34TH MEETING

NATIONAL BIOETHICS ADVISORY COMMISSION

September 17, 1999

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The Grand Ballroom
1489 Jefferson Davis Highway
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I N D E X

P R O C E E D I N G S

OPENING REMARKS

DR. MESLIN: I am going to get us started. Dr. Shapiro mentioned yesterday that he was not able to be here, so I think we will get started. There may be some other Commissioners on their way.

Diane Scott-Jones called to say that she had to return to Philadelphia because her house was flooded by the hurricane.

DR. CASSELL: Do you think it is because people do not like --

DR. MESLIN: We are glad that Eric Cassell was able to come in.

I spoke briefly with Harold last night and he made the following suggestions for today: I know that people have departure plans and the like which may have been disrupted by the hurricane.

DR. CASSELL: Do we have a quorum?

DR. MESLIN: Do we have one or do we need one? We are just starting a conversation here. We can ask Dick Riceberg (?) whether we can start talking at this point.

The suggestion that Harold made was that we should continue with the agenda as it is, which includes the proposal for a discussion that is found

in tab III-A and B of your briefing book, a memo from Jonathan and I about the "Comprehensive Report" and then a very sort of preliminary working draft based on that proposal. Obviously without all the Commissioners here, a decision does not have to be made or need not be made at this meeting and conversation can continue by e-mail, et cetera, but I would be just outlining what the general proposal was to see what Commissioners think.

Secondly, if there is any remaining time, we may want to go back to the priority setting memo that was distributed yesterday that you may now have had a chance to read. If you have not, we can discuss it anyway, but now that we have heard about the extension, at least it is a legitimate conversation to have about what reports will be taken up next.

So that is the general plan if that is okay.

I think what I will do is just very briefly remind Commissioners how tab III-A and B got to where they were. The memo should be self-explanatory.

The Commission had been speaking for some time about an ongoing and rather large report, affectionately called the Comprehensive Report for lack of a better expression, that was intended to collect many of the ongoing issues in human subjects

protections that had been on its plate for some time, including such issues as the appropriateness of OPRR's location and function, issues around IRB activity, the extension of the Common Rule beyond the signatories to other federal agencies and perhaps even beyond that to the private sector, and a number of other matters. It appeared to be a cumulative project that looked rather encyclopedic.

For a number of reasons, which I think are self-evident, Jonathan and I, and in discussion with Kathi Hanna, who hopefully will be here shortly, she is driving in this morning to be with us, we thought a somewhat less exhaustive approach would be helpful so we came up with the idea of an annual report or a status report on the state of human subjects protections, a model that would allow for a regular and relatively brief report to the White House on an annual basis. It afforded the opportunity to be both descriptive where needed and prescriptive if necessary.

There is nothing about either the memo or the working draft that is in any way carved in stone. We had asked Jonathan, who again regrettably could not be here today, to work on this kind of draft over the course of the summer and then through a number of

reworkings it made its way into the form that is in your briefing books.

So the first question really just to open it up -- I will not make any more remarks than that because everything else is commentary, is whether that general idea meets with your approval. If it does not and if you would like to forego or delay discussion until Kathi and others come, we can do that. We can do that, too. But I am, you know, happy to chat about any of the items in the document itself.

There is nothing magical about the strategy except to remind the Commissioners of the letter that Harold sent to the White House in May that this is part of our ongoing commitment to human subjects protections, that the letter on the 4th of May that mentioned several of the Commission's concerns about human subjects protections could be captured in this kind of there-part approach or two-part approach.

Eric?

COMPREHENSIVE SYSTEM OF HUMAN SUBJECTS PROTECTION

DISCUSSION OF PROPOSED DRAFT REPORT

DR. CASSELL: Well, I am a little unhappy to see the idea of pursuing the IRB question fall further down the agenda. I mean, we have repeatedly -- in anything we talk about, we talk about IRBs and then we

say how unhappy we are with this, that, or the other thing, and then when we start to make an agenda, we push that centric back down. The IRB system needs some help. That is charitable, isn't it? If the IRB system needs some help, let's go and try and figure it out, and if the result is to say we cannot figure out anything better then we ought to do it and say that.

But to talk about human subjects protection and then go through for individual research issues without the really underlying method by which we protect human subjects I think is a mistake. I would like -- I would like to put myself on record, Dr. Meslin, as moving that back up to the -- back up because it was up there for quite a while, and I think it should stay there.

DR. MESLIN: Just one point just to clarify. I think the draft document -- again we need not discuss this tab III-B -- spends a lot of time talking about what studies have been done on IRBs, what remains to be done. So I think there would be an attempt to keep it high on the agenda but you are making a plea for an individual report only on the IRB issue.

DR. CASSELL: Oh, yes. I must say that --

DR. MESLIN: Yes.

DR. CASSELL: -- if we want to have an impact as a Commission, one of the impacts we will have is we reform the IRB system or at least declare we cannot figure out how to reform it.

DR. MESLIN: Larry?

DR. MIIKE: I thought in the next section, our discussion about priority setting, that would be one of them.

Eric, we are going to be discussing what other reports we should be taking up. It seems to me natural that that can be brought then.

DR. MESLIN: Bernie?

DR. LO: Yes. I just want to add my agreement to what Eric said. I think that when I read the Human Subjects Protection 1999 Status Report, I think it is a very nice sort of overview summary of what we did, but it does not have the punch to say, look, IRB's are a major problem, perhaps the major problem that is on our agenda, and by not having -- have either its own report or a lot of prominence, I think we lose our -- we lose the opportunity to really try and make a difference.

I think we need a report that has specific recommendations -- I mean, we sort of said that we need to -- we need to do more. We need to extend the

Common Rule and do something to make IRB's more effective. But to be really specific and say we recommend A, B and X, I think, is what I would like to see us do, and we need to get some more information on that. I mean there is a lot of information out there. We have not really reviewed it. We have not really argued it out.

And I think applying ourselves to that either -- you know, I am not sure what the proper format is. I am not sure this is the report. This is a nice summary, but to follow Eric's thing, maybe it needs its own report and maybe that -- I would sort of argue that should be at the top of our list of future consideration.

DR. BACKLAR: I am going to echo and agree. I can only remember that a year-and-a-half or however long it was ago when we had a meeting in Portland, somebody in the public comment section stood up and said it is interesting you keep referring in these reports to the IRB but the IRB is going to do this, that and the other, but you also talk about the problems of the IRB, and we have -- yes, everything that Bernie said is true. We need to discuss it. We need to think this through.

DR. CASSELL: And then there is this

Commission's version of the weather, you know, when everybody talks about it, and nobody does anything about it. It is called education. We bring it up again and again. Remember education, remember education, please think of education when you think of progress.

(Laughter.)

DR. MESLIN: Okay. We will.

Bette?

DR. KRAMER: You know, I agree -- absolutely agree with everything Eric has said, but I would not even put it -- as strongly as I feel about education, I would not even talk about it in the same breath as the IRB because I think, you know, in every single report that we have written we make reference to the fact that IRB's need improvement, and we throw more and more burdens on the IRB when we know they cannot handle what they are doing now. So it seems to me it is even a matter of our own integrity. To just let this slip I think is sort of irresponsible on our part.

DR. MESLIN: One of the things that is possible in this proposal is a version of this 1999 report is something that can be done within the next month or two. It provides the sort of -- it keeps the

promise that Harold made in his May 4th letter that in the coming months there will be a more comprehensive summary of some of these problems.

What it sounds like -- Alex, we are talking about the status report -- that these are not incompatible ideas. A fuller report on -- whether it is IRB's or the extension of the Common Rule is, as Larry may be saying, the subject of a specific report, whether it is the 2000 annual report, and I am not wedded to this model per se, I am just suggesting that the idea has two purposes. One is to respond somewhat immediately and demonstrate comprehensively what we have said and the other is to pick up particular issues or items for the next report on human subjects protections.

DR. LO: If I can make a specific proposal, on page 43 right at the end of this very nice annual report, we said, "Over the next year, the NBAC proposes to consider the extension of the Common Rule." And I do not know if we are willing, as sort of Bette was saying, to sort of really follow through on what we have been promising all along and say that we propose to have as our primary focus or our next major focus both the extension of the Common Rule -- it seems to me we have several things we have been

promising. One is the extension of the Common Rule and the other is attention to how to improve and strengthen IRB's.

I would suggest that maybe we want to sort of package those together as things that we have talked a lot about doing and now we ought to turn ourselves to actually doing something about it.

DR. MESLIN: I think at the risk of asking you the same -- could you say a bit more about the Common Rule part just --

DR. LO: Well --

DR. MESLIN: -- partly for the benefit of the Commissioners who may not be here and have to read the transcripts but also because you have been thinking about it a bit.

DR. LO: Well, I think it is very much in the spirit of common sense that everyone else has been making that in all our reports we have said this is something that we want to highlight as being important and we are going to get back to it and really devote as much attention as it deserves.

I think now is the time to get back to what we have -- we have -- many times, and I think we passed a resolution at one point saying we believe that all human subjects ought to have the protections

of the Common Rule, not just those that are covered under the certain categories. So we have sort of said that is our position, but we have never really talked about what would that mean, how would we do it, other transition issues, who should be doing what, what else needs to be done to make it work, how do you bring privately sponsored research that is not going to be submitted to the FDA and not subject to multisite, multiproject assurance.

All those difficult issues, and we have not really tried to talk to those who are doing privately funded research who now are not subject to the Common Rule to say what would you think about that. Do you accept that? What do you see as the problems? How do you address public concerns that animals get more protection than humans do? Those sorts of things.

So again I think we are clearly on record as saying we think it is a good thing but just being on record is not going to have the impact, I do not think, as really sort of looking through the issues in a systematic and thoughtful way.

DR. MESLIN: Bette?

DR. KRAMER: Eric, I am wondering if there is any way that we could accomplish a report on IRB's without the full Commission having to devote a huge

amount of meeting time to it because I think that is the problem.

You know, we all got the OAG's report when it was issued, and I sure would not want to take a test on any of the particulars right now, but I remember reading it at the time and thinking it was very thoughtful, and it was very relevant. I know that there are -- I am sure, I do not know, I am sure that there probably are a lot of other proposals out there for redoing the IRB system.

I wonder if it would be possible for the Commission to engage a person who could pull together -- who could pull together for us the proposals that have been made, an outline of the proposals that have been made, could pull together from our own reports recommendations that we have made, you know, additional duties that we would like to see the IRB's take on in terms of -- on top of what they already have and kind of present us with a lot of the background that would make it easier for us to go forward and put together a document that we would be comfortable signing off on. I am just trying to figure out a way of shortening the process.

DR. LO: Well, I mean, I agree with Bette that there is a lot that can be done to kind of jump

start us, and I think her suggestions are sort of putting in one place all the things that we have suggested IRB's take on in addition to what they now have to do and that other proposals that have been made -- you know, just in the same way that, you know, long, long ago at the -- sort of the fertilization of the Human Biological Materials Report, we went and collected everybody's policies on research and put them together and said, "God, what a mess. A and B, A does not agree with B on anything and B does not agree with C." But at least we sort of identified what the issues are.

Then I think we have to sit down and say given all that is floating out there and what we suggested, is this feasible, how do we make it work, who -- what recommendations do we need to make as to specific people, organizations or groups doing certain things, and is that really going to do it? I think we have to be very practical in saying that given how stretched the IRB's are, how they are under staffed, how people are all volunteering, how there are really tremendous pressures now to use commercial for profit IRB's, what is going to happen.

DR. KRAMER: Right. And I think one more piece of that might be at some point, I do not know

whether it is before we take a look at it or after we have taken a first look at it, to sit down with OPRR, with Gary Ellis perhaps, and say, "Okay-dokey, you know, what would your office -- what would the system need in order to accomplish these following -- you know, the following proposals that we think are really critical to the IRB functioning?" And just kind of see if we could compile everything that is out there. If there is anything else needed, maybe we will think of it.

DR. MIIKE: Well, I think that is just part of the normal process we go through to put our report together, so it seems like we are already on the second part of our agenda, though. I mean, I have not heard from Alex, but I would guess he would agree with what has been said, but that sounds to be me like -- at least for the group that is here, that is our number one next report priority. I have some suggestions for some others, but I can wait.

Just returning back to this report, I think it is a good idea to have an annual report. The first one obviously would -- I think would be much more comprehensive, and I would like to discuss what the subsequent year one would be because they seem to be more perfunctory, and I would guess that if we

concentrate too much about what kinds of things have changed in a year, we are not going to see much progress. I do not think you see much progress in a twelve-month period. So I would endorse the idea of an annual report along the general lines of what has been recommended here and then try and move on to what subsequent reports might look like.

DR. MESLIN: Alex, did you want to --

MR. CAPRON: Well, my sense about the IRB process has been that until someone is prepared to talk about a percentage of research budgets being devoted to the assurance of the ethics of research we are going to -- most institutions are going to spin their wheels on this.

I mean, the -- I think what happened at UCLA is a good example. From all that I know, after the trouble that they got in a couple of years ago, they decided they had to spend a lot more resources, and they brought in additional people, brought in a new head of it, really beefed it up and anecdotally I believe it is running fairly well.

I suspect that Duke and the University of Illinois at Chicago and other places that get slapped are going to take a look at what they are doing and say we have got to spend more money. We have got to

have more professional staff on this. We have got to be able to answer our obligations of continuing oversight, genuine annual review, et cetera, et cetera.

I mean the issues have all been identified by us, by the Inspector General, that does not change things. Now there are issues which the report identifies here about the -- and identified by the burden lifting group that NIH put together about some things are being examined that ought to be dropped, that is to say, well, you do not really have the same set of concerns when you are doing certain kinds of polling, telephone polling or the like, and maybe that definition of research has to be refined or something.

The other thing that -- well, I will just stop there. I mean, I have a sense that at some point, we or some of us are going to have to come to grips with that. And the other good recommendations for tinkering around are just going to remain ideas until there are resources to do it.

DR. KRAMER: Well, maybe that is what we need to do.

MR. CAPRON: Yes. The other concern I had, which was specifically about the way we put things here, is I do not like talking about what amounts to

sort of internal -- not internal questions but questions that are being handled by our own research now. On page 43 there is a statement at the end of that paragraph that begins, "Finally we are currently conducting an analysis of the commerce laws."

I mean, when we have our analysis, if there are serious doubts that the federal government has the ability, as part of the process of oversight of activities, that I think are almost certainly going to have some commerce, interstate commerce involved with them, if it turns out there is a problem, we address the problem, but let's not. And there is just something, to me, that is awkward with saying we are currently conducting an analysis. That means somebody is doing some research. We do not have -- there could be 50 points in this thing where we would have that. It just -- it is not a way I want to express it to leave it unsaid.

DR. MESLIN: Bette, were you --

MR. CAPRON: I mean, I think what to me remains the issue with this draft as an idea of what we should do is the report on what the federal agencies are actually doing, what we make of that strikes me as a bigger task already, and it is a task that we have had -- is it three years now?

I mean, we began like gang busters on that initially, and all the federal agencies were doing what they were supposed to do in 90 days or something and then other things -- cloning came along and this came along and it just sort of put -- and this does not begin -- this report does not begin to provide that, and that seems to me at a minimum ought to be between covers of an annual report. Whether it is called an annual report or a first report on something, I --

DR. MIIKE: That would be covered by a Common Rules issue, right?

MR. CAPRON: I am sorry I missed that. I was under this impression, I had written down in my book we were starting at 8:30.

DR. MESLIN: Bernie?

DR. LO: I would sort of like to go back to sort of what Larry was talking about. We have got a couple of discussions going on here, and I think one discussion is on this annual report. The other is on our commitment to doing something on IRB's plus or minus the Common Rule and then other future research -- other future reports.

Just so we finish out the 1999 annual report, I think we all write annual reports, and we all get

them in the mail, and my guess is that I read only a fraction of the annual reports that get sent out.

DR. CASSELL: It would take a year to do it.

DR. LO: So I am just thinking, what are we trying to achieve here? Some of it is that -- you know, it is just a record that this is what we did in case you were curious, and so it is an archival document, but I think it is probably worth trying to think of who is our -- or who are our audiences because I think there are multiple audiences.

And what really are we trying to convey other than here is -- if you do not want to take up all the things outside the briefing room here that are the reports in toto here is a, you know, ten-page summary because, I mean, there are two ways to do it. In my cynical moments, I just say, well, just get something out that just is a laundry list. We did this, and then we did that, and then we did this. Or do we want it to be more of an integrated, you know, products looking up this year or storms ahead or something.

So a lot depends on -- we just want to do it, get it done, and say we did it. If you want to know what we did, here is where you find it. Do we want to put a little more time and just shaping it more so it has a message intended to reach a certain audience or

not?

I think, you know, if you take out the IRB stuff, which I think, you know, we are now saying ought to be a separate report and not sort of mixed in with all this, then I think what is left is, you know, we did this report and now here is something of what has happened in the time since that came out, and our next report was this and here is what, you know, and that is okay.

I mean, it is clear. It is readable. It gives a nice summary. I am not sure what impact we are hoping that will have, so it is just a question, and it may not be worth the time to really make it better. I mean, the version of the glossy brochure that, you know, a Fortune 500 company puts out may not be appropriate for us.

DR. MESLIN: I can tell you what Jonathan and I had chatted about, and Kathi may want to comment as well, that the idea is not simply the one report as the Fortune 500 model that you are describing but at least a first status report accomplishes two goals. One, it demonstrates the commitment to human subjects protections in more than -- in more ways than just the three-page letter that was sent on the 4th of May.

Secondly, Alex's point, I think, which is a

good one, about the status of federal agencies, this -- - "serves notice" is the wrong phrase, but it indicates a continuing interest on the part of the Commission and not simply in a single report that there is a regular and persistent interest in the state of human subjects protections in this country.

Now whether that is accomplished in a descriptive report for 1999 and a more focused report in 2000 where the topic is the Common Rule and in the 2001 status report it is some other topic collecting things, that is for you all to decide. But the idea was to take a strategic approach to human subjects protections over a period of time rather than simply to write the big mother of all reports right now. So this was an attempt to do that. But as you say, it may not be the best way to accomplish that goal.

DR. LO: Well, if I can just follow up on that. If that is what we want to do then under each of our reports there needs to be "C: Recommendations for now and what needs to be done." So the way it reads now, it is more like this is what we did and this is how people have responded.

If what we really want to say is here is what we think people ought to do then I think that should be the focus of what we want. Then it becomes more

than just a description. It becomes a proscription for what should happen next but then we have to talk recommendations. What do we recommend to implement our cloning report? That ignored most of the recommendations.

DR. MESLIN: Eric?

DR. CASSELL: Well, I like that because I mean a real big annual report -- I always suspect people who have the time to read annual reports and -- but if we did lay out here are some concrete things that we think ought to be done. For example, we think a portion of each research budget or the overhead must go to the institution's ethical review process or Trish wanted to make clear that money has to be devoted in a research budget that is going to examine the competency of research subject.

There has to be -- that is a concrete recommendation, and it can put people on notice, watch out, here it comes down the line, the next -- the one that is really comprehensive is going to say 12 percent of their budget has to be given over to so and so and the it is very concrete, and a number of others. And we are putting you on notice that these are things we already know are important, and they will be the subject of further things, but it makes it

clear that they can start getting defensive now.

And since we have already discovered in the human subjects one that we did do that it is defensiveness that moves things forward -- there is no power like the power of guilt and the same thing might be here.

DR. MESLIN: Larry?

DR. MIIKE: I, for one, would have a problem with an annual report in that format in the sense that the way that we have been putting our reports together is that we have a good body of knowledge and analysis behind the recommendations. So it would -- and I do not think we would be able to put out an annual report particularly in that format.

I would suggest something that is more like a kick in our pants which is that our annual report identifies those areas of human subject protection and remember we also have a charge that is outside that. For example, this request for xenografts and, you know, gene patenting, et cetera, which is not -- so it is not a whole agenda.

But I was thinking more that we -- this first annual report can say what we consider the critical issues in human subjects protection, what we have so far done about it, what we are going to be doing about

it. And then for those reports that we have already agreed on recommendations you can include in them, for those that we have not, we can identify the key points that we intend to put out recommendations on and, you know, one can lay out a range of possible options that may be coming up in our report if we have the time to do that.

And to me that would then let people know that there are some unresolved issues in our minds, and there are some resolved ones, and we want to see what we -- what people would do about our recommendations. And then it is also a means of getting us to keep on track so that we will come out with reports in these areas.

And the annual report is a mechanism to see whether we actually delivered on our promises in those areas.

DR. MESLIN: Alex?

MR. CAPRON: I think I agree with what I understand Larry and -- were you also agreeing with Bernie's?

DR. LO: Yes.

MR. CAPRON: It does not seem to me that the phrase "annual report" -- that the subject of annual report is NBAC's activities. The subject of the

annual report should be the protection of human subjects. And so that the chapter 3 that is in here now should not stand anywhere like what it looks like here, which is report by report, but rather closer to something I thought that Bette was saying as I came in, which was what are we putting on IRB's, what are we putting here or there.

I mean, we have made recommendations for several types of national review, several additional functions for IRB's. They should have representatives. If they approve research involving people with diminished capacity, they should have such people -- two such people at a minimum on -- as members, et cetera, et cetera.

And I would do it that way, which is sort of what recommendations have we made about this or that and where do they stand. None of them have been implemented with the possible exception of some of the things that may have happened at the national level for NIMH where they may be putting into place some things.

But obviously there has been no statute on cloning, stem cells is much too recent. I do not think anything has happened from the Biological Materials Report. So, I mean, someone should be able

to look at it and say what things have you recommended and group them by their function, not by our report.

Does that make sense?

DR. MESLIN: Yes.

MR. CAPRON: So it is not a 1999 annual report of NBAC. It is a 1999 report on the status of, which is what the label on this thing says but the --

DR. MESLIN: Which is what the intention was.

MR. CAPRON: -- content was not quite making it that way.

DR. MESLIN: Yes.

DR. BACKLAR: So that as we were able to go back and see that the mentally infirmed report by the national Commission was not implemented because the report that the President's Commission alluded to the problems there so people will be able to track.

MR. CAPRON: Yes.

DR. BACKLAR: This is exactly what I was saying. Right, I agree. I actually thought that was what it was intended to do.

MR. CAPRON: But you see it is funny because in chapter 3 there was a laying out and status of implementation and then you get over to 4 and it says status and responses to NBAC reports again. So it is sort of redundant at the very least there.

DR. BACKLAR: Right.

MR. CAPRON: But we do not want to emphasize -- what I have just said -- what we have done but rather where the recommendations are by type.

DR. BACKLAR: And so this is to jog people.

MR. CAPRON: Right. If we said such and such should be clarified, has OPRR issued a clarification or begun a process of issuing a clarification.

DR. MESLIN: Larry, were you --

DR. MIIKE: No.

DR. MESLIN: Bernie?

DR. LO: If I can sort of try and distinguish between different purposes to which we might do that, I think certainly for our internal purposes, it is nice to have a sense of what it is we specifically recommended and sort of what has happened to those. I think Pat was suggesting that for future Commissions or historians it would be nice to have the track record.

I am a little concerned. It kind of sounds whiny to issue a report saying we recommend all this stuff and no one paid any attention to us on all these issues, which is what I am afraid it is going to sound like. So again I think one thing is just to recapitulate it. This is what we have done as sort of

a simple sort of abstract -- you know, what I did over my summer vacation type report.

Another is to sort of signal -- I like Eric's idea to signal what is coming next so people will have a chance to sort of get defensive and start, you know, mobilizing.

A third is to actually help us just sort of, you know, make good on our commitments and to start us on the process of doing some background work that we need to do for our next report.

But I think we should try and be a little clearer as to what we are trying to do and then sort of see is it worth doing because, you know, you better than any of us, Eric, you know, we are -- we have a lot of constraints as to both time and personnel. And so if we are going to put more effort into an annual report that has already gone in, is it worth it? Is it worth the effort given all the other things we could be doing? And what is the impact we want it to have?

I mean, I would hate to do an annual report just so the next Commission that comes along can look back and say, "Oh, these guys were actually sensitive to the ideas and took their place in history."

DR. MESLIN: One thought is to try and never

use the phrase "annual report" to get that concept out of the mind because that was not the intention of this and Alex's points, I think, are extremely well taken.

MR. CAPRON: Status report.

DR. MESLIN: The title may belie the content.

But a fourth version, Bernie, of what you were suggesting was it has nothing to do with look at us, NBAC, but rather look at not only the agencies, look at whether or not other programs have been proposed by other groups, public and private. The best practices model that you referred to on a number of occasions.

So when we, on behalf of the Commission, on behalf of the President issue a status report on the state of human subjects protections, which links very directly to what the Executive Order said, please assess the adequacy of human subjects protections in this country, that was intended to be what this was going for, and I have no idea, as we have heard now, that it accomplished that.

(Fire alarm test.)

DR. CASSELL: That is not my cell phone. I would just like you to know.

(Laughter.)

MR. CAPRON: Answer it, will you?

(Laughter.)

DR. MESLIN: Larry, you were going to say something?

DR. MIIKE: Yes. No, I agree with all that. This is -- and the title actually has "status report of human subjects protection."

I think that -- well, for one, just the organization, I think chapter 2 and chapter 1 should be reversed. We should say what the current system is like and what the reviews are like.

And I do not think it needs to be self-serving. You know, along with the reviews we can also say which areas we have focused on and which areas we are continuing and have not finished our work on, and leave it at that.

In other words, you can both simplify it and complexify it by doing that. Instead of being a sort of landscape issue, it is sort of like here is the current system, here is what has been identified, weaknesses, what other people are recommending, what we have recommended, and what, if any, kinds of changes have gone on.

And so the first report might be a longer one but the following ones that come up are basically referencing in summary fashion the issues that are

identified the previous year and then move on from it.

I would also say that a report like this should have at least an appendix that identifies the key reports that are relevant to the area so that you just sort of -- and maybe even put the summary recommendations of some of the key reports just in a little appendix. For example, our recommendations or the GAO recommendations, et cetera, just so that people can have a short synopsis in a comprehensive fashion.

DR. MESLIN: Bernie?

DR. LO: I like this idea of sort of saying it is a report on human subjects protections. It is not an NBAC report. And then I guess my question would be, in that light, this almost reads like a first draft or background research to an NBAC report on strengthening the protection of human subjects; extending the Common Rule and invigorating IRB's. So then my question becomes, given all it takes to sort of put out a report, is it worth putting out one report which is the state of human subjects 1999 with the promise, I think we are saying at least among the people here today, that we want a big -- our next big NBAC report should be on IRB's and the Common Rule or something like that.

Should we -- how much of it should we put in having this preliminary report and then the report that really has the thought through recommendations?

I mean, to come back to what Alex said, if what we are going to do is recommend that X percent of the budget of research grants goes to ensuring the process of human subjects review and the like, should that all come in a later report because a lot of the chapters here could be very nicely part of a big report. It is the background work that needs to be done and again I am just wondering if it is worth putting out a separate report if we are committing ourselves, which I think we ought to put out a report some time in the year 2000 on IRB's.

DR. MESLIN: Alex?

MR. CAPRON: Well, I had a sense that it was sort of a political issue here, which was some need for us to have a document which is responsive to one of the two primary charges in the charter at a time when the charter has just been renewed for another two years and we have -- it is not as though we have not been doing this, but we have not as directly, as one might have wanted, responded to something that was fairly explicit. In fact, there are two explicit charges. The gene patenting and what is the status of

federal compliance.

And I -- my sense was, when we started on that, we thought what we were going to be doing -- this is before your time, Eric, but what we thought we were going to be doing was issuing a report on what the federal agencies were doing and what we said to --

DR. CASSELL: That is right.

MR. CAPRON: -- ourselves was we have got to be careful not to say that what they say they are doing on paper is actually happening in the country, so we cannot say this is the status of human subjects protection but this is the status of federal implementation of the basic design that was behind the Common Rule.

And what we have discovered, as I recall, when we first got a year later those synopses of what was going on was that some agencies did not really have anybody who knew that they had -- that they were participants in the Common Rule and others had -- you know, OPRR -- a very elaborate office, et cetera, et cetera. We found all sorts of good things and bad things and just in the process of looking got a few of the agencies to say, "Oops, something we have been neglecting. We better get on that."

You know, we could -- and we were in a

position -- we never thought that was going to be our last report on these issues. That was our first report and it did have a sense that we will be back with something more as it developed and that has not -- still has not gotten out. And I got a sense that the reason for saying in 1999, before the end of 1999, we ought to have a report on the current status of the protection of human subjects was to deliver some of that because it is -- the whole thing about the best is the enemy of the good or something.

I mean, it would be nice if we could have that wonderfully comprehensive thing that does everything but we have been holding up a lot of stuff that we could report on to wait for the point where we are able to report on it all, and it just is not a good idea. I basically agree with Larry's points.

DR. MIIKE: I would say that we cannot in our -- in this status report put in specific recommendations that we have not really discussed thoroughly. However, I do not see any problems in stating conclusions that are background studies or background work, for example, on the goal of the federal agencies because it then says here is what we have found so far, but it does not say what we are -- what we formally recommend should be done about it,

but it should be pretty clear we said something has to be done about it. It also sort of forces us to finish that study on the Common Rule and package it with IRB reform.

DR. CASSELL: And just practically speaking, Eric, you better go after that data because it is going to just disappear because it got -- it sort of trailed off, and in a little while, Diane will be gone and anybody who had any connection to it will be gone, and you will not been able to put it back together again. A lot of work was done. It just was not -- it just could not be completed for some reason.

MR. CAPRON: Jim, in the D.C. area, as I understand it, we are very involved in --

(Fire alarm test.)

MR. CAPRON: -- and sat in with the agency interviews.

DR. MESLIN: Kathi, did you --

DR. HANNA: I jut wanted to say that the federal agencies survey data has kind of been plaguing us for some time, and now that I am almost gone, I can probably say without fear of reprisal that I am very suspicious of some of the data that were collected. I have gone back through files.

I spent some time trying to validate some of

it. And I think there was a layer of subjectivity that was inserted into that process by some of the people involved, and it is very hard to sort out how much of it is subjective and how much of it is accurate observation. So I think one of the problems that has paralyzed us in a sense is trying to figure out now what to do with what I personally believe to be suspect data, and I do not take it lightly that, you know, we cast certain agencies as being out of compliance or not caring or not paying attention when we do not have really good reliable data to support that.

So I think that part of the issue is what do we do about that now? Do we try and -- we cannot start over again, but we do have to make a decision about what we are going to do with vast amounts of data, some of which I am sure are quite good, but it is sorting out which is good and which is bad is the daunting task.

DR. LO: Kathi, could I ask you are the data flawed in one direction or in both directions? I mean, if people come to you and say, gee, we do not have anything to implement the Common Rule, the officer sort of retired 18 years ago and no one else has been appointed, are they, in fact, mistaken and,

in fact, there is a huge well-run office in their program? Or is it more the other, are all the biases the other way? People say, oh, we are doing great, we are vigilant, we take this seriously when, in fact, you suspect there is not a whole lot going on.

Because if what the data we have are best case, and there are clear deficiencies then I think we can make use of the data. If, in fact, we cannot -- we have no sense at all whether things are better or worse than the data we collected then I think we are in big, big trouble.

DR. HANNA: I would suspect that it goes -- it possibly goes in both directions.

DR. LO: It goes in both directions.

(Simultaneous discussion.)

DR. CASSELL: That is the way to look at it. That is what the swan song sounds like. Your data is flawed.

DR. MESLIN: Bernie, one of the reasons why the Commission -- just to remind you -- decided to have Harold write to the President on the 5th of May was to try and summarize as carefully and as accurately what the nature of the concerns were without -- and as confidently as those were and there are some fairly dramatic, and they are in the briefing

books for the public who are here, fairly direct and profound statements about the status of human subjects protections, about agencies having difficulty with interpretation and implementation. This gets back to some of the questions we had yesterday about identifying resources so to speak. I think certainly Harold stood by and the Commission has stood by this May 5th -- May 4th letter. So it is an open question to you as to whether you want to try and mine what may be data that is not as helpful and for what purpose or whether another study needs to be done and the like.

Bette, and then Larry?

DR. KRAMER: I was one of the Commissioners who were at that meeting with the representatives of the agencies, and it was pretty apparent that the data were so -- it was so flawed. It was -- as to be -- it was hard. You could not even make a determination as to where it was accurate and where it was inaccurate. It was just almost a -- you almost had to dismiss it as of no use if you were going to do the responsible thing. That was my impression, overall impression.

DR. CASSELL: Oh, Jesus. You know how long it took to get all that stuff?

DR. KRAMER: Well --

DR. MESLIN: Larry?

DR. MIIKE: I think there is a way around it. We do not have to rely about people or conclusions about how well an agency is doing. All we need is to match or to take -- as long as we know what kinds of research agencies are doing because we are not -- we do not -- I do not intend for us to put out recommendations that said, hey, this agency is bad and we should do something about it. It is a question about what is an appropriate IRB and Common Rule application across agencies that may be doing very different kinds of research.

For example, if you are doing basically survey or mail type research -- and I think we all agree that there has got to be some leeway in that versus someone who is doing fairly hazardous types of human subjects research in say clinical trials or something like that.

So I think it is more a question about, yes, all the federal agencies should be following the Common Rule but does it make sense that there is one rule for everybody that is ironclad where you might want some more flexibility in that? It seems to me that that is the way -- the direction of our analysis without having to do the research all over again with these agencies.

DR. MESLIN: Alex?

MR. CAPRON: Now I am puzzled. That sounds like a worthwhile project, Larry, but I have a sense that sounds like a bigger undertaking. I mean, in terms of meeting time and when we should get on it and put it on the agenda once we have something to say about it.

I am disappointed. I had not realized how -- I mean, how bad this was. I mean, I feel -- if this were a board of directors I would be very upset sitting here thinking that our -- that a process that we have had going on, which I thought was more or less a straight forward process and probably had been executed well, and the problem just was that we were holding those data for inclusion in some bigger report and we were not getting the bigger report done, and their major problem was probably that they were stale, not that they were, as you put it, flawed.

Now there is one corrective there which -- and I do not know, Bette, how much this happened at that meeting when you are saying it became obvious, whether what we were dealing with --

(Fire alarm test.)

MR. CAPRON: -- agencies saying you have got it wrong, here is our demonstration but what we are

really doing is X, Y, Z, please correct your statement on this. Now the solution to that is simply reiterate to them what our draft statement of their level of compliance, the problems that they face, whatever. I do not remember. There was a big instrument that they were using. It seemed well organized as an instrument. And say is this accurate. If not, tell us why not. And please do this by the end of October because in December we are publishing this stuff and if you do not want to look wrong, then you better tell us and then you are going to have to have staff to sit down and substantiate that if we are being told that X, Y, Z is happening it is happening.

DR. MESLIN: Alex, that did occur on a couple of occasions in a couple of different ways, including a meeting which is the meeting that Bette was referring to that was held with federal agencies at the White House Conference Center in October of last year.

MR. CAPRON: Does that correct some of the flaw?

DR. MESLIN: Yes, it does correct some of the flaw. There is probably an issue that we need to have more of the Commissioners here present, including Jim, who played a central role in understanding that report

and speaking with federal agencies about it, but just for purposes of maybe bringing closure to this little part of the conversation, there were several opportunities when agencies were given both drafts of summaries of the material relating to their agency, in particular, and asked whether it was accurate or not and they did have that opportunity. And in many instances not only did they correct the description --

(Fire alarm test.)

DR. MESLIN: -- but in addition on -- I would say a moderately frequent basis we are either getting telephone calls at the NBAC office or are receiving documentation from agencies telling us what they are doing. "You reported a while ago that we are doing this. Well, as a matter of fact, we now have a policy in place so please, please do not report that we are out of compliance if you are relying on 1997 data."

So I just want to -- your concern -- your board of directors' concern is valid but it is not entirely accurate.

MR. CAPRON: Okay. But then -- I mean, then the picture is not as -- quite as dire as Kathi has expressed it. There is a remedy. And part of the way this is written it up, it seems to me, should indicate that the very fact that we have been conducting this

oversight operation has brought people more in compliance with their own description of what they should be doing to the extent that is true.

I do not think -- by the way, looking at the May 4th letter, what we have is the second bullet here. "Despite widespread implementation of federal regulations by those departments and agencies, et cetera." What one would expect to follow from this are the specifics, please. Which agencies are part of the widespread implementation and which ones ain't?

And if we give people an opportunity to tell us and if we do not get a response from some agency because, in fact, when you address it to their human subjects office it sits in the mail room because no one knows where to deliver it -- I am not too worried about reporting that they are not in compliance if that is the problem. And maybe it is -- some of the stuff is a little too subjective and not perfect data but we give people an opportunity to correct.

DR. MESLIN: Bernie?

DR. LO: I think I have had a large number of senior moments at these meetings because I really was not aware of problems with the quality of the data. I guess I would like -- Kathi has done so much for us while she has been with us. And if before you leave

we could get a really candid -- even brief -- what are the limitations of the data because I have the sense there is a lot of problems here that we really have not heard about and thought about.

And rather than trying to settle it now, I really want to see -- as would happen if, you know, we were the PI's of a research project. Someone says, well, you know, I have real concerns about the quality of the data. I think we really need to pay a much closer look. And to then be honest with ourselves and say what -- of what use is that data, what inferences, what conclusions are there to draw from them?

And it may well be that we may not feel comfortable naming agencies by name. We say in some agencies we could not get the questionnaire delivered because no one knew they had a thing, others the director did not seem to know what was going on, others we had trouble keeping up-to-date because things were changing. They may have been spurred, or they were actually doing something. To go through all that would be fine if we did not attach sort of names of people, but if we are actually going to sort of identify people, then we have to be very clear as to the accuracy of what we are doing because all of us will get caught in this sort of contest of you were

wrong; no, we were not; yes, you were.

DR. HANNA: One of the -- I mean, it would -- in some cases you cannot avoid identifying the agency because after some of the data were collected and analyzed, it was only as we started to -- started having additional conversations with some of the agencies did we find out that there might be other laws and statutes on the books that they -- are binding for that particular agency that NIH, for example, does not have to comply with because they are not subject to the same acts or whatever.

And so a lot of the interpretations were done not in the context of any specific constraints but existing statutes that, for example, the FBI or the Department of Education or whatever has to comply with. And so that is to point out why one agency might not be quite doing it the same way. You have to identify it because there is a law on the books that required that it has some kind of a countervailing influence.

DR. LO: Yes. I guess, I would like to say this -- it seems to me this discussion we should not be having right now, but we need to have -- again I think what you are helping us understand, Kathi, is that there are lots of different things going on here.

To the extent that some agencies are bound by other regulations or laws and others are not, we need to understand what those laws are and to state them explicitly and make some recommendation as to what goes on.

Now there are other more generic things, I think where like knowing those who have an office that do claim to have it. Well, that is a real problem and, you know, we do not have to name the agency necessarily and say every agency needs to, you know, do a one shot --

DR. CASSELL: Name them. It does not do any good if you do not name them. I mean, they can always say we are wrong.

DR. MESLIN: Larry?

DR. MIIKE: I have three points. One is that over a year ago I wrote a letter. I think, Eric, when you had came on, and at the time I was concerned about the lack of products from this Commission. And I said we did a survey of agencies, why can't we just publish that, and so I got an inkling about what is wrong with the study quite a while back.

Two other things, though. One is that if we are going to publish this as part of say, which I see where at least we are heading towards a separate

report on the Common Rule and IRB's, which would probably be reasonably deliverable early summer next year or something like that. We can do the GAO style. You know, we make our statements, we let the agencies comment, if we cannot resolve the issue, we just sort of print their rebuttal within the report itself so that there is a countervailing conclusion other than our's.

And then the third thing is, Alex, you had made a comment about what I had suggested would take a whole lot of time. I did not mean it in that sense. I am saying that if, within that body of information that was collected, we at least know what kinds of research different agencies are doing, then we have a sense about the variety of human subjects at risk among those agencies because one of the areas where we would have to reach conclusions and issue recommendations about trying to make the Common Rule more appropriate to the different types of research that is being conducted.

So I was only suggesting that as a means of something that might be more easily objective within the information that already had been collected.

DR. MESLIN: Eric?

DR. CASSELL: Well, I think you are hearing

the voice of the minority of Commissioners that you have got in front of you is asking you to drag out that report again and give us a status report on the report and see what you have got.

MR. CAPRON: Yes. Actually I do not want a status report on it. I want the staff, by whatever mechanism, to produce data written up in a way that you would like us to publish that you feel confident enough about that we could -- like any other report.

If we state that stem cells are produced this way or that, I mean I do not want to have a discussion of how you came to that conclusion, I want some language which represents that conclusion that you would say I feel confident that if we give this to a molecular biologist or an embryologist or something they will say, yes, you have got it right. I want an equal description of what the agencies are doing that if we give it to them or to objective observers they would say, yes, you have got it right.

And if some of the data you have are good, we can use those. If you say as to this or that agency or as to some aspect of all the agencies we have got to go back because the way the data were gathered or the blinders the people wore or something meant that this is not reliable, do not tell me it is not

reliable. Get something that is reliable.

DR. MESLIN: Bette?

MR. CAPRON: Do you agree?

DR. CASSELL: Yes, sir. That is affirmative.

DR. KRAMER: I was going to ask Kathi if she thinks that is worth doing.

DR. HANNA: I think so. I mean, I think the problems -- when I started seeing that there were problems with some of the data from some of the agencies, I did not want to just assume it was problems with certain agencies.

I had to assume that there could also be problems with all of the agency data, and so it really requires some kind of spot checking to start out with to get a sense of the agencies that we have just assumed the data were collected appropriately and analyzed appropriately. We need to go back and check and just not assume that that is okay.

I mean, there are a lot of assumptions right now because nobody has had the time to really systematically go through it all.

I think somebody has to systematically go through it to decide which data we can use and which we cannot. I mean, I -- off the top of my head I know that I would -- I am very suspicious of some of the

findings from at least three of the agencies.

DR. MESLIN: Bernie, Eric?

DR. CASSELL: I still second what Alex said.

DR. MESLIN: Bernie?

DR. LO: Yes. I agree very much with what Alex was saying, but I would like to make what may be a significant revision, which is I would like to know what we have and what the staff's assessment is of the quality of the data and the limitations and not to go back and collect more data until they have come back to us because I think collecting more data has got to be factored into our priorities for other things and do we really want them to do that now, sort of going back and rechecking and refining the data as opposed to move on to other things? But I would like very much to know what they have and how reliable it is and how much they think needs to be done to make it more reliable to be able to draw certain conclusions.

DR. CASSELL: But this is a -- but that makes it a research Commission. That is fine. This is an administrative Commission. We are charged to go and find problems and suggest solutions. And we have this data, and if we do that, it is going to just do what it did already. It is going to just peter out.

DR. LO: But, Eric, if we tell them, as Alex

said, to go back and get the data really solid, we are committing them to doing certain things without asking what else could they be doing with their time that may be more --

MR. CAPRON: This is such a fundamental thing.

DR. CASSELL: They are not mute. They will tell us, don't you worry.

MR. CAPRON: I cannot imagine taking on a list of a variety of other topics that we might and never having produced this fundamental building block of the process which was when we were --

DR. CASSELL: Who is doing what in human subjects research.

MR. CAPRON: This came out of the ACER (sic) of the whole process of looking at the problems with the human subjects in the radiation. I mean, that is -- I have a sense that the President -- whether he was persuaded he ought to have a Commission or thought he ought to have a Commission -- said, "Well, let's find out what is happening in the federal government. We have got this system for protection. How is it working?"

And we recognized that was a two-part question. How is it working at the top and how is it

working at the research level? We thought it was a fairly straight forward process to say how on paper at least is it working at the top. Are there -- not just on paper but as implemented at the top.

And, yes, it will take resources, but I cannot imagine our -- after three years -- continuing to turn our back on a fundamental basic part -- if you read our charter it stands out.

DR. MIIKE: How many agencies are we talking about? How many agencies and departments are we talking about?

DR. HANNA: Twenty something.

DR. MIIKE: Twenty something. Isn't that a simple straight forward use of time, to summarize what we can out of that from each one, send them back to each individual agency saying we are updating our original survey, please correct and update this? It seems to be fair. And then they would have an opportunity to look at it, and I think what we do is we take them at their word with documentation whatever they respond, and then we have got an updated information. It seems pretty straight forward, but it is something that a research assistant could do.

DR. CASSELL: Remember part of this problem is a personnel problem. The personnel is the problem.

I mean -- and we all recognize that. What Larry just said is absolutely correct. Somebody striving to come to a conclusion will come to a conclusion and get that data.

DR. MESLIN: In the interest of not so much time but your fellow Commissioners who are not here, can I make a suggestion that we will prepare a short proposal for the Commissioners and send it out on e-mail and you can agree to it?

MR. CAPRON: You can do it that way. I do not know what the proposal would be. I do not think we should be --

DR. CASSELL: We have to look at it and tell us what you have got.

MR. CAPRON: We are not a board of managers. We are not here to decide how resources in the sense of X, Y, Z personnel should be deployed. We need a result. You figure out -- and obviously with Harold --

DR. MESLIN: You have not agreed on what the result is that you want.

DR. CASSELL: Yes, we have. We will make it clear. You want to make a statement of what result -- I heard your's, and I was happy with it.

DR. MESLIN: Restate it.

MR. CAPRON: Let me see if I can restate it. I would expect that, by the end of the year, as part of this status report, we would report on what the federal agencies have done to implement the Common Rule, and that would involve telling them what we have on them now as what we will be stating about it and getting that back. You then prepare, as you would on any topic, the language that reflects that. It would probably have some tables -- I mean, you do not want to write out in paragraph form everything -- with whatever appropriate summaries.

I mean, I feel odd saying it. It is just so straight forward. Is that --

DR. CASSELL: No, I think it is straight forward. I want to reiterate. It got unstraight forward because of a personality problem. You just have to know that sometimes. It is straight forward and up to a certain point there is just what Alex wants, and then we get -- then it gets muddy, what Kathi is talking about, but clarifying the mud.

MR. CAPRON: It may be slightly more complicated than Larry described, but I think he is basically correct as to what is involved.

DR. MESLIN: Bernie?

DR. LO: I mean, I agree with what Alex

wants. I just want to ask Kathi and Eric how do-able is that and what constraints does that place on other work we are planning to do in terms of a new -- starting a new report and finishing up what we have? I mean, given your current staffing and the fact that Kathi is leaving and, you know, you are going to have new people working on this, how straight forward is it and what kind of resources are we talking about?

DR. CASSELL: I would rather work for you than me any day.

DR. MESLIN: My comment, which was to Alex's remark, was not to tell us what it is you want when I suggested we would send around a note. It was as a courtesy to the other Commissioners. You have made a decision that you would like some specific information. It may be that your fellow Commissioners have some different views about that.

I do not think there is any disagreement that a status report should include -- in fact, there are sections in this report. It says "to be written." It could include exactly what you are looking for. I wanted to get direction as to whether you want it contained within this body, within a separate -- as a separate instrument, as a separate document.

As Eric Cassell says, we will tell you what

the labor requirements are to get certain things done and if you want it done in a week, it cannot be done and if you want something comprehensive it cannot be done in three weeks. That is not the problem.

DR. MIIKE: I have a comment specifically on that. I think it may be a problem to include the complete information in the status report, and I think that is what you folks have to decide, whether it is do-able, what Alex suggested. However, I also believe that information has to be published at some point in time. It is just a question to me whether it gets published in a status report or as part of what we are heading towards, a separate analysis of the Common Rule. And the improvements in the IRB.

DR. MESLIN: Bernie, were you going to -- you had one more point?

DR. LO: No.

DR. MESLIN: Trish?

DR. BACKLAR: I just -- I would like to agree that it obviously has to be done, and it cannot be swept under the rug and that it is -- I am surprised, and I did not realize that this had occurred, and it is very important one way or another that it is addressed.

DR. MIIKE: But I still think there is a

simple solution. Just summarize for each agency, send it back to them and let them comment. They will have reasonable time to comment. If it is too outrageously bad, they are going to be furious and send you back a correction. If they do not say anything, then that is their problem. We have given them the opportunity.

DR. MESLIN: I am going to suggest just if anyone needs to take a quick five or ten minute break. I know there are people who are -- may have to do checkouts or something.

Trish asked me to ensure that we have a break between the two parts of the agenda, so I am just going to propose that we take a ten minute break and then come back to the priority setting memo for the last minutes.

(Whereupon, a break was taken from 9:31 a.m. until 9:58 a.m.)

DR. MESLIN: We are going to reconvene. Again for those who are here, we are going to be shortening our morning since Commissioners are going to be having to leave. So for those who have made their entry now awaiting a long -- rest of the morning, our morning will be cut short in a little while.

I know that Dr. Lo has some things that he

wanted to put on the agenda right now.

DR. LO: Yes. I wanted to start by following up on something that was just alluded to before the break and that is Kathi Hanna is leaving the Commission. I know the Commissioners have communicated informally our -- both our sadness at Kathi's leaving but more important our real thanks for all the things that she has done for us and this Commission. She has really put in sort of unbelievable hours and dedication sort of recrafting kind of the confusing and contradictory things that we have said and has really been instrumental in kind of helping to shape our reports and just putting in extraordinary hours far and beyond sort of the call of heroic duty.

She has been a wonderful colleague and just, you know, gracious, good humored, dedicated, caring, and I think all of us really want to say on the public record thanks terrifically, we are going to miss you and good luck in what you do next, and take a vacation before you do anything.

(Applause.)

DR. LO: No speech?

DR. HANNA: No.

DR. LO: That is the best thing about Kathi.

She is not as long winded as we are.

DR. MESLIN: I, too, will add my thanks to Kathi who has made my job extremely enjoyable. There will be other opportunities to thank Kathi. I know there was an intended gathering last night that Hurricane Floyd interrupted so that is delayed but not canceled.

I know that at least Alex and Bernie may have to leave in a little bit so let's just come back to a couple of suggestions that Bernie wanted to make about the discussion we just had.

DR. LO: Yes. I wanted to kind of move us -- I thought -- it is actually useful to sort of try to think through some of the things we thought through this morning. I actually think we are a lot closer than we may realize to sort of making some important recommendations in a major report.

There were two themes that we heard this morning that I think we need to sort of develop. One is education as Eric has been talking about and the other is Alex's suggestion for funding in terms of making IRB's and protection of subjects really work.

I would like to suggest for the next meeting we really sort of -- I think we have kind of made a commitment to sort of do a major report on IRB's and

perhaps the Common Rule as well. One aspect of that is to really push forward Eric's suggestion of let's do something about education.

And I would like to say let's try and flush out what specific recommendations we might want to think about making. So who are we recommending do what to make sure investigators and IRB members really get educated about research ethics?

I would suggest we might want to bring in some key players in that process. Those who are trying to teach research ethics to IRB members and to young researchers. Is there a role to -- something that we can recommend so that deans of medical schools, the AAMC, the boards that write the certification questions to include some questions on research ethics, who is going to pay for it, can we get some foundations like maybe PEW who have been interested in professionalism to say this is part of that, you should put some seed money into it. So to really flush it out.

I mean, Alex is very right in saying we talk about it. It is a good thing. What can we recommend that would make it more likely this is going to happen? How do we know what works and who should be doing it? And if we can sort of start to use staff

time and invite some speakers then I think it would push us towards making recommendations.

I thought one of the things we did in the stem cell report, which was very helpful, is we asked people to make some sort of draft recommendations fairly early on so we could sort of play off against them and even if we did not end up with a document, it was good to think about what we are going to recommend. So I was going to recommend that we ask Eric, who has been so eloquent and forceful in this topic, for the next meeting to give us some sort of rough drafts of specific recommendations we might want to consider to sort of move that process along.

The second thing is I thought that Alex's idea of making this tangible by saying a certain percentage of the research funding dollar needs to go to the support of the infrastructure for IRB's, for training and the like is a really good idea. It needs to happen otherwise they will just be empty words.

What can we do to kind of arrive at what that figure should be, who should pay for it, and what impact it is going to have? So again to talk to IRB people about how much it would cost to really do their job well, to talk to funders, both government funders and private funders. Are they willing to ante up for

this. Do they have the resources to do it? What do they think is a reasonable amount?

And I would particularly be interested -- one of my pet peeves is that some of the foundations who support the biomedical research that actually is now with genetics increasingly dealing with human subjects do not think this is part of our purview. They think they are buying lab equipment. So I would like to get people like Howard Hughes to the table and say, look, is this important to you, training all these people who are going to end up doing research on human subjects and not just on genes. Is this part of their training? Should it be? Are you willing to pay for it? Are you willing to spearhead it the way you have spearheaded, you know, sort of the basic science training?

And finally I think that we have a lot of information that sort of is in part of this outline we are talking about that if we could see it summarized in tabular form. So we talked already about sort of wanting to see as best we can do it sort of what the data are from how the agencies are implementing the Common Rule.

I think Larry's suggestion of having a table or Bette's suggestion of what have we recommended in

other reports, let's see it in black and white of what we have asked IRB's to do. What have other reports on the regulatory process recommended so that we can either affirm them, disagree, revise?

All those things it seems to me will move us quite a bit along a path to having a report that really makes very specific recommendations to implement, I think, our genuinely unanimous agreement that there needs to be tangible support for the people who are trying to oversee research and to train investigators and IRB members. And then if you get the support, how do you actually do it in a way that, you know, education really has the effect we want?

So I just would like to kind of help you plan some concrete things to move us along.

DR. MESLIN: Eric?

DR. CASSELL: And of course the two, the funding and the education, go together. Absolutely. And if we got the people in here and said how much of your budget are you willing to commit to this and really talked to them and had some impact there that would be really wonderful.

DR. MESLIN: Bette?

DR. KRAMER: I would request that in talking to IRB's that we make a point of including community

hospitals as well as academic centers.

DR. MESLIN: Trish?

DR. BACKLAR: I am passing.

DR. MESLIN: Alex?

MR. CAPRON: I had a question about something that we have talked about and Harold has talked about, and that is the development of a concrete proposal tested out in some fashion for an accreditation process for IRB's that would mean that the oversight of IRB's would not be limited to investigation of egregious complaints and a paper assurance but would have some kind of an ongoing regular accreditation.

That I assumed was not on this list because it was part of the more comprehensive report. I just want to make sure that I am correct in thinking that.

DR. MESLIN: Yes. I mean, it was -- the mention of accreditation models including audit proposals of the kind that the Commission has already made in previous reports was at least for this purpose contained in the status report but it could easily be spun up it’s one of the things that could be spun off like others that have been suggested as a separate stand alone or as a supplement to --

MR. CAPRON: Well, I just thought of it -- I mean, maybe I have gotten this wrong, but we have

several topics like the eventual location of the oversight in the federal government, the extension of the Common Rule, and some questions about the details of the Common Rule, and I would say also this accreditation issue, which I thought were for a future report.

DR. MESLIN: I did not mean this one. I mean, the report model.

MR. CAPRON: Okay.

DR. MESLIN: I apologize.

MR. CAPRON: The report model. Okay.

DR. MESLIN: Yes.

MR. CAPRON: All right.

DR. MESLIN: Larry?

DR. MIIKE: I assume that -- I do not see any dissent -- I do not expect any dissent from the other Commissioners in terms of this being a report that we should be doing, so I guess you are just going to go ahead and try to tease out the areas in which we would be prepared for the next meeting.

I guess we are -- oh, we are going to move on to other studies.

DR. MESLIN: Yes. Maybe we should stop talking about the status report model and return for a few minutes if we can -- I know Bernie and Alex have

to leave -- to talk about the priority setting memo.

Trish, and then Larry?

DR. BACKLAR: I just wanted to -- just back about the education and IRB's. A few years ago or a year ago -- as you know, Eric, you put this together -- there was an RFP that went out to the various -- to -- for people to respond about educating ethical issues and IRB's, and it might be interesting to tap into the -- those who were awarded.

DR. MESLIN: That is a very good idea.

DR. BACKLAR: And to see what they are doing and give us any kind of results or whatever just to find out what is going on right now with the group of people who won those awards.

DR. MESLIN: Larry?

DR. MIIKE: If we are going to move on to priority setting areas and since we -- there is not general agreement -- there is general agreement about the human subjects side, and I understand we are going to be putting on -- at least our report -- we may not have recommendations, I am not sure, about the gene patenting issue, but I guess that is something we are going to talk about later.

But the Commission does have two really distinct charges. One is the whole genetic area. And

there is a suggestion from some group about the xenotransplantation. If we are going to be looking in that area, I would rather enlarge that to any human/nonhuman type interaction therapy. I think that -- for example, I was thinking about chimeric issues. We could look across the board about anything that would be including nonhuman genetic therapy or organs in the therapy area in humans or we could look in gene therapy in general.

I only raise this latter issue because now there seems to be a big controversy about in the plant world about using genetically modified genetically modified products, and it seems to me that that is a forecast to me that somebody is going to start getting very worried about gene therapy in general, and it seems to me that there are just so many ethical issues involved around gene therapy and particularly in the area about nonhuman/human interactions that I, for one, would like to see us approach that issue.

DR. MESLIN: Alex?

MR. CAPRON: I think it is an interesting area. I believe that it might be a little lower on our agenda given the fact that there is this ongoing process called the Gene Therapy Policy Conferences that are held several times a year and the Recombinant

DNA Advisory Committee is a group constituted like our's of scientists and nonscientists and so forth and meets publicly on that issue.

So that among topics it would seem to me that the gene patenting issue has been more ignored and the whole set of issues around reproduction have never been addressed at the federal level. The positive side of reproduction, not sterilization, contraception and abortion but the new reproductive technologies. We brushed up against those particularly in the Cloning Report.

DR. BACKLAR: And stem cell.

DR. MESLIN: Although this is not a decision making quorum, the memo that we sent around made a suggestion for having staff prepare a number of background papers that could be presented at the December meeting. I already mentioned Stu Kim is engaged in the gene patenting intellectual property background paper. And there can be several others. We can produce, you know -- the budget is the only rate limiting step. We could produce a half a dozen of those papers if you wanted to see them. You then have to make the priority setting decision. How many reports can we write in two years knowing what is already on our agenda and what we want to accomplish?

But do you at least informally like the idea of producing these background papers and should that be one of them?

MR. CAPRON: Well, I would -- in that context I would suggest that rather than a background paper that at our next meeting we get briefed on the status of the discussions about the gene therapy and the extent at which the genetically modified crops issue is one that is not getting the kind of oversight. I mean, I think Larry is right. It is an interesting area. I would have put it second or third. But if we are going through a process of having a background paper on gene patenting, a background paper on --

DR. MESLIN: Reproductive technology.

MR. CAPRON: -- reproductive technologies and so forth, I think we could even have one of those prepared between our next meeting and our December meeting if the next meeting revealed that -- or left us convinced that this area is not getting the level of attention through the existing mechanisms of the RAC.

DR. MIIKE: I would suggest that -- I think besides the annual report and our -- besides the annual report and the international project, three is

a reasonable amount of projects to consider over the foreseeable time frame of a year. Maybe we will be able to publish it. I would rather that we juggle several as we move along rather than sequentially. Otherwise we will just dabble in the sequential ones.

My suggestion would be that staff prepare some fairly short background papers on maybe four or five so that we do not get stuck with just the background papers and that sets the course for us to decide what we are going to do. Then we can decide how do we pare that down into something that we would issue a full report.

DR. MESLIN: Bernie?

DR. LO: Yes. First a question to you, Eric. I think Larry raised an important issue. How many projects is it feasible for us to be working on sort of simultaneously with different time frames? I think we need to look to you and Harold as to guidance as to what is feasible to do given, you know, those kinds of practical constraints.

And, secondly, I like the idea of having background papers. I would like to ask the staff to pay particular emphasis to sort of opportunities for NBAC. What is going to be the value added of an NBAC

report on top of everything else that is already going on? So it should not just be kind of how interesting is the topic, how important is the topic, but what contribution could we make over and beyond what else is being done.

DR. MESLIN: I think that is exactly the idea that we were envisioning. What unique contribution can NBAC made following from the Executive Order's criteria for priority setting.

We have a -- we are in the process now at staff in being able to at least have a gene patenting paper, a paper on reproductive technologies research, perhaps a paper on public health research, and outcomes research. We have heard some conversation about xenotransplantation. We can do some of this on e-mail but the list of bullets in this memo is not meant to be exhaustive. It is just what has remained on the Commission's radar over the past several years.

I am assuming that you are not saying you would like one on each of the eleven bullets that are here. Are there some that informally you all might think you would like to enjoy seeing?

Trish?

DR. BACKLAR: I think the issue of

compensation for research injury has lingered on for years. This is a problem that is really not adequately addressed. And if we are concerned about protection of human subjects I really do not see how we can ignore it.

DR. MIIKE: I have a comment on that. Perhaps about a dozen years ago I was on the task force at Keystone trying to look at that. If we are going to look at that subject, and I am not adverse to looking at it, I would concentrate on the ethical side of it and not on the legal remedy side. If we get into the legal remedy side we are not going to get anywhere.

MR. CAPRON: Yes. I guess I would disagree. I think the ethical side has been well-limned in a couple of reports. The President's Commission had one, NIH had one before that. The real -- I think it is at the practical level. And what would be worth looking at is there are, I think, actually a few more programs than when we wrote about it that provide voluntarily work out compensation schemes, they either regard subjects as temporary employees if they are in a state system, they make them temporary employees, or they have worked out with their insurance carrier how they are going to handle it.

And I agree, Larry, it is not a matter of the legal remedy. I do not -- you know, in other words, could one develop a common law ability to sue or something. It is really what would be involved with the mechanism of costing out what it would cost to add that to the budgets of research projects.

But I think the legal -- the ethical arguments have been rehearsed fairly well.

DR. MIIKE: Well, then my conclusion out of that is that this is something not worth discussing. No, really, because if the ethical issues have been -- I just remember if we get into the compensation side we have to talk about alternative compensation mechanisms, who gets off, who does not, and then we get into -- all I remember is that we went around and around and around and around, and there are people who are so wedded to the tort system that any end roads into modifying, therefore, a more certain compensation system will -- I know the morass we would get into.

But I am not adverse to that being a short discussion topic that we can raise up at the next meeting.

MR. CAPRON: Could any of these be done before the December meeting? I mean, it would seem to me if we could pace ourselves and have --

DR. MESLIN: Yes.

MR. CAPRON: Okay. I think that would be more sensible. And maybe on the gene therapy and on this compensation issue you really would be pulling together and trying to identify someone who could present what is out there so it really becomes a question that addresses Bernie's issue. Is this the best use of our time or has this been well enough handled or is it being well enough handled by somebody else?

DR. MIIKE: One last thing, Eric, is that I would not suggest that background papers, however short, be prepared on all 11 topics that are in there. I think you should poll the Commission and say which ones would we rather just lay aside for the moment rather than spend all the time --

MR. CAPRON: Yes, but do four or five.

DR. MESLIN: Yes, that is the plan. Five.

Bernie, your hand was up?

DR. LO: My hand was up. Let me just suggest that one of the five -- I am not sure which rank -- address the issue of health services research and the very blurry interface between health services research, disease management and quality improvement. So this old chestnut of what is research, it has been

typically argued clinical research versus patient care.

I think in the health services research area can you use personal health information stored on computers for research projects. It is actually easier to use it for things that you call business necessity, quality improvement, things like that. It can be the exact same study with none of the protections. So given how much of that is going on as part of managed care I would like to see us look at that because no one else is looking at it.

DR. MESLIN: That was one of the -- at least the -- one of the four suggested ones. And then there were four.

DR. MIIKE: I think in the future meetings we should have scheduled two full day meetings knowing full well we are going to have a one-and-a-half day meeting.

(Laughter.)

DR. MESLIN: In the interest of attrition management, unless there is anything that other Commissioners want to bring up about the priority setting memo or other matters maybe we should enjoy the rest of our morning.

Dr. Cassell, did you have any other things

you wanted to --

DR. CASSELL: No. I am looking over the list of dates. Did you all act on that yesterday?

DR. MESLIN: No. We have not acted. There are a couple of folks who have not given us the dates for the next meeting but just to let the public know, we will be meeting in Baltimore or Annapolis. The physical location has not been confirmed but we will do that as quickly as we can. We had to wait for our extension to find out that we would be meeting so we found that out yesterday but we will be meeting in the Baltimore area on the 21st and the 22nd of October. Other dates will be on our web site as soon as they are confirmed.

Other than that I think we should wish everyone a happy rest of their Friday and God speed and avoid the hurricanes.

(Whereupon, at 10:21 a.m., the proceedings were adjourned.)

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