NATIONAL BIOETHICS ADVISORY COMMISSION
6100 Executive Boulevard, Suite 5B01
Rockville, Maryland

HUMAN SUBJECTS SUBCOMMITTEE

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National Institutes of Health
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Bethesda, Maryland

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The meeting was convened, pursuant to notice, at 7:43 a.m., DR. JAMES CHILDRESS, Chairman, presiding.

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I N D E X

P R O C E E D I N G S

UPDATE AND OVERVIEW

DR. CHILDRESS: Welcome to the meeting of the Joint Session of the Subcommittees. And this welcome is only to subcommittee members. And we thank all of you for being here this early, but also to others who are joining this session.

And for members of the public, we do have at least three who have indicated they plan to testify during our public hearing open session at 11:00 o'clock.

If there are others who would like to participate, if you would let Pat Norris or one of the persons at the desk know, that would be helpful.

We have three major tasks today. The first is a discussion of the decisionally-impaired subjects, the draft report and draft recommendations that Jonathan Moreno has prepared on the basis of his work and Rebecca Dresser's contract paper, as well as our various discussions along the way, including the public hearing.

And then, a report, a discussion of the

draft report and recommendations of the Federal Agency Detention of Research Studies.

And then, I will talk some about immediate and future plans which will include a discussion of where we stand on the OPRR reports.

And why don't I just take a minute. Let me ask first, west coast people, we moved you to the other subcommittee anyhow this afternoon, right?

Alex, you can tell me when you're leaving.

DR. CAPRON: About 12:15.

DR. BACKLAR: Not at three.

DR. CHILDRESS: Anyone else? Is there an earlier departure for anyone?

DR. MORENO: I will probably leave at four.

DR. CHILDRESS: About four. Okay.

At some point, we need to talk about the immediate and future plans, including the OPRR report.

So I will just mention some now. We have two contract papers that should be in within three to four weeks.

And I'm in a discussion with the person about the third contract paper which would deal with

OPRR and possibly covering both private and publicly-funded research.

We have things we've worked out on that particular one before, but, you know, the actual contract is going to be altered. But let's say we will have a paper in that area as well.

We've had some difficulty in identifying someone to do it, but it looks as though that we have a person that can work out the details.

We also have for a discussion after the first of the year when we get the preliminary results of the two IRB studies.

We have to think about what we want to do in that area and what else we want to do in order to be able to think about developing over time.

We have perception of children of adolescence. That will come up some time next year.

And we have the discussion of international research raised two or three times in our discussions.

We need to talk about a way to come to terms with this that will be helpful in providing a framework for those who are making decisions about it, not to approve or disapprove any particular

cases, but whether to try to sketch a framework. And we need a helping hand for that.

Now, those are our major tasks, three major tasks. But before we get into those, I would like to see if Dr. Shapiro would like to say anything to the subcommittee or --

DR. SHAPIRO: I think it's great so early on Sunday morning. I appreciate it. That's all, John. I look forward to the discussion.

How did Clemson do yesterday?

(Pause)

DR. SHAPIRO: I think we did better, win and undeservedly as did southern California probably deservingly in that case.

DR. CHILDRESS: All right. Any comments from anyone on the subcommittee about the agenda for today?

DR. FLYNN: Can I ask a question?

DR. CHILDRESS: Sure.

DR. FLYNN: It doesn't relate directly to today. And it may be that some material has come. I just haven't yet seen it.

We had talked at earlier points about hearing from members of the research community about

the issues that are of concern here and trying to get a perspective as to how they wrestle with these issues and what some of the problems are.

I wondered, given the very sharply critical nature of the -- some of the testimony that was heard at the last session, you stated some very strong allegations about conduct in various studies that one really could not get a completely -- a complete picture because the others were not available to speak to their -- to their methods or intent.

I wonder what the plan is to hear from individuals who are routinely involved with conducting clinical research with impaired subjects.

Is there still a plan?

DR. CHILDRESS: We have not developed a plan. That is one of things that we need to do I think after looking at the draft today is to decide what else we need to do.

And we have heard from several researchers, but I would say that there are many more we could hear from as well and perhaps a representative of other kinds of research.

As suggested, there are all kinds. We

might want to look into energy research as part of this.

DR. FLYNN: Yes.

DR. CHILDRESS: So there are several things we could do. And I think one of the things people need, it would be helpful if you would keep in mind during our discussion today. It would be, all right, we have this draft.

And thanks to Jonathan and thanks to Rebecca Dresser for the fine work in getting us to this point where I think now we can begin as suggested last time.

We really don't know where we would go or where we are going to try to go until we can make some decisions about some concrete matters.

And then, we can ask the question, what else do we need to have a respectful and perhaps helpful report? And this may well be one thing.

Now, there are a couple of ways to go about that. One of them is to set a fairly systematic discussion with a variety of researchers on this.

Another would be to try to draft conditions, say, extending what we have here,

modifying them seriously, etcetera, and then using those as a basis for discussion of the researchers who might reflect on it or just slide with the current. This is not to modify them.

So there would be different ways we could go.

Would you like to add anything to that at this point?

DR. FLYNN: No. Just that I think from the standpoint, at least it would be valuable to have the opportunity for some give and take on a somewhat more practical level about how these things are actually being dealt with and what are some of the difficulties that researchers in identifying and how are they are dealing with some of the kinds of issues that were raised in the last meeting.

I just think that I always benefit from that kind of give and take. And moving from the broad to the actual application is often a difficult issue. And I just think that in this area that we understand it.

DR. CASSELL: Yes. I agree with that. In some ways, we've built in the researchers early and then had the public hearing.

That is not that we did an exhaustive discussion with the actual researchers, but with a number of them.

DR. CHARO: And also, when you get to the stage of talking about the materials that are in the last chapter of Jonathan's draft in which there are specific suggestions for implementing policies, you know, consent monitors, the role of the family, in some cases the Maryland legislation that tied its obligation to X, Y, Z.

It struck me that that's the place in which if we were inclined to take some of these suggestions seriously, we might actually have very good questions of people who have come to testify.

So it might be that if we can narrow things down to a set of two or three alternatives that we are serious about and then bring in these people with an agenda on our side also of testing out the work of some of these ideas.

That might be a real way to get the most value out of the public testimony.

DR. FLYNN: That would certainly I think be beneficial because again, I am interested in hearing about the practicalities of the actual work

involved in trying to implement some of the ideas we've had.

DR. CHILDRESS: And along with workability, it seems to me one big question that certainly surfaces in draft, too, is cost.

What do we -- how would this -- if some of the recommendations here were actually adopted, what would be the impact on some of the research in the day-to-day, the way you kind of described it, but also the kind of investment that would be required on part of the institutions to make the recommendations really work?

Alex.

DR. CAPRON: I agree and support concerns that Laurie often has raised.

I want to suggest an additional reason to have some of these researchers here, specifically some of the researchers whose conduct on the face of the testimony that we heard last time seems most questionable and particularly, obviously those at NIH and NIMH whose work is directly under federal aegis.

It seems to me that we would want to offer those people the opportunity to reply to the in

effect accusations that were leveled.

And I say that out of a sense of fairness to them, but also out of a sense that without that reply, it will be harder for us to know what to put into the report on those issues.

And certainly, if there are grounds to believe that everything that we were told last time is true, those would be powerful illustrations to put into the report of some of the problems that need to be addressed.

I would be less confident about putting them in if we have only heard one side.

And yet, on the other hand, I would not want to leave them out if there were substance to them.

We are not going to be in a position to hold a fact-finding, judicial hearing on that, but I think we could get a better sense whether indeed there may be some of those practices which if the person would admit it where they think there is a good justification for it or a different interpretation.

DR. CHILDRESS: I guess let me raise one concern here. And that is, can we go that way,

along the lines you've suggested without in effect becoming an investigatory body, that is looking at particular cases in a concrete way?

And so I have a little reservation about the -

DR. CAPRON: Let me offer an alternative for some of that at least as to the federal. I believe that it was voiced. I voiced it. And there was some support for the notion.

But what we heard on the face of it should impel OPRR to make inquiries as to the process by which products are reviewed and administered at, you know, whatever their clinical setting is at the NIMH research hearing that is going on.

They do have the capability of making those inquiries.

DR. CHILDRESS: Yes.

DR. CAPRON: And if it were clear from our need for that information that that process should be for them perhaps a more accelerated one than they might otherwise have no other need to report by a particular date.

I think we should make that clear to them. If that requires a motion here and a resolution by

our commission that that is what we expect to see from OPRR, then I would make that motion at whatever point you entertain it.

But I also have a sense that beyond that, there would be some value in allowing people to come before us because we allowed the public testimony on the other side.

DR. CHILDRESS: Sure. So we allow it as a matter of principle. And anyone could do that and say it in a public hearing.

But in my discussions with NIMH, the issue was raised as whether we wanted a specific response. And in our discussions, it seemed to be difficult in terms of the requirements of privacy and so forth for that to be done.

And second, for us to request it, I think would at least from the people who have been charged in the public hearing with doing certain kinds of things, I think it would put us in a role that I'm not sure we can and should play.

DR. CAPRON: As a person who was -- who said and who was describing one of the commentaries with regard as having made a cold or unfeeling comment --

DR. CHILDRESS: Right.

DR. CAPRON: I want -- when we were hearing about things over which we have no ability to do anything, I was just cautious.

I was trying to caution the person that if she were coming here thinking that we were going to resolve her problem which had not been resolved by others to whom she had turned, I didn't want her to go away and then in six months say another group led me on and then let me down.

DR. CHILDRESS: It's the same old thing, right?

DR. CAPRON: Right. It's the same old thing.

Whereas, the statements about what was going on at NIMH reflected -- I mean, this is the highest level of psychiatric research. These are the people who I just assume by their positions there are among the most productive and respected researchers in the field.

If there are patterns in which the entire field accepts as the right way to go about things, we ought to know about it.

It's not just a matter of trying to

determine whether there was wrongdoing. I don't think we're in a position to do that.

I think OPRR is in a position to do that.

But there are examples which I think would make our report more compelling.

As I say, I am somewhat on the basis of a description from a patient to say that we know that that is what happened.

PROF. CHARO: If I may? You know, somewhat different from the investigation is very consistent with you're saying is the following.

I've heard a lot of people talk about the way they were treated without it being clear from the descriptions whether that was happening was because they were getting experiments of therapy or they were in research.

And I think it's very common, totally aside from the area of --

DR. CAPRON: Yes.

PROF. CHARO: Menalomas.

DR. CAPRON: Yes.

PROF. CHARO: For this to be a profound confusion on the part of both patients and on the part of the professionals.

And a discussion with the NIH or NIH people about what they thought they were doing in comparison to what the patients were getting might reveal some interesting information either about patterns of abuse in research or even perhaps just the continuing difficulty of separating these two concepts.

And that does shed some light on the kinds of protections you might want to delve into research because of the difficulty in relating people to the appropriate level of care and concern that they can expect from their professional.

DR. CAPRON: Yes. I totally agree with you. To the extent that what we were saying was the perception on the side of the patients/subjects.

We don't need the researcher to tell us whether or not that's true.

What we're hearing the person saying this is how I felt.

And I would take one step further, not only was there that confusion, but there was a sense that with certain illnesses that basically this is my only alternative.

PROF. CHARO: Okay.

DR. CAPRON: In a sense that I'm being not coerced in the sense of someone holding a gun to my head, but my circumstances constrain my ability to do otherwise.

And I think we can convey both of those.

There was a further step though. There were statements, for example, about a researcher coming in with a whole stack, and be it a black binder, filled with consent forms and going through them one right after another.

Now, putting aside any of the comments that were alleged to have been made about, oh, here is a -- or something, just the fact that consent would be obtained in that way, if that's the case, seems to me to raise an issue, again, not an issue that we would say, you know, throw the man in jail.

We are not in a position to say that. And we would obviously have to have a level of fact finding to make that determination.

But if this is the sense that this is an acceptable interpretation of the requirement of informed consent, I think we can again address that.

Now, we could address that simply because it was stated that this had happened. We don't know

whether it happened or not.

But if it happened, this is the problem.

I think it would be better to get some sense of maybe it did happen and maybe the person has some reason to think that that is acceptable, if we could be convinced by him that he was right and my presupposition is wrong.

Or we could see that if to the extent that people don't feel they're doing anything, skirting the rules, they think this is quite acceptable, if we came to an opposite conclusion, we ought to address that.

And so that is an additional factor beyond those that you've mentioned.

I think we're all in some agreement about this. I'm not aware of what your discretions with NIH have been, John. Perhaps you could --

DR. CHILDRESS: Well, just what I had told you. Were the researchers involved or --

DR. CAPRON: No, we're not --

DR. DUMAS: And what was the outcome of that?

DR. CHILDRESS: Well, basically, just what I said that we know. Whether we expected -- well,

it was a conversation, telephone and E-mail about expectations of the impact regarding this and an indication perhaps that NIMH perhaps could respond in a letter if they could get the issues of privacy and so forth obviously for them respond without having the patient's permission.

With certain kinds of information, it gets very tricky. And you can well understand.

DR. CAPRON: Yes.

DR. CHILDRESS: In such a matter.

And yet, my indication, my response was, well, we are not requesting that you get the response on these particular cases because to do so would thrust in the role of then trying to decide which side is right on particular cases.

I think we can learn from particular cases and perceptions and then check for the one which the ideal standards and practices are understood at an institution like the NIH.

DR. CAPRON: Yes.

DR. CHILDRESS: Without actually getting a response to a particular case.

And that would be the way I would be inclined to go.

VOICE: I agree with you.

DR. CASSELL: I'm interested in more responses either directly or some other way because I think whenever those -- whatever that testimony reveals, you have to look in part.

The recommendations we are making, would it have stopped those problems? And my concern is the answer is no.

And the only way I can think of going further than that is some kind of monitoring either from OPRR or some other way so that patients have a recourse, somebody to call or go to complain about the service.

But that's when we're beginning to talk about money. It costs money to do that.

On the other hand, it may be the only way to get good psychiatric research.

So my sense of it is what we have to do is find out, well, what would be the ideal to protect these subjects? And can research go on if that's done? And would that met the objections we've heard?

So I'm still interested in hearing from people.

DR. CHILDRESS: From what I'm hearing, it seems to me your comments are more on a general level.

DR. CASSELL: Yes.

DR. CHILDRESS: Relative to proposed possible recommendations.

DR. CASSELL: Yes.

DR. CHILDRESS: And their potential effectiveness. I was going to say that initially I thought that if we could get people in here that have done the research that is controversial, but what I'm -- I'm just thinking out loud now, hearing Alex's comments and all.

I think it would be rather, number one, inflammatory. And I don't think it's going to -- even if we get the people in here, we're not going to hear necessarily the actual way the research was done or the details that we need to hear.

And I think one of the things that is more general that we do need to hear because I think that if we get someone in here that has done research that has been considered within the ethical guidelines and what the challenges were to get that research done, etcetera, that might be more

fruitful.

I mean, to quote what Eric said at one of the earlier meetings I think is that most of the research that is unethical is not done by unethical people, something to that way.

And I think that's where we need to concentrate on. I think no matter what regulations you have and what laws, there is always going to be researches done unethically.

But I don't think that is what we're trying to accomplish here. I think we're trying to provide regulations or guidelines for most people that are not unethical people, but sometimes do unethical things.

So I think it would -- we need some general guidelines, not the specifics.

Other comments?

DR. DUMAS: Yes. I would agree. I think that we would be remiss not to go further to try to understand the nature of this problem and the scope of the problem.

I would agree that we shouldn't concentrate on specific cases, but rather on the more general rule or the better issues that are

reflected in the specific cases.

There is a series on television now related to the treatment of mentally ill. It has come up on CNN.

Has anyone here seen that?

So there is a building, amounting public concern around the treatment of the mental ill patients.

And I think that we have a responsibility to try to understand the nature and scope of these problems and to address them in our work.

So I don't think we should drop it.

DR. CAPRON: I agree. And I'm particularly uncomfortable with this excuse that confidentiality, whether it's used to not address those basic questions.

DR. DUMAS: No. Right.

DR. CAPRON: I mean, I found it hard to believe that the patient from Philadelphia was the only one who on a unique, ad-hoc was asked to fill out a whole bunch of consent forms at once.

Now, it might be that that is the case. And it might be that the excuse has something to do with his diagnosis, but that strikes me as

improbable.

Therefore, one doesn't have to address his case. It is for the researcher and for the chairman of the IRB that approved that research to tell us whether this is a standard practice.

And if so, how it's justified within the accepted norms of what informed consent is suppose to mean with the freedom to make decisions about research that is --

DR. CHILDRESS: What I've heard on the part of the patient subjects without being case specific is namely find out what the practice is and the standards of informed consent.

DR. CAPRON: Yes. Exactly.

DR. CHILDRESS: That's a very different matter from investigating a particular case.

It seems to me there's other well within our mandate. And it can be done and in part response to proposed recommendations, an effort to see how those might fit with current practice, as well as the standards that are offered in the normative standards.

DR. FLYNN: I think that's important because the difficulties in trying to understand

what really happened in an individual situation. And that's really not our charge.

My concern is that we understand and have a balanced picture so that we do not either over respond or under respond to individual allegations and that we try to base it on what we believe to be in fact the operating standards and practices in the field.

I for one am not persuaded and have had from the large membership I represent no major communications that indicate that there is widespread ethical breaches going on in psychiatric research.

That's not to say that there aren't some. And that's not to say we don't want to strengthen protections.

But I feel more comfortable determining the level and intensity of that effort if we have at least an opportunity to hear something about what are the normative practices and standards that leaders in the research community are working with.

And I don't think we've had that. And that's why I raise it as we begin to look at specific safeguards and approaches to strengthening.

I feel the lack of that part of the dialogue.

DR. CHILDRESS: One way perhaps to address this to meet both concerns would be to invite testimony.

We need to talk about obviously which individuals, but assuming from the NIMH structure and the people that they would recommend and basically try to find out how the standards are interpreted, what kinds of practices occur at which time it would be appropriate to ask questions about how do -- what efforts are being made to prevent mass consent in terms of a large number of forms.

DR. FLYNN: Right.

DR. CHILDRESS: It seems like that would -- would this be a way to basically meet the variety of concerns?

DR. FLYNN: I think so. I think, too, we -- there is some session that is being held in December.

DR. CHILDRESS: Right.

DR. FLYNN: Is that meant to be informative?

DR. CHILDRESS: It's probably about work.

And one thing I want to say, I haven't gotten to the chapter 4 yet. We will get to that shortly.

Will be that whatever we do today and in a subsequent meeting will be far short of a final draft because we do need to incorporate what goes on at the -- what would go on the 2nd and 3rd of December.

And I passed out information about that last time. And I have a few copies of the draft schedule which is being revised.

But I hope it would be particularly if we meet on the 1st. And we need to talk later today with the 23rd of November and the 1st which I am wide open.

We may need both days. We may need only one. If we need only one, which day would be better for people to travel? And that's hard to say, given the Thanksgiving weekend.

But it may be the Sunday before the 1st. It may be one of the two busiest days of travel of the year. It may be a hard one. But anyway, we can talk about the dates.

But the 2nd and 3rd of December would be

the NIMH conference.

And Rex is here actually. Would you like to say a word about that at his point?

DR. COWDRY: Yes. We're still -- we now have the panel.

(Pause)

DR. COWDRY: We --

DR. CHILDRESS: Identify for the record also.

DR. COWDRY: Sure. Rex Cowdry. I'm the Acting Deputy Director of NIMH.

We have the panel identified who the large number of them have experience are IRB members.

Part of the goal of this is to identify good practices for IRBs in dealing with this population in particular.

There will be a series of presentations and draw a hope from those presentations and from their own experience from service on IRBs to try to identify what are good practices.

And I assume they would address both detailed issues, like good practices in terms of how you present consent forms to potential participants in research and also broader issues in terms of the

approaches to surrogacy, for example, that have been employed by IRB.

The location isn't clear yet in part because one of our co-chair's attendance is not clear. Senator Domenici has -- it's depending on his being in town or not.

But we will have that up to you within the next 10 days in terms of venue, details about the speakers and panel members.

DR. CHILDRESS: So it's not clear that it will be at the Double Tree.

DR. COWDRY: It's not entirely clear.

DR. CHILDRESS: Okay.

DR. COWDRY: Because there is some advantages to holding it downtown.

DR. CHILDRESS: Okay. Thank you very much.

Any questions about the meeting?

I do have three copies left over from the last meeting of the rough draft of the schedule. And I'll go ahead and pass those out, knowing that the schedule is still subject to further development and change.

And if the location given here is not --

DR. CAPRON: One question for Rex.

DR. CHILDRESS: Yes.

DR. CAPRON: In looking at the schedule last time, I don't have it in front of me now, it seemed to me that the concerns that Roy raised were well addressed.

That is to say that you were hearing from the research community.

I don't recall that you had scheduled to hear from patients or patient representatives. Is that correct?

DR. COWDRY: We now have on the schedule in the morning, actually early on right after the first discussion about IRBs and their roles, a series of presentations by groups who have actually developed policies, patient groups who have actually developed policies with this, and then, also a public presentation section as well.

So I think that --

DR. CAPRON: That is a change.

DR. CHILDRESS: Well, on the schedule here from 10:45 to 12:00, public statements and comments.

DR. CAPRON: Right. But there is a difference between open and inviting people to come.

I mean, we all know the difference here.

DR. CHILDRESS: Right.

(Laughter)

DR. COWDRY: Specifically, we felt that both the Maryland group, NOMI, and the Alzheimer's Association, for example, who have developed explicit concerns and statements would be interested.

And if there are other groups that have developed these, we would be delighted to actually schedule those presentations in addition to the general public.

And if I might, I would also like to say, we very much like to address the larger issues as you have suggested quite apart from the individual case which we are restricted in terms of the Privacy Act, to address the broader questions because I think there are some very useful lessons to be learned from that and really in both directions.

DR. CHILDRESS: Thank you very much.

Trish.

PROF. BACKLAR: I guess I could say that we already know from the Advisory Committee that there were large problems with informed consent with

the general population.

So I think that we are very likely to find that with this population that may have greater difficulty in consenting that the same problems obtained and maybe even more difficult.

That was -- we've already found that out about the general public.

DR. CHILDRESS: Any other preliminary comments?

(Laughter)

DR. CHILDRESS: Before we get to a discussion on the --

(No response.)

DR. CHILDRESS: I think this actually has been very helpful and sort of a list of things we need to do. And we will proceed accordingly.

As I mentioned, we are grateful to Jonathan Marino and Rebecca Dresser for preparing materials that could get us to this draft report and draft recommendations so that we could begin to make some decisions about actual the text and the like as well as deciding what else we need to do.

And we have discussed over a number meetings, and indeed at every single meeting of the

Human Subjects Subcommittee, we've paid some attention to it.

Again, this was done superbly by staff with the input from subcommittee members. And I have really enjoyed working with Jonathan on this.

It is that the subcommittee and then NBAC as a whole needs to own the report and its recommendations.

And so what we are trying to do today is just see how much here we want to own and how much, if I can put it this way, we want to disown.

But this is a way we really have to come to terms with the issues here and make this so that whatever comes out is our report.

And again, the final version, we have to be thinking in terms of something after January for two reasons.

One is the NIMH conference that we need to attend as many as possible and at least to draw on the resources.

But also, I'm sure there are other things we will need to do.

We have already heard the things that we need to hear about general practices and standards

and from researchers involved with these subjects.

But I'm sure there are other things, too, we'll decide in the course of the day that we will need to do, we need to work up and get information about before we can put this in final form.

So that is something about the direction.

DISCUSSION: RESEARCH WITH DECISIONALLY IMPAIRED SUBJECTS (ISSUES); CONCEPT OF VULNERABILITY

DR. CHILDRESS: I have asked the individual subcommittee members to kick off the discussion relating to a particular parts, as well as to the draft as the whole.

And I have asked, first of all, Trish Backlar, Laurie Flynn, and Alex Capron to help us think a bit about the overall structure, direction, and tone of the report.

And if it is all right with the group, we will just start there and then move on to particular topics.

Would one of the three like to volunteer to go first or do it alphabetically?

DR. CAPRON: You want them listed between Laurie and myself.

PROF. BACKLAR: I've already told you everything. So now, I will have a hard time remembering. I've given it away

Do you want me to start?

DR. CHILDRESS: Please.

PROF. BACKLAR: Overall, I felt that the structure of this was very well done. There are a number of things that I am concerned about. And I do not want to spend a lot of time on that now.

And as I discussed with you, Jim, what I think I will is things like using word terms that might be incorrect and we want to be thought about.

I will send those to Jonathan instead of boring us as I go through the --

DR. CHILDRESS: It might be helpful actually to send them to the subcommittee, too.

PROF. BACKLAR: Right.

DR. CHILDRESS: When they are fairly major recommendations for the draft to go ahead and send them to the subcommittee, too.

So if there is anybody who has a very strong reaction to that --

PROF. BACKLAR: Right.

DR. CHILDRESS: Could also engage in the dialogue.

PROF. BACKLAR: So what I'll do is send it to Henrietta. And she can make a copy of it and send it out.

DR. CHILDRESS: That will be fine.

PROF. BACKLAR: I am a little concerned about the tone. That's one occasion.

And I -- specifically, I know that you are trying to write this in a way that is very even from both sets of interests.

But I think the commentary on page 20 about the subject who was -- who committed suicide is -- it seems that you are absolving the UCLA study.

And I felt a little concerned about that. It isn't that you are inaccurate. You are accurate, but there were other problems at that time.

I found certain things rather confusing. And on page 42, you say at the top, "Instead this report will concentrate on the question whether the research should be permitted on those who have been found to be decisionally incapacitated rather than those at risk or --"

DR. CHILDRESS: I'm sorry. That's a typo.

PROF. BACKLAR: No, no. I know, but I knew what you meant.

DR. CHILDRESS: Yes.

PROF. BACKLAR: The patient was

incapacitated. Those at risk for decision or capacity. And what additional protections should be provided then, if any.

And I am assuming as I read through this that you actually are talking about people with fluctuating capacity or at risk for capacity.

Or are you only -- when you say at risk for capacity, for instance, when we think who is in very early Alzheimer's and is not really yet decisionally impaired, are you leaving that group out?

And in fact, what I found myself concerned about throughout the report is that I see there are four categories of decisionally impaired or potentially decisionally impaired or fluctuating decisionally impaired persons.

And I didn't know whether we should -- this is such a heterogeneous group. If we are going to write a report which addresses all of this group of people, are we going to make sure that we are assuming doing that?

And I saw -- the four categories that I saw were fluctuating capacities, schizophrenia, bellicose, dementia.

Perspective incapacity, Alzheimer's, early dementia, limited capacity, for example, would be able in some way to make an objection clear or an assent, but not much more than that.

And no capacity, that's late stage Alzheimer's and dementia.

And I'm asking this as a question. Are we addressing all those groups? And if so, then we need to make that clear.

DR. MORENO: I think what -- I think you've expressed the problem well. What I was trying to capture was a concern about trying to rule out or anticipate all possible incapacities.

And that it seems to me would probably go further than what I understand the mission of the subcommittee to be since we are all potentially incapacitated.

Although, I have to say that some of the potential recommendations do go, for example, toward some kind of research agendas which cover in theory everybody, including all possible incapacities.

So let me work on that language on page 42, but I see the problem.

PROF. BACKLAR: I have a lot to say about

it, but I think --

DR. MORENO: That's correct.

PROF. BACKLAR: They're going to wait about that.

DR. CHILDRESS: The more general direction in terms of --

PROF. BACKLAR: Right.

DR. CHILDRESS: So the overall sense of the report and recommendations.

PROF. BACKLAR: I think there are -- that the section -- the few sections, page 111 and 112 perceive a -- and I think there was another section.

I think we need to think this all through it, the discussion that we as the commission and the subcommittee have not really addressed.

DR. CHILDRESS: Yes.

PROF. BACKLAR: We got more material about this in our handouts for today in our briefing book.

We certainly have not discussed anything about the so-called challenge studies which come into the issue which we have not really discussed, the imaging issues and what's going on there.

So that this is something we have to think about and talk about together.

I don't feel that we are ready to get to these recommendations. I just don't. We haven't talked enough.

I cannot address the recommendations at this point.

The one recommendation that is -- there are two recommendations I absolutely can agree with.

One is that no study should be done on this particular population unless it addresses their particular medical problems.

And the other is that, yes, I do agree that if people are incapacitated and they are -- they should be told that they don't have capacity.

They should at least have the chance to fight back, so to speak.

DR. CHILDRESS: Well, a few of the draft recommendations is challenge recommendations because they are designed basically to challenge us to think about where we want to go.

PROF. BACKLAR: Right. Yes. Right.

DR. CHILDRESS: Not that they are the ones that we would go forward with, but we do have to make some decisions. And they are designed to help us decide whether this direction is a plausible and

defensible one or not.

PROF. BACKLAR: And I think that the comment then in terms of that, the comment about risk and the minor increment and should we turn that over to the IRBs, I think we have to think this through very, very carefully.

I am not willing to turn anything over to the IRBs unless we know what we are talking about at least.

That's really -- I mean, I have an enormous amount here, but I think that's enough for now.

DR. CHILDRESS: And some of it will come into play in the past directives.

PROF. BACKLAR: Yes, yes. That's actually a big part of it.

DR. CHILDRESS: Okay.

PROF. BACKLAR: Right.

DR. CHILDRESS: Okay. I will suggest that we follow the order listed on the sheet I sent.

And so, Laurie, you get the opportunity of going soon.

DR. FLYNN: All right. Again, some of my concern, I expressed earlier. I've read through

this now three or four times. And like Trish, I'll send some specific comments.

But I was struck by a sort of a sense that surfaces early on in terms of the history and then moves through in recounting some of the things that were presented at the last meeting and then sort of impelled by this both history and presumed evidence of widespread abuse.

And the moves move forward. And I struck me, as I mentioned, that we have not really had very much of an in-depth dialogue around the extent to which such abuses may be occurring.

We don't yet have the information from the IRB study as to how this is being routinely handled.

So I felt a little concerned about kind of accepting and moving forward with an assessment that seemed to dictate a fairly aggressive set of actions.

It may be that we need to take them, but like Trish, I didn't feel ready based on current knowledge to accept the series of recommendations.

It may be easier. I found the structure of this a little bit difficult to follow. I kept wanting to look almost at a chart.

I kept wanting to look at some way to keep the different levels of impairment and the different levels of risk connected to what would be seen as the most appropriate ways or the options that might be considered for providing protection.

And I found somewhat difficult to follow and just conceptually as the document unfolded.

I would have wanted to have seen more emphasis on -- and I don't know if this is not here because the study has not yet been returned -- on what is happening at the IRB level.

Many of us who look into these issues believe that the variance -- that the widespread variance there is a very big problem.

And it doesn't seem to me that we address those strongly, how we would propose to deal with that.

Most of the activity goes to looking at what level of risk may be present and what level of them protection would be assigned in each of the individual situations.

But I think that we need to address the basic system in place which is the IRB system.

And perhaps, as we get more information

about that, we will be better able to do so.

I appreciated the comments that were there I think in several places about the important role of families and care givers.

That is the first time to my knowledge that such comments have been included in a report like this.

And I thought that that was an important recognition of the particular role that families play.

It was noted that there can be situations where their ability to act on behalf of their relative may be comprised or compromisable, but I thought the tone in reference there to the role of these care givers was important.

I for one would like to see, assuming that there is a wide audience for this kind of report, a little further discussion of the critical realities of these disorders.

I think that they are not well understood. And in fact, those of us who work in the arena know that much of what people think they know is actually not true.

And so a little greater discussion of what

the range of clinical realities is for these disorders and how can they effect.

We have stated that they vary, but there is not much detail. And I think it is tremendously important given the fluctuation and abilities that has occurred with these disorders and over time that that be perhaps a little bit more explicitly defined and stated.

DR. CHILDRESS: You would be in effect proposing something similar to the kind of categories that Trish had suggested to get at this. I guess --

DR. FLYNN: Well --

DR. CHILDRESS: Or is it something different that you are proposing?

DR. FLYNN: Well, I think we should be looking at that. I think we need to have some ways of approaching this that we are not entirely explicit in the discussion.

DR. CASSELL: Can I pick on that for a just little bit?

DR. FLYNN: Sure.

DR. CASSELL: I take it that what you're saying is that while can classify failure or

Parkinson's disease and so forth and the classification does pretty well to tell you it was the person even though there is variation.

In psychiatric disorders, it really fails to tell you.

DR. FLYNN: Right.

DR. CASSELL: And it gives you a false sense that you are treating one thing when in fact a derivation may be so great that protection for subjects -- potential for subjects is also required in great variations.

DR. FLYNN: Yes. That is what I'm saying.

DR. CASSELL: Well, that is an important thing to make clear because the usual scientific understanding is that a category of a disease does represent a thing.

And I take it that this is not the case.

DR. FLYNN: That is most -- that is very helpful, a summary.

And that is indeed not the case. And I think it needs to be made clear that simply knowing the diagnostic category does not in and of itself give you very much insight into the decisional capacity of the individual at any given point.

And we know that the categories themselves, the ability to make an accurate diagnosis continues to evolve.

It's not uncommon for individuals over the course of a psychiatric illness to have three or four different diagnoses as their condition changes and often based upon their response to various treatments offered.

The other think that again is kind of line with my concern about the critical -- I'm sorry. Do you pursue that?

PROF. BACKLAR: No. Actually, I wanted to go back to another point. When we're talking about -- that I forgot to say when you brought up about the family.

DR. FLYNN: Right.

PROF. BACKLAR: How pleased you were as I am, too, that Jonathan included this.

I am concerned that we just needed the family. I would prefer to use the term and define it and say internal care givers because it is not simply family that may -- they may not be relatives, but they may be close friends who also are being caregivers.

So one would want to expand that and particularly since we start to get into the issues, I want to make sure we haven't just identified them.

DR. FLYNN: Just another couple of points. Somewhere in here, I think it's on page 21 -- and again, it may be that it is supported somewhere.

This, I don't need to point to the page. But there is a comment made that clinical investigators feel uncertain about how they should conduct themselves when working with this population.

And that may or may not be accurate. I think it's an important thing to know, to what -- I mean in terms of the variety of approaches we would take to addressing and the different places to which we would like to direct comments or suggestions, I for one think it would be useful to know why we believe that.

And if indeed do, on what -- how would we move forward to address these issues?

Because I think ultimately no matter what we do, we are reliant upon individual interactions between researchers and subjects.

And if there is a widespread concern or

lack of guidance or desire help, I think that's important.

And I wish to know in what area is there a desire for help. Where is there a sense that more guidance is needed and how might we address that need guidance?

And what other groups or organizations or societies might we direct the comments to, since I believe there has been relative lack of attention to that issue? So I was struck by that.

I would have wanted a little more conversation that recognizes a particular place we are in the treatment advances.

One of the interesting issues we are confronting here is that at a point where we are dealing with heightened concerned about protection of human subjects and understandably and particularly the potential compromise position of this vulnerable population, we are also in a period of extraordinarily rapid advances in our understanding of the basic mechanisms that underlie these disorders.

And both the advances and the basic science which in and of itself does not advance to

the potential, immediate benefit, direct benefit of any patient. It's critical.

And we have also seen the introduction over the past 10 years of an enormous array of new psychiatric medications, psychiatric medications which represent a great advance in medications, both in terms of reaching populations for whom previous treatment was never effective.

Very frequently, we have a much more benign side effect profile. Somehow the sense that came through here was that these psychiatric medications were a problem, were dangerous, that there had been -- there was a reference early on that even the possibility that widespread of the first psychiatric medications 25 or 30 years ago, they had been for reasons other than alleviating a symptom.

There was a sense of mixed message about the whole enterprise of bringing new treatment to the population.

And there were references to commercial possibilities.

All of these things are part of the equation, but there didn't seem to be an effective

reference to the fact that this is a population that has suffered enormously.

They are in a very stigmatized position with very few effective remedies until quite recently.

And it just seemed to me that the balance that you want in terms of looking at what's happened historically with the population, the goal that research plays for such a population, the particular place we are now in research as we look at the very understandable concerns about the appropriate way to design these medication trials.

PROF. BACKLAR: And in fact, of course, that is a very important point in terms of when we get to our discussion about placebo.

DR. FLYNN: Right. Exactly.

DR. CHILDRESS: Jonathan, do you have --

DR. MORENO: No. I just have a general question, namely, how to put on the table a service of the summary of where we are now in the research as you put it.

I don't feel qualified to do that. So Jim and I or Jim and you, Jim and Harold will need to think about how to commission a service of the

summary of that process, of that evolution.

DR. CHILDRESS: Right. I agree with Jonathan. It is an important addition.

DR. MORENO: One reason that this draft didn't go into that question a great deal is that my impression has been that the subcommittee supposes that research will go on. And it is important in this area.

But I think you're right that the reasoning needs to be articulated. Thank you.

DR. CHILDRESS: Jonathan, did you want to say anything about the comment on investigators?

I'm assuming that you're basing it in part on the literature.

DR. MORENO: I'm basing in part on the literature and in part on experience with psychiatrists and others who work with this population.

I mean, I've had experience with an Alzheimer's researcher in New York who has struggled with the problem of how to get consent on an ongoing basis.

So I have to say it's partly my own experience.

DR. FLYNN: And that goes really to my last comment. And it may be, too, that it was just my difficulty in pulling out the key conceptual issues just from the way it was organized.

And I understood how it was organized, but I kept wanting to pull pieces from different sections and put them together in a different conceptual framework.

For me the issues of informed consent really go to the heart of this. And I would like to see a bit more explication of some of the challenges there.

DR. MORENO: Obstacles to consent.

DR. FLYNN: Obstacles to consent, as well as any -- occasionally, you gave some brief examples of different ways that one might approach this.

And I think a little fuller explanation there is important.

I'm looking for ways to strengthen that area because I think it is the crucial interaction.

And it is every bit important for me as setting as setting up hierarchies of level of risk and level of protection.

I think if we don't have real integrity in

the informed consent process, everything else is going to be called into question.

So anymore development there would be helpful.

DR. CHILDRESS: Trish.

PROF. BACKLAR: Yes. The issue which leads to that, the problem of evaluation of capacity which is something that we may have not addressed.

And I still go back and think that Dr. Applebaum is so precise about it that we do not yet have an agreement on the amount of impairment that we will permit in our society, at what level do we agree that somebody does not have decisional capacity.

Some levels are very clear. But there is a very big gray area. And I still think this is something that this commission really should be addressing in one way or another.

You know that I would love to have Dr. Applebaum do some -- get involved and do some research on this.

DR. FLYNN: That is a critical area though. You're correct.

DR. CHILDRESS: And one thing also that

struck me, of course, Jonathan is building on his work and Rebecca's work that have been submitted.

And there is not much here there on this particular discussion. We had a lot actually when Dr. Applebaum came.

And this is one area we might be able to beef up quite a bit actually.

PROF. BACKLAR: And he is very interested in exploring this further, as you know, even though he has done many studies.

But this particular remark of his has not yet really been explored.

DR. CASSELL: Could we excerpt that as an area that we might discuss separately the whole issue of?

DR. CHILDRESS: Of competence?

DR. FLYNN: Of competence?

DR. CASSELL: Of competence. What do we mean by the capacity?

DR. CHILDRESS: Actually, it's next to the top. It's decision impairment and incapacity and informed consent.

DR. FLYNN: And those are all -- yes.

DR. CHILDRESS: We can move into a really

hard discussion on it. Yes.

DR. FLYNN: Good okay.

DR. CHILDRESS: Okay.

DR. FLYNN: I just want to say having -- as we all do when you're asked a comment, go through and find those places where you would like to see things slightly differently.

I was really very impressed with this. It was very, very thorough, you know. One has quibbles here and there.

But I thought you just gave us an excellent document to work from, although, like Trish, I'm not ready to adopt your recommendations.

I appreciated them as a challenge.

DR. CHILDRESS: Right.

DR. FLYNN: And they did sharpen the focus of my thinking.

DR. CHILDRESS: Right. And Jonathan has done a lot of this sort of stuff and co-author stuff. And these settings, we -- you just -- it's not a --

DR. MORENO: Even those are good --

DR. CHILDRESS: Yes. It's not a -- so he understands.

I underline that again, we really are indebted to you.

DR. FLYNN: It is really an excellent document.

DR. CHILDRESS: Okay. Thanks Trish and Laurie.

And you allayed something. Did I --

DR. CAPRON: I'm glad that we have all acknowledge and I would acknowledge our gratitude to you for this.

I was impressed by, if nothing else, it's size, given the relatively small amount of time you've had to work on it.

I'm less pleased than the others, however, with the presentation of the material here.

And I found myself, I think the reasons different than Laurie, being unhappy with the opening, this history.

I couldn't tell when I was reading it what I was supposed to be gathering from it. Was it recited to show that this is a vulnerable population that is often abused?

Was it recited to show the difficulties of getting consent?

Was it recited to show the failure of past attempts at regulation, particularly vis-a-vis the criticisms of the existing common rule.

I think I share those criticisms, but I realize that until we have the recommendations that we know we are going to be able to make substantively, much more helpful recommendations, I am always worried about that casting stone because it will not only rather than crack someone else's window, it will bounce back on ours.

I thought it would be more helpful if we could begin -- and I tried a lot of rewriting. And then I decided my problem was not just in what was here on a line by line level, but the organization of it.

To begin by making the objectives of the report a lot clearer, what questions are we trying to answer?

And I saw that there were several. And they would lead us in several different directions.

The first is the question, who is impaired? Who is really impaired?

And I'm not still clear having read this whether -- I thought Trish's comments were very

helpful in this regard.

Whether we are in the end only concerned with incapacity. And we are regarding -- the phrase, the title of the report and supposedly what we're dealing with decisional impairment merely as a preliminary question.

So that it would be even within that, we have now decisionally impaired or those who are sort of possibly impaired. We actually say is -- their capacity is doubtful or some such thing.

Suspect, I think we said. I would think that is sort of labeling. It sort of sounds like you are suspect.

What we're saying either you're impaired or maybe you're impaired.

But in the end, it sounds as though we say that all of that is only of interest because maybe you're incapacitated. And that being impaired isn't the issue.

And I thought what this report was going to address was the more difficult set of questions of people who are not incapacitated.

And then, when we got to the recommendations, as far as I can see, what they end

up saying is, well, if you can give informed consent, then you can do all these things.

And then, I found myself wondering, well, then are we saying then that there is no impairment? Or can you have impaired consent?

I mean, I really -- I don't have an answer from reading this report. I don't know. I haven't heard it discussed this way by the commission. I don't know where we come out on that.

But that is the first sort of question, who is impaired?

And then, the question, how is such a decision to be reached? What is the process by which that would be?

And in order for us to make a contribution to that, I think we have to be much clearer then about the kinds of things you were just referring to which are the sort of things that Paul Applebaum could bring where we would be quite substantive in saying this is the way one would determine that.

So that our IRB reading our report or the federal government trying to draft the specific regulations would know what kinds of criteria should be established.

And then, the question, what kinds of protections are therefore appropriate once one is found to be in one category or another?

And you do address that obviously. You talk about -- you mostly address it by setting up what seems occasionally to be a straw man which is the rule-out alternative, the exclusion of whole categories of people.

And the argument that is raised in response to that, as far as I can see, is an utilitarian argument.

And yet, it is not explicitly recognized that we are going to end up with some ethic difficulty if these arguments are being presented on kind of an ontological or not ontological of the duties that one owes to people and respecting them.

And the others are these utilitarian cross currents.

And that then leads me back to the question, what indeed do we think is morally significant about any of these categories?

And I know we had a discussion of this, but seeing it here on paper made me troubled.

There is a section where we recognize that

children are not impaired simply because they don't have decisionmaking capacity.

And why is that? Well, because it is normal for children not to have decisionmaking capacity.

Well, that is fine. And then, there is a discussion. In fact, the section is called something about pathology or something, pathological decisionmaking impairments.

And I found myself in the end saying, ethically, what's -- I mean, we don't want to -- if we consider the word "impaired" or "incapacitated" a pejorative label, we don't want to label an individual child in that way.

But we have as a society viewed that in fact as to having then make decisions for themselves, they don't have that capacity.

So what's the difference in the end? We then end up saying either there is no research or we find a means of permitting research that has been reviewed in a way that takes special -- pays special attention to the fact that you are dealing with someone who is not going to be giving their own consent.

But is there more here? Are we -- and we don't get into this.

And I didn't think that role of the family thing belonged where it comes up at all. I mean, I just thought it was totally out of place.

And what we're missing was precisely because it seems to be the role of the family would normally come into the discussion of sort of what means we're going to have available to deal with the fact that we're facing a person who can't make their own consent.

And here, it becomes relevant, it seems to me, but I defer to my colleagues who know so much more about this.

So talk about the potential differences between a parent deciding for a child who faces a medical condition, but who is otherwise has been a normal member of the family and so forth versus a parent or other care giver deciding for a person who has had a long-term incapacity due to a psychological or psychiatric problem which has been the family in a whole bunch of other ways.

Now, it is apparent that when you read accounts of people who have physical burdens that

their families deal with, you get some of the same concerns raised with a parent saying, you know, I wish my child were dead. I mean, I wish he had died back then rather than recovering.

And I mean, this is not said by a person who does not love their child, but it is just I'm so worn out from this. I'm so unable to deal with it. It seems so hopeless.

And I can go back and find some of that material if it's useful.

So it's not as though there is a sharp difference. The difference may have to do with carnicity and burden and so forth.

Or does it have to do with the nature of the illness? I don't know. We really haven't made clear.

But certainly, if we were only thinking about incapacity, one easy solution would be simply to say plug the decisionally incapacitated adults into the children's regulations if it were just lack of capacity.

And yet, we have a sense that that is not appropriate.

Part of that also arises I think because

of the difference which we don't contextualize very much here in the relationship between the treaters and the patients.

Now, obviously, a good deal of the treatment is no longer institutionally-based treatment, but some of it is.

And certainly, some of the ones that troubled us the most when we heard about it here were people who basically felt locked up wherever they were and maybe were locked up despite their desire to leave.

And maybe, that's a difference. But I don't know what role that plays here for justifying a whole separate set of regulatory concerns.

DR. MORENO: I'm sorry. You mean, the commitment situation?

DR. CAPRON: Well, it's not just commitment because many of these were voluntary admissions to the hospital.

DR. MORENO: Right.

DR. CAPRON: These were not people who were civilly committed.

DR. MORENO: Right. But then, feeling unable perhaps to --

DR. CAPRON: Feeling unable either because they are told basically you are such in bad shape that if you walk out the door, you will, you know -- we are taking you off your drugs. If you leave here, you're going to, you know, do something awful. And the person knows he's going to do something awful to myself.

DR. MORENO: Right.

DR. CAPRON: And fights and feels trapped for that reason.

Now, it is also true that a child who needs a liver transplant or something and is being maintained in the hospital in a precarious situation is equally constrained and not free to go home.

DR. MORENO: Right.

DR. CAPRON: So again, I'm not sure that there is a sharp difference, but I think we had a sense that at least some of the historical view that you're dealing with, a different population comes from that.

And finally, of course, there is the whole social prejudice against people with mental illness which makes them less a matter of concern to society.

I mean, if we knew that large numbers of healthy children were being used in a way which was problematic, we could get very upset.

And yet, we have histories here of -- I mean, those children at the Fernault School. There was no particular reason that they were the right people to study radiation on.

I mean, they didn't go to Hoskitch or Hanover and take a bunch of boys who were there and say they we're going to feed them radioactive isotopes.

They went to a group that are marginalized in society.

And yet, although the examples are in there, that conclusion isn't drawn from them.

DR. MORENO: Right.

DR. CAPRON: So I mean, I think there is a lot to go on here, but the present presentation -- and I could walk through sections, but I think I've conveyed my primary concerns.

I think we have to be much clearer early on about what questions we think we are addressing.

I do think that historical stuff belongs in the report, but I would use it maybe not in a

block, but use it selectively to illustrate and enrich our presentation of particular issues.

DR. CHILDRESS: Okay. I just want to get on that. We are opening up to pursuing this, the general discussion of structure.

DR. CAPRON: Oh, one other major thought that I do want to share and something I started writing pages about and then decided that it properly is premature. I will give them to you, but I don't know.

It seemed to me that part of what was at work here in making this maybe more difficult or more complex task than it even was for the national commission is that we have had a challenge to the basic paradigm of this field.

That challenge has not overthrown the regulations themselves, but it has lead to a different application of them in many instances.

It is different between what I would call the protection model which is embodied in the regulations themselves and is the outgrowth and the post-Nuremberg and then the reviving of interest in the '60s and so forth which is lots of abuses, lots of harm.

The purpose of intervening socially in this and having outside review is to protect. And the correct presumption is that research should not go forward unless it's get over hurdled.

We now know that there is a major challenge to that which is what I call the access paradigm. Here are potential treatments.

There is very little else, whether it is a fatal illness or one of these psychiatric conditions that is available.

And the major problem is people getting access to it. And then, the underlying second step of that is the whole population of people has access to or the benefit of the findings of such research, either basic findings about the condition itself or specific tests of treatment.

And it seems to me that it is hard to understand some of the tensions that we see here over what's the harm of having either excluding people from research or saying we really want to make a big effort to include them without contextualizing it in the present debate which is not always an articulated debate and certainly may not be familiar to all the readers of this report.

And I think we should make it advertent.

It is obviously a much broader problem. But in no certain way, this area raises it with great force.

DR. FLYNN: I just really thank you for that. You have said what I was trying to get at earlier when I talked about having more of an explication of some of the clinical realities and some of the historic issues, sort of a greater elaboration.

The concern that Alex raises about access is very, very real and is an important piece of the history that because this was a marginalized population, because there has been a history of lack of reimbursement for care, other than in the public sector, because the illnesses are so misunderstood and there have been so few treatment.

The issues of access and the desire for an opportunity for research is perhaps stronger here. And it is a very important new way to look at the whole issue that is different than the historic way of seeing these as folks who were, if not ready to be plugged into the children's protections, usually in that very maternalistic way, and given that one

had no sense of there was much we could do about them away, the big issue is really very, very strong protection of their potential for harm.

We should never compromise the concern about the potential for harm. But there is a very strong issue here around access for the individuals for whom clinical care may be virtually unavailable otherwise and for the class as a whole because the group as a whole.

It's a large group. It's a very large group. It's the largest single disabled group in American society, people with severe and chronic mental illnesses.

And there has been until recently precious little hope available.

So I just appreciate your having articulated that so well. I think it is an important piece that we didn't find in here.

PROF. BACKLAR: And actually --

DR. CHILDRESS: Trish.

PROF. BACKLAR: I had -- did you get my book?

DR. MORENO: I didn't yet.

PROF. BACKLAR: You didn't get it. I'm

sorry. I have arranged for it to go everybody. And something went wrong.

But that leads to exactly the problem in terms of research and the therapeutic misconception.

DR. FLYNN: Yes.

PROF. BACKLAR: Because if you don't make this part of the piece -- and if you would have had my book, you would have understood that many people as I noted the other -- at our last meeting when one mother felt so guilty that she had put her child into a research protocol and the child had been so harmed because she thought she was doing good for the child.

DR. MORENO: Yes.

PROF. BACKLAR: And it turned out to boomerang and be awful for both the child and the -- the adult child and herself.

So that piece --

DR. FLYNN: Absolutely.

PROF. BACKLAR: Therapeutic.

DR. CHILDRESS: Yes.

DR. BRITO: I just want to emphasize again what Alex said at the beginning. The discussion of the history at the very beginning, it was very

confusing to me. And I wouldn't -- it didn't give me a clear understanding of where this leads to.

And one of the suggestions I had was maybe history comments, an introductory section where we discuss vulnerability in a general context and invulnerability to this particular group and really emphasize because I think there was a lack of emphasis here on the lack of -- or the -- yes, the lack of protection for this particular group in federal regulations.

And somewhere, that is lost. I know it's mentioned several times, but it's lost somewhere in the body of the paper.

So maybe if we do that right from the beginning, that would help.

And then, in terms of the generalities, I think there needs to be a discussion. And I think this on the context of what Alex and Len were just discussing, the balance of research versus lack o response.

We don’t want to assume the pendulum. you know. The overall tone of the paper seemed to be assume the pendulum too far towards the -- so much protection that we are going to be ignoring the fact

that research can do -- it can be very beneficial to this group as well as other groups.

And Len has already commented on the clinical -- related to the clinical disorders and clinical outcomes, etcetera.

And once again, I think there is too much emphasis on the history here. And I think putting the history of the context of each individual's problem as we discuss it will be a little bit better. I'm very pleased.

DR. CHILDRESS: And some of that might be clear with the exception of how to write the history since we had never agreed on --

DR. BRITO: Right.

DR. CHILDRESS: On sort of outcome and have -- and really objected to the use of the language.

DR. BRITO: So when we decided --

DR. CHILDRESS: This discussion today may help. And maybe, we need to try the history in a couple of different ways to see whether it should be partial throughout the document or whether it should be kept in the whole, but with a clearer focus.

PROF. CHARO: Jonathan, just to get you

completely confused, I thought the history section was very good and very helpful.

(Laughter)

PROF. CHARO: And I enjoyed it enormously and urge you to keep it.

DR. CHILDRESS: Well, I agree with that, too.

(Discussion)

DR. CHILDRESS: Wait. Let me go back. I don't -- I think it was confusing at the beginning. What is confusing about it is it wasn't real clear right off the bat what it is we're trying to accomplish.

And my suggestion here is that I agree with Dr. --

DR. MORENO: No. I think -- is right about that. This can't be --

(Laughter)

(Discussion)

DR. BRITO: Although I generally did actually find it helpful. But I would like to build on a couple of things that came up in the comments already and continue to add to the list of things you might want in this report.

I sense, by the way, that this is going to be a report that will probably go beyond what is absolutely necessary to justify the recommendations.

And will certainly be a more generic summary document that will recite a fair amount of the thinking that has been going on in the last 15 years.

And thereby, a lot of its value will be as a future teaching document and a records document, as well as pure support for the recommendation.

I urge you to feel free to be beyond what is needed in the specifics.

On the issue about notions of vulnerability and how they play into the access paradigm, I think there are two other factors that probably should be taken into account.

One is that this strikes me as an area in which we are unable to rely on the traditional notions of lab and animal testing before you go on to human testing to the same degree as in other fields precisely because the illnesses are uniquely human.

And this poses a huge challenge to the kind of careful scaling of the research that we are

accustomed to when we're looking at physiological disorders that are mimicked very precisely in other animal models.

It is true that as we learn more about physical substrates of the various kinds of mental illness that we will perhaps be able to get more use out of animal models than we have.

But it is exactly one of the reasons why we have been leaping forward into human experimentation often as blindly as we have.

And that needs to be understood because that is a continuing challenge in the appropriate way to approach here as opposed to other areas.

The second is in the interaction --

DR. CAPRON: Alta, could I just ask? How would we go about substantiating that?

DR. CHILDRESS: It sounds right.

DR. CAPRON: It sounds right, but I remember so often sitting in the V&A Advisory Committee and we would get to the point of asking was there an animal model? And people would say we have no animal model for this disease.

PROF. CHARO: I think perhaps -- and Laurie mentioned it when she was asking about

something that talks about kind of state of the research here might be where this kind of thing can happen.

If one can identify specific symptoms which cannot measured in animals, but are a real concern in humans, that might get a handle on it.

So, for example, it is difficult to measure depression in animals. You can measure a lot of secondary behaviors that are associated with depression in humans and say if your mouse is less physically active, sleeping inappropriate hours, eating inappropriately, that is a similar set of symptoms as humans.

But there is not a whole lot of confidence that this actually represents the mouse equivalent of depression.

And there is a tremendous amount of anthropomorphizing in the way in which we use animal models when you're looking for mental illness.

And anything here that simply even just began to explain the challenge of using animal models may help us.

Then, too, if we need to justify later some degree of experimentation in humans when you

factor in the demands for access and major treatments because in fact you cannot have as careful a development for certain kinds of human illnesses as you can for those are about cardiac muscle function where you might be able to get highly accurate animal analogs. It is very important.

DR. CAPRON: I mean I agree with the point. And I guess I would like to put it down in writing and share it with a lot of medical scientists.

PROF. CHARO: Sue.

DR. CAPRON: To see where any of them, yes --

PROF. CHARO: Absolutely.

DR. CAPRON: Tell us something.

PROF. CHARO: Right.

DR. CAPRON: And I guess I would also be more comfortable if we didn't feel that it was necessary to make comparative statements about this area versus others.

I mean, if there are particular barriers which people would substantiate what you just said that it is not possible to have an animal.

They can't even conceive how one would have an exact animal analog because it's a cognitive thing. We have to talk back and forth to understand.

PROF. CHARO: Right.

DR. CAPRON: That would be fine to include without saying that this is a totally different ball park from --

DR. SHAPIRO: I really agree with that because the other ball park, so to speak, is hotly contested.

PROF. BACKLAR: That's right.

DR. SHAPIRO: But I agree, that kind of information --

PROF. BACKLAR: And, for instance, there have been studies. And I can't give -- I'm not a scientist. So I can't describe them to you.

But I think Weinberg did a study in which there was certain physiological alternations made.

And they were for -- for instance, they noticed like they were disheveled like a person with schizophrenia was, the similar kinds of --

PROF. CHARO: I remember, before grooming, they would knock -- before grooming.

PROF. BACKLAR: So it is not totally impossible to do this.

(Discussion)

PROF. BACKLAR: So I am very concerned.

PROF. CHARO: Right. Just to put it on the table because I suspect that there might be something here.

DR. FLYNN: That is an important point.

PROF. CHARO: The second thing though, and it is related kind of from the opposite, has to do with the vulnerability and last-chance medicine that several people have referred to.

I think it's probably worth noting interactions here with the Food and Drug regulation. I'm talking mostly about drug therapies.

PROF. BACKLAR: And early -- so then actually, the access, there are some good therapies that are available.

The problem is that many people don't have access.

PROF. CHARO: Because of the insurance, etcetera.

PROF. BACKLAR: Because of the insurance or because of difficulty in getting treatment or

because in fact they become psychotic and refuse treatment.

And therefore, it is very difficult to get them into treatment.

PROF. CHARO: I'm not suggesting that there are no good treatments for any of these illnesses. I didn't mean to say that.

PROF. BACKLAR: Okay.

PROF. CHARO: But there are situations. There are situations where there are no good treatment and where people are desperate.

DR. CHILDRESS: Rephrase your suggestion then. In that situation, what are you suggesting?

DR. BRITO: I'm saying that it's worth examining the interaction between FDA rules where there are no good treatments and the only thing that's coming down the pike is a drug that's not yet use for another use.

So that off-label fermentation in the context of experimental clinical care is not an option, that it pushes researchers towards a research protocol approach which in turn is inconsistent with the expectations of the patients and their care givers, are frequently inconsistent

with the expectations patients and their care givers.

So that we get people coming in thinking that they are going to be cared for when in fact they are being used for research.

And just to acknowledge that this is part of the overall set of constraints that has drawn people into these --

DR. CHILDRESS: It sounds like it might be good for a couple of paragraphs from you on that as a way to --

PROF. CHARO: I know I'm not making any sense.

DR. CHILDRESS: No, you're making a lot of sense.

(Laughter)

DR. CHILDRESS: If you would sharpen it up. And it would help in terms of the experiences relative to this.

DR. MORENO: But your question --

PROF. CHARO: They might. They might.

DR. CAPRON: Are we also talking about here the difference between no effective treatments and treatments which are effective, but which have

problems?

PROF. CHARO: Even --

DR. CAPRON: And where the researcher may be saying, well, what I'm trying to do is to see whether we can use less of that problematic drug or whether another drug would be better.

DR. FLYNN: You have both. You have a subset of individuals.

DR. CAPRON: I'm saying all of these, yes.

DR. FLYNN: For whom no currently available treatment works. You have those.

DR. CAPRON: Right.

DR. FLYNN: Who are just not reached by anything available.

DR. CAPRON: Right.

DR. FLYNN: Then, you have another group who are reached by some of the older, sort of therapies, but for whom the side effects and perhaps the long-term impact is really very, very problematic.

DR. CAPRON: Right.

DR. FLYNN: And the issues about dose and looking for treatments that can be better tolerated become over time imperative.

But I think your point is a good on.

DR. CAPRON: Yes.

DR. FLYNN: But combined with the economic issues, we really do have a subset of people for a variety of reasons are quite desperate for anything new. It may be the best and the only chance they have of any semblance of a normal living.

PROF. CHARO: I mean, it might lead to suggestions, for example, when it comes to options about could we in certain subsets of groups to focus on research being committed only, for example, on using compassionate use protocol which allows highly individualized attention.

Understanding difficulties of getting data from that that is going to be generalizable, but using a kind of balance between the moods of individuals, the fact that they will be.

It's like you everything you say under certain circumstances approaching this with a patient rather than a subject mentality.

Perhaps, the balance in some subset of cases may be that you have to reduce the generalizability of the data in order to develop it, but still be able to do the experiments as long as

it done in this highly individualized, patient-oriented way.

DR. CASSELL: I'm developing hives as you speak.

(Laughter)

DR. CASSELL: I'm not a researcher. I'm a clinician. And what you're talking is going back to pre-experimental medicine which took a large effort in the scientific community to get back out of.

You can't get that in those ways, unless the person is part of a protocol designed specifically to do what you're trying to do.

What you do is you get a set of anecdotal patients. And unless its -- and pneumonia in which case everybody got better where everybody died, it has virtually no value.

Now, that happens all the time. And it also produces horrors because it's being used for the wrong patient, wrong dose, wrong duration because there are not enough guidelines for the use.

The fact that people are desperate and the desperation drives them to do desperate things, since Socrates' time, will never change.

But in terms of trying to find a way to

both enhance the access of sick people to care that they would otherwise get while at the same time they're defended against the problems that that makes, I'm --

PROF. CHARO: See, I'm not suggesting that these things be addressed as part of increasing access.

I'm suggesting specifically they be addressed as part of enhancing protection.

DR. CASSELL: Well, then you have a research paradigm. Then, what you should say which I think is correct that the way we've been looking at research is merely placebo control and so forth. It is inaccurate to this group and new experimental methods are what are --

DR. CHILDRESS: And that certainly raised the part of the discussion later.

PROF. CHARO: Yes.

DR. CHILDRESS: In this document.

DR. CASSELL: But that was not my point.

(Discussion)

DR. CASSELL: Mr. Chairman, that was not my point that I've been --

DR. CHILDRESS: No, no. I'm trying to

balance as best I can the interaction around the particular issues that we are raising.

(Discussion)

DR. CHILDRESS: And I have Harold on the list for a longer, more extended comments.

DR. DUMAS: All right. This is -- because I think it got lost in the shuffle. One of the things you referred to had implications in my view for the nature of informed consent.

When you mentioned people who might come in thinking they're coming to be treated and actually they are coming to participate in a study that will not necessarily -- without any therapeutic benefits to them.

And I think that is something that should not get lost, how do -- how to deal with the issue of informed consent where that is that liability of misunderstanding.

PROF. CHARO: Of course, you realize, Rhetaugh, that no matter what you do, no matter how hard you try, right, the empirical data studies we have today are the ones that are probably going to come out of the latest rounds of grantmaking are going to show that when people have no satisfactory option, no matter

what they know cognitively, in their hearts, they are going to be a goodly number of them that are there because they think --

DR. DUMAS: They want to be treated.

PROF. CHARO: This is for their health and treatment, right?

DR. DUMAS: Sure.

PROF. CHARO: And that, I don't think we can just afford to ignore that phenomena.

DR. DUMAS: That's right.

PROF. CHARO: We can acknowledge it and work it around it.

DR. DUMAS: That's the point --

PROF. CHARO: We can't pretend it doesn't exist because we've given them all the right papers and then say if they made a mistake, it's their problem.

DR. DUMAS: That's why I thought it was so important to come back to that statement that you made that kind of got passed over.

I think we need to keep in mind.

PROF. CHARO: Right.

DR. DUMAS: And try to find some way to at least highlight that dilemma.

PROF. CHARO: Yes.

DR. CHILDRESS: And -- will stay on this. And then, Alta has two more points. and then, Eric has several. And then Harold has several.

DR. RAUB: Right. My point just really builds on Eric's comment. The distinction between the question of whether the array of research paradigms is sufficient to deal with all of these questions, as distinct from the frequent assertion of something not -- I don't usually hear it called experimental medicine.

I usually hear it called innovative therapy which is not a label that takes it from under protections altogether of protocols and informed consents and IRBs and those things and the like. So -- okay.

PROF. CHARO: Related to these, by the way, Jonathan, there is an unspoken, undiscussed question underlying a lot of this about the notions of clinical apropos.

In many places, in the draft, there are moments where it is appropriate to talk about the expectations of the investigators in terms of the likelihood of benefit to the patient.

And undiscussed though is the kind of myth of research which is that the investigators exist in a moment of true apropos generally don't have a clue of what's going to happen.

And that in turn is essential to the justification of a fair amount of a randomization that goes on with or without placebos, randomization among control placebos.

And yet, here, we are demanding that we no longer think about this as a situation of clinical apropos.

But as soon as you do that and as soon you acknowledge certain expectations, there are a variety of concerns that arise of how soon you break the blinds about how you soon you inform people about preliminary indications of messages that they can be re-consented to continue in a randomized fashion as opposed to demanding access in a more clinical therapeutic mode, etcetera.

I think at some point, we need to at least acknowledge the underlying challenge this poses throughout here.

But it's not Jonathan's field, but it's one that very much applies.

Finally, and I have a feeling you guys are going to get --

(Laughter)

DR. CHILDRESS: Which guys?

(Laughter)

PROF. CHARO: In the discussion -- and this goes back to Alex's -- justifications which I think was very well taken.

In both the area of children and in the area of incapacitation, I want to say incompetent as a kind of broad category of subjects, we constantly are justifying the imposition of risk, whether it's minimal -- over minimal or more than that based on the need to have this research done for the benefit of all society.

And this is absolutely true. But I think that -- my personal inclination is that we're going to be more credible if we actually acknowledge very openly and handily exactly how that -- what that argument means instead of dancing around because I think we've danced a little bit in this draft.

It's a medical draft. It's exactly what it is. It's a draft system. We draft people who are uniquely capable of defending the United States.

And these are people whether it's children or people who are incompetent with illnesses that can't be treated -- can't be researched in any other group of people who are being used without any issue of their ability to volunteer.

It's a draft. And I think you have to acknowledge that openly and then justify it openly because, number one, I think you can only gain credibility if you don't give people the chance to say they weren't really to acknowledge the hard issue underneath this.

And it's just as true for children as it is for the incompetent.

And the second is I think it does begin to open up one's mind, and we will discuss this more when we talk about benefits and risks, to the equities of the situation.

If you think of it as a draft, then the benefits to the larger society may be one part in terms of the patient, but there may be a need to provide benefits to these people directly.

And even if you can't benefit them through the research, maybe you have to put them into an institution that is a four-star hotel version of a

hospital for their illnesses, just like we give veteran benefits for people who have been drafted into the Army or the old draft, you know.

There is a notion in the property area of taking where the government is allowed to take property only where there has been a quid pro quo for it.

And we are being very nervous about saying this in the area of human beings because it comes very close to saying we could draft a portion of the population to serve in, you know, involuntary servitude to the rest of us.

But that is precisely what we are talking about. And I think if we were to say it as boldly as that, we might be willing to then, if we're going to justify it, be much more generous in what it is we think these people are owed in return.

And maybe, then, make it something that is more equitable in the end.

DR. CHILDRESS: It's Buck versus Bell.

PROF. CHARO: Oh, no, that's not fair.

DR. CAPRON: It is Holmes' famous language. I mean, having looked at the statute on involuntary sterilization, he said, how can a nation

that asks so much from its finest not ask this one small sacrifice of giving up reproduction from those who are impaired?

DR. CHILDRESS: And who want experience in the sacrifice anyhow.

(Laughter)

DR. CAPRON: That is interesting. It is Holmes' explicit language. I made reference to it, but -

DR. CHILDRESS: All right. Are there any other reactions?

(No response.)

DR. CHILDRESS: I had anticipated more.

It seems to me that if one works it out along the draft model, you have to deal especially with the kinds of recommendations here with the role of ascent/descent with others actually being able to give authorization or not and with then the direction of the recommendations for the benefit for this group of subjects as it applies.

And so there are certain kinds of restrictions being built in that would make it -- the old technology less --

PROF. CHARO: They make the draft more

tolerable, but in the end, it is still involuntary dragging people into the service of others.

VOICE: Not voluntary.

VOICE: Not involuntary.

PROF. CHARO: Nonvoluntary.

I just don't think -- I don't think you can avoid the kernel here.

And dancing around by making it as a limited group and as pleasant experience as possible doesn't get around the kernel of the objection.

And although you do acknowledge it, you do it in a sentence that comes at the end of a little paragraph.

And then, you go, but the little side benefits will also be mentioned as the answer. And then you move on to the next subhead.

And I mean, I just think that unless we are willing to say, yes, that's exactly what it is and here is why we think it is tolerable and justify it. Well, here are all the things we are doing to make it as inoffensive as possible. And do it very up front. It makes us vulnerable.

DR. CAPRON: I think the issue is a basic underlying issue that has to be addressed.

I'm not sure that you advance the average reader's ability to address it by making an analogy to which there will be so many objections.

PROF. CHARO: Right.

DR. CAPRON: Let me add.

PROF. CHARO: You mean, in the draft?

DR. CAPRON: Yes.

PROF. CHARO: Oh, no, you can drop that.

(Laughter)

DR. CAPRON: Okay. Well, let me just add one more which would be supposedly when we have a draft, it is a result of somebody we recognize, a national authority concluding that this particular demand is appropriate to be made.

I don't think the same thing can be said of this area of research. Certainly, we have public funding for it.

And you might say that that is part of it. But a lot of the research is not publicly funded.

And I don't think we can put aside who decides for a variety of reasons. They would want to go ahead of a particular project in the same position as the Congress and the President who are much more publicly accountable for something like

that and where the decision is much more likely to be seen as something which we all have a right to say yea or nay to.

I mean, you see the point.

And so in a way using the depth analogy for our own thinking might help us to tease out some of the elements that are not comparable which become rather important.

PROF. CHARO: Sure. If only because they make it seem even more outrageous. There hasn't been a national decision.

DR. CAPRON: Right.

PROF. CHARO: There is not a national imperative. It is not being done with national rules.

DR. CAPRON: Yes. All right. Okay. Okay. And the other thing I don't know on what basis whether it was rhetorical or hyperbolic or what about the rear efforts to the equivalent of the four star hotel for the hospital.

But in a certain way, one of the problems that have arisen in this area and other areas of research, like research for prisoners, has been precisely offering the good accommodations, the only

decent accommodations in some cases to the people who would agree, quote, agree, to do this to be research subjects or -- I mean, the example and all the prisons where the medical research world was the only place where you had any chance of not being raped and assaulted. So --

PROF. CHARO: But the problem there is not in giving people good accommodations.

DR. CAPRON: It is under inducement.

PROF. CHARO: It is in the absence of good accommodations generally.

DR. CAPRON: Yes, exactly. But that's certainly true in the view of some people for the patients.

I mean, it's a further --

PROF. CHARO: Right.

DR. CAPRON: Illustration of there is no good alternative.

PROF. CHARO: Right.

DR. CAPRON: If you don't have funding for the drug and the only way you're going to get it is to go into this. It is the same kind of --

PROF. CHARO: Well, that's why when we get to the benefits section, I think we do need to talk

a lot about these kinds of issues.

DR. MORENO: Jim, this is on point of your discussion.

DR. CAPRON: Yes.

DR. MORENO: There is a historical tale to be told that helps to embody your intuition. And that may be done in the following way.

The degree of acceleration in the use of human subjects in research happened during the second world war when the notion of conscription in a national/side service vein, something like your home site became well recognized and accepted.

And there is a sense in which some of that sensibility slopped over to the early cold war period I'm writing about now in this area.

So there actually is some sense to be made historically of your proposal.

But I think Alex is right that this needs to be drawn out very carefully because the lay reader will not understand the point you said of conscripting people to be in research.

DR. CHILDRESS: David Rothman's piece in the New England Journal, for example, doesn't do that.

DR. MORENO: Yes.

DR. CHILDRESS: I will take two more sets of comments of a general nature. And then, we will probably just take an early break and then come back and talk about the particular areas.

Okay. I have Eric. And then, I have Harold.

DR. CASSELL: An early meeting deserves an early break.

DR. CHILDRESS: Right.

(Laughter)

DR. CASSELL: My comment I think really picks up on the things a number of people have said. And it is a very simple one.

We are moving away from the understanding that the function of regulations is the merely the protection of human subjects.

And that movement away from the function of an -- commission that we know -- but I'm sure what word goes instead of "protection".

But we are trying to understand the way in which people are both given access and at the same time prevent -- harm is being prevented.

And I think we have to -- I think if the

gist of this draft would make a real move, an intellectual move in our understanding of research on persons who have difficulty consenting.

And I would like to extend that one further that as we go and study what this means, because I think we are really required to do that, we will find that impairment is present in all of the sick. I mean, I know that because I have studied it.

Impairment is present. Thinking impairment is present in all sick persons.

And yet, we want to protect them at the same time as promote their health.

I'm trying to figure out a way to say that. I'm not too sure how, but I think it ought to be. I think it ought to be.

That is the --

DR. CHILDRESS: If we think about it at all.

(Laughter)

DR. CASSELL: I had said the creative use of language is one of the functions of philosophers, to give new words.

DR. CAPRON: And commission drafters as

well.

DR. CHILDRESS: Anything else?

Harold.

DR. SHAPIRO: Well, one of my comments really picks up exactly I think what Eric was saying.

And that is this is a population which as a number of others have mentioned, can be stigmatized in very unfortunate ways.

And one of the ways our report may help in that particular regard is by noting that really all of these problems fall on really all sick people. It's just in a slightly different way.

And their vulnerability, their capacity to make decisions to their own best interests, their inducement to try to find something because they are very desperate or whatever it is, in my view own, it's for many of these cases matters of some degree.

So it might be that we can find a framework like that which shows that these people like all other people in cases.

PROF. CHARO: Right.

DR. SHAPIRO: Who have very particular symptoms and very particular -- so that just might

be helpful.

It is right along the lines that Eric was suggesting.

Another suggestion is there is a question of fact. That is Alzheimer's was mentioned earlier on.

What is in fact going out there? What is going on at NIMH or anywhere else? Or what are the researchers feeling about this, that, and the other thing which are very important?

There are some issues we cannot decide without knowing more about the facts.

Running over a series of issues are probably not fact dependent which are dependent on how we feel about individuals and how they ought to be treated whatever their circumstances.

And then, it also might be helpful as we go through this and try to organize this to understand better which things we're saying really depend on some finding that we still -- on which depend on a set of arguments which you would like to mount which in some sense stand independent of exactly what researchers or others are doing out there.

That it may or may not helpful. I'm not sure. But it seems like it helped me as I went through this draft to try to distinguish those things.

On the issue -- one of the thing that comes up during -- as I read this report, Jonathan, sometimes, I was not clear whether we're dealing with -- rather it is called innovative medicine, experimental medicine, whatever it is versus research.

In some of the examples, I thought that you dealt more with how people ought to behave in a clinical situation, some of the material of some organized research.

And I think it's important for us to be clear what it is that we're thinking about in that sense.

Finally, just to the issue of access, as I understand the points made here about expanding the notion or framework around which we are going to discuss this, I think that is useful.

But access to treatment, appropriate treatment in the clinical context is very often held back as much by a doctor's unwillingness to adapt

what is already shown to be useful is probably the biggest single access problem that we have here.

That probably lies beyond our scope of concerns here because we have not taken on the whole system I don't think.

But that probable is as important as any other thing when it comes to just access to care.

DR. CAPRON: Can I ask a question, John?

DR. CHILDRESS: Sure.

DR. CAPRON: If the point of talking, as you were and as Eric was right before that, about the comparability in terms of vulnerabilities of people with different illnesses, given the fact of illness is to say that we ought not too quickly to make the move of saying that we want to step in and protect which is basically a way of saying we want to take away your own role in protecting yourself and supplant it with somebody else.

Then, that makes sense because then what we are saying is if you really follow that line, you would be doing the same thing for every heart patient and every kidney patient and so forth.

But if the point is carried too far, I think it does miss something which is a reality

about that stigmatizing role of mental illness.

And maybe, some of it has to do with the frustration that so many of these things for long time seem so intractable.

But maybe it's also due to the way in which people's mental illness is more disruptive of my life than their physical illness usually is.

I mean, if I'm dealing casually in the street or in my work place or something with somebody who is mentally disordered, it is likely that it is going to be more bothersome to me.

And I'm going to be more annoyed about it and less forgiving. I'm not bragging about this. I'm saying I think the reality is like that, than if the person were suffering with cancer.

And we are equally, you know -- accommodations were required.

And I think that that risk, that that widespread conclusion is going to affect the way in which this really plays out and what kinds of things get done that in stepping back from it don't seem as though they should have been done, and the risk that we are taking and the harm that was done gives me pause about how that argument is used.

And contextualizing it, when it's used for one purpose, I'm comfortable.

When it's pressed to the next step of sort of saying maybe too much is really being made of all of this. It's really not so different than and so forth.

Jonathan, I thought, overstated it when kind of said it would truly allies this to compare this to the problems that occur to anybody in illness.

I don't think it trivializes. I think there is a good use to be made of that.

But I think at some point, it denies what is -- what has set this area apart.

DR. SHAPIRO: I agree with you.

DR. CAPRON: Okay.

DR. SHAPIRO: I don't have any problem with what you said.

DR. CAPRON: Okay.

DR. CHILDRESS: It's just finding the right balance of this.

DR. CAPRON: Yes.

DR. CHILDRESS: As I said, we have Alta and then Trish.

And then, I would see -- we've had fairly statements, most of them were written.

I was going to say, if you have anything else to add or -- and then, we will take a break.

PROF. CHARO: One thing that I'm concerned about is around the table, the sense I'm getting that there is a consensus developing that we ought to move to a model that protects access more so than is currently protected.

I just thought I would give you a forewarning.

(Discussion)

PROF. CHARO: Excuse me? It has -- right. I'm not there yet.

My inclinations are still to be focused on protection.

DR. CHILDRESS: Right.

PROF. CHARO: And even at the risk of denying access to people who desperately want it and don't have good options in the clinical therapeutic area, because until we've got complete confidence in the procedural implementation, that's at the local, the IRBs, their staffing and their capabilities throughout that country and our confidence

procedurally at the federal level in terms of oversight with either OPRR in its current location or a different offices that is set up to go oversee things for the government.

I am extremely nervous about anything that that is a way to a highly protectionist approach.

I recognize the cost. And I don't discount them. But not only do I think there is a real risk of abuse to subjects with the numbers on both sides being unknown and unknowable, but there is a huge issue of public confidence and the research endeavor as a whole and the credibility of research.

So although obviously everybody here is open to discussion, I'm not really yet to jump on-board to say we need to be moving to a less protectionist --

DR. CASSELL: But --

DR. CHILDRESS: I think it's a balance issue again.

PROF. CHARO: Right.

DR. CHILDRESS: And I didn't hear anyone say -

PROF. CHARO: I know --

DR. CASSELL: But rather I am trying to find some like this because we didn't have enough.

(Discussion)

DR. CASSELL: Not just balance, but how to -- how do we meet both needs, you know.

PROF. CHARO: Well, but the thing is, you know, a research protocol is not the place to get treatment.

And to try to guarantee access through research to treatment options I think is a fundamentally bad idea because research protocols are being designed to test scientific theories.

They are not being designed to provide care to patients.

If for some people, there is a therapeutic --

DR. CHILDRESS: But --

PROF. CHARO: I think that's incidental. But we can't make that a goal.

DR. CASSELL: No, no, no. The research protocol is the place to get treatment for melanoma because there is no other effective treatment whatsoever.

And the reason for being in the research

protocol is that your treatment at least will not only serve you, but it will also serve the --

DR. DUMAS: But, see, I would argue for access for a different reason.

DR. CASSELL: In general.

DR. DUMAS: And that is that there are groups of the population that may have problems that are peculiar to a particular group.

And they should have some options for studying and understanding those problems better.

PROF. CHARO: But that -- right. In order to make the scientific information generalizable to everybody, you need to make sure that all of --

(Discussion)

PROF. CHARO: All of the groups are being recruited and used.

DR. DUMAS: Right.

PROF. CHARO: So that your data is valuable.

DR. DUMAS: Now, that is the access that I'm talking to which is different from access for treatment for a particular problem.

PROF. CHARO: Right. I'm not unsympathetic, Eric. It's just that, you know,

we've got a problem already here in which people are being enrolled in research under the impression or with the secret and undeniable hope that they are going to get treatment out of it.

And I hate to exacerbate that because it is -- that is one of the key elements in the problems that underlie this area generally.

DR. BRITO: Is that a problem of perception? Or is that a problem of -- in order words, if people know that -- if it is made clear to someone that they are not necessarily going to get a therapeutic treatment, then is it wrong to use research as a means of providing care?

PROF. CHARO: I think what ideally would be better would be to focus on how to move things out into treatment more rapidly when there are no good treatment options in existence, how to more rapidly disseminate research into treatment against the backdrop of bad treatment.

That might be a more appropriate way to do it, but just -- but doing it --

(Discussion)

PROF. CHARO: Really research protocol is a back door of clinical care that carries with it

huge problems.

And I just -- I resist it with every bone in my body. I resist going that route.

DR. CASSELL: Well, what you do is not go that route. Just find an alternative.

(Laughter)

DR. CASSELL: That both provides treatment that is justifiable and protects the person from the uncertainties that go with the treatment. And just go that route. And then it's solved.

(Discussion)

DR. CAPRON: I think the argument -- there really remains an argument, despite the wisdom of what you just said that that notion of protecting the individual from the risk that goes with unknown treatment is the way we have chosen to resolve that uncertainty, saying we will be on the side of protecting the person.

And they had better protect it if they are in a protocol which is likely to yield results.

I think Alta is simply saying one could raise the argument that they are better protected if they are not in a protocol and only their own individual needs are being addressed.

Granted that one result may be that they get a treatment which with all the attention to their individual needs turns out to be harmful to them in ways that people would not anticipate.

And they are worse off than if they had been on the placebo or on a control trial.

So I mean, that is still a choice. It is an ethical choice that we prefer to put our emphasis one way or the other.

And I take that to be what Alta is raising. And this is simply not the only context, but this is a simply a good context in which we would draw attention to this that there is a competing paradigm that is getting attention.

And the one answer in the AIDS area has been that when they set up protocol, they set up a parallel tract for people who do not get the drug as an untested, innovative therapy rather than as a protocol.

Now, then, people say that is going to ruin the protocol itself because the people selected to go into that will be a biased group. And it will leave us, you know, all these kinds of issues arise.

But it is an alternative approach.

And I certainly -- I'm not sure I'm willing to say it's a good approach yet. I mean, I'm sort of troubled in the same way.

But if the people that we had heard from here had all been people who had been offered the same treatment if there is no other treatment for their disease, individually calibrated to them where they were never going -- the next step was not going to be taken.

They were not going to be automatically titrated up or whatever, but it was always going to be just adjusted to them.

Or they could have gone into the research protocol which has the advantages of being more scientifically rigorous and so forth.

Then, I think some of the issues would not arise. It would be at least very clear to them that when they go into the research protocol they have rejected what's being offered to them as an innovative individual treatment.

But now --

PROF. CHARO: I just --

DR. CAPRON: Whereas, now, they go into what is the research protocol. And some of them or

many of them think they're getting the individual treatment.

PROF. CHARO: Right.

DR. CAPRON: But Alta's point, I understood you to be saying it goes beyond the question of whether they are consent or they are confused about this therapeutic misinterpretation.

DR. CASSELL: I also accept that what you're suggesting is that the way it exists now does have these dangers.

Alta is saying that the dangers are so real that there ought to be a way to get treatment that is individualized to you.

And now, I say, okay, now bring them together.

DR. CAPRON: Okay.

DR. CASSELL: You just offered one alternative, the AIDS mode. Bring them together. We ought to be able to figure out either a way to bring them together or a route towards a way to bring them together.

DR. CHILDRESS: This gets back to the time that I suggested to Alta that she actually prepare some paragraphs, but it's now up to a few pages.

(Laughter)

DR. CHILDRESS: But you really need to get that on paper for us to discuss more. Okay.

All right. Just three quick comments.

Trish.

And then, we will take a break.

PROF. BACKLAR: I just want to remind us that at our last session, we heard from people who talked about well known centers of research, one area that we have never heard from.

This is why I'm very interested in what Alta says about the issue of protection. I am very, very concerned about it.

One area that we have never heard from are where research protocols are going on outside of the universities, where they go to sort of off -- IRBs that are -- that basically are not being very careful.

And I mean, these research centers, so to speak, that are outside universities.

And nobody is really finding out what is going on. Occasionally, we read about it in the Wall Street Journal.

So these issues of protection are very

important, not just --

DR. CASSELL: No, it's not the Wall Street Journal. It's a wonderful paper.

(Laughter)

DR. CHILDRESS: Associated book reviews, probably look at interests there.

Okay. Rhetaugh, any last word from you for this part, for our general discussion?

And then, we are going move into particular areas.

DR. DUMAS: I don't have very much more to add. I think most of the concerns that I had have been voiced by other people.

I felt that most of the issues that I would be concerned about are here. They are embedded in the content.

And I think that speaks for reorganization and highlighting certain areas to hit the points that we have mentioned here.

And anything else that comes to my mind, I will write it out and send it to you.

DR. CHILDRESS: Okay. Thanks.

Do you have a final word?

DR. BRITO: We are going to discuss the --

DR. CHILDRESS: Yes, we are going to go to the particular areas after this.

DR. BRITO: I was just want to say that I think part of -- I hear what Alta is saying. And I agree with a lot of it.

A lot of it I'm resisting because I think it's such a complex issue. And I think that's part of it.

What Alex said about the -- made me think about the public testimony, what he said about the AIDS trials, etcetera.

One key element there, it may be simplistic, very pollyannaish in a way, but I think it's something that we don't need to lose focus on is that a lot of the problems with research that we heard in public testimony has to do with deception, you know, when people feel they have been deceived and not been explained things.

I don't know if we have controlled for that when we're writing regulations or recommendations for regulations.

But I think that is a key element. For instance, if somebody goes to and decides to go a certain way with the AIDS medications, etcetera,

they know -- assuming they are not cognitive impaired at the time.

They know what it is they are doing. They're making that decision. And that becomes a very -- the nature of dealing with this population like this.

But what I was hearing in public testimony, most of what I was hearing, the problems were with the way people were treated, not the fact that they were research subjects.

You didn't really hear much about the --

DR. FLYNN: It's important to distinguish the problems at the ethical level and the problems at the clinical care level.

And sometimes, those get very confused.

DR. CHILDRESS: Right. Okay. Thank you very much.

I think it has been a very fruitful discussion, lots of good ideas, important ones for reshaping and restructuring parts of the report and in getting the directions clear and so forth.

We will come back right after break. And let's shoot for 10 minutes. Be back at five 'til. Okay.

DR. CAPRON: The break is exactly on your schedule.

DR. CHILDRESS: I know, but we are going to be faster.

(Whereupon, at 9:44 a.m., the meeting was recessed.)

AFTER RECESS

(10:07 a.m.)

DR. CHILDRESS: Okay. The meeting will come to order. Thank you very much.

So much for asking you to be back at five 'til. I didn't even realize what time it was until it was five after. But thank you for getting back.

And we are going to cover three areas. And I'm not as concerned about the time, but we do have to move along fairly efficiently.

But a number of these issues have been already been flagged in some way in our larger discussion.

And now, what we want to do is talk about three general areas in the report. The first is the

decision impairment and incapacity and informed consent.

And then, the next is risk and benefit.

And then, the last would be special procedures on sections as advanced directives and the like.

And here again, I've asked particular individuals to kick off the discussion.

And so for decision impairment and incapacity and informed consent, Arturo first and then Eric.

CONTINUATION OF DISCUSSION:

RESEARCH WITH DECISIONALLY IMPAIRED SUBJECTS (ISSUES); CONCEPT OF VULNERABILITY

DR. BRITO: In Chapter 2, Decision Impairment and Incapacities, some important issues were raised, particularly towards the end where there is a distinction made between impairment and incapacity.

The problem I had with it was I think maybe the order could have been -- the way it was

organized does not maximize the information there.

And with a couple of the subtitles, I had a little bit of problems with the names in particular.

Alex has already discussed one. And the pathological decisional impairments, the phrasing of that maybe is a better wording for that because that does have negative implications there.

DR. MORENO: I'm sorry. Which one was that?

DR. BRITO: Pathological decision impairments.

DR. MORENO: Right.

DR. BRITO: Referring to the --

DR. MORENO: Right. Got you.

DR. BRITO: Okay. And then, chronic impairment, I understand the distinctions you are trying to make here, but I guess the confusing thing for me is that you can have chronic condition, but that does not necessarily involve chronic impairment.

DR. MORENO: Right.

DR. BRITO: And I'm not sure that was as clear as it could have been. And that includes a

chronic mental health illness. That does not necessarily mean you have a chronic impairment. So somewhere in there, that needs to be more clear.

DR. CHILDRESS: And that would fit with well with Trish's and others concerns this morning, too.

DR. BRITO: Right.

DR. CHILDRESS: To draw distinctions. Thank you.

DR. BRITO: The introductory paragraph, I thought the important point there, the second sentence, those with cognitive impairments are not always impaired with regard to particular sorts of decisions.

And those are not specific. Identifiable cognitive may never -- I guess that goes along with what I'm just saying here.

So I think that's a real important point to keep that in there and to emphasize that a little bit more.

I don't know how detailed you want to get.

DR. CHILDRESS: Basically, I would suggest the thing in terms of the key ideas and concepts. Any suggestions for organization, moving dots.

DR. BRITO: Okay.

DR. CHILDRESS: We're looking for detail in sentences. Let's do that.

DR. BRITO: So basically what I'm saying is I like the tone of this chapter, except I think some of the wording, as I said, and some of the subtitles and the organizational.

And maybe, do a little more discussion of the difference between impairment versus incapacity earlier on.

And then, a little polishing of the chronic impairment subtitle in that subsection.

DR. CHILDRESS: Okay. And we did have another suggestion about the role of the family. And that particular section is better placed elsewhere.

DR. BRITO: Right.

DR. CHILDRESS: Harry.

DR. CASSELL: Well, I want to focus on one point which is not very clear enough here is that the capacity to make decisions here is of a particular kind.

And it is the capacity to make decisions in which oneself is involved.

And that is the thing that makes it different. For example, it is easy to demonstrate that sick people are unable to be centered in the same way that healthy people are.

And you can show that. I've never done this with people with a psychiatric illness, but I am positive that it will come out the same way and with enough force.

You can show a person one day post-operatively from a big enough operation of child block A, B, C, D block.

And show them all sides. And then, put the A side to them and ask them what's on the opposite side. And they can't tell you.

You can show them a picture, a thing where there is a picture on one side and a picture. And they are really quite striking pictures.

Turn them around. And they can't you what's on the other side.

And the failure is not a failure of memory. It is a failure to be able to see anything from a perspective other than where you are at the moment.

Now, those are crucial in this kind of

decisionmaking because this is what you brought up before.

So at the present time, I am working with some lawyers. This has a lot to do with people's abilities to make wills and so forth when they sick or to change their will when they are sick. And the legal standard has no applicability whatsoever to sickness.

So I am wondering whether we don't have to acknowledge the special nature of this incapacity if it is present or the appearance of capacity when it is absent in which we may not begin to able to have to say that particularly with certain groups of people they have to demonstrate the capacity.

Otherwise, the person should not be making the decision.

Actually, there are also ways around this problem. You can help somebody who can't have a perspective see the other side.

But that requires a different stance on the part of the investigator than simply getting permission, the thing that Alex brought up earlier. And that's not clear either.

What is the investigator's place in

determining capacity and enhancing capacity and so forth?

DR. CHILDRESS: Anything else?

(No response.)

DR. CHILDRESS: Okay. It's open for discussion on these central ideas.

Alta.

PROF. CHARO: A question, since it has been so difficult to come up with clear categories of progressive degrees of impairment or complete incapacity, what is the purpose in avoiding the categories that are currently used?

That is simply competent and incompetent with a single break line distinction.

We know that it is difficult to identify. But it has been used consistently.

What is the purpose in not using that category?

DR. MORENO: Well, maybe, I've been reading too much of the literature and, you know, the gradations of confidence in the translation of the competence language to capacity that is so popular in bioethics.

I guess I wanted to try to exhibit a

little more subtlety than that.

PROF. CHARO: For purposes of understanding the problems, I thoroughly appreciate the need to be more precise.

But when it comes to translating these concerns into suggestions for regulatory approaches, I guess the questions is whether or not is that what one might want to re-collapse things for the sake of --

DR. MORENO: I think that the draft of chapter 7 does that.

PROF. CHARO: Okay.

DR. MORENO: I think in fact.

DR. CHILDRESS: Is it one reason for avoiding some of the discussion of competencies and incompetencies frequently that is tied to legal adjudication?

DR. CAPRON: Yes.

DR. CHILDRESS: So is that a good reason for avoiding the language?

DR. CAPRON: I would have thought so. I mean I am --

PROF. CHARO: This was not an argument. This was a genuine question.

DR. CAPRON: It was a genuine question. Okay. There is the notion that competence is a legal, judicial interpretation.

The whole development of the somewhat awkward language about decisionmaking capacity was that it was supposed to be more clinically oriented, done by physicians, nurses, and others in hospitals.

The second thing is that although this is not literally true that a finding of incompetence is global.

Usually, a finding of incompetence is not supposed to be global, but often ends up being treated that way.

Again, the lovely list that Trish had about fluctuating, perspective, limited, and complete incapacity suggest that that would be a wrong approach and to the extent one would have to fight the competency determination to get that out.

I would think that would be a --

PROF. CHARO: Let me just put on the table and keep in mind that whether or not it would be valuable to return to a more simplistic language that tracks legal definitions, but they tend to be legal, I agree, may in turn depend upon the basic

direction of the regulatory proposals.

If one's goal is, for example, to be highly protectionist, then one can say that people are going to frequently be considered incompetent if they have any of these versions of impairment or incapacity at any time.

And that if you then have protectionist regulations that basically make it very difficult to enroll people who are incompetent, what you have done is you have now made a very clear exclusionary zone for large numbers of people.

I mean, the choice about whether or not to use these broad categories may in turn depend upon whether we are trying to exclude large numbers of people are selectively allow some people to participate, but only if they are able to exercise their control on their own of their own situation.

DR. CAPRON: I think I agree with the trust of what you're saying which is the definition you are using depends in part on what purpose you are trying to serve by the definition.

PROF. CHARO: Yes.

DR. CAPRON: And it does get us back to that earlier conflict of paradigms.

In the treatment area, I think it has been true that a lot of people and who act as mental health advocates have resisted findings lack of decisionmaking capacity or incompetence because it means that the person just loses their say in what is going to be done with them.

In this area, as you have just suggested, if your major thrust is protection, then the fact that the person becomes ineligible for research is declared a victory. You have protected them from the harms of research.

PROF. CHARO: Right.

DR. CAPRON: But to the extent that there is this other current, and not saying that we decided how much of that we are going to endorse and how much we are simply going to recognize that it is there, where it is an opportunity to get either on a protocol basis or on an innovative treatment basis access to, then perhaps disqualify them.

PROF. CHARO: That's a good point.

DR. CAPRON: Right. But then, the further quick note is if you are plugging that into a system which has an alternative method for approving the research, that is to say with this kind of surrogate

or with this kind of advance directed we could still go forward.

PROF. CHARO: Yes.

DR. CAPRON: Then, it becomes less crucial. It becomes the reason to go to that alternative method which the individual has already selected or is comfortable with.

And it is not the disqualification.

And then, it becomes much less important that we be able precisely to define what incapacity or incompetence is or how exact the method is by which it is determined at any one place.

PROF. CHARO: One more sort of footnote to add that, too. If you went to a more global, large-scale notion of incompetence/incapacity, you could nonetheless to the rules that apply there say that once this category has been achieved, what is triggered is your incompetence for making so low decisions to consent.

In other words, you have now triggered the need for secondary -- a second person to be involved.

DR. CHILDRESS: And you still have the --

PROF. CHARO: But you may always be

considered despite these incompetencies fully competent to object.

And so that in the substance of what entitlements go along with this category, sort of things that can affect whether or not you should use fewer categories that are obviously imprecise for the sake of simplicity of administration or whether you need to try and come up with much narrower identifications.

DR. CHILDRESS: Jonathan, do you want to --

DR. MORENO: I think that is consistent with the direction of the draft recommendations also.

DR. BRITO: I have a question for Jonathan about the references here, the sliding scale approach to decisionmaking determination. Can you elaborate on that a little bit more?

DR. MORENO: What page?

DR. BRITO: Page 31. Because I think that might help with the --

(Pause)

DR. MORENO: You want me to elaborate on that in the text?

DR. BRITO: Well, elaborate now.

DR. MORENO: Now?

DR. BRITO: Yes, a little more information about what exactly, how this approach has been used in the past.

DR. MORENO: I'm not -- you mean by clinicians?

DR. BRITO: By clinicians.

DR. MORENO: I wouldn't claim to be an authority on how it is to be used by clinicians.

DR. BRITO: Okay.

DR. MORENO: I mean, the --

DR. BRITO: The reason I ask is because I think one of the difficulties is being careful not to -- since this is such a gray area here, I was curious to see if that has been successful approach.

And I think Trish wants to say something about it.

PROF. BACKLAR: Oh, I'm sorry. Alex had showed me something that we had talked about a few weeks ago.

Actually, the first article that I know about sliding scale is by a man called Draine.

And there were a number of articles in the

Hastings report and around which were in terms of clinical treatment.

DR. BRITO: Right.

PROF. BACKLAR: And so if you had a bad cold and there was some kind of treatment about that, the capacity to make a decision about that would be much lower than if you were going to have an operation on your heart, for instance.

So then, you would have to -- then, you would probably not -- may not be the person to make the decision about it. Maybe, you would have a surrogate making the decision because of the capacity.

In other words, the greater the risk, the higher the bar.

DR. BRITO: Right.

PROF. BACKLAR: In terms of capacity.

DR. BRITO: Okay.

PROF. BACKLAR: Does that --

DR. CHILDRESS: Another version focused on the issues of complexity and not simply the risk benefit.

DR. CAPRON: Right.

DR. BRITO: But I thought that was the

question that Arturo was asking was --

DR. CHILDRESS: How does it work?

DR. BRITO: How does it work?

DR. CHILDRESS: How does it work? And how practical is it to utilize it?

(Discussion)

DR. CHILDRESS: In relation to what Alta was saying.

DR. BRITO: Can you rephrase the very last thing you said about the -- just rephrase what you last said?

PROF. CHARO: That you could large, fairly imprecise categories, such as incompetent and competent or incapacitated and fully, whatever, impaired and not impaired.

DR. BRITO: Right.

PROF. CHARO: And then say certain purposes. Like you're always fully competent to refuse, but you may no longer be competent to consent alone and need to have a second person also consenting with you, things like that.

DR. BRITO: Right. And who determines the categories, the person conducting the research? Or are you free to determine that?

PROF. CHARO: That is Eric's point which is a very good one in terms of -- and exactly why there is a lot of concern about the complexity of the category.

The more complex they are, the more difficult it is to imagine, delegating responsibility for assessing the potential subject.

DR. BRITO: Right.

PROF. CHARO: And characterizing them accurately and objectively to somebody who is closely associated with the protocol.

DR. BRITO: Okay.

DR. CAPRON: There is reference in here to one of Dr. Shindler's studies I think which indicates that there were 28 schizophrenic subjects, all of whom were found to have decisionmaking capacity.

I do not know exactly where that was. It is an example that somebody could -- again better to use it in context of making a point than to have it as part of this.

DR. CHILDRESS: And we will mention some of the concerns he had or thoughts he had about the discussion of impairment and incapacity and consent.

Bill, do you want to raise those quickly for us?

DR. FREEMAN: It seems -- unless I've missed it that the discussion is limited to the person's characteristics about capacity.

And yet, Applebaum's research suggests that it is the interaction of the person's capacity with the environment or the context of the decision that it is important.

So you had a person who could not -- with schizophrenia who could not make a -- or at least could not understand it, could not reply back what is the purpose of the research and stuff and inside of 15 minutes of a very complicated consent form, but over two days, 30 minutes at a time in small bites, can end up with that, understanding.

The implication there it seems to me, I don't know how you -- whether it's possible to put that into rules and regulations.

That's a real problem, but certainly the reality is that things are much more complicated.

And a person with the same characteristic is incapacitated in one context and yet is noncapacitated for the very same research in another

context.

PROF. BACKLAR: There is an important aspect of that. He was talking about the element-by-element disclosure.

But also, Applebaum in his research also noted that just repeating the information does not help the capacity to comprehend it.

PROF. CHARO: Teachers who have learned from their students.

(Laughter)

DR. FREEMAN: If I understand, he has not gotten the results yet on that next point.

But it is pretty clear that if you don't even get to the point of being able to say what it is you haven't incorporated.

So it does seem like the context, if it is possible to put into simple rules about a regulation, I don't if that's possible or not.

DR. CHILDRESS: Right.

DR. FREEMAN: In the context of a regulation, it may be important to include it.

DR. CHILDRESS: We will take one or two more points and then turn to --

PROF. CHARO: Just a question again.

There is a mention in here, John, of a melanoma protocol protections in which there is a reference to an assessment tool, to assess capacity, impairment, competence. I'm not sure exactly how it was phrased.

I am curious. In light of the variability of the conditions and of the things being studied in these research protocols, how realistic is it to think that there is -- that there are one or two or three, some small number of tools that exist or could be developed that could be used fairly uniformly to assess at the moment at which somebody is actually about to get started on step one of the research?

So that whether they were briefed once, twice, or 15 times, all at once or element-by-element, at the moment that they are about to start the research that one could double check that they really are appropriately going forward on their own steam.

Is this a completely impossible thought? Or is it within the realm of feasibility?

DR. CASSELL: It is feasible. It is feasible. It is an interesting to that mechanism.

But sure, it's feasible.

One of the problems of testing, the question is who is doing the testing?

Is it being done by someone who wants to show that a person has the decisionmaking capacity in which case it is one test?

(Laughter)

DR. CASSELL: Or is it, you know --

PROF. CHARO: Right. Well, if it were possible that some small number of tools that are available to be used that are fairly objective so that they are not prone to the expectations of the person who is giving it, it might provide a very nice standard way for IRBs to say, yes, you can forward, if on day one, you know, when they show up at the hospital, they are given this test.

And they continue to show appropriate --

DR. MORENO: There is an example. I have seen a -- it's probably a provocation study. It was with schizophrenic patients, a quiz at the end of the consent form essentially that asks them 10, 15 questions about the basic or conditions of the study.

And if they get them all right, then that

is used as one basis for admitting them in the study.

DR. SHAPIRO: I have often wondered whether anyone has given any consideration to what might be a wild idea, namely, to take people such as you have described who pass the test to become those who administer the informed consent to further subjects.

And that would separate them from the interest in the research.

And so I don't know. It may be a wild idea. I'm just asking now if anyone has ever had a model like that. That's all, you know.

PROF. CHARO: I have never heard of such a thing.

DR. MORENO: I think in the HIV context of women, there are peer -- peers are associated with those studies. In Brooklyn, that has been done.

DR. CASSELL: Well, you raised it. I mean but it really raises a very intrigue. If you just stick this little corner up, it raises an intriguing idea about protection in general where peers are better protectors in some regards than another population might be.

DR. CHILDRESS: Who are better protectors?

PROF. CHARO: Peers.

DR. CASSELL: Peers.

My daughter who runs a program for retarded people who are there, their -- are all managed by them. They manage them all and do a much better job.

DR. SHAPIRO: This -- well, I don't want to discuss this scheme. I haven't given enough though to this.

This is a mistake of the researcher. In that case, they are actually having peers of clinical -- who provides the clinical services apparently from what Lee described.

But I was just thinking of all those involved, of researchers recruiting their own subjects, though I haven't had any good practical advice about how to get around it, so I've tried to learned to live it with.

But as I was listening to this discussion, the issue that came before that there might be for people who pass this test -- I wasn't really aware of this test being applied some time.

Well, that is for another time. I don't

want to distort it.

DR. CAPRON: This is a new version of the watch one.

(Discussion)

DR. SHAPIRO: It's pass the test and become the teacher.

DR. CAPRON: Right.

DR. CHILDRESS: Are you welcoming other comments?

VOICE: I'm actually heading toward risks and benefits.

DR. CASSELL: One trivial comment, but it's actually -- you made reference to animals on page 25. And you make an error about the decisionmaking that you ought to pick up.

And you say lower animals ought to behave in certain ways that demonstrate desires, such as inertia -- but they don't necessarily decide.

The question is do they eat? And what do they eat?

PROF. BACKLAR: Do we know?

DR. CASSELL: This rather than that, this mate rather than that mate, this place rather than place.

My -- had no trouble with that whatsoever. But you've got set up in sort of a behavioral view of animal action.

And a few changes. Those aren't decisions you mention. Desire is the stimulus for a decision, but it isn't a decision.

DR. MORENO: Yes.

DR. CHILDRESS: Okay. I have also Trish. Did you want to get in?

DR. MORENO: That's why I said they don't necessarily decide. We don't know. I mean, there are no assertions in the paragraph.

DR. CHILDRESS: Different points.

PROF. BACKLAR: I'm concerned that we are having this discussion about capacity. And we are not talking about advanced directives with this because I think it goes in hand and hand.

So I want us to remember exactly where we are when we get back to the advanced directives. There is a lot of issues there.

And one of the tests that you can do for capacity is the Morehouse Wistaub. Is that the right --

DR. MORENO: Westhauf.

PROF. BACKLAR: Capacity test or a capacity to make out an advanced directive. And I have that in that article that we had --

DR. CHILDRESS: A long time ago.

PROF. BACKLAR: A long time ago.

DR. CHILDRESS: Right.

PROF. BACKLAR: And so people could go back and look at that. And I would be glad to get it to you again.

DR. CHILDRESS: Right. And we will come to -- right. These are obviously overlapping areas.

PROF. BACKLAR: Right.

DR. CHILDRESS: But we had to sort them out some way.

Alex, the last point on this subject.

DR. CAPRON: Okay. Actually, I will be very quickly. I want to encourage us to press towards more practical help in terms of what kinds of measurements have been validated here and make this a richer chapter.

And some of that could then be elaborated in an appendix of a guide for researchers and for IRBs and so forth.

The second is a point that in rewriting

this, you hope you pay attention to keeping separate the question of the what from the what effect follows from it because I know that it is usually sort of a very cardinal thing that lawyers bring to these discussions in saying, well, your definition depends very much on what use will be made of the definition.

But the way certain of these things are asserted about capacity and so forth here, they seem to be more intended to be descriptive.

But mixed in with them is this constant ethical undercurrent of statements about losing the right then to make your own decisions.

And it's worthwhile having that as a context rather than sort of sticking it in with each point.

I mean, it's sort of is that being raised as an argument against a very strict standard?

DR. MORENO: Is there something you've identified, a paragraph?

DR. CAPRON: I'm sure I can find examples of that. And I'll bring them to your attention.

DR. MORENO: Okay. In the meantime, I will keep that.

DR. CAPRON: And the final one is I wanted your help because I thought this might be something, a bigger issue, the fact that it's in a footnote.

In footnote 41, are we saying that this is a morally significant problem?

Down at the bottom, you say, "To the extent that an older child or adolescent is unable to provide a meaningful assent to research participation, that constitutes a morally significant obstacle to enrollment in a study of this kind."

Now, I just don't understand what that means. Is it a morally significant problem because older children are being precluded from being considered?

DR. MORENO: Oh, I see.

DR. CAPRON: Or is this okay because any assent provide would lack meaning?

DR. MORENO: The latter.

DR. CAPRON: Really?

DR. MORENO: That was my intent. I mean --

DR. CAPRON: Okay. Well, I think that should be stated.

DR. MORENO: Right.

DR. CAPRON: And then, I'll decide if I agree with it.

DR. MORENO: Right. Right.

DR. CAPRON: But I just didn't understand what you were saying.

DR. CHILDRESS: Okay. Thanks. Alta, Rhetaugh, and Eric on risks and benefits.

PROF. CHARO: I am just going to do these kinds of risks based on my notes. So I apologize that they are not in the right order.

First, there is mention that there is a special mechanism already in existence for approving protocols that can't be approved under current regulations.

And it comes up in the context of research with children that exceeds minimal risk without direct benefit.

It would be of interest to know how often that procedure has been invoked and how successful it has been used.

I understand it involves appeals of the Secretary for special review.

It is mentioned in footnote 75 on page 46 for the first time. And I am just not aware of any

current information on how well that's been used because it is certainly one of the regulatory outcomes that is going to come up.

DR. MORENO: And again, I will respond to that. Well, Rebecca did send us an addendum.

PROF. CHARO: Oh, she did.

DR. MORENO: That indicates that it has been invoked three times, that secretarial approval has been twice.

Jim, was that --

DR. CHILDRESS: That is my recollection as I recall. And I'll make sure.

DR. MORENO: And the third one may still in process. But I think --

PROF. CHARO: It would actually be interesting to get even a little bit more of a narrative about it.

I mean, why has it been invoked so infrequently considering the number of occasions one could imagine people having a need for it.

DR. MORENO: Right.

PROF. CHARO: Especially prior to the -- for emergency research.

DR. CHILDRESS: So I will get that

information out then.

PROF. CHARO: If it's -- I mean --

(Pause)

PROF. CHARO: Next on issues about assessing risk. We heard in the public testimony last time somebody who insisted that risk and benefit ought to be assessed on a very individualized basis with these kinds of subjects rather than being assessed globally for the population and that the individualized risk benefit assessment should be used for the consenting process.

And that is an extremely interesting idea, although one can immediately the obstacles, financial and time, in terms of time to its implementation.

But I thought it deserved at least some more attention, especially because it had been brought to our attention during public testimony.

The categorical questions about the way in which we use the phrase "minor increase over minimal risk" and the tie in with possibly a better notion of minimal risk versus risk that is commensurate with the current life, medications, and treatments

of the specific subjects which again implicates individualized assessment.

It might be something worth exploring in a little more depth.

(Pause)

PROF. CHARO: I'm sorry. I'm going -- because I'm trying to do it very, very quickly.

The section on benefits generally avoids the question of financial payment as a form of benefit and avoids mostly, although it is there a little bit implicitly, assess to health care professional time and services that is not available to this person otherwise either due to lack of insurance, geographic inaccessibility, etcetera.

And in the understanding of overall risk benefit assessment, I think we need to take head on whether or not we are willing to take those into account.

I think here, by the way, is a place where there is a natural connection to the concerns about research in developing countries because there, the assessment is frequently made that their care is so poor in many cases that there are a lot of indirect benefits coming to them by the virtue of this

research.

Contact with a health care professional at all, for example, may be a benefit.

And whether or not that is factored in when we do the transnational ethics analyses has always been a matter of dispute on my own IRB.

It strikes me that we are being disingenuous to think that exactly the same calculation is an issue in the United States.

The concerns in third-world countries and the concerns in the United States are not so terribly different.

And we need to make an overt decision about whether or not to put these things into the calculation.

And if we do, we then have to incorporate into that what Alex was mentioning about the fact that access to better facilities, etcetera, etcetera, has frequently been cited not only as a benefit, but as potentially a coercive level of inducement.

So that it is a double-edged sword, like Shindler's funny as a sting once again.

DR. CHILDRESS: So you are recommending a

discussion on 55 and the following benefits.

PROF. CHARO: Right.

DR. CHILDRESS: Expanded and --

PROF. CHARO: And it comes up again also on page 63 in terms of the justifications for doing this kind of research, you know, in the United States, contacts.

And then, finally, and I will turn it over to somebody else, was on page 60 where you're discussing the American College of Physicians' document about surrogate consent of incapable subjects where they talk about only possible with additional risks are not substantially greater than the risks of standard treatment, etcetera.

And scientific evidence indicated that post treatment is reasonably likely to provide benefit.

This is the place where I thought discussion of clinical apropos had to be incorporated or get referenced.

Also, the significance of this for the availability of the subjects for so-called me-too studies because it struck me that this would essentially eliminate a phenomenon of me-too studies

where companies want to test a drug to see whether or not it will be equivalently.

And thereby, a second drug company now has a -- drug.

And whether or not we have a generic preference for or against me-too studies in terms of their effect on the market, competition and prices in the long run, etcetera.

That's it.

DR. CHILDRESS: Rhetaugh.

DR. DUMAS: I want to pass because I didn't give special attention to --

DR. CHILDRESS: Okay.

DR. DUMAS: For this one, I just read through it generally. I am not on the message system.

DR. CHILDRESS: Oh, that's right.

DR. DUMAS: So I did not know I was assigned to do special --

DR. CHILDRESS: I'm sorry.

DR. DUMAS: But I will. And I will let you know.

DR. CHILDRESS: Okay. That's fine.

Eric.

DR. CASSELL: I have only a couple of comments. One just as a matter of point, on page 50, you say further the approach simply permits children with healthy conditions to be exposed to research.

The experiences for them are normal going through the medical and other procedures necessary to address their health problem.

An example is venipuncture which may be more stressful for healthy children.

No. It's the opposite way around. The more pain you have, the less pain is tolerable. The more procedures, the fewer procedures are tolerable.

That's why you see children or a child with leukemia screaming at venipuncture.

You would think, why haven't they gotten used to venipuncture? It's because it isn't the pain. The pain isn't the pain. The risk isn't risk.

It is whether one tends to look at it.

And so the risk of a lumbar puncture, what's the risk of a lumbar puncture? It's very small risk.

On the other hand, lumbar punctures can be

awful trauma. And the trauma isn't the risk. The risk is the trauma.

And the child that has to deal with circumstances under which how many lumbar punctures has this person had? What does the lumbar puncture mean, much more?

And that brings me to the next comment which you're quite right to point out, that the risk to one group of people may be entirely different than the risk to another. But then, the benefits are that way, too.

And how sick have you been and for how long when this benefit of getting better is promised?

And if you've been sick enough or completely ruined by your illness enough just a chance of getting better is worth a great deal of risk if there is no other alternative.

So that there is this element of risk embedded, but having to do with the nature of the illness involved.

Now, the problem is, how do you translate that into IRB regulations?

Well, in a way, I think it's possible, at

least to some extent, that people who are doing research in special groups should know that.

People who do research on patients with a psychiatric illness should know what is special about them and what is most frightening to them and so forth.

And I think we have a right to request that their statement of risk and benefit is specific to the group they are working with.

Now, it may be that most of the time that does not apply at all. But in some occasions, it will apply.

DR. MORENO: I was going to say I value your experience with respect to the venipuncture in the case of sick kids and healthy kids.

This is in the context of an account of the reading of the group in this report.

If you feel -- if any commissioner obviously feels strongly enough that they want to get into disagreement with another group, that's fine. And I will note it.

I don't want you to read this draft, another draft, a second draft and see that it is still in there.

DR. CASSELL: Oh, no. I would just like to --

DR. CHILDRESS: And this is an example used by the --

DR. MORENO: Yes, yes.

DR. CASSELL: If I could point out, that is one of the things that happens when people talk about risks for other people.

DR. MORENO: Right.

DR. CASSELL: They assume it in terms of their own ideas of risks. And there are two things that are different about it.

One, they are not the group. And two, they are perfectly healthy and they are not about to undergo the risk. So, you know --

DR. MORENO: Right.

DR. CHILDRESS: Seemingly, this discussion built in a lot of the hostile ways to interpret is one of the questions.

I wonder if there is a bottom line to this discussion of risk that could be stated more clearly because it does seem to me that the different elements are present.

DR. CASSELL: Yes. Oh, I mean, I think

the discussion is excellent in that regard. But it ought to lead to -- that it gives you an opportunity to lead to a more concrete set of conclusions or a pre-proposal, a possible proposal that should be considered.

DR. CHILDRESS: Alex, did you want to comment?

DR. CAPRON: I was just thinking as Eric was telling it. I was put in mind I think of a story Clifford Kurtz tells really in some country where a person was there on the street, selling little animals that you buy.

He sort of whops them over the head. And he is saying, isn't this awful. He says, oh, let me tell you, I've been doing this a long time. And they get used to it.

(Laughter)

DR. CHILDRESS: Okay. Any other points on --

(Laughter)

DR. CHILDRESS: Any other points about risk and benefits to raise?

(No response.)

DR. CHILDRESS: Okay. Our last large

area, all other protections. And we will start with some of the issues about advanced directives.

And I've asked Trish and Alex and Alta to focus on any of these other issues that need to be dealt with and in this context.

So I will just leave to you all to begin to think about the kinds of recommendations that are being offered here which we really haven't focused on so much, but obviously, you can think about a bit.

Trish, do you want to start with advanced directives?

PROF. BACKLAR: Right. And one of the reasons I originally when I began with the discussion today talked about clarification by types of impairment is because if we are going to think of research, advanced directives, it is going to be for a smaller group of people than everybody.

Clearly, people who have no capacity for decisionmaking can't possibly make out an advanced directive.

I just would like to say about advanced directives in general. It appears to me that one of the reasons for advanced directives for end of life

treatment that they have not been successful is that if you are making out a substantive directive, you are making it out for something you have never experienced.

And as you are only going to experience it once, you are not going to be able to do it again, so to speak.

And I am sure most of you have read that paper by Jo Ann Lynn where she says basically she would have a proxy, a surrogate decision-maker for her end of life care.

And that is based pretty much on the understanding that you really don't know what it is going to be.

It is going to be very uncertain. And it certainly may not be at all what one hopes it would be.

So the reason I became interested in making out advanced directives for psychiatric treatment was because they would be for people who had experienced a psychotic episode.

And they knew what, pretty much what might work for them and what might not work. And therefore, they could think about what they wanted

at a time that this would happen again should they lose capacity for decisionmaking.

So there is an element in a research advanced directive which in a sense mimics end of life care and makes it much more difficult to imagine what will occur, unless you use that advanced directive precisely at the time that you are thinking of a research protocol and you have been approached as a subject.

And in a sense, the research advanced directive can become part of the informed consent process.

So am I -- are you still with me? Okay.

And at the moment in rethinking about research advanced directives, I believe that this is probably -- I suspect that this probably the only way that one could use them effectively.

I also think that in this paper, it's not -- I think it's gotten sort of muddled up between procedural and substantive.

And I think one would want to explain the advanced directive in the way that this was a combined process that certainly some -- look at somebody with fluctuating capacity who certainly

could make out an advanced directive in the same way that a psychiatric advanced directive because they are entering a research protocol.

And they -- and it possible that they may lose capacity for decisionmaking during the research protocol.

So they would have appointed a surrogate which I think is very important in exactly the same way we look at end of life advanced directives and say that probably having -- doing it without a surrogate would not be wise.

So I just want to state again that I see this as -- I see this as probably only working in combination with the informed consent and that the surrogate must be appointed.

No, sir, I think that in this paper, the surrogacy issue becomes rather complex. And I would like that clarified.

I always thought that the Maryland Working Group Paper made it rather complex. The health care agent, the surrogate is the health care agent is different from a surrogate, is different from a research agent.

And I think we need to get rid of all these various

categories and that one would consider that as Sax would say that there are people who can make -- who can acquaint a surrogate decision-maker who may not be able to make the rest of the decisions, the substantive decisions about what would happen during the research.

And I think that I have -- I'm not certain that that is something that I would want to -- I know that the advanced directive for somebody of fluctuating capacity, I could see that it could work.

The appointment of a proxy without some indication of what someone prefers I think is already I'm a little concerned about that.

I think I'm going to let the --

DR. CASSELL: Can I ask you a question?

PROF. BACKLAR: Yes.

DR. CASSELL: One of the funds for the advanced directives' in terms of terminal care is that they specify bunches of machines and treatments that the person doesn't want, when in fact they have limited knowledge of those machines and technology changes.

But they do know something which only they

know which is what is important to them about how they are cared for or what happens if they lose consciousness or if they are never going to be restored to reading and so forth and so on or things that are particularly humiliating.

Nobody else can know that but the subject. And that kind of advanced directive, then lays it on a physician, this is who I am and what I want. It's your job to make it happen technically.

The technology is not my problem. It's your problem. My concerns are me. And that's what I'm transmitting to you.

What in fact is your advanced directive transmitting, your research advanced directive?

PROF. BACKLAR: I see it actually as a document in which you could put in safeguards for the person when they lose capacity.

And I don't -- I wrote an article about this in which I described that in considerable detail. And I don't want to repeat the whole thing.

DR. CHILDRESS: You probably ought to circulate another copy.

PROF. BACKLAR: Right.

DR. CHILDRESS: The material has been

coming in over so many months.

PROF. BACKLAR: Right.

DR. CHILDRESS: That's it's hard to have --

PROF. BACKLAR: I do feel the big change that I've made in my concept of this is that I would tie it to the informed consent process.

And I feel that it was interesting, the paper, indeed, the Alzheimer's paper where the surrogate was involved.

It was a dual consent process with the surrogate also going through the consent process with the principle would be a very important addition.

Now, those are changes in my concept with the research advanced directive.

DR. CHILDRESS: Jonathan, do you want to respond?

PROF. BACKLAR: You will get the details.

DR. MORENO: No.

DR. CHILDRESS: Okay. Alex.

DR. CAPRON: Well, the organizational suggestion that I have is that we give separate attention as the chapter title does in the outline

that we have to this whole issue of advanced directives and surrogates appointed under advanced directives separately from a lot of the discussion that now opens chapter 5 which is really more about the competency, capacity determination in which either belongs in chapter 4 as a conclusion to that discussion or over in chapter 6.

And I thought -- I mean, I just found it very confusing. I guess I would like to press Trish the way you were pressing Alta before because this is a subject she has thought so much about to perhaps, rather than simply circulating the paper, particularly through the extent that you are thinking of change --

PROF. BACKLAR: Right.

DR. CAPRON: To try drafting --

PROF. BACKLAR: I would.

DR. CAPRON: You may have done it already.

PROF. BACKLAR: I will. I will because I'm writing -- I mean, rewriting the paper anyway for another journal.

DR. CAPRON: Well, when you're doing that, let me clarify because really the presentation here by Jonathan presents sort of a literature review, s

it is.

I mean, the American College of Physicians says this and Bonnie says that. And, you know, and one person.

I had read -- and I'm not sure I heard you correctly. I have always read Jo Ann Lynn's well known piece about why she doesn't have a living will to make the point that what is really at issue is having decisions made by a person you have selected because you trust them to make the kinds of decisions you would want not because you force them to make the kinds of decisions you would want.

And it is an argument against much specificity. And that seems to me possibly consistent with what you were saying.

That is to say, I would pick a person after a consent process in light of what I now understood to be the issues that will stake differently than if I were just picking generically.

I mean, I might say my wife generically. But if I were dealing with certain kinds of problems, I would appoint Eric as my surrogate because I would have a sense that he knows me well and could make a good decision.

But he would understand what the doctor was talking about much better than my wife would.

So I mean, that could be part of it.

But the emphasis on it being part of the consent process suggests more of that specific orientation towards the kinds of procedures and policies, the relevant risks and benefits that are involved was what you had in mind, as opposed to the appointment of a surrogate.

Being good in and of itself as rather than just relying on or a general assumption that family is a good surrogate or something.

It seems to me that the appointment in the context of end of life care to the extent that any analogy is being made suggests a conscious endorsement of people paying more attention to this particular person than they might otherwise feel inclined to pay just to your relatives because they are your relatives.

Do you see what I mean? I mean, it embodies the person's faith that they will be best treated if you will listen to this person.

And they do not want to unusually constrain that person.

And it is different than a statement that the common law or that the statute would make. This is the person that you listen to.

It is a much more particular expression of their own wish.

PROF. BACKLAR: Right.

DR. CASSELL: Is that okay?

PROF. BACKLAR: Right.

DR. CASSELL: Okay. Then, we're in agreement.

PROF. BACKLAR: But I would rather pick my husband than Eric.

(Laughter)

DR. CAPRON: Fine. Fine. But I thought that the --

DR. CASSELL: Want a transplant?

(Laughter)

DR. CAPRON: I thought that the reason you were saying that this would be in the context of the informed consent was in part having to do with the informed consent making you better aware of what issues are likely to be important issues.

But is not that what you just said.

PROF. BACKLAR: What I'm saying is that if

you are thinking of going into a research protocol.

Let's say I have schizophrenia. And I would like to be in a research protocol for altruistic reasons or for reasons of my own self.

I would know who it is that I trust to be in a sense my partner in this.

DR. CAPRON: Yes.

PROF. BACKLAR: My companion through this.

DR. CAPRON: Right.

PROF. BACKLAR: Somebody who I have known before when I lost capacity because I have experience in losing capacity was there for me.

DR. CAPRON: Yes.

PROF. BACKLAR: And so in a sense, I would maybe pick my surrogate before I made my advanced directive, before we got into the issues of consent and the research.

DR. CAPRON: Right.

PROF. BACKLAR: And would it be before or would it be in combination? I can't tell you because the situation, I don't know exactly.

But probably, one is thinking ahead of the person you trust. And then, you get involved with making out some kind of an advanced directive which

you will see I build in all kinds of safeguards for the -- during the research protocol into that advanced directive in a way that it may be easier to do it this way than having many regulations.

That people are capable of doing this instead of putting all kinds of other things into the common rule.

DR. CAPRON: Yes.

PROF. BACKLAR: And then, when you go to -- so you're thinking of this research protocol. And at the same time that you're getting -- you're going through the consent procedure, the information whether you will agree to be in the protocol or not, your surrogate is there with you.

And both of you can talk about this and so forth at the same time.

DR. CAPRON: Okay.

PROF. BACKLAR: That's what I'm saying.

DR. CAPRON: Fine.

DR. CHILDRESS: So you will get that for us.

PROF. BACKLAR: I will.

DR. CAPRON: Now, another issue --

DR. CHILDRESS: Can you just wait one

second?

I have four people listed as hoping to testify. And we have kind of allotted five minutes for each: a Mr. Boyce, a Mr. Thompson, Mr. Girard, and Dr. Shamoo.

Is that correct?

If all four are here, would you raise your hands so I can make sure --

PROF. BACKLAR: There is one behind you.

DR. CHILDRESS: Okay. Thanks. All right. Good. So we are going to cut this in about four minutes or five.

And we will pick up the very beginning this afternoon of this. I want to get your recommendations and see what we need to change.

Okay. Alex and then Alta. And then, we will stop on this.

DR. CAPRON: Okay. Another thing, Jonathan, that I think it would be worth going into more here is the objection that is often raised to advanced directives at the end of life -- or not often raised, but has been raised by Rebecca and could be thought to be a broadly principle is the notion that it improperly locates in person A the

decision about person B.

But I wanted to endorse something that Trish was saying about the potential difference here and apply it to that argument which has to do with the notion that the person who is not at the end of life and permanently vegetated or seriously impaired by their illness, on their way to death, but rather is in a position of perhaps cycling through an illness and is much more -- it is easier to see that as a person who on day one has a good idea about what the person on day two will be and will once again on day three be the person they are now.

And so it's a way of talking about that false objection and saying perhaps it doesn't have the same applicability, the argument doesn't have the same force as it does in the other area of it being sort of a misallocation of autonomy.

And then, finally, I did think that it was useful having these alternatives, special protections each considered.

And I guess we just need to press a little bit further about any particular one of them.

But the chapter 6 discussions of consent orders and re-consent and so forth, I just would

move some of the stuff that is now in 5 and put it, integrated it more with that.

DR. CHILDRESS: Alta.

PROF. CHARO: Very brief. I have no disagreement with any of the comments that have gone on about the substance of these.

I would suggest that perhaps it would be valuable to make mention of the existence of existing law and regulations, state and federal on health care processes and advanced directives and to search for ways to combine the paper work for clinical health care processes and advanced directives with research in order to make it at least even theoretically practical on the ground since patients now go into hospitals are always getting a request; do you want to make out an advanced directive? Do you want to make out health care processes, etcetera?

With that said, you know, with the agreement that we need to simplify it with the suggestion that we look for ways to build on the existing -- Self Determination Act to simplify, I would just like to say that I don't think that this is likely to wind up affecting a very large number

of people over all.

And as a matter of resource management amongst the staff time and in a number of cases we've noted, I just don't want us wind up focusing too much on this to the exclusion of the more generally applicable questions about general protection.

It is very attempting to do this because you are right. It does fall into all of our autonomy stuff. We love this stuff.

(Laughter)

PROF. CHARO: But in the end, I don't think it is really going to make a difference on the ground the way the other, the more general mandatory top-down protections will. And I would love to keep our focus there.

DR. CHILDRESS: Makes the necessary condition with certain parts of the research has some recommendations -- you're doing. Then, you've had a major impact on it in terms of reducing numbers.

So that is why we will need to come back and at least just quickly run through our recommendations.

PROF. BACKLAR: It is. What I am describing is simply for a narrow group of people.

PROF. CHARO: Right.

PROF. BACKLAR: People with fluctuating capacities, psychotic disorders.

DR. CHILDRESS: Whether you are going to require that.

PROF. BACKLAR: Right.

DR. CHILDRESS: Is it a necessary condition rather than simply allowing it as a direction.

DR. CAPRON: But certainly we need -- if we're talking about presumptions that Alta has articulated that are still a very protectionist model. Protective model is better.

And you're saying a way out of some of the more burdensome methods of protection would in for patients for whom it is possible to use this method.

DR. CHILDRESS: Right.

DR. CAPRON: Then, you haven't said in every case you must.

DR. CHILDRESS: We have to clarify is all I'm saying.

DR. CAPRON: Yes.

DR. CHILDRESS: What's been said. All right. That's all because the draft recommendations actually do make it a necessary condition.

PROF. BACKLAR: Right.

DR. CHILDRESS: I'm afraid I have to call time or we would -- if we are going to start up again this afternoon, we have to get our public hearing in before the 11:30 break. And we have 21 minutes in which to do it.

(Laughter)

DR. CHILDRESS: And so each of our persons will have as usual five minutes to present.

DR. CASSELL: Not let one point leave your monitor.

(Laughter)

DR. CHILDRESS: Okay. Mr. Boyce.

(Discussion)

DR. CHILDRESS: And again, I hate to be the clock watcher, but given the shortness of time, I will hold everyone to five minutes.

Yes.

STATEMENTS BY THE PUBLIC

MR. BOYCE: My name is Truxton Boyce. I am the Secretary-Director for the Society for the Ethical Treatment of Humans.

I was a research subject at Johns Hopkins Hospital over a period of 38 years, both in biomedical and behavioral research.

I was very pleased with the first research where I was a cretin, was treated with thyroid medication. This was back in 1949.

Before that, my physical growth and my intellectual growth was very satisfactory.

When I was transferred from the research project in the pediatric clinic, I went to the psycho-hormonal research unit where Dr. John Money, a psychologist, was to monitor my recovery psychologically from the thyroid therapy.

Then, over the years, this doctor was very abusive. At that point, my parents did not know what to do. We continued on because we were getting free treatment.

And as the years went by and my years with this doctor, in fact, I met with Dr. Childress which was very enlightening.

As a human subject, where do we turn for help?

I've been looking at newspapers and see that people are (Inaudible). I can see that the Physicians Committee for (Inaudible) Medicine. And these people all deal with animals in research and how they are injured.

The last few -- let's see. The last month, the Canadian Broadcast Corporation on prime time live has done a story on this Dr. Money at Johns Hopkins on his controversial research.

I was in there for thyroid, an I-2. Others were in there for sex change operations.

When I was injured in the study in the 1990s, I came here to the fifth floor, right below us.

I had found it through my Senator Joseph Biden.

It was a very painful experience. I had to review a lot of personal things just to find out where to get help.

Once I got here, Dr. Belize was exceptionally understanding. A nine-month investigation ensued.

Johns Hopkins was found in violation of numerous human subjects protection violations.

So what I had thought like Candy Lakner who founded Mothers Against Drunk Drivers, she had to determine, well, where to go?

So I said, well, I didn't find anything in my readings. So it was a good thought to found it myself.

So I thought I would bring it before this group and see if you had previously had any issues where human subjects say, hey, where do we turn when we need help, support, and understanding?

And that pretty much is it.

DR. CHILDRESS: Well, thank you. Thank you for testifying.

DR. CAPRON: And we offered him a short answer. The answer I think is, yes.

At our last hearing, we heard from any number of people who found themselves initially searching for somebody to whom they could turn to help understand what had happened to seek regress for what had happened.

And often, the bureaucratic response has not been very helpful.

So I think you were not alone, sir.

MR. BOYCE: Well, the one nice thing is when I gave talks before Johns Hopkins people during the grant rounds, there were like 100 doctors out there. And they were lot less user friendly to most groups.

It is really nice to be here, to have your smiles and your, you know, casual comments I've heard during this period of time.

Thank you.

DR. CHILDRESS: Any other question or comment for Mr. Boyce?

(No response.)

DR. CHILDRESS: Well, thank you very much. And thanks for submitting materials as well.

And for others who are in the audience and public, we always welcome written materials that we can circulate.

Mr. Thompson.

(Pause)

MR. THOMPSON: I appreciate the opportunity to come before you. And I am impressed that you have been here from 7:30. I did not get up until 9:00 o'clock myself.

(Laughter)

MR. THOMPSON: In 1947, the Nuremberg code banned, as I understand it, any kind of forced treatment, although we didn't call it in that language.

The western world I guess confident -- confidence returning maybe uberous in 1964 opened the door to some research on involuntary patients.

And I think what we've come to know, turning the concept of the advanced directive on its head as a device for allowing forced treatment, although we don't call it by that candid name when we're talking about decisionally impaired, is an unsavory concept.

I was here for the full day or almost the full day of the testimony that you heard in September.

And I was -- I can't say I was startled because I have been involved in these issues for about 10 years.

But I was surprised at the absence of bold recommendations by the people that did testify.

I would like to suggest that you consider returning the United States to any ban on kind of

forced experimental research.

And I also want to give just because this is a topic I talk about in lectures I infrequently give, a new idea or a slightly different way to look at this and just something for your consideration.

I think most psychiatric research has turned into something that more nearly resembles a secular religion than anything that should be called scientific.

As I listened to the feelings of the people who testified in September, they seemed to be feelings that were more akin to something you would hear in church, religious and devotional rather than objective and scientific.

My reading -- and I want to thank Emily Feinstein for mailing me a copy of the President's executive order that founded this committee.

My reading of it is that you have a mandate that could be broader than just the narrow subject of forced experimental research.

And I would like to offer you the challenge of taking on the leadership challenge of holding a hearing on the concept of forced treatment generally, the idea that we can -- the idea of

violent health, that we can both assault and help people and assault them at the same time.

That is a deeply rooted idea. I think it is possibly quite wrong.

I am with some other people. I have been trying to get a Congressman, any Congressman or Senator to hold a hearing on forced treatment, taking the testimony from people that didn't like it and didn't agree with the concept because there is a lot of people that thinks it's okay, but not for them.

There are a lot of ideas afloat in contemporary -- in the contemporary scene that suggests an ever expanding reach of forced treatment.

More of the population is subject to it. We have a plague of outpatient commitment laws.

I am sure you are all familiar with the sexual predator law that was okayed by the Supreme Court in Kansas.

And we also have the very strange idea that we need insurance parity between mental and physical illness without anybody taking account of the fact that you can be forced in psychiatric

illness and you cannot as a matter of routine with regard to medicine.

So I hope you will not just be a rubber stamp for the shallow and narrow conventional wisdom that we've got to have some kind of forced treatment, but will consider trying, putting the United States in the forefront of a ban on this.

And I will suggest lastly that this issue was not ultimately data driven.

Thanks for your time.

DR. CHILDRESS: And thank you again for providing good materials, as well as testimony.

Any questions or comments for Mr. Thompson?

(No response.)

DR. CHILDRESS: Thank you very much.

Mr. Girard.

MR. GIRARD: Thank you.

I would rather stand up. Is this mike working?

DR. CHILDRESS: Yes.

MR. GIRARD: I feel relaxed to stand up.

In 1982, an obscure congressional office published a study called -- the congressional office

was called the Congressional Clearing House on the Future.

And they published a study called "Future Agenda". The theory of the obscure chairman of the obscure clearing house was that Congress was always running around, putting out fires and that the Clearing House on the Future should take a look at the future by polling all the subcommittees in the House of Representative and asking them what would be burning issues before their subcommittee in their area of oversight 10 years in the future, just a 10-year horizon.

Now, in two places in that report, "Future Agenda", the words "offensive microwave weapons" are used.

And in one place, the words "offensive microwave weapons" is linked with the words "and mind control mechanisms".

Now, I have never seen the words "offensive microwave weapons" used in any other government report.

I have -- we have never had the discussion of offensive microwave weapons which should have occurred by 1992.

They are out there. They are in special access programs. They have been used on women's groups, like the (Inaudible) of Common Women, the Women's Encampment for Future Peace and Justice.

They sent it to an Army depot in New York. They have been used in women's groups I have been told. I have no firsthand knowledge of it.

The women's group in the pantex facility down in Amarillo, Texas I believe.

Now, I am essentially here to talk about mind control mechanisms. Because of my interest in the technology, I am contacted from time to time by people who believe they are being assaulted with microwave weapons by the government.

Someone at the last meeting suggested there ought to be 800 number for people to call who become victims of human experimentation that they don't like.

It seemed like a simple-minded idea, but sometimes, the most simple ideas are the soundest.

I am doing the government's work for it. I am doing your work for it because I am accepting and interviewing and listening for hours upon hours to people to try to separate out the cases that are

credible from the cases that are people who are ought to be victims of government research.

And paranoids, there are a few.

Now, I want to tell you why I use the words "offensive microwave weapons" in the title of my committee here because that obscure chairman of the Congressional Clearing House on the Future is now Vice President of the United States, Albert Gore, Jr.

So we know at the highest level of government, people are aware of mind control mechanisms and offensive microwave weapons.

Now, the government, I want to point out that we have an unblemished history of dealing with experimentation now dating 65 years without relief.

For mind research, I would say that if there was any gaps in that record, they may have occurred under when William Colby was the Director of Central Intelligence.

But in general, the record is in tact, 65 years of crimes against humanity which has gone unpunished and for the most part unacknowledged, unremarked upon certainly.

I want to tell you, you will be happy to

know, the government is no longer experimenting on the poor and vulnerable.

It is now experimenting on nice, middle class people like yourself: psychologists, engineers, social workers, Christians, Jews. It is an equal opportunity killer.

And the one glimmering exception which may require -- requires a lot more thought is that of the more than 100 cases that I find credible, there aren't any homosexuals in what I call the electronic concentration camp system.

There is a regular profile, single, lives alone, weak family support, highly verbal people, very intelligent people, preferably diarists, because the idea of experimenting on voluntary human subjects is to get feedback.

You can't get verbal feedback out of a monkey.

And these people have no known political connections. They have never been dissidents. They have never marched against the government, but they are all in the camp anyhow.

I would be happy to come back. The last time I spoke in public, I had overhead

transparencies.

I have government documents. It took me about 92 minutes to finish what I had to say, allowing five minutes to talk about a problem of a matter in which probably thousands of Americans have died already with this electronic.

It's called biological process control. It's so pervasive that it is no longer considered mind control.

And I have brought along for you an Air Force essay in which biological process control is characterized as science fiction, something to come.

I can only tell that you all the symptoms, all the effects that are noted as hypothetical and possible in the future have been reported to me now since -- for the past -- since 1990 is when I began to get calls from the fields for help.

DR. CHILDRESS: You're past the five minutes. Could you make a couple of concluding sentences?

And we would welcome the material. I can't imagine having 90 minutes for a session, but we welcome the material to be submitted to us.

And we will circulate it to all the

members, not only to the subcommittee who are here right now, but also the whole National Bioethics Advisory Commission.

So I would have to ask you to bring it to a close.

MR. GIRARD: Yes. Certainly, I will conclude. I don't have any confessions of Vice President Gore or anyone else who has been on the inside of these experiments.

I've only have documents which I can string together with some, you know, comments and remarks.

I just --

DR. CHILDRESS: Okay. I'm sorry.

MR. GIRARD: Wanted to tell you that aside from the 800 number, the one thing that people come to me for more than any other aside from how do I stop this, how do I mitigate the effects of the electronics is the legal counsel.

Everyone feels that there is some legal way to end this. And all the attorneys I have spoken say electromagnetic radiation leaves no legal evidence. You have no legal basis. We can file a case. It will be thrown out in discovery.

And there is -- although there are many humanitarian groups in Washington, even national lawyers feel there is no one despite the history of the subject that will take on anyone claiming that they have been victimized in a mind control experiment.

DR. CHILDRESS: Thank you very much.

MR. GIRARD: Thank you.

DR. CHILDRESS: Okay. Dr. Shamoo. And I am going to hold you to the five minutes. We will finish exactly on time.

DR. SHAMOO: Thank you for your generosity.

I will be very, very brief. I have two points to make. And one is on the degree of emphasis. And that is the issue of vulnerability.

All of you have mentioned that they are first patients and second that their illness basically affects their decision or their ability.

But the third point which you didn't mention yet, not emphasize, and that is the health care system for the mentally ill is the worse and the lowest.

It is precipitously lower than other

somatic illness. And that is important because you have three categories of how mental health services are received.

One is the private sector. The second is the public health system. And the third, the uninsured, they have no insurance.

Now, in the private sector, the majority of the private sector all across this country, only infuse another additional layer of vulnerability to this group, to their parents, to the care giver.

They are desperate. They are desperate for health care.

And, of course, they will volunteer. And that is very important that are not like all other patients, including Alzheimer's.

The insurance pays for Alzheimer's care, do not pay equally to the mental health service.

The other one I want to mention, the National Alliance for the Mentally Ill have been cited several times.

And as some of you know, I have served on the board of that organization. I have great respect for that organization for a lot of issues they advocate for.

But on this issue of research, it is important to be on the table and for the public record that the majority of budget of the National Alliance for the Mentally Ill comes from the pharmaceutical industry.

And therefore, in my view, I take their view is on the issue of research subjects with a grain of salt.

And I thank you very much.

DR. CHILDRESS: Thank you.

Any questions for Mr. Shamoo?

DR. FLYNN: I would just make a comment, speaking as a person who for 13 years has been Executive Director of the Alliance for the Mentally Ill.

I can state that it is not now true, has never been true, and I think, Dr. Shamoo, by charter will not be true that the majority, half or even as much as 20 percent of our budget comes from the pharmaceutical industry.

I would be glad to give to this group, mail to you the annual report of the organization so you can see precisely where the resources do come from.

But we do not feel in any way compromised in our abilities to speak for these subjects and have a long and an enduring interest as participants in research and equitable protection as well as continued access to research.

DR. CHILDRESS: Alta.

PROF. CHARO: Just a question. I'm not sure. A good point about access and different systems of insurance is an interesting one.

And it makes me realize that people with decisional impairments are going to group demographically in different ways. And it now has an insurance implication.

The dimensions associated with diseases of the elderly will group in people who are covered by Medicare.

Schizophrenia, however, may be disproportionately represented among people who are totally uninsured or perhaps the Medicaid.

And the eligibility for the SSDI becomes an issue now and the changing rules.

And I am realizing that to the extent we are going to be looking at research against the backdrop of access, is there any -- is there a way

to try to get gross demographics of the various kinds of illnesses we are talking about and how that affects where they fall in this insurance scheme in terms of their employment and then age and subsequent insurance status?

DR. FLYNN: I can get you some kinds of information. Yes, there is something.

DR. FLYNN: I am not sure how we would use it exactly, but it strikes me that it might turn out to be useful.

PROF. CHARO: And Medicaid is the largest subprovider.

DR. FLYNN: Okay.

DR. SHAMOO: I just want to add that the budget commissioner is going to provide all the subsidiary in the organization for it. I mean, not just direct operational budget.

Thank you.

DR. CHILDRESS: Thank you.

All right. Pat Norris has an announcement to make. And we will --

MS. NORRIS: I would just like to let commissioners, staff, and Mr. Moffitt know that box lunches are available in conference room 8 for pick

up. And then, we will return for the joint session of the subcommittees.

Also, for everyone else, I understand that the cafeteria is open in the Clinical Center which is building 10 which is right up the street from this building.

And I have been asked to let everyone know there is a soda machine on the fifth floor.

Thank you.

DR. CHILDRESS: Okay. Thank you. I thank all of you.

(Whereupon, at 11:30 a.m., the meeting was recessed.)

AFTER RECESS

(12:00 p.m.)

GENERAL BUSINESS

DR. SHAPIRO: I apologize for interrupting lunch. However, we have done better than schedule. We scheduled zero time for lunch. And we managed to take a half hour. So we have some of you to credit here.

And I really think we will able to give some time back to each of the subcommittees to either get a little more done or finish a little bit early depending on what their status of their discussions are, since I don't believe we are going to use the time until 12:30.

Let me just say some general things. The commission is now in its second year of operation. And as you know, there is a kind of rotation of commissioners, as was anticipated.

Some of us are appointed for two, some for three, some for four years and so on.

And in addition to that, everybody has had a chance to have some experience in the kind of work

the commission does, what we're doing.

You may be loving it or despairing. I don't know.

But this is a time to think of two things. One, how you feel about your own continued participation.

Is this something you enjoy and would like to continue and so on?

Or if you feel otherwise, if you would free to let me know.

And, of course, people's circumstances may have changed, making it difficult, making something that was possible before very difficult now.

This is a time to kind of reassess in your own mind just where you are and let me know what your thinking is, both with respect to your own future participation.

And, of course, since there will certainly be some turnover, if you have any suggestions, recommendations.

I have already received some from some of you regarding open spots that may occur on the commission.

So that is just something you ought to be

thinking about. And please, let me know.

I would like for you to think about it as thoughtfully and carefully as you can and maybe let me know something in the next month just what your own thinking is.

Second, we do -- of course, I would have said what I am about to say almost three weeks ago, four weeks ago. And I was sort of in a little bit of a holding pattern in that respect.

I have decided on a preferred candidate for our Executive Director position.

There are a series of issues that have to be resolved. I think all of them I hope are fairly straightforward before I can make any further announcement, but I had hoped that that would be behind us by today's meeting.

And I guess whatever the term is to say that whenever you think you are over the last hurdle, there is yet one more to go over seems to be operating here.

And so I am sorry to say that I don't have any announcement to make today, but I certainly hope to before we meet the next time.

Finally, with respect to the general

business of the commission, Jim has laid out and he may say a word about this in a few moments and as will Mike and Tom something about the future agendas of their subcommittees.

But we will have the capacity I think to expand the agenda, supplement, complement our agenda with other issues of importance.

I know that I am going to get some communication from some members of Congress and others regarding their views on this matter and not in any coherent, organized way, but just individuals.

I will certainly bring those to you at the appropriate time.

But I am hoping that there will also be ideas among the commission members themselves as these -- as we hear from Jim and Tom regarding the future agenda of their subcommittees whether there are other -- of course, there are other important issues.

There is a long list of other important issues. But whether you think there is some -- of those issues there something that we might address effectively and bring some light to.

We ought to be discussing those pretty soon because that will have some impact as we begin to roll out our staffing next year and so on and so forth.

So I mentioned that briefly last time. I'm mentioning it again today.

Please do, if you can, spare some time thinking and let me know just what your thoughts are in that respect.

That's all I have today by the way of general business for the commission, except to inform you that I must keep forgetting which meeting we had last and when I knew what.

But our budget situation at least is resolved in an effective way. And so that it is really in pretty good shape. And so I feel very good about that. Okay.

Any particular questions?

(No response.)

DR. SHAPIRO: If not, let me turn first to Tom, since you are just listed here first, on a report of the subcommittee activities and discussion.

After Tom reports, others on this

committee may want to add something. And then, there might be questions from other members.

DR. MURRAY: Before I go into any substance -- and I am going to try to be very brief. And then, we will go as long as we have questions. I don't have a lot of business that I wish to bring before the full commission today.

Is there any member of NBAC staff who cannot hear me?

I would very much appreciate it if someone will bring in my briefcase from the other room which is the brown canvas bag.

Thank you very much.

It is not staff. It's just a nice person.

(Laughter)

DR. MURRAY: Thank you.

We are still continuing our work on the tissue samples and their origin, their fate, etcetera.

We had planned. And we will be talking later today. We are going to try to stay to the ambitious deadline of issuing a report some time in January of '98.

I don't want to speak for the commission because we haven't had the conversation today about whether that is still a reasonable deadline.

We will have that conversation before we break. I am hoping that -- I am fairly confident that we can do it if we really needed to.

Are there questions about the tissue sample report?

(No response.)

DR. MURRAY: All right. Thank you.

Lisa Eiseman who was so good as to bring my bag in is actually -- is doing some work for us to find out how many tissue samples there are and in what forms, etcetera.

And it may come -- it came as a surprise to me that the number may well approach 100 million in the United States.

So that in itself will be of interest I think when we do our report.

PROF. CHARO: Does that include the --

(Laughter)

DR. MURRAY: I'm hoping to get my monopoly on that. I've been touch with Publisher's Clearinghouse about this.

Thank you, Alta.

No. It does include those. These are the ones that are actually for pathological reasons.

In terms of future research, we early on were given -- we looked at the executive order and decided that we needed to do two additional reports to fulfill the spirit of the executive order.

One would be on genetic privacy and discrimination. And one would be on gene patenting.

We have -- in every meeting we schedule for the subcommittee, we schedule time to talk about future plans.

And in every meeting that time gives way to the discussion of current work. So we have yet to have in the -- yet to have the discussion as a subcommittee about which of the two to do next or whether to in fact see something else as an even greater urgency.

But we will have -- I am determined to take the last 15 minutes at least today, of today's meeting to have that conversation.

That's really all I have to report by way of the official report of the subcommittee.

Anything, any questions?

I invite other members of our, the Genetic Subcommittee to add any details they want to add or any other member of the commission to ask any questions they might have.

DR. CAPRON: I would like to know substantively if you can suggest where you are going on, as you put, the origins and dispositions issues?

DR. MURRAY: Well, Zeke laid out a very nice -- he has been developing really over the course of our meetings a nice set of distinctions for thinking about the issue.

DR. CAPRON: Does it appear on this chart?

DR. MURRAY: It's on the chart. I think that chart incorporates all of -- yes.

DR. EMANUEL: Under tab D.

DR. CAPRON: Those were blank boxes. They are a grid on which one might make indications.

And what I really was saying was have you begun to fill in the boxes?

DR. MURRAY: I think creating the right grid is no small feat.

And, yes, we have begun to fill in the boxes.

DR. CAPRON: It was a question.

(Laughter)

DR. CAPRON: I am delighted to see your grid.

DR. MURRAY: Yes.

DR. CAPRON: It is very helpful.

(Pause)

DR. CAPRON: Let me -- just one of the things about not operating as a whole commission on these issues is that at some time between now and January, those of us who haven't been on whichever subcommittee we haven't been on are going to need to be caught up very quickly to date.

DR. MURRAY: Right.

DR. CAPRON: Something that will -- we won't have seen grow. And so I was just wondering if you could give us some sense of where you are tentatively thinking.

DR. MURRAY: Sure. And I don't want to be alone on this. I want to invite all members of the subcommittee who want to contribute to do that.

I will start us off. We do think that the distinction -- well, the retrospective/prospective labels, we have abandoned.

We are going to now talk more descriptively about tissues collected up to the effective date of whenever our recommendations -- whenever we believe our recommendations ought to be effective.

We think -- I believe we think as a group that the distinction between research collected with the primary purpose being a clinical purpose, patient care-related purpose, that is an important category versus things collected with the reasonable expectation that they would be used for research, and that the consents under which those tissues are collected under those two circumstances probably ought to be different, with the consents collected under the purpose of research being much more explicit about the likely research uses.

But let me invite Zeke or anyone else to comment further.

DR. EMANUEL: If you look at the chart, I think that there are four kinds of distinctions there which are substantively relevant.

And we've only gotten through -- well, we've gotten through three of them. One is this, what was labeled there erroneously prospective and

retrospective.

And Tom has just clarified to mean collected in the past and collected after the report or some effective date.

Then, the clinical research distinction, then what is listed there is anonymizable versus identifiable.

And as correctly pointed out, it really should be anonymous, not samples, but research, anonymous research, research that is done on an anonymous sample and research that is done on an identifiable sample.

And then, along the left -- those three, I think -- I believe those three, we have --

DR. CAPRON: By identifiable, you mean the identity part of the research.

DR. EMANUEL: Yes.

DR. CAPRON: Okay.

DR. EMANUEL: And anonymous means that it may have -- the sample may have been kept. It may still exist in an identifiable, but the research is being conducted on it in an anonymous way, although you may have clinical data linked to the sample.

There is a useful diagram in the next

room. But --

DR. CAPRON: No, I understand.

DR. EMANUEL: Okay. And then, the distinctions along the side which have been a source of some discussion that, you know, at the last meeting or two meetings ago, I can't remember either, of whether an individual with no community implication -- having some community implication, but no stigma.

And then, having some community implication and some potential for stigma, we actually haven't gotten to discussing it at this point.

There was some suggestion led off by Jim at some previous meeting about collapsing the two groups. We just haven't gotten there yet.

Within those categories, within each one of those boxes, one, there are probably four questions we are going to have to address:

whether IRB approval is needed for the research;

whether the IRB can simply decide whether the research fits into the box;

whether -- what level of individual

consent there should be.

Should it be presumed consent with an opt-out which we heard from -- that is being used in some countries?

Whether it should be a general consent, whether it should be an explicit consent.

And then, also for the community, the fourth level is for the community, whether that should be some general -- presumed consent or some explicit consent required for that kind of research.

And then, one of the things we tried to do was to come up with a variety of examples, both genetic and non-genetic.

And you have some of them in the notebook further on, but there are others to try to illustrate for ourselves the kind of research that falls into one of these categories, whether it would be possible or not possible. How were the samples? How did they exist? How might that exist, etcetera?

DR. CAPRON: Could I ask a question?

DR. EMANUEL: Sure.

DR. CAPRON: The distinction which Tom addressed which you didn't spend time on just now is the clinical care versus research setting

distinction.

And I guess the reason for the distinction is the use suggestion about greater need for consent or whatever it is, the projection or something with research studies or be more explicit had to do with the notion that a person in that situation -- excuse me -- the researcher in that situation really has an opportunity to focus on that at the time the sample is collected.

Whereas, if it arises out of clinical care, it would much, much likely that that person would have in mind what those uses could be.

And it would be less realistic I suppose to expect that they would have made it explicit what's involved.

I wonder is that a correct reading?

DR. EMANUEL: No.

DR. CAPRON: Okay. What was the reasons for what Tom was suggesting?

DR. EMANUEL: There are a variety. I think we've considered in the last hour or so a variety of reasons.

Part of what you were getting to is that if you collect the sample for research, there may be

some research endeavors you are planning to do, but there are also going to be a lot for which you have stored the sample which you cannot anticipate now.

So one of the examples we have used is a physician health study where they knew they were going to do some tests, but, you know, there has been a lot of tests that they have done that they could not have anticipated when they originally collected them.

DR. CAPRON: Right.

DR. EMANUEL: Although a lot of the research is, you might say, in the spirit of what they did collect it for.

But at least in the research setting, the person participating knows it's research with no anticipation of individual benefit.

There is an opportunity for a more explicit consent process and an exchange with either an investigator or a proxy.

And I'm not blinking on some of the other distinctions that we got.

Whereas, in the clinical consent -- oh, and also, you are tracking these people. So that if you wanted to inform them in some manner, at least

they are more readily available to you.

In the clinical --

DR. CAPRON: Is that across the board in research or only in certain kinds of research?

DR. EMANUEL: No. Where you might want to go back, it's potential.

For example, in the physician's health study, it is. They are contacting them every two years.

Some of the studies that have --

DR. CAPRON: Go ahead and make your point.

DR. EMANUEL: Some of the studies have raised a problem. They are tracking them over time.

In the clinical case, initially, there is a benefit to having taken the sample already to the person. The sample was taken with the intention.

DR. CAPRON: Right.

DR. EMANUEL: Well, or if they are -- or whatever.

Second, as best as we can tell, the vast majority of them never make it to the research setting to be used for research at all.

And the attention whey they are collected is not to necessarily use them for research.

And then, also the possibility of consent, we've heard as well as from other experience, know that around the time of surgery or around the time of biopsy is not going to be an effective time to get valid, informed consent for the future.

And so the kinds of other kinds of consent you might want would not have the opportunity for an interchange with the investigator.

And so you would probably need a different kind of consent if we think that is a valuable thing to be able to use those samples for research.

DR. CAPRON: I guess I've been much more concerned up until now with what you were calling retrospective.

How do we treat the samples we already have before we work out a good set of requirements to follow in the future?

DR. EMANUEL: Yes.

DR. CAPRON: And I guess I'm now confused. I thought Tom was saying that you were going to require a higher level of consent for the research.

DR. EMANUEL: Yes.

DR. MURRAY: Yes.

DR. CAPRON: In the future.

DR. MURRAY: For samples in the collected in the future.

DR. CAPRON: None of this applies to samples in the past?

I mean, none of that differentiation applies to samples in the past?

DR. EMANUEL: No. If you look at the chart, it does apply in the past. Under retrospective, no longer labeled retrospective, but under what --

DR. CAPRON: You separate them.

DR. EMANUEL: Yes.

DR. CAPRON: Why would you not require a higher level of standards of work for the clinical care because the people in that situation would have had less sense that whatever researchers do which is for the benefit of science is going to be done to them out of participating?

Why wouldn't the sense be that their consent such as it was -- it was out of therapeutic, get this diseased organ out of me. Or diagnostic, find out if something about these I am giving this up.

And then, I am not even by implication

saying that I have any desire to advance to science.

Now, obviously, you wouldn't have any question if the research that you are talking about was one in which a person had consented to the genetic analysis of their tissue.

I mean, that's -- and that's what we are now coming to, the genetic analysis of their tissue.

If they didn't consent to that, but they consented to other research studies, it would seem to me that you would have a better argument that that is a -- at least as to some kind of future genetic or present-day genetic studies an indication that they would not be bothered by your making this use.

And it is less of a violation of their expectations when their tissue is taken that it is now going to be used by a somewhat different scientist for another scientific purpose.

I mean, it may not be enough, but it certainly would be less of a surprise for me to learn, for example, if I were in that situation than if I had gone in for a diagnostic study.

And it turned out, my samples are stored by them, the institution because it is also a

research institution. And now, they are being used for a study when I had no thought that that was being contemplated.

DR. MURRAY: One reason we have undertaken the series of -- is to get a deeper understanding of what people understood and believed about why their tissue was taken and what uses will be made of it and a similar set of tissues.

And that is how we began today. Actually, it was a report on that from the group that is conducting the main hearings.

My comments previously about higher standards were looking at samples that will be collected in the future per our recommendations.

And my comments about, quote, higher standards, does not have a more expressed --

DR. EMANUEL: Right. I think we need to be -- researchers need to be fully open and candid if they have an expectation that a sample to be collected will be used for research.

And that is what we are going, you know, to want to make the standard here on it.

DR. MURRAY: Understandably, that did not happen in the past universally.

DR. CAPRON: Right.

DR. MURRAY: Typically, the samples were collected with a very kind of minimalist. We may use this for research education. It is something. Do you agree? And yes or no?

I understand that. And I think in that context, your comments are well --

DR. EMANUEL: Well, if you accept that, Alex, just think about what you might -- think about the kinds of consent you might go about trying to obtain in the past.

If we are now going to say from here on end, if you collected the samples in the past, you can't use them unless you get consent.

You have to go back and contact everyone again which is going to be a very difficult or impossible feat, first of all.

Second of all, many of those people are just going to be dead.

I mean, in the Mayo Clinic, 75 years of X disease, it's going to be an impossible kind of study to do anymore if we have your kind of --

And it seems to me that there is, you know, some sense here of public good about -- that

we heard from David and I think makes some sense, you know.

This is a sample which can be a benefit with no harm to you. Right.

We are not harming you. We are not making -- if we are making it obviously, it's identifiable, we have to go back and get consent for it.

But if it's an anonymous, we are going to use it in an anonymous manner. It's not going to harm you.

Now, we may add onto it, recognizing something that isn't there in the common rule that there could be some harm to a community.

And in that case, we are talking -- we are going to talk about possible, you know, levels of consent that you might want.

But it seems to me if you think through, we've now got this bank. We've heard from, you know -- the armed services has 2.5 million samples. We have this bank.

If we adopt your -- the things you're thinking about, that is the end of that, any research that can be done on those 2.5 million samples.

DR. CAPRON: Well, no.

DR. EMANUEL: Baring --

DR. CAPRON: Just as you might expect some gradation of the requirements, you could also say that you have a gradation depending upon the uniqueness of the resource.

If there are 100 million samples around, maybe a great many of the studies that need to be done could be done on samples that were collected for research purposes.

I have no idea how many of the 2.5 million Army ones were collected for that reason.

Do you know?

DR. EMANUEL: Well, have some sense.

DR. EISEMAN: The 2.5 million are all samples of --

DR. EMANUEL: Of clinical care. The vast majority of samples in this country are going to be clinical care.

DR. CAPRON: I understand. But I mean, again, it may be a case-by-case determination. Are you dealing with a resource where the only possible resource is a pathology, clinical care?

Or are you dealing with one where there

are other, maybe slightly more expensive, maybe more difficult to find samples in which people at least knew that they were in research?

And then, there are harms. And then, there are wrongs.

And I think I gave the analogy early on that, you know, if someone comes into your house and looks around your house and looks at all your stuff and doesn't take any of it, and you come in and you don't even know they have been there at that moment, you may still have been wronged.

And if you were told that someone had done that, you would feel wronged, even though you haven't been harmed.

They don't tell anyone else. Or anything they find there they publish anonymously as it were.

There is a sense of a violation.

Now, I think it is easier to say that after a person who is deceased, that violation was attenuated because then it is sort of the sense a violation of one's relatives having been used in research without knowing it rather than oneself.

And the individual probably no longer has an interest that we --

MR. HOLTZMAN: Alex, just for clarification though, the argument you are making would equally apply as we look at future collections.

You are saying that the conditions of consent from use in research of the clinically collected sample probably should be more stringent than in the research context.

DR. CAPRON: What I'm saying is in the future given the obvious gold mine that these kinds of things are, I would require a lot more foresight on the part of people who are collecting the sample to say if it is likely that my colleague from genetics down the hall is going to come, knocking on my door a few years from now and say you've removed 1,000 pancreases or something.

I would like to go on a study of X, Y, Z genetic thing. You know that now. You can put that in your, quote, clinical consent form.

And we could develop -- although we have got some criticism of the form that was being put out by the National Center.

Do we all get that for this guy who does readability? Or did I just get it?

DR. SHAPIRO: I got it.

DR. CAPRON: Yes. I think it came directly.

But in any case, I mean, there are concerns. How well can this be done?

But it certainly be part of the process.

And then, we can say, now it becomes the clear presumption that it is only people who have been informed that this is in prospect.

DR. MURRAY: But that's not where we're headed, Alex. And all I can tell you is I don't agree with that analysis of it.

DR. SHAPIRO: I don't either.

DR. MURRAY: I think it's quite impossible to anticipate.

DR. CASSELL: When you say somebody has walked into your home, then you are implying an identification of you in the home.

If I would change it and say the analogy is somebody came in blindfolded and was introduced to your silverware drawer which they looked in and then went out blindfolded, then in fact, have you really been harmed?

DR. CAPRON: No, you've been wronged.

DR. CASSELL: I've been wronged. What's the wrong?

DR. DUMAS: They had no business coming in the first place.

DR. CASSELL: That's in the first place.

DR. DUMAS: Right.

DR. CASSELL: But the tissue is removed.

DR. CAPRON: There is still more tissue.

DR. EMANUEL: No, wait a second, Alex. One of the things that we --

(Discussion)

DR. FLYNN: The only thing I have. Even though I'm sure, Alex, you will say that the many hearings on this are not necessarily representative of the population as a whole.

But there has been a strong expression, regardless of age or education or other variables, that if it already exists, by all means, move it, don't waste it.

DR. EMANUEL: And also, it's not me. We've heard -- I mean, we haven't heard from anyone. And it is not unanimous, but it is clear consensus that that tissue isn't me.

There isn't the sense I own, you know. It

is part of me.

We are not locked in that sense, you know, that my body -- whether it is removed or apart from me, it's still me. That is actually is not peoples presumption interestingly from these mini hearings.

Now, again, that may not be your view.

DR. CAPRON: Well, I haven't -- I mean, all I've had on the many hearings I think are some questions that Bernie raised about --

DR. EMANUEL: No, no, no.

DR. GREIDER: There was a summary.

DR. EMANUEL: A summary.

DR. GREIDER: Summaries this time. And there was one in the last time.

DR. SHAPIRO: Okay. Let's continue the discussion, but let's do it raising your and so we can get to see -- Eric.

DR. CASSELL: Yes. And then, the question then comes about this, all of those samples can be made anonymous to a researcher, can't they?

DR. EMANUEL: It depends on what the researcher wants, what the research is.

DR. CASSELL: But I mean, they could be made anonymous. If they are not, maybe this

research can't go forward.

But if they are, other research can go forward.

DR. EMANUEL: Yes. Let me -- yes. I want to - unfortunately, there is no blackboard here.

But in principle, you are right. What we are now trying to -- I think where we are. I don't want to speak for the subcommittee.

But I think where we are at is to recognize two categories of research where you now have an anonymous sample.

It may have come from an identifiable slide and an identifiable --

DR. CAPRON: Yes.

DR. EMANUEL: But it has been made anonymous.

And you have an identifiable sample that you need to have identifiable for the kind of research you are doing, maybe a family pedigree type study. And you are going to publish seven families and their pedigrees.

You are right. So in the case we are referring to, you still might have the slide. You might have the medical -- information from the

medical record.

But to the researcher, it's patient 100. And he or she cannot walk backwards.

DR. CASSELL: Alex, is that still harm in your terms?

DR. CAPRON: Wrong. It's still wrong.

DR. CASSELL: Is that still wrong in your terms?

DR. CAPRON: Let me make clear. It seems to me that a determination that something is a wrong does not mean it is prohibited.

DR. CASSELL: I didn't say that. I think that.

DR. CAPRON: I don't think everyone thinks that. I would be surprised. I want to look at what the Center for Health Policy Studies is finding out here and how they are posing the question.

People collapse those two things. Then, they are making the judgment that on the balance, more good will come from this use and better to use it than to waste it.

And that is a different judgment than a wrong has been done.

And maybe, a wrong is justified by other

good that can come from it.

DR. CASSELL: But it's still a wrong to you though. This anonymous tissue down the line and so forth, is that a wrong?

DR. CAPRON: I think any study about a person -- and this is -- you are saying it isn't just -- at this point, it is no longer just a tissue that is being studied.

It is the fetatypical manifestation of this. In other words, you are not counting how frequently this mutation occurs in the population.

You are saying this mutation is associated with X, Y, Z problem that family X had.

For one thing, family X, depending on how rare it is, may see themselves in that result.

(Discussion)

DR. CAPRON: Other people may see them in that result.

DR. EMANUEL: Alex, let's clarify something here. First of all, I think it is very important why we have the Genetic Subcommittee, it has become quite clear that this cannot be restricted to genetics in any way.

And if you will actually look at the

papers that were submitted, part unconsciously and part just because I didn't know the genetics -- those papers are not genetics by and large.

And it is very relevant for all of us to keep in mind that we should not restrict it to the genetics because the rules should apply across the board.

Second of all, if the family could recognize themselves in the published report, that by definition -- that by our definition I believe -- again I don't want to speak for the -- makes it identifiable.

If you can walk backwards, it is identifiable. And you do need very explicit consent. There is just no question about that.

DR. CAPRON: The history of writing on this subject of research is replete with examples of people who thought they were publishing anonymous information.

And it turned out, other people seeing that information were able to figure out --

DR. EMANUEL: I think we -- since we are intent on it, I think there are some ways.

The subcommittee has been thinking about

it to try to make at least bring to bear another perspective on that question before a researcher is allowed to go out and just use it.

In fact, is it anonymous or identifiable is a question that someone besides the researcher will have to ask.

But I think the other question here and I think it's worth the full commission, the philosophers do make this idea of the fact that people can be harmed without their knowing about their being harmed.

(Discussion)

DR. EMANUEL: Right. They are being wronged without their knowing that they are being wronged.

That is well accepted I would say in the philosophy world.

It's actual manifestation for the rest of us while we live I think and how much we ought to take account of it is --

DR. CAPRON: I agree.

DR. EMANUEL: Is a real question.

DR. CAPRON: Because that is where you get into the balance.

(Discussion)

DR. CAPRON: It is the wrong. It is the theoretical that people really don't seem to worry about when you ask them.

And they say scientific knowledge is more important than that wrong. I can understand that, but at least --

DR. MURRAY: It is not clearly even regarded as a wrong.

DR. CASSELL: I always thought it was a wrong.

(Laughter)

DR. MURRAY: In fact, we had suggested --

DR. CASSELL: I don't regard it as a wrong.

(Laughter)

DR. MURRAY: I think I understand part of the -- Alex is correct to point out that particularly some of the practices that local research group created in order to -- from their point of view sort of protected the confidentiality. They say it's published pedigrees.

Well, one of the things we learned early on in the LC work, the junior project, is while

there are L groups agree that this was an issue and L group thought they had the perfect solution, and nobody had the same solution.

And probably, some of them didn't work very well. And some of them involved fabricating elements of pedigrees. And that threw the medical letters in a tizzy.

But what we will I think have to do is provide something more like a sensible scheme that -- or at least some guidelines for a scheme that would be more universally adopted.

And I think it does -- Zeke drew a picture with a kind of barrier between the researcher/user of the information and anybody who would have the identifiable tissues for the medical records.

And the precise sort of character of that barrier and what both substantive procedural protections they would provide to make sure that no one could walk back, I think would be very important. And we are moving to address that.

DR. MURRAY: Okay. Other issues?

DR. CAPRON: May I put aside the particular points that I've raised and just say to me this does reveal the possibility that well-

informed people who have spent a lot of time looking at this will come to different conclusions than those of us who come to it in a naive and ignorant fashion,

DR. MURRAY: Yes.

DR. CAPRON: Therefore, it poses the risk that unless there is a good deal of time to look at drafts of reports and have full table discussions, we could have unnecessary misunderstandings and conflict.

DR. MURRAY: The commission had one report. And that one, we did as a full commission.

DR. CAPRON: Right.

DR. MURRAY: So I think it will go both ways with the Human Subjects Subcommittee having its conversations about its topics.

DR. CAPRON: Both of those predecessor commissions sat always as a whole.

DR. MURRAY: Yes.

DR. CAPRON: And we have chosen a different method. And I just flag that we may be running into some risks.

DR. MURRAY: I mean, part of it is also going to be the forbearance of the other members of

the subcommittee that wasn't actively involved in drafting it to say, well, you know, I'll ask these questions. These are sensible people. And I'll trust their analysis now.

We will have to just work that out. And it is going to work both ways.

DR. EMANUEL: Actually, I second that in my sort of fear and trembling of what the human subjects is going --

(Laughter)

DR. EMANUEL: The potential that, you now --

(Laughter)

DR. EMANUEL: Especially under that chairmanship of Childress.

(Laughter)

DR. EMANUEL: But I mean, it may be useful for us to think about the next meeting. I think we may have more substance in which to be able to present, actually have some tentative ideas to what we're going to propose.

And it may be that we want to allocate a couple of hours to have, you know, 15 minutes of presentations.

This is kind of the rules our policy proposal. And have it shot at by people here because -- and vice versa, of course.

DR. MURRAY: Well, we don't intend to keep the groups in isolation from each other.

And if any want to offer anymore time available, then we will schedule.

DR. CASSELL: I want to bring up something. Alex and I yesterday were privy to a presentation about science -- biotechnology in 2010 which is not very long from now.

And one of the startling things was a presentation of what they call the 90 systems data collection.

The 90 systems data collection, the sampling and analytical device are all one. And they are as big as a computer chip.

And they produce data in amounts that just pass the imagination and about anything.

(Laughter)

DR. CASSELL: So that I mean, they will do away with the clinical laboratories and things like that because everything will be done on site.

But they produced data of amazing

quantities. But they raise issues that are relative to what you are talking about that are terribly important and about privacy and confidentiality. And it's -- that are related to this.

And so I think this has to be done with an eye to what is going to be in expediential terms a presumption of information from specimens where their capacity for wrong and harm is large.

DR. SHAPIRO: The score of the example with respect to being wrong remind me of the quip that the Allen people said.

They woke up one day in this apartment and found that all his furniture had been stolen while he was asleep and had been replaced by other furniture exactly the same.

(Laughter)

DR. SHAPIRO: I don't know if he's wrong.

(Laughter)

DR. SHAPIRO: Okay.

DR. MURRAY: I have one parting word.

DR. SHAPIRO: Yes.

DR. MURRAY: I have -- some of you may be aware that there is momentous social event taking place.

DR. CAPRON: Called the World Series.

DR. MURRAY: Called the World Series. And I -

(Laughter)

(Pause)

DR. MORENO: It is dangerous to do that in this metropolitan area.

DR. SHAPIRO: Okay. Let me turn again to give a report and to see what issues might be on people's minds with respect to the subject of protection.

DR. CHILDRESS: Well, there is a veil of ignorance slightly here.

(Laughter)

DR. CHILDRESS: They were concentrating on two major areas, first a draft report and draft recommendations regarding research involving decisionally impaired subjects.

And we have been grateful to Jonathan Moreno and Rebecca Dresser for the contract paper.

And Jonathan has developed a fine draft that everyone may see.

We spent this morning working over that. And we have a lot of suggestions for revision.

Furthermore, we will not reach any final formulation until we've done some other things.

We will participate in a National Institute mental health conference on the 2nd and 3rd of December.

We want to get more input from our researchers and responses to particular proposals.

To those on the other subcommittee and again back to the whole who are interested in seeing what we are doing, I would probably recommend concentrating on the next draft when we get a chance to do that because we did mention the revisions in the - proposed revisions in the structure and so forth, although you can get some ideas from what we discussed, that is the draft that we discussed this morning.

What are we shooting for? Early next year. And beyond that, I will have to wait until our discussion later today to see what really seems feasible getting into things that we need to do with this particular report.

The second area we are focusing on is our mandating task of looking at federal agency protection of human subjects.

And we are grateful here to Bill Freeman, Susan Katz, Joe Mangel, and Emily Feinstein for the work they have done in developing the draft.

And we hope to make that report this year. But whether we do or not will depend on how our discussion goes this afternoon.

And again, everyone received the draft of that report.

Now, in addition to these two areas, we have contract papers underway. And two should be available in the next three to four weeks on the placement of OPRR.

So John Fletcher is writing one. And Charles McCarthy is writing one.

A third paper is under discussion that was concerned about simply the placement of OPRR, but possibly expanding the role of OPRR to deal with private as well as federally-funded research.

DR. GREIDER: A point of order. These are really not about placement of OPRR really. That's just shortened it for placement of a office --

DR. CHILDRESS: Right.

DR. GREIDER: That is going to be used --

DR. CHILDRESS: Right. Right. Thank you.

And then, we have discussed and we hope to resolve later to day whether and what sort of thing we can do with international research ethics.

And we are going to spend some time on that and how to go about it.

Obviously, we've gotten back numbers and received a lot of material circulating on this particular topic.

Here, I will remind us all that the task of bringing back is not -- we are considering another in that area.

We will have a community paper that I think the contract is maybe close to be being developed and maybe another one that may be developed on the justice. So we will be looking at those areas as part of our reflection as well.

That is a quick sketch.

Let me turn to the subcommittee members and see what they might want to add.

VOICE: Or subtract.

DR. SHAPIRO: Any comments from the subcommittee members or questions from other members of the commission?

DR. CAPRON: I would add only that the

draft that Jonathan prepared was widely praised in our discussion for getting us off to a very good start.

And at the same time, everyone had a lot of suggestions about major changes and how to proceed as well as detailed ideas about things that should be done to it.

So that those who are reading it without the benefit of that should know that I'm sure Jonathan will welcome comments from them as well, but also if there are things there that don't seem quite right, they may have been identified by our discussion already.

DR. CHILDRESS: And that is one reason I mentioned, I think the next draft will be if the subcommittee -- other subcommittee members who don't have a lot of time recommend that we wait until the next one and then dig into that.

So I think we -- this is really the first time, even though we have spent a portion of each of our subcommittee meetings on this particular topic, and during the major public hearing the last time, this is the first time the subcommittee members really began to try to determine where we want to go

with this.

And as Alex mentioned, Jonathan's paper incorporated -- and Rebecca Dresser's paper really provided an excellent start in that direction.

DR. SHAPIRO: Thank you, Jim.

Any other comments?

Yes, Steve.

MR. HOLTZMAN: I have a question. somewhere in the middle of -- we passed a resolution pertaining to resolve this resolution about any research, human subject research in the U.S. should be subject to the common rule.

I don't think anyone in the world heard us make that recommendation. I was wondering how that is going to fold back into what you're doing in making that.

DR. SHAPIRO: Alta.

PROF. CHARO: I'm hoping when we get to the point of discussing the overall regulation of research in the United States and the best place within the federal government to provide leadership that we can revisit that question.

MR. HOLTZMAN: Okay.

PROF. CHARO: To see how one can

operationalize that idea and what implications that has for existing offices being reshuffled, changed, added to, subtracted, etcetera.

DR. SHAPIRO: Steve, I would say the comment, your comment that no one in the world knows is only approximately true.

(Laughter)

DR. SHAPIRO: Because I have been speaking to various congressional staffs and members of Congress on both the issues. I have told them about it.

And we ourselves don't have much more to say right now. But -- so I think we will be back to that issue. And it is on some people's minds.

MR. HOLTZMAN: What is the status of the Glenn bill?

PROF. CHARO: Going nowhere fast. The staffer in charge of shepherding the bill for Glenn has left and moved to some obscure place in the middle of the country.

So I'm not sure --

MR. HOLTZMAN: Can we continent something as sure as that or --

(Laughter)

MR. HOLTZMAN: I won't tell any of --

PROF. CHARO: What I used to call fly-over country. And --

(Laughter)

PROF. CHARO: And anyway, I don't know who picks up the leadership on that bill, if anybody.

DR. EMANUEL: Two points I think relevant here. One is it might be helpful for the commission because it sounds as if both subcommittees are working in directions of modifications of a common rule.

You with respect to mentally impaired subjects, us with respect to at least some portions that deal with stored tissue, what exactly the process is for modifying the regulation and just for us to understand what we might need to do since I think our recommendations, you know, may change depending on how difficult it is or easy it is for this way or that way.

The second thing is at least from what I hear, you guys may be suggesting some changes in the overall federal regulation of research more broadly.

I for one would feel that we need -- the other subcommittee needs to be included somewhat

since of our recommendations obviously are going to assume a certain structure of that regulation and so before we go too far and it feels like our recommendations are out, barely hot off the press before the commission has said, no, we are changing everything again.

So I think at least on that level, there needs to be some clear coordination that we don't make a proposal that assumes a certain structure that you are actively contemplating revising or suggesting be revised.

DR. SHAPIRO: That is a good point.

And in fact, the issue of the common rule, I am sure, will come up again this afternoon when we deal with the federal agency implementation.

That is a very good point. Perhaps, we can focus somewhat on that.

Alta.

PROF. CHARO: And, Zeke, if it is any comfort to you, even in the context of discussing the right approach, the right balance of protection and protection against abuse and access to research and promotion of research in the context of decisionally-impaired people, the issue of the

regulation research generally and how likely that it will stay the same is dogging us as well.

So if it is any comfort, you are not alone.

(Laughter)

PROF. CHARO: On both subcommittees. So all of this stuff is going to be done against the backdrop of some uncertainty.

DR. SHAPIRO: Any other questions regarding --

(No response.)

DR. SHAPIRO: Okay. Thank you.

Is there anything we need to discuss today with regard to future meetings?

DR. QUINLAN: I just distributed at the table of dates for meetings going all the way through July 7th.

Some of them -- most of them were already agreed upon. The dates are pretty much fixed. The locations have not been fixed.

PROF. CHARO: And February 23rd, a couple of dates, that is definitely --

DR. QUINLAN: Well, the idea was that --

PROF. CHARO: Right.

DR. QUINLAN: Miami would --

PROF. CHARO: Right.

DR. QUINLAN: The majority of the members of the commission had expressed that they would indeed like that.

PROF. CHARO: Sure.

DR. QUINLAN: Especially because of this, by a conference that many would really like.

PROF. CHARO: Sure. What is the conference on?

DR. CAPRON: It's genetics, about technologies and international symposiums, international symposium of genetic --

DR. SHAPIRO: Is it the so-called Miami symposium?

DR. CAPRON: Miami symposium.

DR. SHAPIRO: Yes.

DR. QUINLAN: Unless there is some real objection, we would like to plan ahead. And we now have a support contract. And therefore, we really have to plan ahead considerably.

And so if anybody has any problem with the locations or the dates, you know, please speak up now instead of two or three months from now.

It becomes more and more difficult and expensive.

PROF. BACKLAR: I think everybody agrees that -- will be great.

(Laughter)

DR. DUMAS: You have noted the Miami already.

DR. QUINLAN: Well, I would like to have just some general agreement that this is indeed doable.

The cities where -- the idea is that we ought to circulate around the country. And these are some of the places that have come up.

If there is some, you know -- some rearranging, I would prefer it be done now, at least if someone really objects to any of the locations or would really like to insist on some other location so that we can plan.

PROF. CAPRON: As one of the people who was very encouraging of our meeting other places, my thought was that it was advantageous for us to alternate.

We seem to have gone through a year and a half period meeting only in Washington.

And now, we seem to be facing a year in which depending upon where Nunn is -- is that, no?

DR. QUINLAN: Actually --

(Laughter)

PROF. CAPRON: We would -- entirely outside.

DR. QUINLAN: This only goes to the right.

PROF. CAPRON: All right.

DR. QUINLAN: It is not going to the rest of the year.

PROF. CAPRON: But even within that, I gather from the staff point of view -- and I don't want to be conservative of the staff researchers -- a lot more burden and expense, meeting elsewhere.

DR. QUINLAN: Actually, that is not a big problem. I think that the expenses, the average expenses now versus elsewhere with the contract support, the difference is not that large.

PROF. CAPRON: Okay. I found when I was doing out-of-town meetings that the expense of getting everything there and having the staff go there and so forth, just I would wonder if we wouldn't want to get on more of a --

VOICE: Home-away.

PROF. CAPRON: Home-away, home-away sort of thing or home-home-away, wherever the cities are rather than contemplating a whole month.

DR. QUINLAN: Well, how does everybody else feel?

DR. SHAPIRO: The main thing we have now is these dates are held. We can think about that, Alex.

And you don't have to decide exactly now whether this sequence -- we all work with the staff on that.

DR. QUINLAN: Okay.

DR. SHAPIRO: But the dates are critical.

PROF. CAPRON: Okay. And the only other comment I have is it would seem to me that the notion of going to Tuskegee ought to be timed with the release of a report on the subject of human subject protection.

And we should have in mind that if our federal report is going to be done before then and it doesn't make sense to hold it until then, we ought not go to Tuskegee without the ability to give a final eye, a yea to a report which would then be in effect and released by you, Harold, at a press

conference there.

I mean, the purpose of going there is to highlight the effect that the Tuskegee study has had on this.

And so I would -- if that is not going to be by March, for example, the incapacity of subjects topics is not going to be done by March, but it would done by May, then I would go to Tuskegee in May, although being there in March is probably climatically more comfortable.

I don't know what the hurricane season is or the tornado or whatever it is.

But in any case, I think we ought to think strategically about these rather than randomly.

DR. SHAPIRO: That's a good point.

PROF. CAPRON: On that thing, the question, is the January 7th meeting intended to release the two reports, the -- or not?

I don't know. I can't speak for Jim. I doubt that we will be releasing the two reports as things are going.

DR. MURRAY: It is possible that we might have the federal agency. But we won't even know that until our discussion this afternoon to see

where we are.

But that would be the only way we would not have the other report.

DR. SHAPIRO: I think actually in March may work well. But that is a very good point that Alex makes. It may work well for release of one of the reports.

We will have to look at it.

And the stored tissue?

DR. MURRAY: I hope the stored tissue report will be ready by about then.

DR. FLYNN: By when?

DR. MURRAY: By January.

The meeting in Miami, one of the ideas of the stored tissue meeting, that would be the time to release the report if it is ready by then, if it is not ready in January.

DR. BRITO: Yes. It would be ready for your meeting there.

DR. MURRAY: Right. That may affect our deliberations where we are pressed for that deadline.

DR. CHARO: Speaking for the people in the

-- country, I just remind you that Madison was the first city offered up for an out-of-town meeting. It has not made it onto your calendar yet.

(Discussion)

DR. SHAPIRO: What else could you ask for?

(Laughter)

DR. SHAPIRO: Again, those are very helpful suggestions and ideas. Just make sure you keep these dates. That is what is going to be focused on right now. Okay.

Any other business before we expand again into subcommittees?

DR. CAPRON: Are we going to discuss the draft outline for our annual report or just --

DR. SHAPIRO: I would be glad to. We have only got that brief outline which we sent around. It's not --

DR. CAPRON: So it's just --

DR. SHAPIRO: Yes. And we are going to be working. In fact, we are already working on parts of it which we will be distributing to everybody. Okay.

This part of our meeting is adjourned. If it possible to take a five-minute break, we will

take a five-minute break.

(Whereupon, at 12:55 p.m., the meeting was recessed.)

AFTER RECESS

(1:00 p.m.)

CHAIRMAN CHILDRESS: I think we had a very very good discussion this morning of the draft report.

What I want to do is just to see, make sure we are clear on exactly what else we need to do and then also see if there are any quick reactions to the recommendations, areas which we didn't focus on specifically though.

Obviously, we did touch on them indirectly, at least some of the indirectly.

One thing we need to decide is when we want to do the next meeting. And I was asking Harold what he had planned for the 1st of December, a full commission meeting.

And I guess one question that is still for consideration there is whether there will be enough

for the whole commission to deal with as a commission versus the subcommittee.

And we have two days. And I guess even if there is enough for the commission as a whole, there would still be the possibility of a subcommittee meeting that day.

So one question we need to think about is when to do our next meeting, whether the 23rd or the 1st.

Now, there are some advantages with each one. I can do either of them. It does not matter to me.

Jonathan, you are --

DR. MORENO: I am totally at your disposal.

CHAIRMAN CHILDRESS: Okay. Thank you. Thank you.

So it is a matter really of what would be best for the subcommittee in terms of the travel, in terms of being here for other reasons, such as wanting to be at the NIMH conference.

Obviously, for the 1st, one of the advantages in the NIMH conference. The disadvantage would be traveling on the Sunday after Thanksgiving.

Then, you have the disadvantage of the previous -- or the advantage of the previous week is that it is Sunday. And that the disadvantage is --

(Discussion)

CHAIRMAN CHILDRESS: Well, I know particularly with the small kids, it's not -- you would need to be there.

It is really up to the subcommittee as to which Sunday we would like to ruin before --

DR. CAPRON: That would make sense to me, before December 1st because we would get a lot more copies to them. We could present it to the other subcommittee members and get more response.

So I think waiting until the Sunday right before wouldn't be as --

CHAIRMAN CHILDRESS: There is still one question as to whether this being on the 1st this may make --

(Discussion)

CHAIRMAN CHILDRESS: Is that right?

DR. DUMAS: Instead of the full committee?

CHAIRMAN CHILDRESS: Well, the question that Harold is having to deal with is how much would there be there for the whole committee.

Now, no one would argue that there are whole things that the whole committee could begin to do.

DR. CAPRON: I wanted to ask -- I requested this a number of times. Is there any possibility -- or are there conflicts that you, Jim, or you, Harold, had the next week?

I have mentioned all along that that last -- the week of December 1st is my last week of teaching.

It becomes increasingly hard to reschedule classes because other colleagues have also missed classes. And they are trying to reschedule.

It also seemed to me that the time between November 23rd and December 1st was simply too short given the fact that Thanksgiving took up a couple of those days.

And the weekend takes up a couple more of the days to expect any real substantive progress between those two days.

On the other hand, a week later, I now see there is already going to be a giant subcommittee meeting, if it were possible to -- on the 9th it says here.

If it were possible to have part of the day as your subcommittee and part a whole committee where the genetics people would get to hear our report and go over with us the draft which would likely have been further revised in light of whatever we talk about on the 23rd.

That seems to me --

VOICE: The 9th.

VOICE: What day is the 9th?

VOICE: It is all right with me.

CHAIRMAN CHILDRESS: I have to lecture.

DR. CAPRON: Maybe, that is the reason that it wasn't scheduled. It is very hard to find dates. I can't remember the details right now.

But it was very, very hard to find dates when any representative on this committee could assemble.

I agree that there are significant issues with that date as to whether it is a good time to meet period.

(Discussion)

DR. CAPRON: To meet at all. And I will talk with Jim after the meeting. And I will talk with Tom and see where he and his committee are

before deciding.

We will look once again of the idea of trying to have it a week later. I don't know. I don't remember any longer what the exact constraints were.

DR. BACKLAR: If we are actually thinking, if we are going to go to this conference, it seems to me we should be on one side or the other of it, the NIMH conference.

DR. CAPRON: I won't be able to go to that. Again, I don't know. So much depends too I guess as you look around and see if they can get facilities.

DR. BACKLAR: I'm sorry.

DR. BRITO: I agree what Patricia said about the December meeting. The other thing is if we do meet on the 23rd, that Sunday, is there enough time around time when the full commission meets on December 1st, if we meet with them for Jonathan to get -- because I feel pretty comfortable about this morning's talk that we are going to progress with this paper, probably change it.

But would there be -- and I think by November 23rd, we can make a lot of changes. But

then, would there be enough turnaround time to have something ready?

CHAIRMAN CHILDRESS: With Thanksgiving, it's very difficult.

DR. BRITO: Right.

CHAIRMAN CHILDRESS: It's very difficult to imagine. And that's why we have to consider that very difficult.

DR. CHARO: Just a clarification, I get in from Boston. Is November 23rd definite or is that up for grabs in the discussion?

CHAIRMAN CHILDRESS: It is up for grabs.

DR. BRITO: It is to be decided.

CHAIRMAN CHILDRESS: It's what we are really discussing.

DR. BACKLAR: And December 1 is not definite either because of the conditions, because it is on such a difficult day to get here.

CHAIRMAN CHILDRESS: And it also depends on what is there for the whole commission to discuss in terms of materials.

DR. BACKLAR: And if we have on the 4th -- if we were to already -- if we were to have benefited from the NIMH conference --

CHAIRMAN CHILDRESS: That's true.

DR. BACKLAR: And if I help us in our discussions rather than having a discussion and then going into the conference. We should reverse that.

MR. GIRARD: Well, Jim, what is the best date for your committee? Put the other commission aside. I mean, I'm hearing --

CHAIRMAN CHILDRESS: Well, the following week. Alex has mentioned the 9th. And again, I just have to be at the direction of the --

DR. DUMAS: I can't come on the 9th.

CHAIRMAN CHILDRESS: But I don't know if others like to do that as well.

DR. BRITO: Is the 8th a possibility?

CHAIRMAN CHILDRESS: the 8th is a possibility.

DR. BRITO: The 8th is Monday and it's easier.

CHAIRMAN CHILDRESS: Okay.

DR. SHAPIRO: Does this committee prefer to meet on the 8th?

DR. CAPRON: Instead of the 1st?

DR. BACKLAR: And then, I come in.

(Discussion)

DR. BACKLAR: I will come twice. I will come the following week to another meeting.

DR. CHARO: I have got to say, one of the things is although you kept saying they were tentative, for all of us -- at least I've been planning around these dates.

And I've got travel. I have said, yes, to other conferences because they were next to this date.

And suddenly, I'm left unfunded with no ticket because I was going to take advantage of being able to piggyback on an anthropology meeting.

CHAIRMAN CHILDRESS: Right.

DR. CHARO: And just changing dates this close to the end of the semester in general is really tough on us. Students are going to rebel.

CHAIRMAN CHILDRESS: I guess the thing about the 23rd which we listed as we have decided. Is that right as a date?

DR. CAPRON: So we are --

CHAIRMAN CHILDRESS: Is this what -- is that okay with the subcommittee members?

DR. BRITO: What?

CHAIRMAN CHILDRESS: For November 23rd as

a definite. This was -- just is going to have to be decided.

DR. BRITO: A one-day subcommittee meeting.

CHAIRMAN CHILDRESS: Right.

(Discussion)

CHAIRMAN CHILDRESS: And the January subcommittee is definitely meeting then. And we can decide if whether to do some joint things on that day. Okay.

DR. BRITO: So what is up in the air now is whether we should meet the 1st or not, whether that is productive or unproductive.

DR. BACKLAR: Or if we can meet on the 4th?

DR. BRITO: Or can I make another suggestion?

CHAIRMAN CHILDRESS: Yes.

DR. BRITO: December 2nd, we can meet. Since the meeting is December 2nd and 3rd, is it possible to meet the evenings of those dates, the afternoon of the 3rd?

The meeting adjourns on the 3rd at 12:30.

DR. BACKLAR: Some of us have to get to

the airport.

DR. BRITO: Well, then, you are going to wait until the 4th? The conference ends at 12:30 on the 3rd.

(Discussion)

DR. BRITO: You are going to wait -- you are going to stay until the 4th. If you would stay until the 4th, wouldn't you stay for the evening of the 3rd?

DR. CAPRON: Right.

DR. BRITO: So why not just meet like between 1 and 8:00 o'clock.

DR. BACKLAR: At the end of the day.

DR. BRITO: It ends at 12:30. So it is going to waste time to wait another whole day.

CHAIRMAN CHILDRESS: Alex can't attend the conference anyhow.

Who could attend Wednesday afternoon, the 3rd?

DR. BACKLAR: That would mean I would lose Thursday. I am not working.

DR. DUMAS: I don't have my calendar with me.

DR. BRITO: Okay.

DR. DUMAS: I looked at the schedule of everything that we had.

DR. BRITO: We are going to attend the 4th, too. I see that most people are going to attend the 4th. But I don't see what sense it makes not to meet that afternoon.

We could meet the morning of the 4th also.

CHAIRMAN CHILDRESS: If people could say.

DR. BRITO: Right.

CHAIRMAN CHILDRESS: And again, the staff would have to work out and see if this is feasible.

But from the standpoint of the individuals involved, how many could make the afternoon of the 3rd which you would basically be trying to work through -- work further and recommendations further in light of what we had heard on the 2nd and 3rd?

DR. BRITO: What is easier for you all to do?

DR. CHARO: I wasn't planning to go to the NIMH thing.

DR. BRITO: Oh.

DR. CHARO: Because I am teaching. I've got two things for Thursday. I've got 16 hours of teaching.

CHAIRMAN CHILDRESS: Will the following week -- of course, we would have to travel back.

DR. BRITO: Are you done with teaching by the following week?

DR. CHARO: Am I finished? No, we are taught, we go into the --

(Laughter)

DR. CHARO: It is still hot.

(Laughter)

DR. BRITO: So you need more class days than ours.

DR. CASSELL: Are we talking about the 8th or 7th? What are we talking about now?

CHAIRMAN CHILDRESS: The 8th.

DR. CASSELL: I can make the 8th.

DR. FLYNN: What day of the week is that on?

DR. CAPRON: It's a Monday.

DR. FLYNN: The 8th is a Monday.

DR. CHARO: That's -- I'm still teaching then. And I can't --

DR. DUMAS: And I can't either.

DR. BRITO: What about on the 1st and 5th? I don't know what's so right about the 7th then.

DR. CAPRON: Do it on Sunday. That's --

DR. BACKLAR: No, no.

DR. CAPRON: Too many Sundays.

DR. BACKLAR: Because I have to be here the next week.

DR. BRITO: Every Sunday would be --

DR. BACKLAR: So the problem of flying on Sunday of Thanksgiving is just being eliminated. Is that correct?

CHAIRMAN CHILDRESS: Well, not necessarily. We are just --

(Laughter)

DR. CASSELL: It is the hardest day of the year, the worst flying day of the year.

DR. CAPRON: The worst traveling day.

DR. CASSELL: The worst traveling day.

DR. CAPRON: On the highways, too, if nothing else.

DR. CHARO: So we are doing a public service not to add our --

(Laughter)

CHAIRMAN CHILDRESS: Okay. We are set on the November 23rd. I am not sure what is emerging as another possible date.

DR. SHAPIRO: You will hear of the -- you might not have to deal with that.

DR. BRITO: Well, it is going to be hard to get other dates.

DR. BACKLAR: Yes. We could --

(Discussion)

DR. BACKLAR: If we all agree to stay. Can we agree to stay after the --

DR. CASSELL: How many of you could stay on the 3rd? I wonder if we could just --

DR. BRITO: Is it possible to have small working groups?

DR. SHAPIRO: It may be it's worth having instead of the 1st, the 2nd.

DR. CASSELL: We don't have the 1st.

DR. SHAPIRO: If we don't have the 1st, maybe at least some subset could stay on the 3rd and build in the materials that come out of not only the 23rd, but come out of the conference.

(Discussion)

CHAIRMAN CHILDRESS: Does that make sense to as you a proposal? I know you can't --

DR. CAPRON: You will have a meeting and I won't be there.

DR. BACKLAR: You can meet again on the morning of the 4th.

CHAIRMAN CHILDRESS: I know.

DR. SHAPIRO: I will have to check that.

DR. DUMAS: Is the 1st on that schedule that we --

DR. CHARO: Yes.

DR. DUMAS: That we got before.

DR. CHARO: Yes.

DR. DUMAS: Okay.

DR. SHAPIRO: The problem is travel.

DR. DUMAS: Okay.

DR. SHAPIRO: Because for that Sunday, if people don't have reservations now, it is possibly impossible to get, like --

DR. CASSELL: Can we prepare for the 1st? Because I have --

DR. SHAPIRO: Well, Jim, I think if this -- if your -- if a subset of your committee can meet on the 3rd after the end of this conference.

CHAIRMAN CHILDRESS: Yes.

DR. SHAPIRO: And at least we can have some -- and the Genetics Committees meet anyway on the 8th or something.

DR. BACKLAR: The 9th.

DR. SHAPIRO: The 9th. We would then just cancel the 1st.

CHAIRMAN CHILDRESS: It certainly would be very useful if you are at the meeting of December 3rd to meet and able to dispel what you think has come out of it.

DR. BACKLAR: Right.

CHAIRMAN CHILDRESS: All right. So the 3rd?

DR. BACKLAR: Yes.

CHAIRMAN CHILDRESS: The first is out. Okay.

DR. BACKLAR: Great.

DR. CAPRON: Great.

CHAIRMAN CHILDRESS: Okay. We are now on a roll. Anything else we --

(Laughter)

DR. BACKLAR: So we can start booking.

CHAIRMAN CHILDRESS: Yes. Okay. Okay.

DR. FLYNN: And we cancel that.

DR. BACKLAR: It is definitely important.

DR. SHAPIRO: We cancel on the 1st. Okay. All right.

DR. CHARO: That was the one player I needed.

(Laughter)

DR. CAPRON: Okay.

(Laughter)

DR. CAPRON: Okay. On a one-day contract just to be --

DR. CHARO: Just to get the last four segments.

DR. CAPRON: Yes.

CHAIRMAN CHILDRESS: Before we go to the federal agency report, what we need, we received a lot of suggestions this morning and very important ones for revisions of the draft. And that will proceed.

And then, we have individuals here who are going to contribute materials. They are called Alta and Irish, for example.

And there may have been others. I don't profess that we have everything now and surely I cannot remember everything, but I believe that was the case.

Obviously, the NIMH conference, we will try to build in.

And then, also, we need to get input, more input from researchers. Now, that is something that we can try on November 23rd. So let's think about that and give me any suggestions you have.

Is that agreeable to build that in as part of our work on the 23rd?

DR. BACKLAR: On November the 23rd?

CHAIRMAN CHILDRESS: Right. Okay. And then, give me suggestions on that.

DR. BACKLAR: (Inaudible).

CHAIRMAN CHILDRESS: I'm sorry.

DR. BACKLAR: (Inaudible).

CHAIRMAN CHILDRESS: Right. By E-mail, if you would.

DR. BACKLAR: All right.

CHAIRMAN CHILDRESS: I will get that to -- okay.

Now, anything else we need to talk about on the draft report on decisionally-impaired subjects?

DR. CAPRON: Are we going to talk about the recommendations?

CHAIRMAN CHILDRESS: We would like to get the response to the recommendations.

But anything else besides the recommendations?

DR. CASSELL: Well, I just want to say briefly, too, that it seems to me that the discussion that we've had now really impacts on how we see those recommendations.

I found them bland. And I thought that what we were talking about today was going to end up changing those recommendations a lot.

So my own sense of it is that it would require looking at the rewritten proposal.

CHAIRMAN CHILDRESS: Right.

DR. CASSELL: And the implications for the recommendations.

CHAIRMAN CHILDRESS: Yes. I agree. I think it would take those. I would just note though that far from being bland, I think there is one on minimal research, not potentially beneficial research is actually very radical and would create tremendous problems.

It seems to me that that is one that needs further attention.

DR. MORENO: Right. Can I -- there are a couple of typos. And they are not -- one is not

insignificant.

CHAIRMAN CHILDRESS: Right. Minimal risk.

DR. MORENO: On page 160, seven lines down from the beginning of number 7.

DR. BACKLAR: Yes.

DR. MORENO: Examples of --

DR. BACKLAR: Yes.

DR. MORENO: I am sure everybody picked up on that one.

DR. BACKLAR: Yes.

CHAIRMAN CHILDRESS: Yes. That was a test to see if we were reading carefully. Is that right?

DR. BACKLAR: Also, at the beginning, something about the National Commission's role.

DR. MORENO: Right.

DR. BACKLAR: That was interesting.

DR. MORENO: Clearly, it should be Advisory Commission.

DR. CHARO: I would to second Jim's holding out of item number 2, the non-beneficial minimal risks.

I circled that one as getting way too tight, particularly in light of my concerns about the workability of these advanced directive things.

And on the great and minimal risks not potentially beneficial, we might want to spend more time thinking about the alternatives.

And Harold was asking other things before we settle on any particular methodology.

CHAIRMAN CHILDRESS: And so we would be sort of working through in doing this.

DR. CHARO: Yes.

DR. CAPRON: I have this underlying question which I got from a nod from Jonathan when we -- when I raised it.

DR. MORENO: Yes.

DR. CAPRON: And you were asleep.

DR. MORENO: Yes.

(Laughter)

DR. CAPRON: And to just look at that very one, Alta, that you were just mentioning. An IRB should approve -- should approve, disapprove this category of research only if the potential subject has given informed consent or is incapable, has executed an advanced directive specifically authorizing research of the kind represented in the study.

Now, that obviously raised questions about

the advanced directive. The type of directive that we are going to be accepting was procedure specific rather than proxy.

But moreover, it did seem to dichotomize the category as those with capacity to give consent and those without, without addressing the peculiar problems of people who were impaired where the capacity question is this more complex thing.

And I wasn't -- and that occurs throughout these recommends.

And I think we need, you know, now or some time to discuss if that's the direction we are going or not.

CHAIRMAN CHILDRESS: And I think the kinds of proposals that came out this morning, building in part on Trish's initial comments about distinguish more --

DR. CAPRON: Yes.

CHAIRMAN CHILDRESS: On the individuals, not simply the level of risk whether it is a direct benefit or not.

That does complicate it. And it complicates it along the lines that you are suggesting.

Thus, we need to spend some --

DR. CAPRON: Well, but it's a little -- it seems to me that it's a little different than that because Trish's were longitudinal categories I thought.

I mean, they were -- to change her wording slightly it's fluctuating incapacity, respective incapacity, limited incapacity, and incapacity or no capacity.

And that it is not the only way we can see in what we're talking about as being impaired. I mean, one could be in the category of --

CHAIRMAN CHILDRESS: Well, if you don't have limited capacity, then you are impaired. So --

DR. CAPRON: But I don't know.

CHAIRMAN CHILDRESS: Right.

DR. CAPRON: Is that -- is limited capacity equivalent to impaired?

CHAIRMAN CHILDRESS: I would assume so, right?

DR. BACKLAR: Then, you --

DR. DUMAS: I would, too.

DR. BACKLAR: He changed the way I

described it. And I don't have my notes right in front of me.

When I was thinking about -- I was thinking about people who had bipolar disorders and people with schizophrenia.

DR. CAPRON: Right.

DR. BACKLAR: The appearance of being to make decisions for themselves.

DR. CAPRON: Right.

DR. BACKLAR: Then, when I was thinking about limited capacity, I was thinking about that group of people who have limited, potentially limited capacity, a group of people who at this moment still have capacity or very early Alzheimer's, some people with dementia. In other words, before things get too bad.

DR. CAPRON: I thought that was the perspective of the incapacity category.

DR. BACKLAR: Perspective.

DR. CAPRON: Perspective.

DR. BACKLAR: Yes.

DR. CAPRON: What about limited?

DR. BACKLAR: I'm sorry.

DR. CAPRON: Yes.

DR. BACKLAR: Prospective is --

DR. CAPRON: Yes.

DR. BACKLAR: Limited is where -- and you could use another term where they have the ability to ascent or object, but not -- or even possibly appoint somebody they trust, but not really the ability to make these kinds of decisions.

DR. CAPRON: So is that what at other times we were calling impairment? It's not capacity, but its diminished capacity or something like that?

I mean, I --

(Discussion)

CHAIRMAN CHILDRESS: That is why the work has to be done.

DR. CAPRON: That is why the work has to be done. And if we do recognize that category, then it seems odd here in the recommendations to have only the polls of you've got to actually give full consent or you don't have capacity.

What about that middle ground which was originally what I thought this report was going to be about?

And then, the report ends up being about

capacity and incapacity.

DR. BACKLAR: Right.

DR. CAPRON: Is a difficult issue, but maybe not as difficult or difficult for different reasons.

DR. MORENO: And I have to confess, Alex, I hadn't the foggiest idea what to do what that.

DR. CAPRON: Okay.

DR. MORENO: And I felt a little more confident about projecting in my fantasy life what commissioners might want to be saying about some of the pollers, the polls, but not -- my fantasy life being so impoverished, I wasn't able to go as far as --

(Laughter)

DR. MORENO: I agree with you.

DR. DUMAS: The thing that disturbs me about this assessment is that we are assuming that the IRBs will make these determinations about whether a person is -- has a

DR. MORENO: I don't think so.

DR. DUMAS: Well, who makes the determination? How is this judged?

DR. CAPRON: You are right to raise the

question. But I don't -- I wasn't assuming it was the IRB.

DR. DUMAS: In here somewhere, it says the IRB should approve only if --

DR. CAPRON: They have a choice.

DR. DUMAS: It doesn't say that that if the person is -- let me read it.

(Pause)

DR. DUMAS: I have trouble keeping up with these pages.

DR. CAPRON: Actually --

DR. DUMAS: Read the first recommendation.

DR. CAPRON: No, it doesn't say if they have determined.

DR. DUMAS: Yes.

DR. CAPRON: I mean, it is vague on this.

DR. DUMAS: Okay. Well, the thing that I think is really important is that the question of who makes the assessment of --

DR. CAPRON: Yes.

DR. DUMAS: Of mental capability.

DR. CAPRON: Should it be someone other than the researcher?

DR. DUMAS: Yes.

DR. CAPRON: Yes.

DR. DUMAS: And then, they are going to make this assessment. And then, the IRB is going to rule based on their assessment, whoever makes this assessment.

DR. CASSELL: I think one of the directions we are going in is being much more specific about the nature of that assessment and who makes it.

DR. DUMAS: That's right. I think so.

DR. CAPRON: And some guidance is given. I mean, I'm looking at the guidance section. It is IRBs may require investigators to identify independent consent.

DR. DUMAS: Yes.

DR. CAPRON: And independent psychiatrists may be required to certify the potential subject's loss in decisionmaking capacity and so forth.

DR. DUMAS: Yes.

DR. CAPRON: But obviously, the --

DR. DUMAS: That has to be pulled out because as I said, there are a lot of important things embedded in the content here.

And it comes up in different areas. But I

think that should really be pulled out and put in here.

And that reminds me again of the section on risks and benefits that I read only briefly. And I'm going to look at that again more closely.

But I think that the issue of who determines risks and benefits needs to be treated in that area, too.

DR. CAPRON: Good. I would second what Rhetaugh has just said and not that the same kind of issue comes up with the phrase about notification.

IRBs should be required to determine that the investigator has provided for notification. And the phrase "provided for notification" is not the same thing as notifying which --

(Discussion)

DR. CAPRON: And that should be the bottom line we care about here. You can provide for it if it doesn't happen ineffectual.

I also was struck that some of these things that are under guidance, I couldn't tell if they were there because you just didn't feel, Jonathan, that we have come far enough towards

saying that they really belong in the regulations.

I anticipated that guidance was going to be more of, as suggested at the beginning, something that is not probably not suitable for the regulations, but where the concern is about why the -- would be informative.

DR. DUMAS: It is very important.

CHAIRMAN CHILDRESS: Yes, we will take just a few more points on the reaction to the recommendations.

DR. CASSELL: And greater and minimal risk not being beneficial to research, and it is not the case at all.

But I also think it is not effective the way it is written here. Under physician monitor, an independent physician monitor decides.

You know that that is pretty tough to do because it has to be a physician. The word "medical" should not be in there.

DR. DUMAS: Right.

DR. CASSELL: But what do you mean by medical, a person who practices in the psychiatric state? Or do you mean something else in passing? It could be anything. It simply shouldn't.

A psychiatric social worker could do that just as well.

DR. DUMAS: Right.

DR. CASSELL: In the terms of getting one --

DR. DUMAS: Right. A psychiatric nurse.

DR. CASSELL: A psychiatric nurse can do that. And in fact, we may be heading towards it.

So this whole thing has a lot to do with who is monitoring all of this.

DR. DUMAS: Right.

DR. CASSELL: And so we may be heading in the direction of making more specific recommendations about the monitoring of consent and all this stuff.

DR. CAPRON: I also -- I'm sorry.

DR. BACKLAR: I actually was going to include that in the research on advance directives.

DR. CAPRON: Right.

DR. BACKLAR: It should not necessarily be a psychiatrist because many people don't have a close relationship with a psychiatrist. And they see them once every three months if they are lucky.

DR. CASSELL: They have an outside

psychiatrist. They don't have a --

DR. CAPRON: Right.

DR. CASSELL: Coming into the institution. So --

CHAIRMAN CHILDRESS: The last point.

DR. CAPRON: Well, it is the verb in that sentence.

DR. BACKLAR: Okay.

DR. CAPRON: And recommend that the subject's participation be stopped on medical grounds.

There are certainly other contexts in which the person that is the monitor can literally put all that to a stop.

DR. DUMAS: Maybe, if you take medical grounds out.

DR. CAPRON: Yes. We agreed about the medical grounds.

DR. DUMAS: Right.

DR. CAPRON: But is it recommend? Recommend to whom, the researchers, to the IRB?

Or is it they have some actual decisionmaking authority to say pull them out, get them back on regular treatment?

CHAIRMAN CHILDRESS: And obviously, there is a lot more to discuss here. And these have been very helpful points for our recommendations.

What I would ask you to do is actually spend some time mulling over these, preferably on the planes back, especially for those on the west coast and see what --

CHAIRMAN CHILDRESS: I would recommend to circulate my list of --

DR. MORENO: Jim, the reason that the word "medical" was there perhaps was ill chosen was to acknowledge the fact that this monitor whether a physician or non-physician is not usually the physician to know the -- may not be the physician to know the subject's views in advance about research.

That may have to be left to a legally authorized representative. This is a best-interest test, in other words, the consent to respond to. But we are sorting that out.

CHAIRMAN CHILDRESS: Okay. All right. Thanks everyone. Good thorough discussions. All right.

Let me shift gears. And we could ask for thanks to Jonathan and the staff of Bill Freeman and

Susan Katz and Joe Mangel and Emily Feinstein.

DR. CASSELL: It is routine.

CHAIRMAN CHILDRESS: It is routine. It gets bigger each week.

REPORT ON SURVEY OF FEDERAL AGENCIES

DR. FREEMAN: Okay. Do you folks want to introduce it? I will do as you wish.

CHAIRMAN CHILDRESS: WE will open it for discussion.

DR. FREEMAN: It was mostly a prior version. You have seen now this next draft.

We tried to focus on the pros on the basis of some feedback from the last meeting, focused the first chapter on what was going to be -- or what is the or what we propose to be the messages or the conclusions and then recommendations.

And then, in the second chapter of findings which was only findings of the first part of the survey which is incomplete.

We don't have all the departments and curves that we would want to have. We are not going

to be describing every department and pros.

We are making categories of -- or kinds of groups of departments or findings that we found.

But I think the range of the findings are there. And so it is fairly complete pro section.

There will be some -- I believe some new conclusions -- I mean, not conclusions, new findings around the edges of those.

I think we found a little bit more complexity on the October 9th meeting the day before this report went out about some of the reasons why perhaps a department might not have had some structures in place, what it thought was risk to subjects.

So we will be -- have more details about that.

But what you have there is pretty much I think the range of what we have already found. And we have not concluded every interview, but we will -- we don't expect to find anything new in terms of new kind of finding in the very few departments that are left.

Phase 2 which is chapter 3 which is the -- let me just go back. The first phases of the

structure, what is in place of the structure in terms of the departments and agencies.

The next thing that we are in the middle of now is the process. It is the process that the structures have.

So we are only going to get places that have mature structures. That's the IRBs.

And we only have a limited number, not clearly what we want, trying to find out what the process is.

That, of course, is not written at all at this point.

And then, the recommendations, conclusions and recommendations which is the next chapter. In addition, we have in the handout that we sent out to you a brief summary of the comments that we have received in response to an open mailing.

And I think there are some that we may want to incorporate more fully into the conclusions as supporting, I think at least support some of our conclusions.

It does seem to me that the commission and this subcommittee at this point faces some choices. We propose some choices, but we realize that that's

only a proposal.

And we were guessing that this is what you would want, but we have been known to guess wrong before.

So feel free to, as you will anyway, say that we guessed wrong.

But in particular as you can tell in my program memo of what is the approach in terms of a range of approaches that NBAC might want to make in response to the conclusions, that some federal agencies have not implemented their own regulations.

A set that we think, as you can tell, we gave our rationale at least for them is what we think you might want to have.

That clearly is your choice. And we will go with what you all -- the approaches you want to have.

I hope that at least in that cover memo we gave clearly the range of responses that you could have.

And if that is not true and if you come up with an entirely different one, again, we will include that.

I think, Jim, that is -- at one point at

one time this afternoon, you may want to talk a little bit about what appeared to be the findings of phase 2 of which is written nothing.

You have received nothing written. I'm sorry.

But you probably ought to focus on what -- and anyone I believe that has gotten Alex's rewrite of chapter 1.

DR. CAPRON: It's not a chapter. It's just the first few pages. And it actually was based on the language from the first version.

And that is the new language in the second version which we probably would want to make sure is included.

My objective in doing that was I was trying to be helpful to you in the process, but to suggest a way of expressing that makes it a little less like a government report and more of something you would want to read.

DR. SHAPIRO: I didn't know that there was a --

(Laughter)

CHAIRMAN CHILDRESS: Why don't you -- Alex, since you have already started with that, why

don't you go ahead and proceed with your -- I have asked Alex and Alta to give us an initial feedback in the hope that the subcommittee will move forward in the discussion of the draft report and recommendations.

And, Alex, why don't you continue?

DR. CAPRON: Well, one of the departments that isn't fully addressed in the recommendations is the extent to which the non-implementing departments, that their non-implementation implicates something more, the need for something more than the kinds of solutions that you've set out here.

And obviously, as a person who has pressed this notion of a super agency, super department thought to get to the issue to have greater attention.

What puzzles me about this is the extent to which these are departments which were at least nominally participates in the interagency task force.

And if so and if that is the present revisement of something that goes beyond the departmental level, I would have to judge that to be

unsuccessful in meeting what I would have thought was the goal which is ensuring that everybody understands and is doing what we're supposed to be doing about the regulations.

The notion that the departments are simply ignorant of their own rules and if we hadn't come along would be going ahead without attending to these regulations is disturbing.

And I think we need to draw some further conclusions on that. And I would be prepared to do so.

Now, I don't know how that works, Jim, with the notion that the conclusions vis-a-vis the location of research protection is a topic that we are only get to in terms of to draft the reports we have for later.

Perhaps, like our move on the non-covered research where we sort of signal that we have reached tentative conclusion, it may be enough to indicate that those findings have these broader implications.

But reaching conclusions on that requires a further examination of the competing considerations.

I wouldn't want to lose that, that set of conclusions.

DR. KATZ: We purposely did not put that in because that has already been on the for you folks and by you folks. And I figured you put it where you wanted it and the weight that you wanted it.

What we do have is the experience as we see it that, first of all, it is not the ignorance of the department because I know of no department that is ignorant.

It is within agencies. For whatever reason I think some are ignorant. But there are competing demands.

It is not like they do not know that the regs exist. It is the competing demands, competing in the sense of either time for other things, also disagreement about whether -- in some cases whether the regulations should apply at all and so on.

So that is why we say that there is a range of reasons. And in a sense the recommendations were changed need to account of that.

There is -- I made this analogy before.

And at the time, I didn't think it through well enough. I think I thought it through a little better.

The first research about implementation of new things, new technology or change was with the agricultural extension agents in commerce actually back in the '30s.

And there was this signal curve. This is time. This is a percent. And it goes like this.

And you have a long time in just and few people adopt that is the latest good thing that everyone should adopt.

And then, you have a short time when there is a rapid increase of the percentage of people doing it.

And then, there is a long time for that remaining tail.

One of the important things about that is the farmers in those three phases are different.

The first ones are risk takers. And they do to whatever comes first. And sometimes, they get burned. And sometimes, it's a good deal.

These people in the middle, the large majority do it. They hear other people do it. They

have their own network.

The last ones are resistant for a whole variety of reasons. And to get them to adopt, you need to sort of find out and particularize the message, what is it that you object to? Or what is the problem? And try to match the change to them.

I think we are at the tail in the federal agencies.

DR. CAPRON: Yes. It seems to me that that analogy which I suspect that the clinical researchers around the table and the physicians around the table could say equally applies to clinical changes.

DR. KATZ: Yes.

DR. CAPRON: It doesn't quite fit from what I understood our situation to be. That is why I asked if these were people who were participates in interagency committee.

To me, it's more like the kid who crosses his fingers when he tells you something and thinks that although I seemed to have agreed, I haven't really agreed because these are all people who signed onto and continue -- not people.

These are all departments which are

embodied that have signed onto and continue to participate in a process that allegedly is aimed toward a common rule equally applied to all agencies.

And yet, you're telling us that some of them know all the language about it, at least in the cover memo.

You said some of them were, quote, simply ignorant, and others sort of -- well, some were so ignorant that it really took asking them questions.

Some of them, as soon as they tried to file a report and realized they had nothing to report said, oh, my God, we have got to do something.

But in any case, in the periods since the common rule came in, they have been inactive.

And yet, they signed the common rule. Their agency appeared when that was reported in the Federal Register. And they continue to participate.

That doesn't seem to me that it is the same as different farmers responding to the agricultural extension agents or different physicians who are unconvinced because it is not as though all those physicians say that they are doing

it.

They are in fact resistant to change. And they don't make any bones about it that they have no intention of going along. They have to be persuaded.

So I think the analogy is more disturbing. I mean, I think the situation is more disturbing than the analogy.

DR. KATZ: I tend to agree, you know. And I think maybe in subset B of conclusion number one, it is less vague for a reader because basically what we're seeing and what Bill saw in his investigation is that there is a range.

And what we're talking about if we can discuss in detail in what is now the draft of chapter 2, when we talk about agencies in which the resistance is implementation seems to be very deeply embedded and historically.

And it may call for a different kind of remedy than with the agencies that Bill is talking about where you really have difficulty in terms of the size of the agency and the dissemination of information or a whole range of other problems that are minimal of different solutions.

DR. CAPRON: Right. When you go to an agency and they tell you we don't do anything that we should have to regulate and then you start going around with them and they do --

DR. KATZ: Well, I think --

DR. CAPRON: It's denial.

DR. KATZ: Ten years ago and also 20 years ago.

DR. CAPRON: Yes. It is a pattern of -- you know.

DR. KATZ: Well, I suspect that this is very much linked to something which in this draft which -- although I've got to tell was hugely, you know, way beyond where we were the last time. So I was very grateful that that much got incorporated really.

I think it's linked to one though that you decided not to put in. And that was any estimate of the level of the actual injury by the physical or dignitary associated with specific failures to implement.

Now, as I read through the descriptions for the various departments and examples of problems, it struck me that consistently, there is a

breakout not in terms of the regulatory coverage, but in terms of people's reaction to the regulation, depending upon whether you are talking physically or nonphysically invasive research.

And on nonphysically invasive research, we've got three categories, off hand I can think of. One is -- I just wrote it down here.

One is going to be survey research. Another one is going to be medical record review. And another one is going to stored tissue sampling, God help us, in which I think it is possible if you were to go back and look at your data again.

You would see a pattern in agency and department's enthusiasm about the implementation of these particular regulations.

And even if the bottom line in the end is that from a regulatory point of view, you still want the same regs to apply, whether it is physically invasive or nonphysically invasive, this may suggest something about the approach to be taken in the recommendations.

Because if the regulations are either in fact burdensome for people that do nonphysically invasive or are simply perceived as such, that needs

to be addressed in order to remove the resistance that you have identified.

But I think it tracks that distinction.

Perceived as burdensome may have to do with not with the fact that the regulations are imperfect to begin with, but because the frequency of the research or the frequency with which the research is not in fact on the line of being minimal risk, for example, means that they don't have the single point person who clearly makes the judgment calls.

And if you need to have review, you don't have a place to focus review.

And indeed, you do speculate there about the possibility of a shared IRB which may or may not be part of the super agency structure as a place to help agencies and departments go when they are really not in this business in a big way for non-minimal risk research.

So I think it is only that these things are linked. And I would urge us to perhaps, even if the regulations are going to change substantively, to look at that breakout, you know.

I've seen Gene Shelton sitting in the

back. And I know he spoke at the second or third subcommittee meeting quite passionately about the need to distinguish nonphysically invasive from physically invasive.

And it may be that the distinction needs to be in the assistance that is given to the agencies rather than necessarily regulatory changes.

I mean, they are two separate options.

But as it stands now, we don't get a chance to pull this out in the kind of lessons learned in the words of the assistance to the agencies.

DR. FREEMAN: We have mentioned -- I think you're right, but maybe it's not as clear as it could be.

We do mention -- and I will say, by the way, behavioral, non-biomedical versus biomedical.

The non-invasive biomedical is still covered well because the biomedical types generally take the whole thing.

And so medical records review is not as burdensome as the non-invasive, as the non-biomedical by the non-biomedical researchers in the non-biomedical departments in the federal government

and agencies of the federal government.

DR. CHARO: You know, this may be true of the federal agencies, but I am amazed because my experience in the university sector is that biomedical research or not, if it's not physically invasive, people do not think of it of something that has to go to an IRB.

And getting people used to the idea that a record review has to have IRB review, just because you are going to be matching records is shocking.

I watched moments that my own IRB get shocked. And they were reminded that is how the regs work. Right.

So I am amazed that the federal government has no such confusion.

DR. FREEMAN: What has happened I think is coincidentally. And so it would be worthwhile to go back and look.

What has happened is those who are doing basic biomedical have some years ago or recently really gotten their act together in response to a scandal.

So now, the entire protection is a pretty good system. And they therefore implemented that

book. That's what we're going to do because we've got to keep our act clean is in effect the response.

There may be in fact -- and I would have to go back or we would have to go back and look that some departments are related and they do basically health-related research, not invasive that may be similar to the non-biomedical researches.

And you may be right on that.

DR. CHARO: It's just -- I'm sorry, Susan.

DR. KATZ: I was just going to say to the other issue that you raised, there is a very brief comment about it or at least there was in one draft.

And it may or may not be in terms of whether or not they are actual injuries, you know. What is the rate, you know, or the distribution of the actual injury?

DR. CHARO: Yes.

DR. KATZ: And basically, we say that we are not making a statement about that because we don't have the data to support it one way or another.

And it may be something that one would want to delve more deeply into if you are going to make actual regulatory changes based on that

assumption.

I mean, if you are going to lay on another whole layer of either bureaucracy or regulation, you would want to know, you know, what are the actual harms and what is the risk factor.

DR. CHARO: But one thing that can be done here whether it is biomedical invasive or just invasive, I mean --

DR. KATZ: Right.

DR. CHARO: But I think it's very obvious to people what the injuries are in theory that come from the basic research.

It is not really clear offhand necessarily.

One of the injuries you are so worried about is non-invasive research.

So if you want to begin to look at the agencies, and I'm speculating, but I'm pretty confident you're going to find a significant association between enthusiastic implementation and invasiveness of potential injury.

Look at the ones that are not enthusiastically implementing. Look at the degree to which they are doing non-invasive stuff.

And step one is going to be to try and explain why this is potentially injurious.

And so the privacy concerns and the discrimination, etcetera have to be explained.

The next step is going to justify why even if you are not sure why these thing have actually happened that the existing regs need to be implemented anyway.

I mean, this is a reprisal in some ways. The discussion that Alex is sounding every time I've raised coverage of non-covered research out in the rest of the country.

And Alex says, show me the count. Show me the bodies. And I've been saying, well, that doesn't matter.

But I've yet to come up with an answer that justifies why it doesn't matter enough to really kind of narrow it down for everybody.

And I guess I'm throwing up exactly the same challenge here. Justify why the regs should be implemented even if we can't count the bodies just because we think that there is a value to the implementation.

But do it with some sensitivity that to

the problems that have been cited by the agencies. And you throw them a carrot out. And we're going to make it easier for you to do it.

DR. CAPRON: Could I ask? Would it be sensible to respond in a situation where a group of agencies have implemented rules and another group has said that they would, but haven't.

And we are now asking, well, is it reasonable to insist that they do it? And do we need to have, as you say, evidence that harm has arisen from their not doing it?

To say at the very least the burden ought to be on the agencies that are not implementing it.

DR. CHARO: To show why they shouldn't have to.

DR. CAPRON: To show why they shouldn't have to because this was something, whatever process this was, it took 10 years to go through.

There was a lot of opportunity to explore. And the whole incentive of the people involved was not to create unduly burdensome rules.

A certain amount of this emerged from a public process of the National Commission and a certain amount from the public process of the

President's commission.

And then, there was this less public process, but at least it periodically was published in the Federal Register for comment and so forth.

It is now on the books. If you want to deviate from it, if it just not a sloppy deviation, just a failure to implement.

If it is in principle, we have now become convinced, show us why you're convinced of that.

DR. CHARO: Yes.

DR. CAPRON: It seems to me it would not be unreasonable for us to say if there is going to be an effect, an effectual rewriting here, it ought to be done in a way which is subject to review based upon evidence that it is justified to change the rules.

DR. FREEMAN: In a way, this discussion, however, is already passe, meaning major --

(Laughter)

DR. FREEMAN: Major agencies that they caved in effect.

DR. CAPRON: Well --

DR. FREEMAN: I will also use a different

term. In seeing that there was going to be a public report by a prestigious national bioethics advisory commission --

(Laughter)

DR. FREEMAN: I think. At least, it is coincidental with the fact that they realized there is going to be this report and received in a draft what we had written have now begun activity.

DR. CAPRON: Could you put in the fact that you are going to publish the pictures of the Secretary --

(Laughter)

DR. FREEMAN: And it seems as though the draft is in effect they are going with their feet in the sense they recognize whatever is the reasons -- whatever are the reasons why they haven't done it in the past is probably not going to look good.

This is my guess. I mean, I haven't gotten on this report.

That it does seem coincidental that that is happening.

DR. CHARO: It is probably just as well because no matter how much you say the burden should be on them, the fact is they are not -- we are not

in a position of advocating civil disobedience in which they are simply allowed to say, no, I choose not to implement the regulations.

(Discussion)

DR. CHARO: Or let me make my arguments for why they don't.

DR. FREEMAN: Yes.

DR. CHARO: But even if they have caved --

(Laughter)

DR. CHARO: Right. I would predict that the actual implementation is not going to be as good as you might like if it is being done in a grudging fashion.

And the way to get rid of the grudging fashion is to respond to what you have picked up in the survey and what they have sent in the comments that Randy summarized about what they perceived to be the obstacles, as well as what you have identified independently.

And this is where it is circling around again and again.

I suspect that the need for a one-stop shopping approach that there is somebody that is identifiable who makes the first judgment call about

whether or not something is research.

And if it is research, is it exempt? Or is it minimal risk where it doesn't need to be reviewed?

And if it needs to be reviewed, do we already have an IRB in place for multiple projects?

And if not, can we send this to somebody else to make it their headache rather than have to go through the single project assurance?

Or if I have to go through the single project assurance, can we make that as streamlined as possible?

It is a kind of step-wise approach to making implementation as rational, as tolerable as possible. And then, maybe get an extreme level of resistance.

DR. KATZ: I think in fact that what you say is the best justification. It is a justification that it will be, you know, in terms of implementation for non-implementing agencies.

And that is, you know, whatever you say, part of the problem that you run into is that there is no structure in place that helps them decide on this, you know, core issues.

So even if there is no research going on of much to anybody or no research at all or very little research or some research that, you know, falls in and doesn't fall in, the lack of a structure in place means that they have no place to go for anybody to make those decisions, no identified place.

DR. CHARO: Right.

DR. KATZ: So the lack of implementation in itself causes these agencies difficulties because they don't have any structure in place to deal with those kinds of issues.

DR. FREEMAN: I'm a little worried.

DR. KATZ: That justification maybe should be brought out more.

DR. FREEMAN: Along the same lines, we are worried. But what I thought was in there maybe hasn't -- we didn't see as strong enough.

When we talk about the -- especially independent agencies that have not signed on and also two departments at least that have not signed on, that for them to sign on, it is going to have to be much more efficient.

The system is going to have to be much

more efficient. And we give the example of the Civil Rights Commission.

I mean, here is a group, the base office, you know. Once in awhile, we will do a survey before -- shortly before a meeting, a public meeting of what is the -- what is the feeling out there in the community where they are doing the survey -- I mean, where they are having the meeting about whatever the problem is.

They simply don't have the infrastructure to have the lead time nor the amount of people to have an IRB and go through that whole process.

There needs to be a way for them to do the research that is exempt or have help in a very quick review of things.

I thought it was in there. And what I'm hearing is that it is not.

It seems to me that if we are talking about, as one of the things in there, that's not just the signed-on departments that this covers now, but all the federal government, that much of the remainder is more like that kind of situation.

The variation in the amount of research done by a given agency, it varies from, you know,

one research, something or the other per year to the NIH obviously.

And in the same way with risks, you know. That is something that we found. And we need to clear it.

DR. CHARO: The agencies and departments are covered. And obviously, you want to make it as easy as possible.

But I think it might actually make some sense to try and see if we can identify any actual injury at all, any because they are not already subject to the regulatory requirement.

The burden of proof is not on them to say, no way, to say, no, I don't want to sign onto this. They don't have to do the implementation.

And yet, I don't think you need to have a pattern of injury. I think when the federal government or any governmental entity is in charge of inflicting an injury on somebody, the injury is doubled because it's not the injury intrinsically, it is also the fact that it was done to you by your own government. That makes it doubly offensive.

DR. FREEMAN: Right.

DR. CHARO: And it really should not be

tolerated. And so it would be helpful if there was some minimal amount of document about non-implementing agencies as well that we could use as an example of why you would want to extend this.

So part one is, yes, you need to make it easier for the ones that signed on.

That becomes a model for the ones who have yet to sign on and see how doable it is.

And here is why they should be told that you really must do it. And it's really at the level of the White House to direct the departments to comply.

CHAIRMAN CHILDRESS: Harold.

DR. SHAPIRO: Alta, several national bodies have decided that it is important to follow a certain process, not only because harm may be done, but because some wrongs may occur.

And it seems to me that you would be fundamentally -- if you are going to hook an agency's signing on to some demonstration of harm, you are going to be in a very fundamental way reversing the judgment of some pretty seemingly groups that it is important to have this structure in place because even if there is no harm, there is

going to be wrongs. So --

DR. CHARO: I am not really thinking of condition. I am saying it strengthens the case.

DR. CASSELL: Yes. But the problem is that it strengthens the case. But then, somebody says, so how common are those instances?

And then, you are stuck up against the idea about that again.

The minute you bring one piece of data out on the scene, you are up against, well, what is the baseline and what is the, you know -- not only what percentage of the injuries.

And you cannot answer those questions.

DR. FREEMAN: But I hear Alta saying we need to make it strong. I would suggest that we not lightly -- we will not be very productive to go looking for cases of demonstrable harm or wrong.

What I'm also hearing is that we have not made the case that -- strong enough about why to extend them. I mean, some of the discussion has been that.

It does seem to me -- and I have asked that it be put at the very end of the agenda something about community perceptions of that

meeting at CDC in the past two days on community participation in research.

There is a lot of anger out there by the sizable proportion of the population about past injustices in research and very recent injustices in research.

And the reason I think to have the regulations is to try to minimize that by every single federal agency the chance of it happening.

And the trust issue between the population and the government is I think the bottom line. That was what after all motivated the National Commission, both the trust on the part of the population --

DR. SHAPIRO: So everything ought really to be debated. And if something comes out, the commission will be aware of the changes that are being made is that we are moving to a point of having something that we want to fairly state in the text.

DR. KATZ: They are on the bottom. I just can't remember having seen any drafts which ones.

(Discussion)

DR. CHARO: It may be this one.

DR. KATZ: Right.

(Laughter)

DR. KATZ: And sometimes, we did cut off or add it.

CHAIRMAN CHILDRESS: Harold.

DR. SHAPIRO: I want to pursue a less important aspect of the issue that Alta raised when she pointed to the fact that there may be some correlation between the nature of the activities and the nature of the attitude towards this common rule.

And there might be some insights available. And I think it is a very interesting point.

I do not know where it will lead, but it will be very important to look at.

That leads to a second issue which I found missing from looking at this. And I call it an issue of scaling.

That is some agency is not a component. I don't know if they do one research project a year or 100,000 research projects a year.

I don't know if they -- what kind of research they do. And so I'm finding it very hard especially when there is so much speculation in the

report regarding what the motives are.

I found it very hard to think about it. I mean, I have no reason to second guess you, but I have no reason to say, yes, I was right.

All because I simply don't know enough myself about the nature of the research that is going on and whether it is not -- if it is reasonable to kind of think that they were exempt, for example.

Isn't that just an artifact --

DR. KATZ: Can I also before you go on throw a question back to you because this is a fundamental issue that I think the commission needs to address to give us some -- and that is how specific do you want to get about agencies?

I mean, our struggle throughout this is that we do not want to target agencies in ways that are not helpful, although we feel that it is certainly appropriate to use agency specific information when it is illustrative of larger problems.

But the kind of thing that you are talking about, we certainly have put in and have cut a lot of it out, you know.

We don't know how specific or how much information you want about different agencies.

DR. CAPRON: I thought that part of the reason it wasn't in there was because you were giving the agencies to opportunity comment on the material you were going to -- before you shared it.

DR. KATZ: It will be in there in tables and thing.

DR. FREEMAN: But before you commented on it.

CHAIRMAN CHILDRESS: This is the question that Harold asked.

DR. FREEMAN: We can put it. And we did not put it in. And I totally agree that it is needed there.

DR. CAPRON: I expected it to be there. And I thought, well, it is not there because you are giving them a fair chance to make sure you got it right before you --

DR. KATZ: It's right in the narrative of the agencies that we actually discussed.

DR. CAPRON: Just the way you said it. Just the way you said it.

DR. CHARO: I think rather than tables,

you are asking the reader to pull it out. A narrative that says, well, we found evidence of a very widespread violation of the common rule with respect to non-invasive research whose risks are primarily risks of loss of privacy, dot, dot, dot, dot, dot, dot, some of which may be seen as trivial, but nonetheless -- which are really quite real and let us explain why.

It is a suddenly a woman's privacy is breached. She is subject to battery because of the information that has been revealed, etcetera, etcetera, etcetera.

So that you get this opportunity to teach as well as to give some scaling.

Then, we found moderate level folks of particular agencies of lack of implementation on this particular kind of invasive thing.

These kinds of physical risks gives the reader a chance to get a sense of what level of outrage or concern or indifference is appropriate as a reader.

And that will then help set up the recommendations.

DR. SHAPIRO: We have --

(Discussion)

DR. SHAPIRO: In evaluating this situation. I don't know long it is.

DR. DUMAS: This discussion makes me very nervous because you mentioned about the lack of confidence and trust people have in the government.

DR. FREEMAN: Yes.

DR. DUMAS: And I find the report rather equivocal which can do a lot to undermine trust if people feel that there is something that is being covered up.

And I think there is a way of giving an assessment of the scope of the problem in implementing a common rule without having to target a specific agency.

So I don't you have to necessarily target an agency in order to give a more accurate picture of just how much this is being -- the common rule is being adhered to and where the gaps are.

And I think we need to be as open and as factual as we can be about this because it doesn't make sense for us to spend the time that we spend trying to develop ways to advise on the protection of human subjects when the government itself is not

doing it.

And I certainly would not want to give the impression that we are going to turn our heads on that.

DR. KATZ: What you are talking about and we have had an ongoing, internal discussion about the way the data should be organized as well.

There is a description of the data in terms of incidence so that you have some sort of idea of, you know -- and that is sort of the last piece. And it hasn't been pulled together yet.

I mean, the data is there. There is a lot of data. And I think, you know -- I don't know of somebody will need to come in and do that or if staff will have time to do that.

But that is the kind of the last piece. We have overall impressions. But you are saying you need in the -- or you are saying you need in the report, you know, a moderate number of agencies.

DR. SHAPIRO: I would need some information so I can make an assessment myself of how I feel what's going on here.

Whether or not it will be in the report, in what form, I am not entirely sure about. I just

don't have the information. This is my concern.

DR. CASSELL: Maybe, we ought to have the data.

DR. DUMAS: That's right. We should have it.

DR. CASSELL: We should ask for the data so that we can look at it and see it.

DR. FLYNN: One of the pieces that was, at least for me, hard to assess was the situations where the agencies felt apparently wrongly that they were not out of compliance or that they did not have to have certain kinds of research covered.

Again, someone mentioned earlier, I would like to know that their thinking was. I would like to know what the scope of that problem was.

It was hard to draw a differential assessment of how well or poorly some of these agencies were doing in the category of not being in compliance.

DR. FREEMAN: It sounds like for balance, I mean, along with what has already been said, that you need to give the same numbers for the agencies that are in full compliance. You have a sense of --

DR. FLYNN: Yes.

DR. FREEMAN: The numbers. Okay. That will be easy to do.

CHAIRMAN CHILDRESS: Harold and then Alex and then Eric and then Alta.

DR. SHAPIRO: I will just say one more thing. And that is when it comes -- again, this, and it may be simply because I lack the expertise --

DR. CAPRON: That leads --

DR. SHAPIRO: That the others may have.

When it comes to recommendations to implement, I'm not sure what the best way for us to proceed is because I'm not quite sure what the procedures are for making changes.

The report talks about the federal government implementing this. I'm not sure if that is the best way to do it.

I mean, are we talking about federal action. I'm not against saying we call for federal action.

I want to understand what type of federal action we called for when we just say amend the federal -- when we say DHS ought to do this or the Justice Department ought to do this. I don't know what --

DR. CAPRON: I thought you were getting to the next level which is as to whether or not the regulations are in practice making any difference.

We don't have data in this report on that. And rather not the best way -- if we thought there was noncompliance at the IRB, one of the best ways to go about that would be to be federal action or some other action.

But I want to make -- I want to be careful. And I want you to be careful when you are writing when we talk about fully in compliance and so forth, the reader who isn't constantly attuned to that issue might think it means that we know that HHS which has procedures and processes to implement is fairly compliant and that HHS grantees are doing what the regulations expect them to do.

We don't know that. And we ought never to imply that we do.

Now, I don't mean to imply -- think that we should imply that it is not happening.

So full compliance or, you know, the regulations are working or something, it just the kind of thing we should be sensitive to avoid.

And we remind the reader of the limited

nature of the present set of findings.

DR. FREEMAN: What you are saying is that we need to make clear that full compliance means, on the one hand, when you are doing the research, you have the structures and processes in place.

When you are paying for it, you assure that they have those structures, but you don't you have the slightest idea about the quality of --

DR. CAPRON: You are sure on paper. They have given you a paper saying that their institution will obey certain rules, whether they are or whether they are like some of the instances we heard of major universities of doing that.

DR. FREEMAN: Yes.

DR. CAPRON: And only adventitious reports or particularly persistent injured patients finally get the spotlight shown.

We don't know whether those are highly unrepresentative, odd instances, or whether there is a more pervasive problem or not.

In recent times, talking to people at IRBs at major institutions, some of them have certainly expressed to me concerns about what their own institution does.

And, you know, how one person will say she was a relatively new member and she was just horrified. But she bit her tongue for awhile because she didn't want to be immediately seen as trouble maker until she saw a pattern. And then, she identified.

They were exempting whole areas of research that needed review.

And once she said, you know -- showed them what was in the regulation was she able to persuade people.

That is a major research institution. And I would bet dollars to donuts that no one here has any reason to think that that institution isn't, quote, obeying the rules.

We don't know. And we should not lead people with a false sense of assurance.

CHAIRMAN CHILDRESS: Susan and then Eric and Alta.

DR. KATZ: I think we also have to keep in mind, and I'm not sure that this is strongly enough stated, of what the limits of the current investigation are in terms of what it shows about efficacy of implementation which is what you are

talking about.

DR. CAPRON: Yes.

DR. KATZ: I mean, we really -- David is really focused on structures and structural issues, although in phase 2, I gather has gone beyond that to a certain limited sense.

But all we could say in the best of circumstances is that a department or agency that funds extramural research has those structures in place which would seem to, you know --

DR. CAPRON: Provide some assurance.

DR. KATZ: Exactly. And that is the limit that we could say based on the current investigation.

If we think that there is a pervasive, we might want to recommend further investigation. The actual ethicacy of implementation is probably the next step anyway.

CHAIRMAN CHILDRESS: Eric.

DR. CASSELL: Well, all of this once again makes me think that we ought to have -- ought to provide the commissioners with the data and because I can see a lot of things happening after the report comes back.

And I can see the newspaper talking about how the government is not in compliance and so forth and so on.

This structure that you are talking about, in fact the data may show something much less than that.

Also, since much of this is interpretation, we ought to see what you are basing your interpretation on.

CHAIRMAN CHILDRESS: Alta.

DR. CHARO: I would like to --

CHAIRMAN CHILDRESS: I'm sorry.

Bill, do you want to respond first?

DR. FREEMAN: I was just going to say along the lines -- and we can't answer that now.

The purpose for being in the pros, the positive agencies, we described them first and then, the ones that needed help, shall we say.

And then, in the conclusions, if you noticed, we reversed the order, very strong and negative.

But then, also a positive conclusion on what to do about that is extended.

That is something that I think the choices

there, obviously, those are yours, how to emphasize what and what sequence, etcetera.

And what I'm hearing is that before we make that decision, you would like to have a look at it, have all the tables, and what is the sense of weights.

I can go through it quickly.

CHAIRMAN CHILDRESS: Sure.

DR. FREEMAN: Scaling and weights so you will know how. Okay.

DR. CHARO: I would like to throw out an idea and just get reactions to it for a different thing to add to this report, totally separate from the data.

Going back to what it is that stormed this inquiry which is the Radiation Committee's work, okay, I am also wondering if it wouldn't be good for public relations purposes as well as for making it more useful to the public and the President, at some point to go back to the major scandals in research that have had any connection to the federal government or through actual direct intramural research implementation.

Approach one of them and say, all right,

in what we have learned about the federal government, could that still happen today? Yes or No. And if not, why?

And then -- I know.

(Laughter)

DR. CHARO: But the point of all this except to figure out whether or not the scandals we are familiar with have been adequately addressed so far.

And part two is, this is where I'm sure we -- but kind of create a little mythical department that doesn't exist and give it a status similar to that of some these agencies that have not completely implemented their regs.

And begin to outline exactly the kinds of things that could still happen today based on our information and why that is a problem.

In other words, try to put a very concrete, comprehensible space to all of these information.

For the purpose of dealing with the credibility gap, it is essential that we address whether or not the things that people are still complaining about are still problems today or

whether we can finally put them to bed.

And then, we need to be very honest about what it is that people should still be worried about and how it is that that then leads to the recommendations.

DR. SHAPIRO: Would you say that it is much likely to happen today?

DR. CHARO: Yes.

(Laughter)

DR. CASSELL: They never made a set of regulations that will keep people from getting around the --

DR. CHARO: Yes, I know this. I understand this.

But, you know, look, some of the scandals took place at a time before we even had any of these regulations.

And it is worth as a public relations issue to say, you know, no, we can't no secret research for which there was no consent and there was no knowledge because we now have regulations that say this is absolutely -- you know.

So at least you can say it's now against the rules.

DR. DUMAS: But I'm exempting those rules.

DR. CHARO: You are personally?

DR. CASSELL: No.

(Laughter)

DR. CHARO: But do you catch my meaning? At least we begin to identify where we need some progress in a concrete way for credibility purposes and then to also to create some concrete situations that exemplify the gaps that remain.

DR. CASSELL: Informed consent is the thing that is lacking from the big scandals that there are out there. It's informed consent.

DR. FREEMAN: But not the only thing.

DR. CHARO: Not the only thing.

DR. DUMAS: That's not the only thing.

DR. FREEMAN: Jim, can I bring up the letters from the last time?

I think realistically having been exposed and listened to these, some of the scandals and at the meeting that it was said for the past two days in which there were a lot of community people very angry that people, researchers who did recently bad things to people in the research of using measles in LA, for example.

Nothing bad has happened to them. Now, the amount of anger and passion to that is -- and then as I thought about it, it made a lot of sense.

I mean, large numbers of people in their communities are being in jail for all sorts of things. How come other people aren't being put in jail when they do bad things?

It is people who are wronged, the person who goes in the house. You get angry. And there needs to be some response to that.

I, as I said didn't appreciate, until the past two days.

It seems to me unrealistic that we will be able to prevent every bad thing from happening by regulations.

But we have yet to pay as a nation or as a system or whatever you want to call it attention to what happens when the system fails.

And so something bad does happen. How do you minimize and respond to it appropriately the resulting wrong?

What happens I think is that the response that generally has been done from at least hearing the community people, their interpretations is that

it compounds the wrong.

Step after step after step, our response, our meaning the federal government's response has been to increase the anger as opposed to deal with it directly.

And one of the questions may be -- this was not the focus of our survey. And I don't know if it could be in this report or if it is something that you want to pay attention to in the future reports.

It's how to plan for when the system fails to prevent the problem, how to intervene appropriately, respond appropriately to minimize the loss of trust, minimize the anger, set things right appropriately, as opposed to long years later and it is still festering.

Do we want to do that? Is it the nature of the problem that really propelled the National Commission which was a concern about the potential loss of trust in the research enterprise?

DR. CASSELL: Henceforth, the government will leap forward to say we did the wrong thing and we are terribly sorry on the first day afterwards.

I don't just see that happening.

DR. FREEMAN: I don't see it happening. But it is also true that the response has not been -- as I said, I think it has made things worse.

I think there is something that could be done. And I'm not saying that means to look.

I'm suggesting that it may be something that you might want to look at and propose for the federal government to learn how to do it better.

My assessment, personal is that the record has been atrocious.

DR. CHARO: I'm not sure how -- let me go back. I will go back to Harold was when he asked for something that will help him understand how to react to all this.

And step one was more of the underlying data. And then, my thinking was that will help, but I don't still think it is going to get us all the way because it still requires too much work on the part of the reader to interpret it.

And so the suggestion was to try to find some way to make more concrete the degree to which the current situation is perilous or comforting.

And maybe, the best way isn't to address how previous scandals would be handled by today's

rules, but I would love to find some way of doing it.

And I think if you want to talk about issues about punishment following a scandal I think is only one piece of the question of how credibility is restored and how much work needs to be done in changing the current situation to make sure that credibility is maintained.

Nobody is claiming that you can create a system that is going to be error free. And that is a straw man that you all have fun in knocking down.

But you can assess whether or not the current regulations even have the theoretical capability of preventing a prior scandal.

Because if they don't even have the theoretical capability of preventing it, you know you've got a big gap.

If they have the theoretical abilities to do it, but your survey has demonstrated that the agencies who haven't been implementing the key regs or don't have the understanding of how they operate, then that's another way you can answer it.

But I just feel that there needs to be something more vivid, more case oriented to bring

out the conclusions that we want to bring out.

DR. KATZ: Can I just make a suggestion? And this may not be responsive to what you're talking about.

But there is a sort of very brief couple of sentences which talk about what actually has happened in response to prior commissions and committees and their recommendation.

And it is quite a lot. And in fact, you know, we are a good bit along the way. And I think it is just in that section where we talk about the five or six things that these commissions have considered in the past.

And in fact, three of them have been fairly completely and well considered and have lead to real actions in terms of both regulations and structures and some very good underlying ethical principles.

That is a hell of a lot that has happened over the past 25 years that maybe deserves greater emphasis upfront.

This goes to what Bill was asking in a decision which you have to make, a fairly fundamental decision which is, you know, what do you

want the report to say?

Do you want the report to focus on what needs to be done and the risks that are still out there?

Or do you want the report to focus on how far we have come, but with some attention to the fact that we need to go further?

I mean, you can write two very different reports from exactly the same data.

The problems that remain may be significant in those agencies. There are fairly significant problems in terms of dissemination of information and interpretation of regulations and all sorts of things which are significant when you talk among yourselves.

They may or may not be significant out in the field. And you may not want to emphasize them that much.

But we need I think some indication from you whether or not you want to go back and focus perhaps in the historical section on exactly what you're talking about which is, you know, how far we've come.

It's only in a few sentences here. It

leaves a lot to those of us who know an awful lot about it, but may not mean very much to people who don't.

CHAIRMAN CHILDRESS: I think one reason it's difficult to answer the question you raise, apart from a sense of scale, to use Harold language, is we don't have for the few agencies and departments that have not implemented the common rule, we don't even have a sense of how much they do. And how many research subjects are involved?

And so that becomes a kind of basic starting point before the questions I think can be raised.

One of the things that we have stressed so long is that at least given what we heard early about the number of departments and agencies that were in compliance and the numbers involved there and the basic biomedical research and basic research, etcetera, that the progress is being one that certainly we would want to emphasize.

But one can do that without denying the dark side, too.

And I guess where the discussion at this point is roughly you persons have done a great job.

We've got -- the report is at a point where we now need to make some very difficult decisions that may shape the tone and so forth, but we need to I guess look at that information and very quickly respond.

And then, we need to think about ways to use Alzheimer's in making the recommendations more vivid and the like.

Is that roughly a fair sense?

DR. CAPRON: I mean, the danger of going too far the way Alta says is that unless you are going to recite examples, and we've heard some here of things that are post-regulation, are post-common rule and are a problem, unless you have a whole bunch of those to recite to indicate that there still are problems, I'm worried about drawing any strong conclusions for the reason that we are just talking about this top level.

And if there are more instances like the ones we have heard, we should be worried.

If those are highly local problems having to do with, as it were, institutional pathology, then we don't have to be as worried and we don't really even lay it at the door of the federal people

who are doing what they can do.

And there will always be some people who skirt regulations or don't understand them or whatever.

So that, you know, we are not talking about the perfection here.

DR. CHARO: Well, for example --

DR. CAPRON: But I just don't feel comfortable -- I mean, I feel comfortable if we have problems in using them because as long as we are not misrepresenting them, they indicate that there are problems.

But the absence of reporting instances to us leaves me --

DR. CHARO: Right.

DR. FLYNN: Agnostic as to whether or not there is something more that we should be worried about.

DR. CHARO: Well, I mean --

DR. CAPRON: And how likely the past could repeat itself.

DR. CHARO: Certainly, things the reports about the VA research in the '80s provide one source of things to take a look at and whether or not that

was due to isolated misunderstanding or if that had something to do with the way in which the regs were being implemented is illuminating.

Some of the concerns that have been raised about survey research that actually does reveal private information and puts people at risk of gang violence or battery or other kinds of responses which is current which was never reviewed.

It is being counted as, you know, part of our research protocol, but clearly never got reviewed.

So it wasn't being seen within that department as something that needs to be reviewed is a current example that relates to the current regulation implementation.

It may not be much. I'm not sure that there is enough there.

DR. FREEMAN: There is actually a fair amount, the part that we wish we had. And then we had the meeting on the 9th. And so we had to scrap what we had written.

The basic substance really hasn't changed. It's more than just privacy. When you are interviewing people about their experience of crime,

there is not a whole different for some people than interviewing them about the death of their spouse or parent.

There is a lot of emotional overlay that comes out that you are not prepared to deal with if you are actually -- them at the time of the interview.

Simply by raising these emotional related issues --

DR. CAPRON: Are these victims of crime?

DR. FREEMAN: What?

DR. CAPRON: Victims of crime? Victims?

DR. FREEMAN: Yes.

As in the example, there are lots of possible wrongs that can occur in survey research beyond just privacy.

And we see protocols that have that as a potential. And it is insignificant. It probably doesn't --

DR. KATZ: I think it's going to be very difficult to go too far down that road because in the case that Bill is talking about, and this is the one agency that I actually went to take part in an interview, they indicated when they talked to

victims of crime that in fact it was quite cathartic for them and they welcomed the opportunity.

So that you need a whole different kind of study again to find out the level of information you're trying to get at I think.

DR. SHAPIRO: One of the things that Alta said was that there is a series of levels here.

Level one is are these agencies making a good faith attempt to implement this regulation in ways that are reasonable and likely encourage appropriate behavior out there in the field, whether it is intramural or -- that is a question that can be answered I think even if there is a lot of that?

And then, they have that. And there still may be a lot of bad stuff going on. That's because there are other steps in this that we are studying that are being implemented properly. Well, they have to be studied some other time.

And it seems to me as I understand what you've done, we are in this first phase. And to take the example you have given, is this interview cathartic or is it emotionally difficult for you?

At the level we are at, that is not the point. The point only is, is somebody asking the

question? Is somebody in a position to know, evaluating this thing and saying, yes, that is a reasonable thing?

DR. FREEMAN: To pay attention to.

DR. SHAPIRO: To pay attention or not. I mean, we don't have to decide at this stage just to take that example. I understand that it is just one of many possible examples.

DR. CAPRON: But certainly if we have the example and the answer is that that agency was not requiring anyone to think about that because they thought --

(Discussion)

DR. CAPRON: Then, that's an illustration. That's an illustration of the category you want, a problem that we can show that has happened.

DR. SHAPIRO: Yes.

DR. CAPRON: Where a harm has happened because the rules weren't being implemented.

DR. KATZ: That will be in there. That, as Bill indicated, was taken out, that whole section.

DR. FREEMAN: Because it needs to be rewritten. It's still the substance that we were

saying.

DR. CAPRON: Okay.

DR. FREEMAN: But I want to get back to what we were talking because some people said people should be put in jail.

I want to be clear that was not my suggestion way back to the previous discussion.

But the question about what to do when there is a failure reminds me of airplane crashes. The major effort is to prevent the crash.

But with the airplane crash, we have also learned that emergency departments near major airports need to be ready for mass casualties. And they practice that.

So when the airplane crashes since it is not if but when, at least there will be a better possible response to save lives than might otherwise occur.

Let me ask. In that context should NBAC be looking at or should we say anything about even now or in the future the system that as far as I can tell is fairly nonexistent which is to fashion appropriate responses to failure of prevention of harm to participants in research?

CHAIRMAN CHILDRESS: That is something that we probably should look into in the future.

But I think there is a problem with the analogy is one worries about a system in place to deal with moral failures because it may well end up being simply then the kind of protect yourself sort of arrangement.

In other words, have a system in place to deal with the failures, I think of may be problematic.

At least it is something we need to think about a lot farther. I think it would take us afield from this.

Actually, we have passed the time for the break. But I sense that, number one, that this has been a very fruitful discussion.

And number two, we are not far from getting finished with this. And I think that we ought to go ahead and move forward and just finish our discussion of the federal agency and not take a break now.

And then, I'm not sure we actually have a lot left to discuss.

DR. CAPRON: Could I invite Bill to write

--

CHAIRMAN CHILDRESS: Yes.

DR. CAPRON: What he was just thinking about. And I don't have clear what the impetus for that is, the discussions you were privy to and to the extent that this is some topics on the record and you couldn't put in the report, particularly if there are other sources other than your own experience with it were published or --

DR. FREEMAN: It was not part of the survey. We didn't ask any question about it in the survey.

But I will write that up as a separate --

DR. CAPRON: What you are reporting was the hearing in Atlanta or a series of --

DR. FREEMAN: The Center for Disease Control response at a meeting, Thursday and Friday in response to the President's Tuskegee apology.

One of the items he charged Secretary Shalala with was to reply within six months about -- which is November 11th or something other -- about community participation in research.

So one of the things they are doing is they got together six agencies. CDC was the lead

agency, but five others, including the Indian Health Service, community members, researchers, and us bureaucratics, a small group of about 80 to discuss it.

And it was, as I said, an eye opener to me. But as I thought about it, not at all surprising, once I thought about it about the anger that persists about unresolved.

DR. CAPRON: Yes

DR. FREEMAN: Okay. And I will write it up.

DR. CAPRON: What I am saying is that between what you know and what is in the Secretary's November 11th or whatever report, it would really be helpful to see it on paper.

And then, get a sense if we are in agreement.

DR. CHARO: Jim, I also think that this something that needs -- that either is going to be or needs to be introduced into the contract papers on the appropriate place within the government, an overseer of this research because clearly in terms of questions about response, the first action that people have is that OPRR can go and investigate.

But OPRR, because of its situation within NIH, does not have the authority for force action on other agencies.

And within HHS, it is faced with bureaucratic conflicts that hamper its independence and effectiveness on the nature of the fact that is low down in the food chain.

So that a lot of the issue about appropriate response is going to be tied up to the appropriate regulatory location for this.

And that might be the place to get handling.

Since the first step to any kind of correction of a problem is going to be investigating what happened, right?

One last thing, I know that a lot of this stuff was about survey research and how that has potential for harm.

But can we make sure we don't get too hyperbolic in our speculations about that harm without hard evidence?

Do you think it underlines credibility if we speculate too wildly on that on the middle-ground level?

DR. FREEMAN: I think -- I'm sorry.

DR. FLYNN: I'm sorry.

DR. FREEMAN: Go ahead.

DR. FLYNN: It would help if we could get, now having settled this, a summary of where we think we are at the next iteration.

CHAIRMAN CHILDRESS: That is, first of all, when we can get information. And that has been requested by the commission, our subcommittee.

Second, when you think chapter 3, is it 3 you will have?

DR. FREEMAN: Yes.

CHAIRMAN CHILDRESS: When you think you might have a draft of that.

And then, when you think it might be possible in terms of the next revision, whether we might have something prior to the 23rd for delivery?

DR. FREEMAN: I had stepped out during the meeting. We are meeting on both the 23rd of November and the 3rd of December.

CHAIRMAN CHILDRESS: Yes. The meeting on the 3rd of December will be a meeting to basically try to incorporate what we gained from the conference, the NIMH, and try to go ahead and work that into the discussion of decisionally

impaired subjects.

So that will be the only thing we will be doing at that point.

DR. FREEMAN: On the 3rd.

CHAIRMAN CHILDRESS: On the 3rd.

DR. FREEMAN: So we will be meeting on the 23rd November.

CHAIRMAN CHILDRESS: Right.

DR. FREEMAN: And you want it before that.

CHAIRMAN CHILDRESS: And when we were discussing that meeting on the 1st, we --

DR. FREEMAN: I did hear from the 1st to the 3rd. I didn't know about the 23rd was still on.

CHAIRMAN CHILDRESS: What do you think?

DR. FREEMAN: We will get something to you before the 23rd.

CHAIRMAN CHILDRESS: Okay. And you can get the information requested in the next --

DR. FREEMAN: I think we will get some information. If you want it all in one package, that might take longer, but we can -- I think if the major players, information on the major players to give you a sense of scale and stuff, probably within seven to 10 days.

CHAIRMAN CHILDRESS: Okay.

DR. FREEMAN: It should not a problem.

CHAIRMAN CHILDRESS: Okay.

DR. FREEMAN: I've got a specific question. It sounds minor, except it is how we write it.

As you sought to propose and in chapter 2 use and thereafter, the word "participant", research participant, research involving a participant, whatever as opposed to subject, all in the past, it has been subject in the U.S. in terms of official lingo and to include regulations.

The Canadian report, and as a matter I quote from it, has gone to the word "participant" because it implies a more accurate role for the person.

Certainly, the best cancer activist have said that they refer to their participants, not subjects of research, the ones that I have heard anyway and others as well.

The question is, should we continue that or should we go back?

It produces a little bit of confusion because of the old style and new regulations, but do

you want to make the change or not?

CHAIRMAN CHILDRESS: Well, I am speaking personally. And let's directions from others.

I have no problem with that as long as we just -- if at the outset will indicate we're using participant to cover the category that's often discussed as subject.

And I think there are probably good reasons, as you have indicated for moving to participant.

But what responses -- any responses from others?

DR. FLYNN: We use the word "participant" for very much the same reasons that it applies a different kind of role as in relation to the decisions and a partnership that it is what we are trying to affect.

And since it appears to be a term that is coming into usage among a variety of patient groups, if there is no objection, I think it leaves its own semantically in good directions.

CHAIRMAN CHILDRESS: Okay.

DR. KATZ: If you want to serve on the other side. There are kind of running arguments

about this. And I will concede graciously if there is a consensus.

My only problem with it has been that -- a, it is has been used historically. And it does appear in the regulations.

So that you are setting up something. You are introducing in some ways a whole other issue.

My impression when that is done is that sometimes it's more of an impediment to understanding than it is a help.

For example, when you start doing "she" instead of "he", you know, I find that all I do is every time I see "she" instead of "he", you know, I then start thinking about that issue instead of what I'm reading. So that's one issue.

And the historical issue and the issue of how it appears in the regulations.

The other thing is that just last week or the week before on the IRB Web site -- I don't know how many of you are aware of it.

It's an IRB Web site where people who are involved in sort of the day-to-day running of IRBs discuss issues.

There was some sentiment done when you

were on the road, some very strong sentiment that if -- that one should not dissemble that in fact when you call research subjects, they are aware that they are in a situation that is different in kind from a clinical situation or from even the ideal situation where they would be real participants.

I mean, in fact, we are talking in this country about a situation that doesn't exist much where people are real participants in the research endeavor when they are subjects.

So there are a lot of issues. And I don't have any major problem with using the word "participant", but I think there are issues that you might want to think about.

CHAIRMAN CHILDRESS: Okay. In response to Susan?

DR. CAPRON: I'm afraid Trish and I were distracted as this was first raised, a kind of a sidebar with Henrietta.

I think from what I just understood, chapter 2 uses participant which I know this. And you were trying to justify that change.

DR. FREEMAN: I didn't raise the footnote.

DR. CAPRON: Right.

DR. FREEMAN: Actually, this is a decision for the --

(Discussion)

DR. CAPRON: I'm with Susan.

DR. BACKLAR: You want subject?

DR. CAPRON: Yes.

CHAIRMAN CHILDRESS: And subject need not imply -- I mean, basically, if you think about it, historically from subject, you meant -- it captured some of the agency as well of one being studied.

(Discussion)

CHAIRMAN CHILDRESS: But historically --

DR. CAPRON: Yes, I always thought the subject was the object of the research.

DR. CHARO: The what?

(Discussion)

CHAIRMAN CHILDRESS: But at certain points, we sometimes mean to shift the language to recapture what's involved.

I don't feel strongly about it.

We had two nos.

DR. DUMAS: I don't think we --

CHAIRMAN CHILDRESS: It's more than a trivial matter I think.

DR. CHARO: It is.

DR. DUMAS: I don't know that we should change the common parlance in this area. And my sense is that subject is more widely used in the research area than is participant.

And although we may make a good argument, there might be some value in not changing the nomenclature.

CHAIRMAN CHILDRESS: We may decide to change, but this may not be the report in which to do it.

DR. CAPRON: Right.

CHAIRMAN CHILDRESS: We might want to do it in --

DR. DUMAS: In the --

CHAIRMAN CHILDRESS: The decisionally impaired subjects.

DR. DUMAS: Well, you might want to --

CHAIRMAN CHILDRESS: Rather than one that is actually trying to summarize where we are in terms of federal regulation.

DR. DUMAS: I'm comfortable with that.

CHAIRMAN CHILDRESS: So I think this may be the reason to -- I'm changing the view I offered

earlier. This gives me a reason to stick with it for this particular report. And then to think further about whether to change for --

DR. DUMAS: If you want to recommend that it be changed in this case, I would agree with you.

DR. CASSELL: Search and replace is done so easily, you know.

DR. KATZ: We have search and replace.

(Laughter)

CHAIRMAN CHILDRESS: Okay. Do I hear consensus to stay with it for this report?

DR. BACKLAR: Yes.

DR. CAPRON: Yes.

CHAIRMAN CHILDRESS: Okay. And then, we will consider whether to do it in the subsequent report. Okay.

Other things that we need to talk about?

DR. FREEMAN: Phase 2, just a brief report. In terms of looking at process, we found some -- so far some problems, nothing like the findings of phase 1 which are, you know, significant.

So I think it was much more important than the problems of not paying attention to certain

things in the process because is a process survey, not a researcher survey.

We have found actually coming up against the limits of the common rule or the regulations things that people expressed.

The most -- parts of the survey are that we don't know what to do with research work that harms or affects third parties that are not part of the people getting consent and, you know, they are not physically there and this kind of stuff.

As one example, genetics is an obvious one. As another, communities. These are IRB people, chairs, who are coming up against those problems and dealing with them.

So I think what I foresee is that the findings of phase 2 will be a listing of variably now realistically 20 year-old, 20 -- actually I guess it's 16 years old. It's '81 that the regs that then with the minor modification became a common rule.

And that modification in '91 was not intended to bring them up to date. It's intended to get the '81 regs agreed to by everybody.

Now, that is 16 years old. And --

DR. CHARO: We have spent a lot of time sitting in the rooms talking about this stuff. And I actually welcome the chance for them to review the documents and make responses and makes comments and feed that in.

DR. FREEMAN: You want them to review.

Now, what we have told the agencies is that they look at -- they will look at them.

First of all, we said their table, we --

DR. CHARO: Yes.

DR. FREEMAN: As a suggestion.

We also, before this meeting, those parts that mention the specific agency, went to the agencies.

The parts that had some mensurative pros with it, it was each agency, but only theirs.

DR. CHARO: Right.

DR. FREEMAN: So we didn't see someone else's.

It would be somewhat a change of rules for the Interagency Committee to see everything at this point. And then again, maybe, you would want to change yours. I don't see what the --

DR. CAPRON: Well, that goes back to a

question that obviously arose during the cloning report.

And I guess I just have a different take on it than everyone else.

We are a public body.

DR. FREEMAN: Right.

DR. CAPRON: When staff members or contract staff or part-time are written a draft. Of course, they work in their offices. They work back and forth on the drafts.

And maybe, stuff they put in, they decide to take out. There is a process here I think of giving people a fair chance to respond and avoid misinterpretations.

But once we come into this room, what's on the table in front of us ought to be available to anyone.

It would be ironic if the Interagency Task Force as collectively has this responsibility weren't able to see information.

I mean, the notion of confidentiality --

DR. FREEMAN: I'm not saying --

DR. CAPRON: Of government departments for their official acts.

DR. FREEMAN: I'm not saying --

DR. CAPRON: Makes no sense to me.

DR. FREEMAN: Yes. I'm not saying it was confidential. I'm just saying what we had said to the departments.

I suspect that the departments would not get upset if it went -- first of all, now that it is here and obviously it can go anywhere.

DR. CAPRON: But more important, in spite of what we said to the departments, this was going to be the sequence.

You are suggesting a change a change in that sequence. It's not because of confidentiality I am concerned.

DR. FREEMAN: All we said --

DR. CHARO: I --

DR. CAPRON: I'm just asking. That's all.

I don't think it's a change in the -- I mean, if you get people's responses and you now have a draft that you would be sending to us, why not say at that point to the members of the Interagency Task Force -- because that is the group.

If we recommend any changes in the regulations, that's the group that's going to have

to agree on those changes and implement them because they would be a change to the common rule. And they would all have to sign off on it.

And we might as well get their responses now. There may be some things that we think are wonderful, but collectively they think they are not. And then, we can be convinced we are misguided on.

CHAIRMAN CHILDRESS: You anticipate at this point problems in doing that.

DR. FREEMAN: I think their next meeting is the 1st of November.

CHAIRMAN CHILDRESS: I'm not saying a problem getting on the agenda, but --

DR. FREEMAN: No, I don't see any problem with it. I don't foresee --

(Discussion)

DR. FREEMAN: Oh, the 19th of November.

(Discussion)

DR. CAPRON: You can save it for the meeting. But if you discussed it on the 19th and we don't meet until the 23rd, then we can get at least an oral feedback.

DR. CHARO: I agree. I mean, without getting into the issue of what is or is not

confidential or what is a public record, I don't think it necessarily is a good idea to make assurances to agencies and then just back away from it.

But I also understand that the assurances are only for some things. Obviously, there was a public report that was going to be used for.

The assurance wasn't that nothing they said was going to get used.

So if there is a way to actually maintain, you know, to keep assurances and promises that were made, I would prefer that. I don't want to create problems that are unnecessary.

But clearly there is a document that summarizes things, that uses the information that is in essence the first draft of a public document.

That would be the best thing to share I think. And it avoids going back on an arrangement.

These are agencies we are going to be working with for a long time to come. And I certainly wouldn't want the commission to --

DR. CAPRON: Could I have the assurance though -- I understood the assurance was that they simply get a chance to comment.

And that is what they are getting now. That is an informational --

DR. FREEMAN: We also said that we would not be giving any -- we would not be giving their information to another agency.

DR. CHARO: Their original responses.

DR. FREEMAN: At this time of review. In other words, we weren't going to give the response.

DR. CAPRON: Right.

DR. FREEMAN: The question was, are we going to get to see the whole report? And we said, not before it's published.

And we said, thinking in the earlier draft process, you know, if it's still in getting feedback from the agency, we are not going to give what we give you for your feedback at the same time to another agency.

DR. CAPRON: Right.

DR. FREEMAN: That doesn't make sense.

DR. CAPRON: Right.

DR. FREEMAN: That is the assurance part.

DR. CAPRON: Now, you are getting that feedback.

(Discussion)

DR. CHARO: So after you've gotten the feedback, agencies can correct anything they think was erroneous.

DR. FREEMAN: That's right.

DR. CHARO: So that there is not an issue of misrepresentation at that point I think is perfectly fine.

DR. FREEMAN: Right.

DR. CHARO: So we can share.

DR. CAPRON: Okay.

CHAIRMAN CHILDRESS: Just for a moment. And that's why I raised the question. You're comfortable with that in terms of your dealing with the agencies that in effect would not --

DR. FREEMAN: What we can do is just simply just to make it clear we can notify them the first of next week that this is what we plan to do. If they have a problem with it, let us know.

But we think it's going to be very helpful. I don't think there is going to be any problem.

CHAIRMAN CHILDRESS: Susan.

DR. FLYNN: Can I just raise one issue that the commission might want to consider? And

that is are you comfortable enough, you know?

These conclusions and recommendations, as Dr. Shapiro pointed out, are very preliminary. They are based on data that, you know, that the staffs who collected it are very familiar with.

But the rest of us even some of us who are drafting the report aren't very familiar with.

Are you comfortable enough with the conclusions and recommendations that this is at the point that you want them to go the Interagency Committee for their discussion?

I mean, you haven't bought them into or signed off on them.

DR. KATZ: This is a good point. And actually, I wasn't thinking about those because I haven't bought into them at all yet because I haven't -- in the body of the report -- the body of the report still is working at making the argument.

DR. CHARO: Yes.

DR. KATZ: And that is actually the area that I was looking to get reviewed, not the conclusions and recommendations, but what was being drawn out of the survey in terms of patterns of implementation, significance of non-implementation,

reasons for non-implementation, attitudes about change.

That is where I was hoping to get some feedback.

Indeed, there is nothing in the conclusions and recommendations that anybody here has voted on or even tentatively.

DR. CHARO: Exactly.

DR. KATZ: And also, the rest of it, I don't know about the timeframe in terms of what you can have done before the 19th.

But a lot of what you are talking about that needs to be organized and then written about and then passed on, I mean, I don't know.

That is a tall order. I don't know if you are also working on phase 2.

And you are also working on -- I mean, realistically in terms of what the comments to do before the 19th.

CHAIRMAN CHILDRESS: Well, we can do what we can before the 19th.

DR. FREEMAN: I think on Monday, we can combine both all the -- and Alex's comments. I mean, first of all, it's clear -- it should be clear

that it would be what we said at that point since there is not another meeting from now and before the 19th is the staff.

DR. CAPRON: It is ours, not yours, not in review anymore by the commission.

DR. FREEMAN: So I will take the heat on it. It's wrong, it's wrong.

DR. CHARO: Why not just share the proceeding sections?

DR. CAPRON: But that is true of the whole draft. I mean, the next draft we will get --

(Discussion)

DR. FREEMAN: You are now saying it would be helpful even though you may end up doing something entirely different, at least you'll have -- they will have an opportunity to comment on what you're receiving at the meeting before the 23rd.

And that is great timing because by that time, it's, you know, what we sent out to you.

DR. DUMAS: I would be in favor in letting them see it as it. I don't have --

DR. CAPRON: If the Washington Post comes in and needs it and publishes something, they only thing we have to make sure if they say this was they

were commenting on a staff draft which the commission has neither approved or disapproved.

DR. DUMAS: Right.

DR. CHARO: Right.

DR. CAPRON: And it may or may not.

DR. CHARO: And I am sure that it will be redone. There will be a paragraph where they say that.

(Discussion)

DR. CASSELL: They can't do anything about that.

CHAIRMAN CHILDRESS: Okay.

DR. CAPRON: We are living in the real world.

CHAIRMAN CHILDRESS: Jonathan.

DR. MORENO: The recommendation you just put a draft on every page. It says that.

DR. CAPRON: Yes.

DR. KATZ: A draft.

DR. CAPRON: Right.

DR. CHARO: A staff draft.

CHAIRMAN CHILDRESS: Any other comments?

DR. CASSELL: I was impressed by that, too, Jonathan.

(Laughter)

DR. CAPRON: Well, you know, actually, Jonathan -- this says the working paper of the commission.

It really should say this is a staff draft being submitted to the commission for its review. I mean something like that to make it clear.

(Laughter)

(Discussion)

CHAIRMAN CHILDRESS: I think again, we have had a number of really good suggestions. I really think all those, the large group working on this.

And, Randy, I did mention you earlier. You weren't on the sheet. But thank you very much for your contributions, too.

But do we have other suggestions?

(Discussion)

CHAIRMAN CHILDRESS: Anything that you would like to add?

(No response.)

CHAIRMAN CHILDRESS: I think that this has been a very productive discussion of this. And, boy, the efficiency of getting out early.

Thank you all very, very much.

(Pause)

NEXT STEPS

CHAIRMAN CHILDRESS: The Next Steps. And I did a brief summary when we were talking about -- when we were meeting with the -- in back of the hole.

But I think we really do need to do something. We are talking about international research.

DR. BRITO: Jim, I want to say something. At the last meeting, Alta suggested that maybe we should approach that before we do the children and subjects.

CHAIRMAN CHILDRESS: Yes.

DR. BRITO: With the reading I've done since then on the international, particular the Ace trials, I think maybe it is more important to do that right now. Or not right now, after these two.

CHAIRMAN CHILDRESS: Given the scheduled meetings, we will be talking about doing something

the first of the year.

DR. BRITO: Right.

CHAIRMAN CHILDRESS: What we need to do is put in place a plan for that. And that means thinking about how we want to go about it.

We have received a lot of materials that have been made available both from a public citizen and from the federal government.

We also have to think about what we would like to do. Would we like to have adversaries at --

DR. CASSELL: I would like to hear adversaries.

CHAIRMAN CHILDRESS: Would we like to have contract papers that get at the issues? Would we like to have both?

And then, we need to get suggestions of people today and very quickly so that we can get something set up for an early meeting.

DR. CAPRON: I have a question about, are we looking at international work?

Or are we looking at certain types of studies where the questions really would arise if they were done here or elsewhere, but we have a sense that it is more likely that they are going to

be done elsewhere?

I'm not clear. The AIDS example is a complicated one.

CHAIRMAN CHILDRESS: Yes, it is complicated.

DR. CASSELL: What cultural rule -- I mean, whether cultural rules apply. What -- do our understanding of what is the right thing to do change as you look at it?

DR. CAPRON: Maybe. But that comment that was in the October 9th New York Times article in which the government official when informed that this was something that could not be approved in the United States expressed surprise over that.

And it implied that it would not have been accepted if that had been understood, known and understood suggested we are just dealing with a question of, well, those are the norms of another country and/or fiscal circumstances of another country that needed to evaluate risk benefits.

DR. CASSELL: That's not the issue. The issue is do those things have impact?

DR. CAPRON: I know. But to the extent that we are using the AIDS example, it's a more

ambiguous example than it originally appeared in which the justification was two-fold.

Well, I am not going to read the whole thing.

DR. BRITO: Well, the point is we are using these just as examples to raise larger the questions of what kinds of standards and procedures.

DR. CAPRON: Right. But are we particularly looking then at the international aspect because that is the one we want to look at.

DR. BRITO: Right. Because as I understand the way the -- right? Is that --

DR. CAPRON: Yes.

DR. CASSELL: But then, we had --

DR. BRITO: International research. I don't see it as ambiguous. Where is the ambiguity with the AIDS example?

DR. CAPRON: In that it was originally presented as -- in this country as something which couldn't be done here now for the practical argument, the reason.

That is now accepted therapy to do the --

DR. BRITO: Yes. I don't have the name. and I apologize for it. But there is someone. And

they think this is someone we can get. And I will give it to you by E-mail.

That there is a lot of U.S.-funded international research in AIDS right now. And the biggest argument here about doing a lot of this work is that because of cultural and financial differences in other countries, you cannot use the same rules as you do here basically for most of it.

Therefore, it is the basic rational being used for placebo control trials in things that have been proven to be effective here.

DR. CASSELL: Yes. But Alex is raising a separate question. Suppose you wanted to do an experiment here. We really want to do it here, but, look, we can't do it here because it's unethical.

Well, let's go where it is ethical. That's a different thing. That's --

DR. BRITO: Right. And let me finish. And there is someone, I think in Boston or somewhere that is doing some research that without the placebo control is comparable to the other research that is funded.

So I will get you that name. And I think we need to --

DR. CAPRON: Well, that is the issue that is going on in Thailand. And the argument as I understood there was it got approved because the NIH said we are doing the placebo in Thailand. Therefore, we in effect will have placebo control on this non-placebo control study.

And of those people, and BU I think it is, want to do that study that way. There may be a Harvard --

DR. BRITO: It's Harvard.

DR. CAPRON: It's Harvard?

DR. BRITO: Yes. There is one Harvard.

DR. CAPRON: Then, we okay that. I mean, if they say those scruples will insist on it. And our science won't be offended by it because we in effect have the control coming out of the same study.

That is a very different --

(Discussion)

DR. CHARO: You know, it seems to me that there is an initial question here about why? What is the scope of the interest?

To answer that, I think we probably all need to come up to speed to a common level of

knowledge about current standards for collaborative, cross border research.

There is a lot out there that exists in regulation. And then, there is a lot out there for CIOMS for the transcribers, the C-I-O-M-S.

And these things cover a wide variety of issues, ranging from cultural brotherhood and what constitutes an ethics trial to variations in what is an appropriate form of operationalization of things, like informed consent to things that are kind of in between, like what is it to be giving by consent and by whom where in some countries, things are really viewed more as a family matter as opposed to the U.S. tradition or at least the Anglo tradition of very much individualistic and everything in between.

And what constitutes coercion, etcetera?

There is a lot of work out there. And it may make sense to try to start first by getting everybody up to speed.

People like Bob Levine at Yale who worked with CIONS and Seth Fluce. He is going to be the chief of the Health Legislative Unit of WHS in Geneva.

Or even Dr. Cook from the University of

Toronto who served with the WHS Special in productive research could probably do a very good job of briefing everybody.

Then, after having gotten up to speed ask them to identify the areas where there has been a lot of consensus that's been workable and areas that still seem to be hot debated.

And we will then have narrowed the universe to questions that are at least still debated.

And we can ask whether or not this is a topic we want to take on and how much of it and what the scope of it is.

So in a sense starting from the AIDS trial of having that. We start with --

(Discussion)

CHAIRMAN CHILDRESS: I agree. The last time I raised some of the issues that --

DR. BRITO: I agree with that. And you have to take the -- prohibition consideration. I'm not disagreeing with that. And starting with the AIDS trial, maybe, it's too specific. Maybe, it's too narrow.

I'm worried that a lot of these cultural

issues are being used and the economic reasons are going to be used by pharmaceutical companies to mask what is really going on.

DR. CHARO: But is not an --

DR. BRITO: No, I understand that.

DR. CHARO: It is --

DR. BRITO: I understand that. I understand that.

DR. CHARO: I understand what you're saying, but --

DR. CASSELL: Well, why can't you -- which is very clear. Instead of diving right into the thing, we ought to find out where are we now, what has been the guiding principle before we start developing new --

DR. CAPRON: The other name in that regard is actually Bernard Dickens.

DR. CHARO: Yes.

DR. CAPRON: Who was Rebecca's husband. And I think those are the principal contract person who worked on the CIONS.

DR. CHARO: That was --

DR. CAPRON: I think --

DR. CHARO: (Inaudible).

(Laughter)

CHAIRMAN CHILDRESS: Okay. Any last word?

DR. CASSELL: Have a nice weekend.

(Laughter)

CHAIRMAN CHILDRESS: Thanks a lot.

DR. CHARO: Thanks a lot.

CHAIRMAN CHILDRESS: Okay. I hear a consensus directed along the lines of this proposal.

Jonathan is signaling me.

DR. MORENO: Can I just note that those members of the subcommittee who would like to get their writs in on this draft by line and/or page, calls, E-mails or faxes me within five or six days because I am going to start cutting and pasting?

And it gets very difficult to follow from one draft to the next what your comment is.

CHAIRMAN CHILDRESS: Everyone could respond by Thursday or Friday. Let's say Friday. Respond by Friday with additional points to Jonathan. Okay.

Any last comment?

(No response.)

CHAIRMAN CHILDRESS: Alta, do you have another proposal before we adjourn?

DR. CHARO: No.

CHAIRMAN CHILDRESS: Thank you very, very much.

(Whereupon, at 3:27 p.m., the meeting was concluded.)

C E R T I F I C A T E

This is to certify that the foregoing proceedings of a meeting of the National Bioethics Advisory Commission, Human Subjects Subcommittee, Bethesda, Maryland, held on October 19, 1997, were transcribed as herein appears and that this is the original transcript thereof.

WILLIAM J. MOFFITT
Court Reporter

1