do it more deeply if you have the opportunity because it is not even October, it is more like July or August if you think of production time for reports. But you have to complete your work for the first round.

And sometimes you will have to tear up some of the stuff you did to begin with when you get into the details and you realize your ideas were unworkable. So there is some inefficiency in it but I do not imagine there is any other way around it. And my kitchen is looking better.

DR. CASSELL: Yes. But it is a bad analogy because as everybody knows who has gone through that it never ends.

Zeke?

DR. SHAPIRO: And then Larry.

DR. EMANUEL: I do not want to be --

DR. CASSELL: Excuse me. I did not see your hand.

DR. EMANUEL: Do you want to go first? I do not want to be skeptical but -- and maybe Alex is right from a strategic standpoint. If you really want to focus attention on the extension of the common rule to vulnerable groups you say it now, if you come back to it you come back to it.

My approach may be -- I mean, you might deafen people. You might make them immure to listening to you by that and I worry that if we do not present a sort of well wrought document about the extension of the common rules outlining the groups we are extending it to, explaining the implications, that we may not be listened to, that we

are going to get a number of statements about the extension none of which is a sort of comprehensive treatment of it.

I, as much as anyone, I think on this desperately want an extension of the common rule to uncovered groups and especially private organizations doing things that look like research. Maybe this may be a misjudgment about the correct way of understanding it. I think a well crafted product on that rather than a sort of general declaratory paper is going to be the right way to go. That is a strategy that --

DR. SHAPIRO: If I could just make a comment here. I think, Jim, if I have understood you and your colleagues correctly that they do intend to provide, to use your phrase, a well crafted paper that is something considerably beyond the superficial treatment of these issues and which as I understand what Jim has been saying would be quite persuasive, at the very least would be quite persuasive that further action in this area is needed. It may go to some specific recommendations or not depending in various areas.

Now that would certainly in my judgment be a step forward. And while none of us can predict with any certainty just who will react to what in various ways, it seems to me that what Jim has described if I understand it correctly certainly would be a step forward. But more than providing a step forward for others it would also be a great step forward for all of us to share a common platform on which to base our continuing work.

So I, in fact, kind of admire the ambition of this group. I think it is important to remind ourselves at the same time of a remark Jim made right at the very beginning, namely that this is an area which

is compared with the genetics area rather well worked. I mean there is a lot of material out there. A lot of thinking has gone on. So I think it is, myself, just plausible that this can really be carried off effectively. I think we will learn more as the committee goes ahead.

Larry, I am sorry. You wanted to say something before.

DR. MIIKE: Two comments. One is I am puzzled by why you have taken compensation for research related injuries as a topic. I do not think it is much of an issue. I mean, I think that when you get into an operational aspect of it all it is a morass. So I would not bother with that as a topic.

My other comment is that to me if there is anything in the human subjects research area that the result of all that work on an institutionalized or system wide basis is the IRBs and the informed consent process. So I think the work that we do in those two areas are ultimately what we will contribute the most to in the long run in the human subject area.

I see the pieces that you would be working on, except for the compensation one, as building the blocks to how we then finally view the change that must go on in the IRB and informed consent.

DR. SHAPIRO: Thank you. Jim?

DR. CHILDRESS: I think you are -- I would certainly agree with the part about the IRBs and the informed consent. The reason we are putting it lower on the list at this point is those are two areas where we just need a lot more empirical work, a lot more information than we currently have available. So of all the areas I think those are the two that really require the most work over time to find out exactly what is going

on in the consent process, exactly where there are problems, to find out exactly what is going on in our IRBs.

Regarding compensation for research related injuries this, as Alex has mentioned, is a topic that has been discussed over time at least for the last 20 years in the work of the DHEW Secretary's Task Force and in '77 or so and the work of the President's Commission, and in other contexts as well including a lot of the literature. And there seem to be at least members of our -- many members of our subcommittee seem to think this and I have to agree that there are some pretty strong arguments for going in this direction.

Now the operational part is not again something that would obviously require a lot more information probably than we will have and we may at this point end up with some arguments for going in a particular direction and there may well be counter arguments on the practical side or the cost side, et cetera.

But it is not -- on the one hand -- I mean I am hearing contradictory things here. But on the one hand I hear the comment it is not much of a problem. On the other hand I hear that it is a morass. If it is not much of a problem in terms of there are not very many injuries and so forth and, in fact, it is not something that would be that significant a drain, but it will be symbolically important for affirming this. And it goes back to our sense of community as well as vulnerability that, in effect, to affirm solidarity with those who participate in this enterprise and who are injured in a nonnegligent way in that process.

DR. MIIKE: Just a comment on that. I was in a group that looked at this when the first possibilities of HIV vaccine trials were

to come up and the issue came up. I think it is going to be a morass because it is quite easy to define in the abstract sense what our compensation system would comprise of. But when you get into the issue of was it the research treatment that actually caused the harm or was it the underlying disease, the issue about absolute immunity if one sets up a compensation system, absolute immunity from the tort system, of course there is always the question about who pays. Aside from the issue about is there undue influence, et cetera, etcetera.

But I read the transcript of your group. I never got the sense out of that transcript that this was a burning issue for your subcommittee. So I was kind of surprised that it popped up as one of your deliverables in the immediate future.

DR. CHILDRESS: Well, I may have misread the group. I would not say burning but I thought one that we felt that enough work had been done on and it would get some fairly strong consensus on, but is that fair, subcommittee?

PROF. CHARO: Yes.

DR. SHAPIRO: Alex and then David.

PROF. CAPRON: I am concerned that in the very first task, mandated Federal Government adherence to the common rule, that we have a high budget and a low budget approach to that. It may be that in the first year it would not even be the budget. It would just be a timing question. If we were to conclude after Joel's work or whoever takes over that task that with certain minor corrections and some cleaning up of some administrative glitches and so forth that the various parts of the Federal Government are all adhering pretty well to the

common rule, and I were to pick up the New York Times the day after our report came out, I suspect the headline and putting aside headline writings, the lead paragraph, would be National Bioethics Commission concludes Federal Government doing a good job of protecting human subjects.

We will not know that from knowing whether or not people are complying with rules because we do not know, they do not know what is going on for the most part. The system is not set up for that to be the case. They cannot tell you how many research subjects there are and outside of adverse report things that rise to a certain level which may not be indications by the way, you get an adverse reaction, may not be an indication anything has gone wrong. That may be even an expected adverse reaction if it is serious enough.

So part of the question is -- I would like to be better informed about what that long awaited NIH funded study on IRB's is going to tell us. So we could scope fairly early in our task whether there is something more that might be done to provide more reliable assurance as to the way in which the set of federal rules, however well complied with by the agencies, are actually filtering down to the subject researcher interaction in that level.

So I would hope that part of the thought process and the work product that goes into that number one is to identify what more needs to be known and to follow up on what Rhetaugh was saying this morning it may be that we would never see ourselves as able to do the studies that would provide the answers to that question. But if it turns out that it is a question we think needs to be asked and answered then

we spell that out even as soon as the first report so that any intelligent reader will know the caveat with which they ought to take our expected conclusion.

DR. CHILDRESS: I think that is fair. I think it is fair and actually in the context of our discussion in the Human Subjects Subcommittee we first deal with IRBs precisely in relation to the question of adherence to the common rule. So I think that we share that and that I think it is important that point should be underlined.

DR. SHAPIRO: Alta and then David?

PROF. CHARO: Alex, I think it is also because this is the effect of having subcommittees and not all being present at one another's discussions. I think that the degree to which how much work needs to be done on number one then will control how much room there is to work on everything else except for perhaps number two which I think is equally high up there although unmandated.

It is precisely why I was saying this morning that I think it is time that the subcommittee members themselves read these reports and do what they are going to do with them including coming to the conclusion that they do not tell us enough because with volunteers you cannot expect people to be putting in 60 hour weeks to get something out in time for somebody else's schedule. That is not a reasonable request.

So the committee members have to do it themselves and I would be very surprised if what happened was that there was a report that would permit a headline that says the conclusion is that federal agencies are all doing everything they have absolutely got to do and are

doing a wonderful job. I would be amazed. Based upon the preliminary reportage we got at the subcommittee meeting which said that there were significant gaps in the detailed information that one might have hoped to get back from the original reports. So this has not passed unnoticed.

DR. SHAPIRO: David?

DR. COX: I would like to come back to something that I brought up earlier this morning concerning ways of empowering groups of individuals whose role in a particular form of research is essential to providing the information and it was at that point that I brought up compensation -- group compensation in one form or other that may be a way of that kind of empowerment. To demonstrate to Steve that I am partially educable I quite agree that that does not have anything to do with powers but maybe this is where we can put it. And that I also agree with Larry that let's get rid of the injured people and stick it in here. So that is a suggestion that we could still deal with compensation, deal with the group in the community issue but maybe fill it in number three there and I would be very -- I would like to see that first one.

DR. SHAPIRO: Laurie?

MS. FLYNN: I would just like to make a comment as one who is I think here to represent sort of the community and the nonexpert that I am hearing some tension and I have been feeling it all day and it is between a sort of a more cautious, slower, very strongly academically and scientifically based process versus a sense of urgency about the rising visibility of some of these issues, the sense that we have some glaring gaps in what we would like to see as the whole of our enterprise,

and I think some recognition that there are other forces which may view these issues with a lot less understanding than this group does.

And it was my sense that that has been played out in discussions not only of whether our agendas are too big or too small or too focused or too broad, but as we heard earlier today in terms of are we planning for lots of money and a long time, or a little money and a short visit with each other, I think it is terribly important to recognize as I know we all do that this is as all activities in Washington at some level it is a political activity and that we need to claim and own this agenda insofar as we believe we have capable individuals and staff available to help.

I would rather and appreciate Jim's laying out an ambitious agenda and appreciate Harold saying, you know, I think we can make some progress and really move the ball. We will do much more in some areas than others but all of it will be important. It will be important in focusing the issues. It will be important in owning a leadership role as these discussions go forward. It will be some visibility that the federal establishment has recognized a need to address these issues.

I believe, Alex, it will require in terms of the cognitively impaired much more than merely reviewing and affirming what was done and said in the past and asking maybe why we could not get some of it done better. That will be important but that is only a first step in my view and, in fact, there are a number of people who have done a great deal of thinking about how to advance and how to assure stronger protection that also does bring in some of these issues of the effective

role of community with impaired and vulnerable subjects.

So I really want to argue for us not to be afraid of the scope of the agenda, the complexity of the agenda, the cost of the agenda. That is what I signed up for and I am eager to meet that challenge.

DR. SHAPIRO: Thank you. Other comments?

DR. CHILDRESS: Well, let me make --

DR. SHAPIRO: Jim, do you have any other questions that you would like to know from us?

DR. CHILDRESS: Well, just we need to get some sense of the group as to how they would like for us to proceed.

PROF. CAPRON: Could you flip back to the first page that you were calling the more conceptual issues?

DR. CHILDRESS: Looking at the issues raised by Belmont particularly in relation to concerning our theme of community and examining vulnerability as a concept that may provide a lens for looking at some of these matters.

PROF. CAPRON: What happened to the whole question of the reorientation of the idea of protecting human subjects?

DR. CHILDRESS: That is part of our discussion of vulnerability of community.

PROF. CAPRON: Well, everybody seems to have a different answer as to where it comes --

(Simultaneous discussion.

PROF. CAPRON: Let me just understand. The common rule part up here is really going to be plugged into the report that is on

the next --

DR. CHILDRESS: That was really a --

PROF. CAPRON: Out of order.

DR. CHILDRESS: -- preliminary point. I had not told Alta when to start writing.

PROF. CAPRON: Okay.

DR. CHILDRESS: That was a preliminary point.

PROF. CAPRON: So the general direction is the exploration of this community question that we had this morning.

DR. CHILDRESS: And vulnerability.

PROF. CAPRON: And vulnerability which got talked about later on in the context of particular --

PROF. CHARO: It is not on the agenda.

PROF. CAPRON: Alta, it is not off the agenda, it just comes up.

(Simultaneous discussion.)

PROF. CAPRON: And vulnerability we have talked about a lot by naming groups that are thought of as vulnerable populations.

DR. CHILDRESS: Our approach was to say that, no, we need to look at what is common in the discussion of vulnerability and take that as a concept where we can look at all potential and actual research subjects, and then recognize that there are different degrees of vulnerability and that may well require different kinds of protection. But this is also a vulnerability to exclusion as well as to abuse within the research.

PROF. CAPRON: Well, I would -- I know we are not at the

point of writing that part yet.

DR. CHILDRESS: No, we are not.

PROF. CAPRON: But there is a question of the way you go about asking what you are after and I think that for all the attractiveness of vulnerability that it is a -- it is very, very strained to say vulnerable to exclusion. I mean if you were talking about an orientation --

PROF. CHARO: Why not --

PROF. CAPRON: I will tell you why. If you are talking about an orientation towards research which says that the major objective is to protect the vulnerable you are talking about a very different orientation than if you are talking about an orientation that says the major issue is to ensure participation and to the extent that in many areas today the arguments about research are that what is wrong is getting kept out of the research then it seems to me that orientation we ought to be -- and it should be either a separate topic as to has there been a change in the whole paradigm and then within that question would be within the vulnerability paradigm do we have to rethink what vulnerability means.

If you have every one who has AIDS -- everyone who is HIV positive or everyone -- every White male between the ages of 25 and 35 who has, or every White male between the ages of 25 and 35 who has an income of more than $50,000 or whatever -- however you want to cut it and you say this group is all the same, then it does not seem to me that you ought to be then talking about vulnerability within this group to exclusion. The whole question is rather is there an entitlement to be in a

research project and, if so, at what stage of the research if you have certain qualifications in terms of your medical situation or are we going to -- that was not the question that the Belmont Report asked and it was not the mental framework in the 1960's and '70s.

In the 1960's and '70s was you have people who have medically interesting conditions and researchers who want to do research on them and they need to be protected. The National Commission for the Protection of Research Subjects, not the National Commission for the entitlement of people who might want to be research subjects.

I am just saying it is a -- we have had a -- there is another paradigm that has grown up. It has not replaced it. There are two competing paradigms and that seems to me it is not captured very well by the term vulnerability.

DR. CASSELL: But that is a different statement.

DR. SHAPIRO: Mike and Eric.

PROF. CAPRON: I am just saying I would like to see that explicitly --

(Laughter.)

DR. CASSELL: What -- I think that the word "vulnerable" we have chosen because Arturo presented it so well but the basis, the background for this is that there is a change in the relationship of research and subject. In the 1960's empirical researchers and endangered subjects. In the intervening 30 years or 36 years or whatever that has changed to a certain degree. Yes, subjects may still be endangered by research but the whole population has entered into

the scientific endeavor in a way that was not yet envisioned in the 1960's.

One of the effects of that is that both researchers to some degree certainly and subjects have a different view of their role and of the need to protect both their own care, the scientific establishment, advances, and the person whose subject. As that happens then the problems of exclusion come about because in the attempt to protect people they were protected away from being able to participate in research that promised them a treatment that they would not otherwise have gotten.

It is not so much specifically that you pick out a certain group and say, well, you know, we -- we are not talking about that being excluded. It is the question of how we can as a subcommittee certainly redraw our understanding of the relationship between subject and research and what we mean by the word subject, of which vulnerability stands as a good -- catchword is not what I mean, as a good quick way of saying it but for a much more complex understanding of what it is to be a subject and what has to be taken care of.

DR. SHAPIRO: If I understood -- there is a number of people who want to speak on this issue. But as I understood Jim and his colleagues talking about this morning is they acknowledge that they too felt vulnerability was a kind of -- not yet quite sure that was the right lens I think to be correctly used, and so that I think that issue which Alex raises needs further discussion by the subcommittee. Whether that is the right lens or some other lens, some other setting so to speak would be better for it.

That is all I understood you were saying, Jim. I think that judging from the comments everyone has made I think everyone on NBAC accepts the notion that Eric just articulated and apparently I think Arturo summarized in something you may have said at the subcommittee level that these -- a lot of the background, issues of change in these 30 year periods, there is a different set of issues which are going to impact just how we feel about many of these things. But I, myself, do not know whether vulnerability is the right or the wrong lens to use Jim's phrase yet. I think we are going to just have to see about that as we think more carefully about the issue and the issue Alex raises may turn out to be important for us and we will just have to see.

Alta and then Rhetaugh?

PROF. CHARO: Yes. Also again just by way of background information I think actually much -- this was developed much more thoroughly than you might have had a chance to find out because, in fact, the subcommittee meeting started with the question of whether the paradigm has changed. It started with that phenomenon of the demand for access, does that change what the basic thrust of the regulation of human subjects research ought to be about. Should it be about dual paradigms? Should it be about one to the exclusion of another, et cetera?

And in the course of that discussion I think that this is also I think what is exactly -- what is appropriate for the whole committee and for the subcommittee tomorrow. I got the impression that the following things were emerging: That number one the problem of access is extremely real and highly emotional for very specific groups

of people who are epitomized for example by people who are HIV positive, who have wanted more rapid access to innovative therapies of all sorts.

Second that although this is a very real problem it frequently is one that is addressed through FDA because so frequently it arises in the context of drugs and devices so that it is already being addressed at the regulatory level to some extent by virtue of changes in FDA's own policy about fast tracking access to certain things which reduces the universe of people who are totally without some kind of concern about access issues.

Next that in terms of who is nonetheless vulnerable as a result of this, ironically it is not the people trying to get access, but to the extent that there are any kinds of groups that are routinely excluded, if they are representative of a larger portion of the population which then goes on to use things like drugs and devices without ever having had testing on people who are similar to them broadly you have created a new class of experimental subjects who are not covered in any way which kind of returns to the very basics of who is uncovered.

Example: We do very little research on pregnant women except for things that are therapeutic for extremely serious medical conditions for the pregnant women themselves and their unborn babies. So with regard to less significant conditions, right, we have a real gap in our knowledge base about the way various drugs would operate if they were taken. This means that every pregnant woman who does take something because for whatever reason it is important enough to take it is, in fact, in the therapeutic context becoming an experiment of one with

no controls, academic or governmental. And in that sense those people, indeed, are vulnerable because of not being covered by virtue of people in their class having been excluded.

So that whether we stick with the word "vulnerable" or come up with different words, whatever, I think that there was already some significant discussion about trying to identify how the problem of access plays into who is more at risk in the long run both from the research itself or from less formal forms of research, i.e. medical practice which is a continuing experiment with every patient.

We may find the right word but one of the issues really is whether or not this notion of kind of the priorities of continuing to focus on gaps in basic coverage of protection with access being something that may follow up since it is partly handled by FDA and maybe comes up later in the paradigm, if that is acceptable or not? Right? That is a real policy question. But this has been thought through a little bit more than may have been apparent by today's discussion here.

DR. SHAPIRO: Rhetaugh?

DR. DUMAS: My comments were more process oriented. I think that what we are dealing here with is whether or not we can accept the broad outline of the task that this group has defined for itself. I get lost after that into the details because I think that once we begin to work on this task then many of the specific issues will emerge and we will have an opportunity again for input on how they should be dealt with.

I think we are dealing here -- I find myself dealing with differences in how we approach work and how we conceptualize the task.

But I do not hear anything that tells me that there are real problems in accepting the general overview of the work that is to be done.

DR. SHAPIRO: My thought on that, Rhetaugh, and it is a very helpful remark, is that there is broad agreement here regarding this approach and what members of the commission are trying to do is to give Jim some helpful hints of what things he ought to be thinking about and working into his thinking as he and the committee proceed. That is what I -- and I think that is helpful because not everybody is a member of the subcommittee.

DR. DUMAS: But it is important for us to understand that we will have another chance.

DR. SHAPIRO: Oh, yes. We will have more than one other chance.

DR. DUMAS: We have more than one chance.

DR. SHAPIRO: Arturo had his hand up before. I do not know if he still wants to speak.

DR. BRITO: I just want to -- everybody keeps quoting what I said at the other meeting. I want to clarify it a little bit. The issue of vulnerability, and once again we did talk about that, I do not know if it made the transcripts or not, I cannot recall, but we did talk about maybe it is not the correct word to use but it is for lack of a better word at this point as what we are using. But the issue of vulnerability, the discussion of it was so extensive because of the following reasons:

This is one of the major points I made at the beginning, is that if we focus our attention on those that have the greatest potential to be vulnerable this allows for protecting all research subjects which

essentially can be vulnerable at some point in time during research. So it is not just minority groups. It is not just the cognitively impaired. It is not just children, et cetera. But looking at those groups first allows us to be more comprehensive.

And I am looking at this here. I am drawing an upside down triangle where we are looking at first these general topics of community and vulnerability, and I think we also need to look at maybe within these two is the changes that have occurred over the last 20 years particularly since the Belmont Report as another general topic that has changed things such as genetic research, et cetera, before we get to the specifics.

I do not see how we can look at the specific topics until we discuss these general ones. It does not mean we have to go into how each and every group is vulnerable, but what defines somebody as being vulnerable as a general concept and then going on and how that relates to communities, not each specific community initially but then later on specific ones.

I guess everything else has pretty much been said that I have written down but I just want to clarify that and I gave a definition of vulnerability a little more extensive than that which is in the transcripts. But we will leave it at that.

DR. SHAPIRO: Thank you very much. Trish?

PROF. BACKLAR: I guess I want to say that I -- going back to something Alta was saying is that I believe part of the demand for access to research may reflect the general problems of adequate access to health care and I just do want to make this statement because

it is important to all the work that we do. It makes for the therapeutic misconception that may cause some real problems in research as in the drug washout case that Laurie and I keep referring to. That is all.

DR. SHAPIRO: Thank you. Yes?

DR. SCOTT-JONES: I would like to say that in areas where there is a real disagreement we ought to have a way to say that there is a disagreement and to take it under advisement when we continue to discuss this. So, Alex, when you were commenting earlier it is the case that you are asserting that you accept that there is a right to be protected from harm in research but you do not accept that there is a right to be included, a right to participate, then maybe we should think about that. But is that what you were saying?

PROF. CAPRON: No. That was not what I was saying. I am glad you asked again. What I was saying was I did not think that the discussion, the very interesting discussion which I read in the transcript, was captured by this notion of vulnerability and I am actually encouraged to hear Arturo in describing it to say that he thought there were three topics, community, vulnerability and this change in paradigms. That is all I was trying to say.

I was not taking a stand on whether one or both of the paradigms should exist and be supported by the way the regulatory structure is. It just seemed to me that the paradigm that is embodied in our present regulations is the paradigm of protection and the other paradigm of inclusion and a right to be included is not well represented. It has been layered on somewhat uncomfortably I believe in light of pressures to be included.

I think I am very comfortable to follow on what Rhetaugh said at this point in not trying to nail everything down at this moment and I have great confidence in Jim and members of the subcommittee. I am worried that we not get too far into the process before we have figured out conceptually what we are trying to do because it is not going to be possible six and eight months from now when a first report is being written on this subject to say, oh, well, actually we should be doing this or that. I mean we will not be able to do it then and we may get locked into some of these things.

Jim described the vulnerability idea as being a family of ideas and it may well be that that family an encompass the notion of therapeutic orphans which is what Alta is talking about. Something that has been in the literature for 25 years in discussion about the way that children and pregnant women get excluded from trials and, therefore, you do not necessarily have the basis on which to prescribe in a safe and reliable way drugs for them. I think that is an important topic. I do not think it is a topic that is much illuminated about talking about them as vulnerable research subjects. I think it is a different policy issue. But if we right now want to use this term and understand we are talking about ten different things I am comfortable.

I want to ask a question of Jim which is a couple of other topics we talked about this morning, one of which might be on the list for our own fast track, and that was the national IRB. The national IRB is in effect the ethics advisory board which is part of the HHS and therefore I guess -- I do not know if it is in the common regulations. Gary, is it. It is just in HHS.

DR. ELLIS: Yes.

PROF. CAPRON: Okay. It contemplates something that is very close to everybody's heart now. That is to say certain categories of research involving very vulnerable patients, and they are enumerated there, are supposed to be reviewed by an ethics advisory board to the secretary. If that was what you meant when you talked about a national IRB or its an instance of a national IRB we might want to look at that.

Again I agree, Laurie, it is not a question just of going back to past reports and saying they were nice and whatever. I very much would like to know what has happened since then on anything. Why hasn't steps that were recommended or are required been taken, et cetera, et cetera? Have a political context for it and I think that is an important part of it. But since that is a topic which could be addressed it seems to me in the fairly short run I would want to know if you would like to see that listed on your things that will be addressed. To me it is in the same category as the compensation issue. It is possible probably to get a handle around it.

DR. CHILDRESS: I think there might well be some interest on that in the subcommittee though I will let members speak for themselves. I was thinking about it in presenting it today more as one of the questions to arise about the whole IRB system. That is what kinds of structures do we need in place to supplement or in some way to improve what we currently have. So I simply saw it as one of several possibilities. But it is -- if the group feels that this is something we ought to hit early?

PROF. CAPRON: You also mentioned in passing and maybe this is on the same level of how do we supplement IRB's and in

the transcript there were some comments by Joan Rachlin about the notion of using -- having certain IRBs take responsibility for a particular protocol and really work it up in a really, really excellent way. Think it through in more detail and give it better review than an IRB that perhaps is processing one protocol every three to five minutes in a busy agenda can do. Where you have multicenter trials going on making -- her term was "Center of Excellence" which is kind of a loaded term. I am not sure if it would work but it conveys an important idea.

There you have a very interesting idea that ties into your notion of community because on the one hand you can see all the IRBs being a community among themselves and on the other the whole argument in favor of having this done at a local institutional level is that that IRB would reflect its community so that if you have an IRB at a Catholic hospital or a Baptist hospital or a nonsectarian hospital, or a research university, or whatever, that each of those might look at the same protocol somewhat differently and how do you allow the IRBs to reflect that while at the same time maybe improving the quality of the protocols that they look at from the viewpoint of the protection of subjects, and can that be done?

It seems to me that you, therefore, tie into what you see as a general issue. But I would like to see that somewhere on the research agenda, too.

DR. CHILDRESS: I think that is important and whether it could fit in with our overall discussion of assessment of IRBs would be important.

PROF. CAPRON: Yes. It probably is a subsetting under

the IRB but it is not something I think that is coming out of Charles McKay's study at all because it was not -- that is not what they are looking at. What they are looking at is IRB functioning now. This is a question would there be a way of improving the quality of IRBs while still taking into account a value that IRBs are supposed to serve of being in some sense sensitive to their own community's particular views and values.

DR. CHILDRESS: Good. Thanks.

DR. SHAPIRO: Thank you. Other comments at this time for Jim and his subcommittee?

Well, you have a full agenda and lots of help which I am sure you will use very effectively. I think it is fair to say that the NBAC is really quite pleased with the general structure that the subcommittee has come up with and look forward to our next chance to discuss these issues which as we all know will be in March.

DR. CHILDRESS: Can I just add one point? I received a note perhaps from a subcommittee member that I have not mentioned anything about education. This morning when we talked about -- I mentioned it in passing that is one of the implementation strategies and it seems to me that it will come out as one way to extend whatever we come up with on these other levels.

DISCUSSION OF FUTURE NBAC ACTIVITIES

DR. SHAPIRO: First of all I want to thank the chairs of both subcommittees once again for getting us off to a good start. We will all have a chance as I said a few moments ago to review in writing these general ideas over the next six to eight weeks or so and then have

a more detailed and probably even more informed discussion at our March meeting.

There are two issues I wanted to raise, two additional issues I would like to raise. There are two additional issues I would like to raise with NBAC right now. One has to do with what we will schedule for the March meeting in addition to reports from and discussion of the work of the subcommittees. The second has to do with some follow up, perhaps some follow up of the international summit that we sponsored in San Francisco in the middle of November.

Let me go to the first of these topics. The question is the agenda for our March meeting. My proposal is that in addition to our most important work which will be discuss the work of the subcommittees and keep pointing us towards our responsibilities in October and beyond. That will obviously be the first and most important item on our agenda.

I thought, however, that it would also be useful to schedule some time for us to hear from representatives of important constituencies. For example, just to take a few examples, not trying to put these in any kind of order at all, but to hear for example from the American Association of Medical Schools or Medical Colleges. I forgot what the A -- AAMC, is that --

DR. _____: Yes, colleges.

DR. SHAPIRO: -- regarding what -- regarding our agenda and what they think perhaps should be on our agenda in addition to what is on it. The same thing to a group perhaps representing practicing physicians, groups representing patients, others and so on. These would

have to be articulated more carefully than I am doing right now. But I do have a sense that it is important to supplement what is available in our public comment section by actually taking some initiatives ourselves and to go out and invite representatives of certain groups to address us.

If that seems reasonable to you we would appreciate any suggestions you might have. I do not think we have time today to discuss that in any great detail but we could take some suggestions and we would try to put together a modest list. We cannot hear from 20 people. We will all be asleep before that is over. But to begin a process at least because we may do this at some future meeting as well, to reach out to important groups in the areas in which we are discussing and give them a chance to tell us what is on their minds.

Jim, do you have a comment?

DR. CHILDRESS: Just a comment. A couple of the areas we thought we would need a lot more information this morning had to do with patients and why they choose to participate or decline to participate in research. And second, what researchers actually -- investigators think about the regulations, the guidelines, the functions of IRBs and so forth. So if there would be any way to work some of that into the presentation that would be most helpful for the subcommittee.

DR. SHAPIRO: No, I think that that -- there is no reason why we cannot and we will look to you for some -- not, I do not mean, Jim, to you especially, but to members here for some recommendations. We will be in touch very shortly on that because it is something we would have to arrange well in advance.

Tom, if your group has in addition to those people that

you are seeing in your subcommittee, if you have people which you think would be helpful for the whole committee to hear from we would be glad to do that.

Yes, David?

DR. COX: Harold, this probably goes without saying, but so that we could have some time where we could have a question and answer with those people because rather than just a prepared statement, but to be able to get their views on some of the things that we are considering.

DR. SHAPIRO: Right. Absolutely. A very good point and we will certainly do that. So we will be cautious in the number that we actually schedule and also ask them if at all possible to give us some written material in advance and to make the actual presentation rather modest in time so that we have time for Q&A which is probably the most effective part of these discussions.

If that is satisfactory to the committee we will proceed to put --

PROF. CAPRON: I am trying to imagine myself being Giordi Coe (?) and the head of the AAMC and knowing what in the world I would say at this point in this body's deliberations compared to being offered the same opportunity to speak to this group in July or September when at least I would be commenting on some initial drafts. It would be one thing to say to any and all of these groups that we would be happy to hear from you early in our process, if just looking at our agenda suggests things to them which are not on the kind of list that is going to emerge from this meeting hearing from our two subcommittees where

they could each on a page list the topics that we are going to be looking at and saying are there things that we have left out. And any group that responds to that by saying, yes, we would like to come and talk to you about something you have left off that ought to be part of it, that would be useful.

I just -- I am a little skeptical about the value to us of hearing that or the value to them of having their shot at us when we have not done anything.

DR. SHAPIRO: Well, again I can speak for those groups that have been in contact with me already. And they certainly are extremely anxious for us to hear directly from them what is on their minds. And it really is that that I had in mind. They want to talk to NBAC about that. And if we are judicious and we try to, you know, there is an endless number of those groups, we can only have a certain number, I think that they will feel very much more included in the process and want to be sure that we hear --

PROF. CAPRON: Is this mostly in effect on our agenda?

DR. SHAPIRO: Yes.

PROF. CAPRON: In effect, things that they want to make sure that we have thought about.

DR. SHAPIRO: Okay.

PROF. CAPRON: That is fine. I mean that is focused because those are people who have said exactly what I was saying.

DR. SHAPIRO: That is right.

PROF. CAPRON: And give them the opportunity rather than saying to whoever at AAMC or AMA or whatever this is a command

performance and they trot out their --

DR. SHAPIRO: Oh, no, no. It is not the latter because that would not use their time or our time very well. You are quite correct.

PROF. CAPRON: But if you have already heard -- you are in effect saying you have heard people and you want our permission to --

DR. SHAPIRO: That is right.

PROF. CAPRON: Yes, okay.

DR. SHAPIRO: Secondly, before we break, I do want to break for a few moments before our public comment session, one to give us a break and, two, I have to make a phone call. But there is one other issue which really does not need in any way to be resolved now but I do want members to think about it. That is I have gotten quite a lot of communication from the international summit we held in San Francisco from our colleagues filling analogous positions roughly speaking around the world eager for us to follow up in the sense of eager for us to continue to be a group they can interact with, both individually and collectively, as they plan their own work in the months and years ahead.

The question is and we can revisit this perhaps in March, is whether we want to take any initiative to continue to either ourselves send delegates to functions like that which will take place elsewhere around the world, if we want to take any initiatives to bring people together again maybe a year from now or something of that nature. In some sense how highly we value some continued interaction with our colleagues in other parts of the world who are addressing in a broad sense similar problems to the ones that we are addressing.

I raise this only because, one, it came up at the very end of the meeting as those who were there will remember and, second, that continue to get mail asking if we are going to continue this initiative in the same way or not. I do not think we have to -- unless there is someone who has something they really want to say today, that is fine, but if not it is something which I will just -- we will come back to perhaps next time.

PROF. CAPRON: If you had volunteers.

DR. SHAPIRO: If we have volunteers who want to do things in this area carry on the work for us and represent us and so on and so forth.

PROF. CAPRON: No. What I meant was volunteer other countries that send -- we would like to host the next one.

DR. SHAPIRO: Correct. And the question is do we want to participate and so on and so forth. We would not have to run this whole thing. I am not saying that. We do not have the capacity to do that.

David?

DR. COX: What I was going to say pertained to a previous thing.

DR. SHAPIRO: Okay.

PROF. CHARO: One quick thing. If we could simply find out what the calendar is for their own public meeting it might be nice for those of us who have other reasons to be traveling already to double check whether we will be in their vicinity and ask then if we can attend as an observer. It is a simple thing but it takes a little bit of lead time.

DR. SHAPIRO: We can certainly do that. Many of them have periodic meetings of various kinds that is sort of special meetings, conventions and so on. I think it is in France. They meet every January and --

PROF. CAPRON: January 16th this year, 15th and 16th.

DR. SHAPIRO: -- and so on. All right. Well, I will -- we will attempt to put some information together for it. If any of you have any further thoughts on that let's bring it up next time.

Okay. Let's adjourn for about 12 and a half minutes and then we will reassemble for public comments.

(Whereupon, a brief break was taken from 3:50 p.m. until 4:05 p.m.)

PUBLIC COMMENT

DR. SHAPIRO: Colleagues, once again could we please assemble?

We have four people who have signed up for public comment. Let me just remind everybody what the ground rules are the committee has adopted in this respect. Each speaker has a maximum of five minutes to present their comments. I will try not to be too rigid about it but remember that if one goes over too much I will -- I do not have anything to pull, or the hook, or that old trap door underneath the table, but just ask people to be considerate of others who are waiting to give their comments to the NBAC members.

The four people who have signed up for today are Dr. Shamoo, Dr. Barash, Nancy Reame, and Chris Kline. I will say a little bit more about each in just a moment. But first on our list is Dr. Shamoo,

who is professor of Department of Biological Chemistry, University of Maryland at Baltimore.

Dr. Shamoo, thank you very much for being here today.

DR. SHAMOO: Thank you. Thank you, Mr. Chairman.

I have to my right Vera Hazman (?), chairman of the Citizens for Responsible Care in Psychiatry and Research, and to my left is Janice Becker, a mother of her daughter --

(Technical difficulties.)

DR. SHAMOO: -- describing my testimony.

My written testimony of course is much longer and you have a copy of it. It is 12 pages, which is essentially an expansion of the testimony I gave to the U.S. Senate Governmental Affairs Committee ten months ago.

I am Adil E. Shamoo from Columbia, Maryland. I am here to speak on behalf of Citizens for Responsible Care in Psychiatry and Research. For the purpose of identification only the following is a brief statement about my background:

I am a professor and former chairman of the Department of Biochemistry and Molecular Biology at the University of Maryland, School of Medicine in Baltimore, Maryland. I am the editor-in-chief of the Journal of Accountability in Research. I have chaired five international conferences in the United States and in Europe on issues of ethics and research. The last such conference I chaired was in January '95 titled "Ethics in Neurobiological Research with Human Subjects." Finally, I served on several boards, among them the National Alliance for the Mentally Ill, an elected position.

I would like to thank you, Mr. Chairman and members of your commission, for giving me this opportunity to inform you of my personal and my organization's grave concerns regarding the current ongoing research practices of using persons with mental illness as human patient subjects in high risk experiments which cause them harm. Our organization's urgent message is one, an immediate moratorium on all nontherapeutic high risk experimentation with mentally disabled persons which may exacerbate their illness such as medication washout and the use of foreign chemicals known to induce relapse with severe symptoms such as psychosis and delusions.

Two, a full and thorough investigation of the past 30 years of neuropsychiatric research experiments that were of high risk and may have harmed patients.

The issue which I bring to you, I believe, is of greater magnitude than the two well known instances in our recent history. Namely the Tuskegee syphilis and the Radiation Exposure experiments. I say this for the following reason: The sheer number of mentally disabled victims who have been used in recent years without their ability to comprehend the nature of these invasive, high risk, often painful experiments and who could not therefore give their informed consent surpasses the number of those who were victimized in the Tuskegee syphilis and the Radiation Exposure experiments.

To illustrate: Two recent studies, one our's -- by the way I brought also a few copies and Ms. Norris will give you copies of these if you want, a paper in '93 which was the wake up call and a paper just appeared recently on the subject. These are sort of from the beginning

to the end.

Surveyed literature for the past three decades of studies involving complete sudden withdrawal of medication from patients, that is washout, with subsequent return of symptoms of psychosis and delusions, that is relapse. These experiments involved 4,365 patients diagnosed with schizophrenia and that is only a narrow window on the subject. The routine inclusion of uncomprehending mentally disabled patients in high risk nontherapeutic research which offers no direct benefit to its subject is a violation of fundamental human rights.

In New York the courts have recently come down hard on the state's psychiatric research policy. In a unanimous decision by a panel of five judges in New York State Supreme Court Appellate Division the court declared that the state violated state and federal constitutions by conducting such nonconsensual experiments on children and mentally incapacitated adults.

The psychiatric community's blind eye and deaf ear to ethical violation by its members is apparent in the professional literature where investigators seem oblivious to the contradiction of their statement when they report. I quote, "28 acutely psychotic patients with schizophrenia..." and I had the words "were the subjects" obviously and I am continuing quoting, "...all of the patients in this study were capable of informed consent and entered voluntarily," end of quote.

The most troubling question that continues to perplex us all is how to ensure that our fundamental moral principles are not compromised in the name of science and how to ensure that human -- that the human rights of the most vulnerable disabled individuals who

are unable to protect themselves are not violated for the convenience of society or more likely for those who are in a position of power.

The first of the six principles enunciated by the Radiation Commission just recently is, and I quote, "One ought not to treat people as mere means to the ends of others." Unfortunately, an important and powerful research organization, the American College of Neuropsychopharmacology whose members conduct psychiatric research with human subjects uphold standards of ethics which have been rejected since Nuremberg.

In their most recent statement of principles of ethical conduct about the subject states, and I quote, "All persons living in society have a moral responsibility to participate in efforts to promote and contribute to the present and future welfare of that society. Research is one of these obligations," end of quote.

It is especially distressing that the Fraternity of Psychiatric Researchers in our continue to invoke a morally unacceptable etiology to lay claim to their unsanctioned right to conduct nontherapeutic experiments on mentally disabled persons. No one has moral obligation to participate in research. We do not conscript our citizens. Mentally disabled persons who are incapable of making an informed voluntary decision should never be exploited for the benefit of others.

Ethicist Tom Beauchamp in a recent article that just came out rebuke of the human radiation experiments applies equally well to the use of the mentally disabled in research, and I quote, "Never in the history of civil medicine has it been permissible to exploit patients

by using them to the end of science in nontherapeutic research that carries a risk of harm," end of quote.

Our recommendations, we have eleven of them, you have a copy of them and I will only state a couple of them: One, enact a national human subject welfare act for all research on human subjects. Its scope not to be limited to the source of funding, federal or private. We ask that humans be afforded the same federal legal protection as are already provided to animals and of the National Animal Welfare Act. Is it not ironic that animals were given greater federal protections than Americans?

Two, unethical experiments with vulnerable mentally disabled human beings are being conducted now as I speak to you. And you members of the commission, you can do something to end such inhumane violations against disabled vulnerable human beings.

In closing, to investigate the unethical exploitation of mentally disabled persons who cannot give informed voluntary or comprehending consent are nevertheless subjected to experimental research studies which are against their own best interests. We believe and the courts have recently agreed such experiments on nonconsensual persons violate fundamental human rights.

I thank you, Mr. Chairman.

DR. SHAPIRO: Thank you very much for your very articulate statement. I do hope you will provide Ms. Norris with those articles so we can distribute them to all members of the committee and, of course, we do have the statement here. I think each member of the committee has the statement which we will review carefully. I want to

thank you for your efforts in bringing this to our attention.

I would also like to indicate that the appellate decision which you referred to in New York has distributed to all members of the committee just before the call to this meeting. But thank you all for being here. We appreciate your efforts very much.

DR. SHAMOO: Thank you.

DR. MURRAY: Harold, could I ask a question?

DR. SHAPIRO: Yes, absolutely. Tom?

DR. MURRAY: I do really want to thank you for coming and giving us this very interesting statement. A question occurs to me. Clearly I agree with you, you cannot justify doing risky -- significantly risky research on someone who is simply incapable of giving a meaningful consent. There is no argument there.

The one concern I have is, is the mere fact of being diagnosed with a mental disease like schizophrenia, I do not take that as evidence that you are incapable of --

DR. SHAMOO: No.

DR. MURRAY: Okay.

DR. SHAMOO: That is not true.

DR. MURRAY: Okay. But what is --

DR. SHAMOO: Comprehension. There has to be determination of comprehension at the time, before, during and after the experiment.

DR. MURRAY: Okay. Thank you.

DR. SHAMOO: By independent psychiatrists. Not the currently used practice of the same psychiatric researcher/investigator.

That is the point. We have made that recommendation as part of the National Alliance for Mentally Ill Ethics Standard which I was co-chairing that committee.

DR. SHAPIRO: Thank you.

DR. SHAMOO: Thank you, sir.

DR. SHAPIRO: Trish?

PROF. BACKLAR: What is interesting, of course, is that the Belmont Report articulates right in the beginning the concern of using the same researcher as the physician. So again we need to go back and reread what has gone before.

DR. SHAMOO: You are absolutely right.

PROF. CHARO: Is there actually time for questions or do we need to --

DR. SHAPIRO: Well, I think if there are just a few very short questions. Otherwise we do not have time because we have others who are coming. Do you have an important question which will be relatively short?

PROF. CHARO: Just to clarify something that they specifically wrote --

DR. SHAPIRO: Okay. And that will have to be the last question on this issue.

PROF. CHARO: On number four in your recommendations which you talk about the need to think about the best interest of the subject.

DR. SHAMOO: Yes.

PROF. CHARO: I just want to be sure I understand how

that would be operationalized. If I am interested in seeing whether a new drug would be better than --

DR. SHAMOO: You are talking about the placebo issue.

PROF. CHARO: No, no. Not the placebo issue. I want to just compare a new drug to an existing therapy.

DR. SHAPIRO: That is right.

PROF. CHARO: But I genuinely do not know if the new drug is going to work. So I do not think I can say that this is minimal risk. It potentially is high risk. I truly do not know but it is aimed precisely at people who in fact are not capable of consent.

DR. SHAMOO: As you know --

PROF. CHARO: I am not sure I understand how number four would respond to that kind of situation which is quite commonly observed.

DR. SHAMOO: As you know, new drugs, and I am a research scientist, not a lawyer, they are all used after a tremendous amount of laboratory animal experimentation and that is the AMA recommendation in 1947. So there are predictivity and the prediction is of a greater therapeutic outcome than the existing medication then you have some justification for the use of that drug. But that is not the case currently practiced unfortunately. So there is ways to do human experiments. Do not misunderstand me. I do support experiments with human subjects but they can be done ethically.

DR. SHAPIRO: Thank you very much for those comments.

DR. SHAMOO: Thank you, Mr. Chairman.

DR. SHAPIRO: Thank you all for being here today.

Carol Barash, who is next on our list, is founder and director of Genetics, Ethics and Policy Consulting in Boston.

Barash? Is Barash here? Oh, here, I am sorry. I did not see you come down. Thank you very much and thank you also very much for being here.

DR. BARASH: I have not submitted written comments but I will leave them with Patricia.

DR. SHAPIRO: Thank you.

DR. BARASH: Mr. Chairman and other commission members, thank you for the invitation to offer commentary to the commission. Briefly I am Dr. Carol Isaacson-Barash, a trained philosopher who has spent the last five years in the field of human genetics. First as director of a Department of Energy funded study of genetic discrimination and now as founder and principal of Genetics, Ethics and Policy Consulting, a small firm dedicated to helping institutions optimize the benefits of genetic technologies through applied research, policy and ethical analysis, education and product development.

I would like to ask the commission to consider today some of the more general and broader issues about -- implied by the issue areas you have discussed throughout the day. I am not entirely sure that what I am asking you to do falls within your mandate but I will offer it nonetheless.

My comments today focus on what I perceive as an unmet need in the realm of bioethics and genetics. Namely the need to

develop an ethical framework which applies to a broad array of genetics and ethics issues not presently or even possibly governed by legislation. Although there is state and federal legislation intended to protect against inappropriate uses of genetic information including genetic discrimination which is arguably the most salient form of misuse, existing legislative solutions are piecemeal, ad hoc and will inevitably fail to solve the breadth of problems. Even fully effective laws will not prohibit the occurrence of morally objectionable outcomes since most value, weight and decision making authority is unbounded by law.

Presently there are numerous venues where institutions are free to determine a person's opportunities or benefits based on judgments about the worth of that individual which in turn are based on judgments about that person's genetic status. Such decision making authority is capable of wielding outstanding personal, familial and societal harms.

For example, adoption agency's ability to decide that a couple, one of whom has a genetic risk, is permitted only to adopt a child having a comparable risk raises not only serious social policy questions about whether children with genetic risk factors are entitled to parenting only by individuals considered deficient to parent normal children. That illustrates the potential for ethically suspect decision making based on normative interpretations of the meeting and significance of genetic information.

Although adoption issues arguably affect a relatively small number of people this issue is appropriate to worry about, both because of the disturbing questions it raises and because of the

enormous significance such types of decisions have on the people involved.

Genetic discoveries are making the unavoidable need to make trade offs which means deciding against ethically defensible interests and values. Our ethical tools are arguably inadequate to the task. Explicit deliberation about the meeting and desirability of genetic risk burden is clearly ethically sensitive if not only because the stakes are often unavoidably high. Appropriate rating of genetic risk questions is central to ethically defensible public policy.

Competing ways of framing opportunity and benefit questions as applied to genetic risks can yield conflicting decisions thereby promoting wildly different views of equity or fairness. For example, results from the DOE study of genetic discrimination revealed inconsistent rationales underlying exclusionary decisions, in particular insurance decisions were arguably premised on prudence, whereas blood donation exclusions were arguably premised on moral authority.

Good social policies should be ethically defensible, ethically consistent and embody maximum public participation. From an ethical point of view it is desirable that societal decisions about the appropriate use of genetic information fully consider values which define monetization as well as ethical principles which unlike utility or prudence are inclusive of nonmonetizable values.

I, therefore, suggest that the commission recommend the development of a framework for ethically defensible decision making about the management of genetic information in areas not governed by law. Such a framework could then serve as a guidance document which

could be disseminated to institutions involved in decision making in areas where these issues arise.

Such a framework would (1) permit explicit consideration of otherwise hidden normative assumptions; (2) permit explicit deliberation about the meaning and significance of genetic risk so as to prevent overvaluing of genetic risk; (3) enable decision makers to explicitly acknowledge the inevitable need to make trade offs; and (4) drive tension to relevant ethical variables and in so doing minimize a false dependency on science as the purveyor of just decisions as well as foster more responsible decision making.

Thank you again for this opportunity to address the commission.

DR. SHAPIRO: Thank you very much for coming here today and for your very thoughtful remarks. I hope you will leave us a copy so we can distribute copies to members of the commission. Thank you very much.

Our next speaker is Nancy Reame at the Institute of Medicine, American Academy of Nursing, Distinguished Nurse Scholar.

DR. REAME: Thank you, Dr. Shapiro. I come to you today as a nurse, a reproductive scientist at the University of Michigan, past director of an NIH funded infertility research center, and currently a health policy scholar at the Institute of Medicine.

This year I am fortunate to be spending my time addressing an issue of great professional interest to me, the bioethics of assisted reproduction involving gamete donors and gestational carriers, commonly known as third party or collaborative reproduction.

I understand that a priority of this commission is to address gaps in the protection of the rights and welfare of human research subjects, especially in relation to informed consent and personal autonomy. I would submit that third party reproduction is in dire need of your attention in this regard.

Back in 1980 as a young faculty member I led a support group for some of the first women in the world to be hired as surrogate mothers through a commercial agency. This was not a research experiment or a well designed clinical trial developed by seasoned investigators but rather the brain child if you will of an attorney who saw a way to create a business venture out of the need of infertile couples. Working with these well intentioned but highly vulnerable young women I had the chance to see firsthand the health care challenges, psychosocial pitfalls and moral dilemmas implicit in this reproductive option and I have written about it and provided you with a reference at the back of the handout.

Now in a follow up study with these same women I am asking them to revisit this major life event for its risks, benefits and consequences to their lives. Interestingly this same attorney that I mentioned continues to be at the forefront of the infertility industry.

As you can see by the ad that I have attached there that came from a recent issue of the Northwest Airline magazine, and I forgot to check when I flew in the other day to see if it is still there. He now has an international clientele. Typically these ads are also in Japanese. And can be reached by fax, e-mail and the Worldwide Web. He is just one example of the infertility entrepreneurs who have emerged since 1978

when the first test tube baby, Louise Brown, was born. Now 18 years later there are more than 350 IVF clinics in the U.S. thus making it very much a part of mainstream medicine.

While the use of gestational carriers contributes a small proportion of the IVF pregnancies, those resulting from egg donation are expected to increase dramatically as the baby boomers age. The growth of the infertility industry has been for the most part unchecked coming at the same time or perhaps as a result of in my view the Federal Government's ban on support for research on human fertilization.

Further, many of the scientific breakthroughs such as egg donation and transfer of cryopreserved embryos were not developed here in this country but in other countries. Ironically one could argue that nowhere has the demand for and implementation of these technologies been greater than in America despite our research sanctions.

Thus in the U.S. today we are faced with a scenario where medical practice has embraced a new technology which is now widespread but locally under evaluated for its impact on people's lives because it is off limits to rigorous scientific scrutiny.

Now as a side bar I must refer you to this morning's Washington Post if you have not already seen it of the story there of the latest twist in American ingenuity, namely human embryo research as a hobby by a particular NIH funded investigator. That is all I am going to say about that.

It is not surprising then that an array of court cases and human tragedies has emerged stemming from not only poorly defined legal statutes but also from unclear or absent procedures for donor and

recipient screening, informed consent, and protection of patient rights all due in part to a crucial lack of data about the health risks, psychological responses and social consequences to gamete donors, recipients and their offspring.

Although the AMA, the American Society for Reproductive Medicine, and NABER, the National Advisory Board on Ethics and Reproduction, continue to scrutinize practice and self imposed ethical guidelines for third party reproduction, they are doing so with one hand tied behind their backs, namely without the advantage of much needed system-wide databased rationale.

Further, without any legislative teeth in these self imposed voluntary recommendations practitioners need not heed their organization's advice. For example, the ASRM has for years cautioned against the participation of its members in surrogate parenting arrangements calling for those who do choose to offer this procedure to treat it as investigational with all the necessary requirements for protection approved by a properly constituted IRB.

One could argue that this has inadvertently spawned the increased use by physicians and couples of commercial gamete brokers who are only governed by the laws of market supply and demand as a way to avoid the appearance of shunning such research requirements.

With the advent of preimplantation diagnosis, cryopreservation and now in vitro maturation of oocytes we are clearly at the leading edge of the translation of even more spectacular breakthroughs from the bench to medical practice at the bed side. The continuing ban on IVF research will only further erode the opportunity to

develop clear effective health policies to protect the growing numbers of not only aging infertile couples but also former cancer patients who are expected to take advantage of third party reproduction, as well as the young men and women who serve as the gamete donors.

Federal funding of this research is sorely needed to provide consistent ethical and scientific review at the national level. No such official standards now exist. The research when it occurs is unchecked in the private sector. I, therefore, call on this commission to get on with the unfinished business of the 1993 NIH Human Embryo Research Panel and to recommend to the President to lift the ban on federal funding of IVF research along with endorsing as a high priority for the NIH the conduct of behavioral studies and ethics research in third party reproduction.

Thank you very much for hearing my comments.

DR. SHAPIRO: Thank you very much and thank you very much for coming here today. We appreciate it.

The last person we have on public comments is Chris Kline, a staff member of the Minority Staff, U.S. Senate Committee on Governmental Affairs.

Mr. Kline?

MR. KLINE: Good afternoon. I am here today to brief you on the upcoming actions that Senator Glenn intends to take with regards to this issue. In October my staff director, Lynn Weiss, briefed you on the past hearings that the committee has held regarding the Human Radiation experiments and a hearing in March of '96 on the protection of human research subjects. Today I am going to tell you about the

next step Senator Glenn intends to take.

Later this month he intends to introduce legislation whose primary purpose would apply the common rule protections to all human subject research and stipulate criminal sanctions for violations of the law. This has been referenced as a needed step by many different panel members today. The legislation would have two secondary goals.

The first of those would be also to prohibit federal funds for non-IRB reviewed classified research and require disclosure to research subjects of certain information regarding classified research. It is my understanding that the President intends to offer an Executive Order that may take these steps later this month as well. But in any case we are going to go ahead and put that in the legislative language.

A secondary goal of the legislation to reduce any potential regulatory conflict of interest within the National Institutes of Health and HHS, the legislation would establish the Office of Protection of Research Subjects within the Office of the Secretary. They are taking that out of NIH.

Why do we think we need this legislation? As very familiar to you, not all federal agencies have adopted -- which conduct or sponsor human research have adopted the common rule. Letters that our committee has sent to agencies have found that the Nuclear Regulatory Commission and the Department of Labor in particular are concurrently conducting research involving human subjects and they have not adopted the common rule. In the case of the Department of Labor the research would meet the criteria of less than minimal risk but in the future they could choose to conduct research that would not meet that

criteria.

Other gaps in common rule coverage include the recipients of federal funding who have not voluntarily applied the common rule guidelines to all research conducted at that facility as well as private clinical facilities and other private facilities which do not receive any federal assistance or not seeking to patent a drug.

As Dr. Shamoo mentioned there is more protection in existing statute for animal research than there exists for human research subjects.

Finally, evidence from recent press reports, the Wall Street Journal, the Cleveland Plain Dealer, the New York Times, as well as the research at the Advisory Committee on Human Radiation Experiments, and the General Accounting Office has given to us suggests that the common rule is inconsistently applied or all together ignored, and often receives little administrative support from the research institutions.

The multiple site research trials and the pressure on researchers to secure grants can often marginalize IRB authority requiring a designated research facility official to regularly attest that human subject research is being conducted appropriately and providing criminal sanctions for falsification or violation of this will substantially strengthen the common rule in our opinion and improve the protection for human research subjects.

Now how would our legislation work? First of all it would require all research facilities to register with the Department of Health and Human Services. The registration shall include first a statement of

principles governing the research facility and its conduct of human subject research. Two, designation of the official responsible for all human subject research. Three, designation of a membership roster of the IRBs at that institution. And four, attestation that the research facility is complying with the protection requirements of the common rule.

The legislation will include a grandfather provision for all research entities which currently have negotiated project assurances with HHS. Obviously the 104th Congress and it looks like the 105th Congress have aversion to additional regulation. So we are going into this very wide eyed in understanding that we cannot just create a new bureaucracy to enforce this and we want to take advantage of existing information that already is in place.

Another provision of the legislation would require a re-registration every three years. Finally, as I mentioned, or in addition I mentioned the criminal penalties would be assigned to violations of the act.

In regards to the classified research the act would prohibit federal funding for such research where an IRB has waived informed consent or where a determination has been made that the research is exempt from IRB review and prohibit federal funding for those activities.

It would also require that for all classified research that the research subjects be provided information concerning the identity of the sponsoring federal agency, a statement that the research involves classified information and an unclassified description of the purpose of

the research. This recommendation was one that the Advisory Committee on Radiation Experiments made.

We are not claiming that this is the be all and end all answer to the problems that have been discussed here today and we are looking in particular at input from this commission as we develop this legislation. We intend to introduce the legislation later this month on the 21st of January but that is just the start of the process. We are very eager to get your comments and assistance and hopefully ultimately your support and advocacy for this legislation.

Thank you and I am willing to take any questions.

DR. SHAPIRO: Thank you very much.

Alex?

PROF. CAPRON: Just a couple of questions of clarification. You mentioned moving the OPRR with a new name over to the Office of the Secretary and then you later on said that all research facilities would have to register with NIH. Did you mean --

MR. KLINE: I meant HHS.

PROF. CAPRON: You did mean HHS?

MR. KLINE: Yes.

PROF. CAPRON: All right. And how would this apply -- by what definition are you categorizing research vis-a-vis research which is either sponsored by another department through an agency -- to a sponsor or an investigator who does not do any biomedical research? For example, Mathematica in Princeton that did the big social science experiment. If that funding had come from HUD let's say or from some other agency and they do not do any biomedical research, would they

still register as a research institution with HHS?

MR. KLINE: Well, I am not familiar with the specifics --

PROF. CAPRON: Well, that was a bad -- I mean, do not worry about the specific example. Just say it is a company that does say social science research and does not get any HHS funding, would they -- is HHS to be the central office for any research institute?

MR. KLINE: Yes.

PROF. CAPRON: I see. Okay. And the final question is how are you defining research in light of some very interesting comments that you may have heard this morning Dr. Emanuel made about the amount of what many people would call research that goes on in health care delivery settings in the way in which care is arranged, not necessarily research on a drug or device, but on how you arrange the care, what barriers you put, what inducements you put and so forth.

MR. KLINE: It is a very burning question. I can read to you the definition that we have now and again this is the whole purpose of the legislative process, is to take in account the other --

PROF. CAPRON: Do you have that definition?

MR. KLINE: Yes, sure.

PROF. CAPRON: Do you want to read it into the record?

MR. KLINE: And again I -- actually tomorrow I am discussing it with some of our lawyers. So the term "research" means a systematic investigation including research development, testing and evaluation designed to develop or contribute to generalizable knowledge, and in those activities for which a federal department or agency has specific responsibility for regulating as a research activity. So under that

-- it is a very broad definition but it seems to me under that definition that this kind of research that was described this morning would apply.

PROF. CAPRON: Let me understand. The final catch language you used was that the federal agency has some responsibility. Medicare, a federal agency, has responsibility for the way in which people, organizations that provide care to Medicare patients organize that care. I mean that is to say they decide are you a qualified organization and so forth. That is not a research concern of their's. In other words, they would not see themselves as conducting research. But they do have a little handle on why a particular managed care plan qualifies to offer Medicare managed care.

Is that a linkage or were you thinking of an agency like NIH that now has research oversight over a company?

MR. KLINE: The General Accounting Office raised the same point with us on how the Medicare issue would be handled and right now that is one of the issues we remain to work out and I would like your comments on that. There are a number of issues here that we are not sure what the impact of this legislation will be frankly. The whole question of physician's use of off label medicines or medications, development of new surgical procedures, these kinds of things are not currently covered as research. But under the definition that we have many might consider that they would be. This has to be developed and clarified during our legislative process.

DR. SHAPIRO: Alta?

PROF. CHARO: Also by way of clarification would this legislation offer protection to any U.S. citizen or U.S. resident who is

enrolled in an experiment in the U.S. or is it any U.S. citizen or resident who is conducting experiments in the U.S. or abroad now that we have lots of transnational collaborations would be obligated to comply with these rules? I am just trying to get a sense of the coverage on the margins.

MR. KLINE: It would apply to research facilities within the U.S. Another issue some of the -- you have seen the Cleveland Plain Dealer articles, the discussion of drug research that is done in a foreign country that did them if the application is applied here, I -- if it was a U.S. company then it would apply. Our law would presumably apply to that. So the protection is extended to the U.S. citizen but the law focuses on the research facility and addresses the issue that way. Am I making myself clear?

PROF. CHARO: I think I am understanding that basically this would cover only research facilities physically located in the U.S. and whichever territories or however you do that part of it.

MR. KLINE: Right.

PROF. CHARO: But an individual investigator not with a research institute in the U.S., just an individual physician who decides to collaborate with some physicians in Canada would not be subject to this and would be subject only to the local Canadian rules.

MR. KLINE: No.

PROF. CHARO: A different set of standards.

MR. KLINE: A research within the U.S. would be covered under our definition. An individual researcher within the U.S. --

PROF. CHARO: Who is not affiliated with any institute

that is registered.

MR. KLINE: Yes. He would be considered an --

PROF. CHARO: An institute in and of himself.

MR. KLINE: Right.

PROF. CHARO: Ah, okay, thank you.

MR. SHAPIRO: Zeke, the last question on this.

DR. EMANUEL: Sorry. Just two quickies. It does strike me that the definition that you have to research is overly broad. I know I am responsible for trying to broaden things out but -- and in this regard education for doctors or providers or people like that that is intended to improve care for patients may be subject to the precise definition that you have suggested. And that could have a huge chilling effect on educational interventions that you are proposing that people want to attempt that are separate from organizational things.

The second thing is I am not clear in the language and I would just ask you to think it through whether some company that does not do research -- that does research through private physician offices would be covered. In the oncology field with which I am most familiar that is a very common practice. You organize, you know, 50 doctors. you send all the people in and you actually do experiments. You know, you give drugs essentially in private offices outside hospitals and outside of other institutions.

I do not know how your legislation would affect that.

MR. KLINE: In the definition of a research facility. Our definition of research --

DR. EMANUEL: Research.

MR. KLINE: Yes. It means any public or private entity, agency or person that uses human subject in research.

(Simultaneous discussion.)

DR. EMANUEL: Okay.

MR. KLINE: Again we -- I will forward the legislation to Mr. Dommel and he can distribute it to you all and we very much are looking forward to your comments and help on this.

DR. SHAPIRO: Well, let me say that I hope you will take back a message to Senator Glenn that we are very appreciative of the interest his staff -- he has taken and his staff taken in the work of NBAC and we very much appreciate the time and effort that you and other members of the staff have given us and we will certainly look forward to cooperating in whatever way we can be helpful to formulate good legislation. So thank you very much.

DR. EMANUEL: It would be helpful if you kept us up-to-date of how this is progressing. That would be really helpful.

DR. SHAPIRO: We are adjourned. Thank you.

(Whereupon, the proceedings were adjourned at 4:46 p.m.)

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