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OPENING REMARKS

HAROLD T. SHAPIRO, Ph.D.

DR. SHAPIRO: Welcome, everyone. I would like to get our meeting started.

I notice Eric, in making out these agendas, lives in the hopeful anticipation that all of us have 15 minutes worth of something important to say, which I continuously disappoint him but nevertheless he keeps on hoping. I cannot help him out today.

I just want to thank everyone for being here today and we do have, I think, some really rather important and interesting projects to review today. Some of which are underway and others about to get underway, which will really be quite important for the commission over the next year-and-a-half or so.

So let me turn the microphone over to Eric who first has an introduction to make and then we will get on with our discussions today.

DR. MESLIN: Thanks very much.

For those in the room, who have noticed that there is a new person sitting on my left, I wanted to let the commission know and the public who is here that are very pleased that Dr. Marjorie Speers, Deputy Associate Director for Science Policy at the CDC, has
through an arrangement with the CDC been brought to NBAC to work with us as the project director for our coming "oversight report." I put that in quotes because it is yet to have an official title.

Dr. Speers is uniquely qualified to lead this project on NBAC's behalf both with her extensive experience in federal policy and in human subjects protections and with her well-known expertise in regulatory structure. I know you will all benefit from her wise counsel and her assistance.

I would also just like to acknowledge for the record how grateful we are to the CDC for allowing us to have Dr. Speers join us. I think it will be of great benefit to the CDC and, indeed, the entire Federal Government to have Marjorie onboard.

So welcome, Marjorie.

You will be hearing more about how the sort of nuts and bolts of the arrangement works. We hope to have Marjorie physically located with us at the NBAC offices in the not too distant future but you will see her participating in discussions electronically and otherwise in the days and weeks to come.

Our general plan for the morning as you have seen in your briefing book is to have three presentations on materials that were previously
circulated to you electronically.

One prepared by Jonathan Moreno, a consultant to us that you all know and love, and Robert Tanner from our --

DR. BACKLAR: Yes.

(Simultaneous discussion.)

DR. MESLIN: A pause for effect.

DR. SHAPIRO: Here, here.

DR. MESLIN: Yes.

Happy Chanukah.

And Robert Tanner from our staff.

Jonathan and Rob have worked together on that first document in your briefing book looking at the IRB issue.

Kathi Hanna, who I think you also know and love as much as Jonathan if not more --

DR. BACKLAR: Yes.

(Simultaneous discussion.)

DR. MESLIN: -- more loving and fondness, has, as you know, been -- we have contracted with her to work on another project. You will hear from Kathi.

The only thing I wanted to say very briefly at the outside was that the materials you have in the briefing book on this oversight project are really initial pieces of what will be a much more comprehensive
work plan for you. So, in particular, the outline as we have defined it in the book, which essentially lists a number of important questions that we think the report will want to address should not be confused with an actual outline, chapters and context, and methodology.

So I just wanted to alert you to the fact that the discussion we will have this morning should allow you to decide what you think should go into such a work plan and we hope within the next ten days to two weeks a more substantive outline of what the plan of action would be for completing that outline will be. And you will hear more from Marjorie about that in a few minutes.

But I did not want you to suffer the misperception that the outline, which we have been trying to provide you for all of our other reports, in this report is what you need to endorse or adopt or critique. It really is a set of substantive questions that describe the scope.

Those are all the remarks I wanted to make to get commissioners up to date on what the plan of action is for this and maybe we can just ask Jonathan and Rob to just walk us through some of their materials.

OVERSIGHT OF HUMAN SUBJECTS PROJECT

SUMMARY OF IRB STUDIES
DR. MORENO: Thank you.

Good morning.

First, I want to say that Rob, as usual, has done yeoman's service in developing the material that you have for this first part of the morning. He did so in the victorious after glow of his successful passage of the bar examination.

So congratulations.

(Applause.)

DR. TANNER: Thank you.

DR. MORENO: That is better than being loved, isn't it?

(Laughter.)

DR. MORENO: You cannot take that to the bank.

DR. SHAPIRO: We will not discuss that issue.

(Laughter.)

DR. MORENO: The project is, of course, the oversight project and as a dreaded punster I cannot help but reflect on the other meaning of the word "oversight."

It is very easy, particularly in a little effort like this, to fail to do justice to the previous reports by our predecessors, particularly -- and what
makes me particularly anxious about organizing material in a summary way like this is that the half dozen or so reports were done under different authorities. Very often by largely different people under somewhat different historical circumstances with different purposes.

So one needs to keep in mind that there are important substantive differences that, for example, Alex over here would probably point out to us in interpretations of the -- for example, the President's Commission's report in '83.

Nonetheless, it is rather clear if one does a review of the half dozen or so reports on the IRB system or that had something to say about the IRB system from the early '80s to the late '90s, that common topics emerge and some common themes of recommendation emerge.

At least in broad -- in a broad fashion. It would clearly be irresponsible for us not to -- for you, I suppose, not to be aware of what previous groups have had to say about this issue since a lot of time and money was spent by some other smart people on this question.

So this memorandum, dated November 23, '99, entitled "Previous reviews of the federal system of human subjects protections," goes through the following
-- a summary of the following previous reports:

One by the President's Commission in 1983 entitled "Implementing Human Research Regulations."

The next by the Advisory Committee on Human Radiation Experiments from 1995.

It is interesting, by the way, that there is this sort of 12 year hiatus in major reports on the system.


And then the Office of Extramural Research findings in June of 1998.

Several state reports.

And finally a report by an academic group with which I was associated at the University of Pennsylvania, Center for Bioethics.

Looking through these reports it is possible to identify at least four persistent topical features and about -- you know, these lists are somewhat arbitrary -- but about eight or so themes in recommendations.
Now perhaps I should just add that although there is this 15-year period over which these reports take place and there is a certain risk again of anachronism in trying to summarize what they have to say, I think it is important to point out that the regulations themselves did not change that much over this period. So there is some background consistency there.

What did change, I suppose, is the environment of research, of clinical research, over this 15, 17, 18 year period. Including not only, as many of you know, the -- as you all well know, the nature of the business which was much more highly capitalized, involved many more subjects, got into multisite research in a much bigger way than was the case in the early '80s, and seemed at least to strike many observers as stressing the IRB system in a way for which it was not designed in the late '70s or early '80s.

And, also, the fact that there were certain public, if you like, scandals that brought the public's attention back to the question of human subjects research primarily expressed in the human radiation experiments controversy.

So there was some background stability in the regulations in this period while at the same time there
was an increasing interest in the public in the question of human subjects research, I mean the ethics of that activity, and that accounts, I think, for the fact that by the mid '90s there is this flurry of new interest.

Perhaps it should also be said that the President's Commission report in 1983 was intended partly, as I understand it, as an attempt to ensure — I wish Alex were here actually to say more about this -- but to ensure that the National Commission's recommendations with respect to the human subjects review system were implemented in accord with the spirit of the National Commission. So that document is an attempt to ensure implementation and provide continuing guidance since the National Commission ended.

And then 12 years later we have this new flurry of activity as a result of the human radiation experiments and other things that have happened.

Well, we tried then to -- and I am not going to belabor the obvious, you have this stuff in front of you, but I am just going to point out on pages 9 to 11 the persistent features of the reviews that we have listed.

First of all, several of the reports mention the importance of monitoring. Both report to — both in regard to the monitoring of the IRB's themselves,
perhaps by the Federal Government but also -- through
the OPRR but arguably also through the universities
themselves that are responsible for these entities. And
there is more talk about the university's responsibility
to make sure that IRB's function well as we go through
the '90s than there is in the beginning of this period
that I am describing.

And then the second sense of monitoring, of
course, is the monitoring that IRB's have the authority
to do but it is generally agreed rarely do, which is
that of consent processes, for example, and other
elements, other moments in the clinical trials process.

Secondly, many -- in several of these reviews
there are allusions to -- and perhaps illusions as well
to the need for some kind of ongoing national forum for
the assessment of novel ethical problems in light of the
rules governing research involving human subjects.

But there is great variation in the notion of
what that review -- that national review should or could
be like, including -- had I added our own report on the
involvement of persons with mental disorders in
research. We also had something to say about that or
you did. I should not remind you of last year.

And there are lots of different notions about
how this national review should take place if it should take place at all.

Thirdly, the reports frequently discuss problems with IRB management, particularly among busier IRBs. This again is a subject that comes up more frequently in the last five years than it did 15 years ago.

There does seem to have been an acceleration in the activity of some university research centers in the last 15 years. A sense in which there is perhaps a greater difference in the rate of activity among the busier centers as compared to the less busy centers today than there was in the early '80s.

And that is reflected increasingly in the reviews in the last few years that some of the busier IRBs are really busy and that perhaps -- and this is especially true in the IG report -- perhaps those that -- -- I am sorry, in the Office of Extramural Research Report -- that perhaps those are the IRBs, the top ten percent that do 40 percent of the protocols, that especially need our help or especially need somebody's help because they are really stressed.

Finally -- oh, and I should also say that part of this concern about IRB management also goes to -- and I think this is quite important speaking as a former IRB
member and a current IRB consultant -- the importance of
IRB member training, not only initial training but
continuing education and training, and institutional
support for IRBs.

Just as a footnote to this comment, my
perception is, I have to say, as somebody who is
watching this from the sidelines, that as a result of
some OPRR and FDA activities in the last few years there
has been an increasing tendency for institutions to take
more responsibility for the support of IRBs. Perhaps
that is a kind of Hawthorne effect at work but my
perception is at least that the public attention to
these issues has increased the level of support at some
of the busier centers for IRBs, including professional
staff support, which can go a long way in helping busy
IRBs.

Finally, among the topics discussed, the more
recent reviews of the system especially have identified
problems in the system of local IRB review, which is
part of the initial spirit at least of the IRB system
and the Common Rule.

Local facility based review is supposed to
have many virtues, including being able to identify
specific problems or specific values that obtain in that
area, in that neighborhood where that clinical center
serves also as a care giver and with increasing
multisite studies and with central IRBs that review the
consent forms and protocols for those studies.

Many local IRBs feel that they are no longer
relevant, that they are virtually marginalized in that
process, and there is enormous pressure on them, as you
know, because there is money involved for their local
investigators and colleagues, and this work cannot be
done perhaps if they are not part of this multisite
study and they may not be part of it if the local
approval does not follow.

So these are the kinds of stresses that have
been part of reports, the more recent reports and the
changes in the research environment that I already
alluded to a couple of times.

Now just going through very briefly some of
the typical recommendations that one sees in these
reports continuing with the sort of meta-analysis I am
doing. First of all, repeatedly one sees the allegation
-- and this is over on page 10 now -- that IRBs have
inadequate resources to carry out their functions. I
have already alluded to some of these problems.

Secondly, there is a problem with the
preparation of IRB members, that they should be given
more education and that institutions should invest more
resources in ensuring that that is the case.

And perhaps also increasingly one sees in some of these reviews of the system recently that investigators also should be trained and perhaps there should be some local certification required of individuals who engage in research involving human subjects. That would be a significant change and my understanding is that there are several institutions that are following through with that as we speak.

Thirdly, there is a -- there are -- is a concern about the jeopardy in which local IRB -- the local IRB spirit, the local IRB philosophy is placed by the fact of multisite studies and that perhaps those local IRBs in some way deserve to be supported and to be ramified in their work and that their input not be excluded from multisite studies.

Fourthly, there is a continuing concern as none of us will be surprised to learn that the regulatory requirements are burdensome, unnecessarily so, particularly with regard to continuing review and to annual reports.

And there is also some concern that -- I do not elaborate here -- that some of the work that is done actually distracts from the really important issues of human subjects protections, that there is too much focus
on paperwork and not enough focus on what is really
going on, on site.

Fifth, a number of these reports contend that
IRBs lack information regarding the competence of
investigators even though the local IRB system, I think,
is partly intended, at least implicitly, to deal with
that problem. We know the local reputations of our
colleagues supposedly. But, in fact, as these places
get bigger and bigger that is not always the case and
one, in fact, may not know, for example, if one's
colleague's protocol has already gone through another
IRB somewhere and has been rejected.

So there are concerns that there is some
information that IRBs do not have that may be relevant
to their deliberations and another dimension of this is
the interesting vexing relationship that ought to exist
between the Data Safety Monitoring Board and the IRB and
the fact that DSMBs, of course, as part of their role
get information to which no one else is privy but which
may be quite important to the IRB in deciding whether,
for example, it wants to step in and monitor an ongoing
research activity.

I think that is a really interesting problem
and one that may well warrant further consideration by
you.
The sixth one is one that I have had to struggle with because I have to say I know a lot more -- feel I know a lot more about the OPRR process than the FDA and yet one does see repeated references, particularly recently, in these reports to differing cultures, the different culture of the two agencies. And that there is a -- that this puts local IRBs and investigators and research administrators and academic officers in a real bind because on the one hand they are set up for this compliance process, which is a sort of a priori process. It is a promise basically.

And then on the other hand when they have the auditors come in to do this after the fact review that there is a lack of continuity. There is a lack of integration between the sort of philosophical approaches of the agencies and it makes it harder for them to know which master they should be serving and how to serve them both adequately.

And I have to say that I have absolutely no creative ideas about how to handle that one but it is a concern that you hear people expressing.

The seventh has to do with the fact that we really -- of course, as often has been said -- do not know how many human subjects are in research and not only that we do not know how often those same
individuals are in research trials repeatedly. That is true not only of people who are sick but also -- quite interesting to me anyway -- it is also true of normal volunteers.

We do not know how much of a normal volunteer industry there is and how many repeaters there are and how many people are, in effect, making a living by moving from one research study to another and whether that is an important policy question or not I am not sure but at least it is an indication of how little is known, in fact, about what is going on in the human subjects world with respect to the people themselves.

Finally -- and I have sort of already mentioned this one. There is a continuing sense that IRBs need some sort of guidance and leadership on particularly complex issues that are not directly or comprehensively addressed in regulation but that have generated public controversy.

Examples are the use of people in research who have impaired decision making capacity, genetic research that may have implications for persons other than the subject, him or herself, research interventions in exotic but very promising fields like stem cell therapy and xenografts.

These are all areas that have been mentioned
in the literature and by some of these reporting groups about which IRBs very often feel quite bereft of help. They feel exposed. They have conversations within themselves and perhaps at their institutions about how to handle these. They end up very often on MCW-BIOETHICS Digest raising questions about how their colleagues handle these things, which is fine, but persistently one sees in these reports some notion that there ought to be a way of helping local IRBs feel less exposed, feel less vulnerable, feel that they know more about what the societal and scientific consensus is about the propriety of certain kinds of research, and under what conditions.

So I am going to stop there. Actually I will not. I am going to say one last thing that is just a procedural matter that I would sort of put on the table for you. That as you continue to examine the IRB system it might be very useful to have at least one sort of hearing or session perhaps with a subcommittee of the commission if not the full commission with IRB members themselves chosen from the grassroots as it were from various different kinds of institutions and nonlocal as well as local IRBs and also, of course, in some way getting to a representative, whatever that means, group of investigators who have to deal with the regulations.
I think that some of what those people are going to have to say would be really interesting. I have heard some -- I have had my ears burned off on more than one occasion when they found out that I was involved in thinking about these issues. And that clearly is something that ought to be part of the process over the next few months it would seem to me.

Thank you.

DISCUSSION WITH COMMISSIONERS

DR. SHAPIRO: Thank you.

Before we go to any questions, Eric, do you want to add anything regarding some of the next steps at least we have tentatively in mind?

And then let's go to questions and see whether that makes sense to the commissioners.

DR. MESLIN: Sure. At least one of the things we have started immediately is to start to network with a number of folks. I sent around on the NBAC E-list a note about the upcoming PRIM&R meeting which is occurring starting Sunday and into early next week. I will be at that meeting on the Monday, as will Marjorie and Ellen Gadbois from our staff, at a workshop that was already on the agenda, which we have allowed to be scheduled on Monday afternoon at 4:30 where essentially we will be there to hear from and discuss with
researchers and IRBs at the PRIM&R meeting concerns and ideas they have related to this report.

        We intended to send out a note earlier, hopefully, maybe later today on the MCW ListServ informing them about this meeting and our willingness to hear their views. This is certainly part of a broader outreach effort that we hope to have in place where other national meetings of investigators or administrators or IRBs we can seek their views in a more collaborative way.

        In addition, there will be -- we do have the opportunity, as Jonathan suggested, to convene either separate meetings or separate hearings in various parts of the country and obviously we will be interested to know what commissioners’ schedules are like in that regard.

        Were there other things you wanted to mention?

        DR. SHAPIRO: No. I do not think there is anything else except let's see what the commissioners think regarding what Jonathan and Eric have put before you.

        Just one other issue which we should include in our discussion as we go along this morning is the issue of how we want to -- and to what extent we want to focus on the so-called independent IRBs, that is IRBs
put together out there in the private sector and what that is and what we should do and how we should find out about what roles they play and how they function and so on but that is just one of the items on the agenda.

Let's just go to questions and comments from commissioners.

Larry?

DR. MIIKE: Jonathan, number six, OPRR and FDA, who are -- who is raising those issues and have different significant problems? It seems to me the only kind of solution I can think of is that there be sort of a systematic contact between FDA and OPRR so that FDA and OPRR can look at what FDA has found retrospectively and say what are the kinds of things they should be alerted for. Basically who is raising that?

DR. MORENO: Mostly I would say that it seems to me to be academic administrators who have the responsibility for compliance who are very concerned about this and that is perhaps another group that you might want to hear from about this.

DR. MIIKE: But is it a big problem on the FDA side?

DR. MORENO: I do not know how to characterize it. I am not sure I want to characterize it for the record but I have just -- I have had people say to me
that they find it -- they feel as though they are serving two masters with different sets of expectations but I do not know that I can say much more about it than that.

DR. SHAPIRO: Jonathan, just to pursue Larry's question and make sure I understand both your comment and what -- and what Larry has asked. Does this occur in circumstances where an academic health center might be doing some kind of joint project on the research -- on a clinical trial of some kind or another and the FDA, of course, needs to be involved and, of course, the academic health center has a multiple project assurance with OPRR? Is that where it arises?

DR. MORENO: Yes, I think so. And perhaps one element of this is also a concern that the IRB -- to what extent is the IRB responsible for the kinds of things that the FDA would be concerned about, which is the methodological adequacy of the study. And not limited to the consent issues. Maybe that helps a little bit.

Many IRBs, as I think most of us know, I see you are nodding your heads, we have been in many conversations in IRBs in which questions are raised about the methodology of the study, the science, whether it is warranted, and then somebody will say, "But wait,
we are an IRB, that is not our job." And so this is an area in which there is some question about slippage of an OPRR kind of issue and FDA kind of issue in the IRB system.

DR. SHAPIRO: Thank you.

Other comments or questions?

David?

DR. COX: Yes.

Jonathan, in terms of your looking this up, out of all the things that you mentioned, and there are things that you hear repeatedly, one of the things that was not mentioned is sort of the grounding in the fundamental principles that IRBs are supposed to be, you know, doing so that there is a common standard by which even locally --

DR. MORENO: Right.

DR. COX: -- and how often locally that is discussed and that it is even clear sort of where the goal posts are. So I do not have much of a feel for this overall. Some places probably do it and some do not. Is this an issue?

DR. MORENO: I think IRB -- again this is somewhat impressionistic and somewhat based on the reports that we looked at. I think IRB members understand that their role is human subjects protection
insofar as that is the sort -- I am not sure of the language. I cannot remember the language they used but the underlying spirit that is supposed to tie all IRBs together in what they do. That is understood.

But somebody said to me actually yesterday how often -- how clearly do IRB members themselves understand the regulations, have they read the regulations, isn't it often the case that IRB members will say, "It is a good thing we have got the lawyer here. That is his or her job or the administrator to worry about the regulations. We are going to worry about subjects protections in a more global philosophical sense."

But I think that is understood but then when you -- when people start getting uncomfortable -- for example, the definition of minimal risk, right, which easily people can then say, "Well, that is a problem for the compliance officer. That is a problem for the lawyers. Not -- we have to focus on the protections question."

DR. COX: Well, just a -- may I ask a follow up to that, Harold, because I think when Dr. Lane came and spoke to us the -- you are right, the types of research has changed over the time but the ethics has not changed.
DR. MORENO: Right.

DR. COX: It is pretty clear. You know, even I understand what the Belmont Report is about. And the -- but how you get that translated is the difficulty.

DR. MORENO: Right.

DR. COX: So everyone is passing that translation off to the next guy. Then, in fact, people -- the road to health is paved with good intentions and no one is being protected. So somehow for us to really sort of focus on this question, which is in some ways theoretical but in other ways really practical, the translation of the stuff, and what I would be less keen about is focusing on, you know, exactly what the nuts and bolts of the administrative operations are and then missing yet one more time how it really gets translated.

DR. MORENO: And I think that is why -- I think that is right. I think that is why people are very interested in talking about education and continuing education for IRB members and investigators.

But again I think it would be -- it is important in my view to assert that -- at least again in my experience -- IRB members are aware that their role is human subjects protections and that at least prima
facia is the case. How -- but how again that -- there
tends to be some slippage there perhaps in terms of
dealing with the specific issues is what your question
goes to.

DR. COX: Yes.

DR. SHAPIRO: I want to come back subsequently
to talk somewhat about the interaction between the IRBs
and the legal system but I have got a number of
commissioners who want to talk first. As a matter of
fact, the list has just gotten a little longer.

But, Tom, you are first on the list.

DR. MURRAY: Jon, as I am sure you are aware,
in some other countries the balance of IRB membership is
quite different from the United States. We have the
requirement for one unaffiliated member or one lay
member.

Now I fully understand that many IRB members
see themselves -- institutional members -- as
beleaguered and unappreciated protectors of human
subjects. Nonetheless, I did not see it in any of your
points you noted, has there been any discussion in any
of these reports or is there discussion among the IRB
people with whom you have talked about the prospect of
changing the composition of IRBs to reflect more intense
input from the broader community unaffiliated with the
institution?

DR. MORENO: Well, this is the other sense of oversight that I mentioned before by way of self-defense. We probably should have, although we did not mention, that there have been some recommendations along those lines. In fact, this commission itself recommended with respect to persons with mental disorders last year that there be a couple -- check me on this -- a couple of people who have -- on the IRB that regular reviews protocols that have to do with people with mental disorders who are familiar with the problems of that population in research.

So the answer is yes although I have to say that that is not a very prominent theme in the reviews. It is -- arguably it is emerging only in the last couple of years, particularly as the OPRR has identified IRBs that have failed to take that requirement seriously and, as you know, intervene very aggressively.

So, arguably, Tom, perhaps if I had number nine, the emerging theme would be the membership issue and sort of opening things up. And there may be a -- also another dimension of that sociologically as perhaps the famous FDA waiver for emergency with research under certain conditions, which requires community consultation.
So I think that is well taken as maybe there is a certain populist movement that is emerging as theme number nine that has to do with opening up the membership.

DR. SHAPIRO: Jim?

DR. CHILDRESS: First, an observation and then kind of an extended question about how we might proceed in regard to what Harold has raised about independent IRBs but a preliminary point. David mentioned about Belmont and its role in IRB deliberations. As I recall the McKay report indicated that many IRB members were virtually unfamiliar with the content of the Belmont Report and so those kinds of principles were -- (Simultaneous discussion.)

DR. CHILDRESS: -- present there without their knowing that they were the Belmont principles and they were operative.

I think Harold raised a very important question that does not appear at least as an issue in a couple of reports and that is what about the independent IRBs.

And I honestly do not know what is available in studies that have already been conducted about a more quantitative matter. How many are there, et cetera, et cetera? What kind of loads do they have? What is their
composition and the like? And I -- if there is not
material available like that then perhaps we ought to
commission a study of that sort.

But, second, I would be interested in
qualitative matters and perhaps having two or three
persons from such IRBs join us for a discussion in a
more qualitative way.

DR. SHAPIRO: I think that would be very
helpful.

DR. MORENO: It is interesting. That is a
nice point there. I do not know that there is any data
about how many there are and how many protocols they
review and so forth.

Most of the concern you hear expressed about
nonlocal IRBs or independent IRBs is not that they are
sloppy but that they undermine sort of the morale of the
system. If the goal is efficiency then if that reflects
badly on the local university based on IRBs, you know,
inefficiency must be a bad thing surely. And then it
has a kind of -- it creates kind of a negative
impression.

On the other hand, what you do not hear is
that there is sort of outlaws exploiting the system but
they -- rather that they sort of undermine the local
spirit of IRB review.
DR. SHAPIRO: Okay. Laurie?

MS. FLYNN: Thank you.

I really want to thank Jonathan and Rob for their report.

I just had a couple of observations that I think pick up on some of your themes.

We did in my organization an effort to recruit people to serve on IRBs as part of our response to the concerns about protection of human subjects in situations where mental disorders are the focus and, indeed, got a number of folks together in July, Patricia helped us train them, Trish helped us train them, and now to date have placed about 16 people directly on IRBs to provide that additional kind of lay perspective.

So I have a couple of observations. Number one, there are a lot of people out there who would like to help and I think we need to think more clearly about bringing the mechanisms together.

IRB administrators to a person that we have heard from are -- besieged is hardly a strong enough word. These folks feel inundated with tasks. They have a very difficult time recruiting the individuals that they need to assist them in those tasks. They point out regularly that it is often a part-time volunteer type position that they have or that they do not have any
staff to assist them and that the burden of the work that is placed upon them continues to pile up.

The comments we got back from the people we trained who have been placed on IRBs, again reinforcing some of what Jonathan indicated, many of them told us that they had been trying -- they had gotten in one day more specific formal training than have ever been given to other members of the IRB about this subject. And we have had a number of requests to reproduce our material, which kind of stunned us. We really were amazed at this.

The recommendation that you made to think about holding hearings or getting input or getting a sense directly from participants in IRBs and investigators, I think is really important.

The administrators, in particularly, are feeling that they are swimming in a very heavy current with increasing expectations, but notably not increased resources, are concerned that we understand the environment in which they are trying to operate. And point in particular to the fact that they seem to be the focus of all the attention and "reform" and nobody is looking at what is going on in these private IRBs.

So the notion that we look at some of these IRBs that are outside the scope of our current, although
imperfect system of oversight, is a strong theme and I do agree that if we listen to this population that is working directly in the arena we will learn from it and we will also, I think, see the need to expand our focus and look more directly at what is going on in the -- on the private side.

DR. SHAPIRO: Diane?

DR. SCOTT-JONES: The question that I have is the one that Tom has already asked, and I would just like to add that, that is regarding the nonaffiliated members of the IRB or the community members, and the specific points that I would like to make is that it would be great to have some information about what kind of education and training are provided to the nonaffiliated members. And then how well integrated those members are into the overall IRB, that is how comfortable are they expressing their views and when they express their views how well received they are by the other IRB members in the review of proposals?

DR. SHAPIRO: Thank you.

Bernie?

DR. LO: I would offer a few more suggestions on the sort of ways we might proceed. I think a lot of the suggestions that Jim and Laurie and others have made, I think, will really help us.
There are two issues that sort of come out that sort of suggest that we try and find more empirical information about these issues. One is education. I think everyone agrees IRB members and investigators need more educational research ethics.

And I am struck at how little there is -- I mean, there are always these calls for education but very little on how is it actually being done. Are there programs that work? Are there things that IRBs and others have tried that do not work? I know from, you know, my other hat -- you know, all the NIH training grants supposedly have a requirement for training in research ethics. So there is some experience out there.

My guess is that the experience is pretty negative. It is very perfunctory and not very good education. But to the extent that people are calling for education but do not really have any clear ideas on how to do it and what has worked for others, we could do a service by bringing together some people who have tried to educate both IRB members and investigators to try to find out what works and what does not.

The other issue that comes up and it was also in the draft outline is the idea that the current regulations were really drawn up with particular
attention to problems with biomedical research and now
that the scope of research has expanded there are
questions as to whether there are new issues that come
up that are not well addressed or whether some of the
concerns that really were first raised in the biomedical
context and put in the regulations maybe do not apply to
the text research.

We got into this to some extent with our
research on human biological materials report.

I do not know if there is a place, Jonathan,
where someone has really gone through and said, look,
you know, these regulations really were made for the
following problems that came out of the biomedical
research context and here are ways which it does not
apply to social science research or health services
research or epidemiologic research.

And perhaps if that is not readily available,
is that something we might want to commission a paper
on? Maybe you guys already --

DR. SHAPIRO: Well, on that issue, Bernie,
obviously every time we go down talking about one aspect
of the issues, the IRBs and how they are really
functioning, we do, as you point out, come up against
broader issues, that is, is the Common Rule structured
correctly for this reason and other reasons, that is
dealing with -- is a single rule dealing with biomedical
and social science and epidemiological and health
services research really a useful idea anymore? And
that is an extremely important issue and I am glad you
have raised it. It will come -- we need to focus on
that in my view directly when we come to think about the
Common Rule as a structure but it plays a role here and
I am very glad you raised that issue.

I think it is one of the important issues we
will have to face as we go through this -- as we go
through this project.

I have got Trish and Rhetaugh next.

DR. MORENO: May I just say one --

DR. SHAPIRO: Yes.

DR. MORENO: -- thing directly in response to
what Bernie said? I mean, I think that also gets well
taken and -- for example, in my university there is the
IRB for -- basically for psychology and sociology and
there is the IRB for the health sciences. And as I
think about it, and Rob should check me on this, I do
not think any of these reports really address that
specific question. I know that the American
Psychological Association has been very interested in
this issue over the years and perhaps someone from there
could come and talk to us about how they perceive this
IRB issue for deception research and so forth.

DR. SHAPIRO: I think, Jonathan, if I could say so, also increasingly important, especially in recent years is this health services research. It is a bigger and bigger issue almost every day and it is different in character than some of these -- at least it is often different in character.

DR. MORENO: The other thing I want to add just with respect to your first point, what educational programs are there at universities and which ones seem to work. Actually you could get a panel of representatives of three institutions that the OPRR says when I call them that they verbally at least refer to these three when people call them. What is a good model? Well, they refer to Minnesota, Rochester and UC Irvine.

All have educational programs of various sorts and I know that in the case of Minnesota and Rochester they actually have it for the whole institution, all investigators. In Minnesota it is animal as well as human. And at Rochester they have developed an exam that people have to pass in order to do research with living things. So we could hear more about that from those people.

DR. LO: Let me just ask a question. Do you
mean UC Irvine or UCSD?

DR. MORENO: My understanding was it was Irvine but do not quote me.

(Laughter.)

DR. SHAPIRO: I have actually seen the exam from Rochester and it came up at another session we had once. I have forgotten exactly what the context was. There was someone here talking but I have actually seen the exam and I have no idea how they correct the exam. The questions are the appropriate ones. It was really quite -- you know, it is -- the questions -- someone had thought carefully about what the issues were. Now what happens at the other end I have no knowledge one way or the other.

Trish?

DR. BACKLAR: I am interested that I do not see anywhere any remarks or concerns about the issues of interests of the IRB and the institution but I am also interested in conflicts of interest. I did not see that here. But as we talk about what I call the offshore IRBs or the offshore research, I am not sure which I want to call it --

(Simultaneous discussion.)

DR. BACKLAR: -- offshore IRBs. I also understand that some institutions review research from --
- not from their institution but literally offshore research and that they get paid for this. And so then one begins to wonder about that kind of conflict of interest, not necessarily where the IRB is the offshore but part of another institution.

DR. MORENO: The figure I have heard is $500.

DR. BACKLAR: Pardon?

DR. MORENO: One figure I have heard is $500 that they charge to do these reviews. I do not know if anybody has heard other things.

DR. BACKLAR: I have heard it is not more than that.

DR. MORENO: Right.

DR. BACKLAR: But I have heard up to that.

DR. MORENO: Concerning the conflict of interest question and I am especially interested in the issue of whether financial arrangements between investigators and sponsors should be disclosed to the IRB separately but also arguably to the subjects themselves.

In all the reports so far as I know there is only one -- the ones that we cover here -- there is only one mention of that and that is in the New York State report on the use of so-called normal subjects in research and it is a kind of a throw away line.
So, in general, the answer is it is not discussed in these reports.

DR. BACKLAR: There was somebody who had spoken about these issues to the conflict of interests, I believe, when we went to NIMH, he is a physician and a bioethicist, and he -- it is hard to pronounce his name.

DR. SHAPIRO: Daniel Someisty (?).

DR. BACKLAR: Yes.

(Simultaneous discussion.)

DR. BACKLAR: It would be interesting to go back and look at the issue.

DR. SHAPIRO: Rhetaugh?

DR. DUMAS: My comment is related to the issue of training for IRBs and also the relationship between CDC and OPRR.

I am aware that there have been training programs in various parts of the country that I think have been sponsored by OPRR. I know that there was one out in Michigan and they have been in various parts of the country.

It would seem to me that it might be helpful -- this might be a good time to bring OPRR back to us again so that they can update us on their intelligence.

It seems -- I have been out on a couple of site visits with them and I have the distinct impression that the
work of this commission has really inspired and fired
the OPRR and I have been impressed with the breadth and
the seriousness of their investigations and also with
what has been found on the two visits that I have been
out with them.

And so I think it would be a good idea to hear
from them again because I think that they have kind of
broadened their intelligence in areas that would be
useful to us.

One of the things that I might mention is that
it seems that the IRBs are serious about having a
community member but they have one person from the
broader community and in talking with those people, from
a sample of two, they feel somewhat overwhelmed with the
responsibility of representing a community that is yet
undefined to them so that their expectations are
overwhelming. And there is a lot that I think can be
learned through that.

DR. SHAPIRO:  Eric, you had something?

DR. MESLIN:  Just two quick reminders. You
may not have seen them buried in the briefing book.
Picking up on one of Bernie's points about health
services research, we included a note from the Institute
of Medicine about a panel that they are putting together
and they hope to be done within a year to 18 months
looking specifically at IRBs and health services research.

So we will not want to repeat what they are doing but we will certainly track what they are doing and perhaps even invite the chair once he or she has been appointed.

Bernie, I do not know if you know any more about that panel yet and whether it has been constituted?

The second -- picking up on something Tom Murray raised before he stepped away regarding lay members and experience from other places, there -- I think it would be useful for us to do a comparison or at least learn from the experiences from other countries.

Fortunately, we have an international project underway which is doing much of that right now but there are several other countries who have different approaches not only to oversight and review of the IRB model but also to the constitution of IRBs themselves. New Zealand is one example where there is a greater proportion of lay members than our federal regulations require. So I hope you will agree that it will make sense to look outside of the U.S. borders to the experience from other countries in review issues.

DR. SHAPIRO: Diane?
DR. SCOTT-JONES: I have a couple of comments. The first is Jonathan mentioned APA, the American Psychological Association, in response to Bernie's question about differences between biomedical research and other kinds of research that are reviewed.

I wanted to let you know that I serve on the American Psychological Association's task force, which is revising its ethical standards for research with human participants, and I can, if you like, provide a statement about the experiences we have had over the past two or three years and the positive and negative reactions to our task force's work and I can also give a copy of the document that we developed.

Then the second comment that I have is regarding, number one, the adequacy of the IRB's resources to do its work in Jonathan's document to us. I think this issue extends beyond what is written here and when there are inadequate resources there are long delays and negative experiences that investigators have, they then alter their opinion of the whole IRB process so it is not just recognized as a problem of resources.

It then becomes labeled as a problem with the IRB generally and it causes investigators -- many of them -- to develop an attitude of great disdain for the entire process and to recommend that the process is in itself
inappropriate.

So I hope in what we do we can try to separate those issues. That is those that are arising solely from inadequate sources from issues that have to do with the process itself and whether we need this type of process.

DR. SHAPIRO: Thank you.

Just before we go on, let me ask everyone, despite the fact this is a small room and one thinks that you can easily be heard, it is very hard for the transcriber to hear us unless we talk pretty close to the microphone.

DR. SCOTT-JONES: I am sorry.

DR. SHAPIRO: No, it is not only -- I did not mean to do it now. It is just that I got the note on a paper in front of me just now. So, please, when people speak try to speak close to the microphone. It just makes it easier for our colleague here who is doing the transcription.

Let me ask Jonathan a question which I indicated I would ask way back at the beginning. That is how all these considerations interact with legal requirements and what it is that -- constraints that may be placed on the IRBs by having a legal requirement which are not directly in these regulations but come
from broader concerns of hospitals. Let me give you an example.

Informed consent. It is one thing to hear calls all the time to have simplified and understandable informed consent documents. It is another thing to hear from general counsel of the hospital what you have to put in to protect yourself from some potential suit down the road and by the time you get through with this you sort of throw up your hands and say, "Well, ask the legal people, I cannot even deal with this anymore."

My question is, is this something you hear often or people bring up? Did I just invent this in my own imagination? Is that an issue at all? Just inform consent is one example. There can be many other examples in the IRB operations.

DR. MORENO: Here I really think -- I hesitate to say much for fear of prejudicing your views. I mean, I have to speak from my own experience.

DR. SHAPIRO: Yes.

DR. MORENO: I may be wrong about this and I think this is another reason for these panels to give a sort of qualitative window on the relationship of legal counsel in the university.

But my impression is that the lawyers do not get involved until there is a problem that is brought to
their attention either by the IRB or by some other party so that, in fact, there is not very much involvement and arguably there may be instances in which there should be more involvement by legal counsel.

So I think it is just the other sort of problem. They tend to put out fires after they have already started.

DR. SHAPIRO: Let me try to push that because while that may be -- what typically happens in many cases like this, although I cannot speak directly with respect to the IRBs, is, yes, a fire happens and general counsel comes in. But then the rules change forever and the bureaucratic system just accumulates these rules. They do not go away.

DR. MORENO: Right.

DR. SHAPIRO: And one fire on top of another fire on top of another fire eventually leads you to a rather complex situation. Again I am not asserting this is the case.

DR. MORENO: It is, in fact, true.

DR. SHAPIRO: I am just wondering if it is --

DR. MORENO: I agree with you in this sense.

One does hear investigators, I am sure others of you as well, complain about some requirement. And then when you point out that that is not a federal requirement,
that that is a local requirement -- I have had countless
conversations with people from my own institution and
other institutions about this, and they will say, "Oh,
well, that is crazy." Well, it may be crazy but that is
the way your institution has decided to do it.

So I think we are in the same ball park here.

There is a sort of local accretion of requirements that
are often confused with federal requirements.

DR. SHAPIRO: Laurie, do you have anything?

And then Steve.

MS. FLYNN: Yes. Just another comment on this
issue of informed consent because this, too, has been a
real focus that my organization and others in the
psychiatric research arena have had. And I have spent
some time going and watching informed consent procedures
and have been struck by the variability of what passes
for informed consent in some places.

It has nothing to do with the document. I
mean, you are quite correct. The documents today are
extraordinary and have very little understandability to
the average individual and are quite challenging if we
are concerned about particularly vulnerable subjects.

So that institutions that are trying to be
responsive to the concerns that are abroad are looking
for ways to supplement. We produced a little videotape
that is aimed directly at the potential subject and kind of boils it all down to the questions you should ask and the things you should know.

But the institutions themselves, I think, feel very much like the lawyers have abandoned them, much as Jonathan said, that the lawyers show up only when there is a threatening letter or a lawsuit arrives, and I think they feel very insecure about how they can meet both the legal test and the real test of protection.

Again this comes back to the IRB in terms of what is their job. How does the IRB really assure itself in the face of these mounting concerns, this voluminous paper, the signature on which does not necessarily imply that real understanding was achieved.

So I think it is a very critical issue and I think it is one that continues to vex institutions and the lawyers have basically taken, if you will pardon the expression, a very narrow legalistic approach.

DR. SHAPIRO: You know, I am struck in this conversation by its relationship to an issue we were discussing yesterday in the international context where we are wondering aloud whether we should, as Ruth suggested, distinguish between the substantive and procedural requirements for informed consent.

And one of the specific issues is, well, what
about something having to be written and signed. Here is one example. And the FDA suggests that maybe that ought to be waived. Well, we will not waive it here but in some sense it is already waived since nobody pays any attention to that part of it and we have to bring up other ways, as you have rather imaginatively -- you and your colleagues have sort of worked on imaginatively to make sure there is understanding that the written and signed part is not the substantive part really. It is what you are able to get them to really understand.

DR. MORENO: May I just add two other comments to this colloquy on the role of the law in this process?

The recent Stanford experience is very instructive. The fact that Stanford knew there was a federal regulation on the use of prisoners and forgot there was a state regulation and had a problem with that. This is an instance in which arguably legal input at the right time would have been very valuable and they did not get it, and again it goes to the point that Laurie is making that it tends to come rather late if it comes at all.

And yet you are right. There is still an accretion of requirements locally.

DR. SHAPIRO: The worst of all worlds here.
DR. MORENO: But they are bureaucratic. They are bureaucratic. They are not necessarily based in the law.

DR. SHAPIRO: Right.

DR. MORENO: At the same time with respect to research involving persons who are not -- who are not -- do not meet some standard of decision making capacity, there is a continuing issue in many jurisdictions, many states I can tell you because I have been talking to people about this, about the extent to which that kind of research can go on to be in strict accordance with the law with respect to who has decision making authority for these people in that state.

And IRBs are being permitted to go along and approve -- I know you know something about this -- IRBs are being permitted at many institutions to go along and approve research with certain surrogate decision makers involved who do not clearly meet what would seem to be legal requirements in that state for the authority to enter those people into research.

You may want to say more about this.

So this is an example in which there is a kind of -- there is a real ambiguity. There is a -- and there is perhaps a certain wink and a nod about what is permitted and about -- and the lack of contact between
the law and what is the actual procedures.

DR. SHAPIRO: Steve, you have been waiting patiently.

You changed your mind. Okay.

Any other comments about this? Obviously we have quite a work plan in front of us dealing with this but I think -- excuse me.

DR. CASSELL: One very quick one. I did hear the word "education."

(Laughter.)

DR. SHAPIRO: Right. So far so good, Eric.

DR. CASSELL: Yes.

DR. SHAPIRO: Okay. Any other comments, questions, suggestions? Again we will have to commissioners well before, I think, the next meeting a coherent set of issues and exactly what we are planning to do, which meetings we are going to attend, what panels we are going to invite it. There were a number of very good suggestions here today which we will try to follow up on.

Jonathan, thank you. Thank you both very much for this. You are certainly welcome to stay and let's turn now to our next subject.

Eric?

DR. MESLIN: I think we are now at the point
that Kathi Hanna can give us an update on -- following up from our request for getting more information about federal agencies.

Kathi?

SUMMARY OF FEDERAL AGENCIES INPUT

KATHI E. HANNA, M.S., Ph.D.

DR. HANNA: I will be very brief because I am really just going to update you on some procedural issues in terms of --

DR. SHAPIRO: I do not think your microphone is working.

DR. HANNA: Is this one working? Okay.

I am just going to provide you with an update on some of the procedural issues that we are pursuing right now in terms of collecting federal agency data. In the briefing book there is a memo that explains and refreshes for you the history of how these data were collected.

Just to give you the short story here, we have -- Rob and I have spent a considerable amount of time going through the files and looking at the data. At the September meeting several commissioners made a specific request that we do that.

We have pretty much gone through the first cursory review of the files and there is a lot of useful
information in there. However, it is dated and what we have decided to do is kind of a two step process here.

One is to respond to the letter that went out from Dr. Shapiro to the federal agencies several weeks ago telling them that we are now going to be asking for their cooperation again.

And what we are going to do is ask them -- we are going to send them back because -- in the interim the person that might have responded to the initial request to the Executive Order or might have responded to the initial interview that was conducted perhaps two-and-a-half years ago might not be there anymore. So we are going to give the agencies the original response to the Executive Order, which vary in length from a few pages to hundreds, so that we -- they know exactly what we are referring to. That will be their -- the first response that was given.

The next set of data that were collected we have in house. It is somewhat irregular. Parts of it are useful. We will not be returning that data to them for review. Rather we will be asking them to give us an update on any changes in their policies or practices that have occurred since they first responded to the Executive Order. If they have any written documents that have been produced since then we would like to get
copies of those.

Now many of the agencies have been providing these to us over the past few years. So for many of them it just means making another xerox copy and sending it on to us.

In addition because we would like to get some uniform information across the agencies that is current, we will be asking them to respond to roughly ten or twelve questions. These questions have to do with their research portfolio, the type of research they do, the research designs that they use, what their infrastructure is for protecting human subjects. So there will be a series of questions. We are trying to keep it short and very much to the point.

They will also be given the opportunity to inform us of any education or outreach activities they conduct in terms of informing their grantees or their investigators about human subjects protections.

We will also ask them to give us input on issues that they think NBAC should be addressing. We have done this repeatedly. There have been many opportunities for them to do so. This will be in a much more formal approach of doing it.

What we plan to do is at the December 13th meeting where all the agency representatives will be
convened is to share this draft set of questions with them to make sure that we are asking the right questions and that we are framing them properly.

One of the problems that I had with some of the original questions that were asked was that they were trying to -- there was an attempt to force categories that all agencies could respond to and I think what we ended up with were some empty cells here and there because the agencies are quite different in what they do.

So I am hoping that with this process it will allow for a little bit more of the texture and the complexity of the agencies to come through.

We will also be taking a close look at any other regulations or laws that the agencies are facing that they have to comply with on a daily basis that are either in conflict with the Common Rule or supplemental to the Common Rule. Much as each IRB at an institution might have developed their own policies and procedures.

Many of the federal agencies have also developed their own policies and procedures so the Common Rule is just one set of regulations that they are dealing with and we need a much better understanding of what other issues they are dealing with.
I think on the basis of collecting that set of data, I think they have until roughly the end of January to respond to us. We will then begin to try and frame the issues that have arisen and rather than providing a report that is an agency by agency review it will be more raising the issues that have come out of collecting these data with examples of particular problems or particular approaches that are working that the agencies can provide.

DR. SHAPIRO: Thank you very much, Kathi.
Thank you for the work that you are doing and getting us together on this.
Jim?

DISCUSSION WITH COMMISSIONERS

DR. CHILDRESS: Thanks very much, Kathi. I am delighted that you were able to actually find some things in the earlier work that could be redeemed.

I think the plan you have developed is really a good one for getting at the kinds of issues that would be important to us in our report and that we were much too specific in the kinds of things that were being asked for earlier.

Thank you.

DR. SHAPIRO: Any other comments?
Rachel?
DR. LEVINSON: I just want to add to what Kathi said about what will be done at the meeting on December 13th. I think the points you just made about what agencies do in addition to enforcing compliance with the Common Rule, any procedures that they have developed in response to the sense that the Common Rule may not be the perfect or complete model that is useful for their agency. I will also encourage them to use this as an opportunity to provide input to NBAC on this report, to provide broader comments on the federal system of oversight as a whole, to give examples of problems that they face within their agencies that make their jobs difficult. These are the people on the line, the intermediaries that are interpreting the Common Rule in many cases for their investigators. This would be a useful time for them to provide that information to NBAC.

DR. SHAPIRO: Thank you.

Thank you very much for mobilizing that meeting on the 13th. That should be very helpful to the process.

Any other questions on this particular issue?

Well, let me say a few things and then I am going to turn to Eric to talk about the broader outline
of this report.

The two issues we have discussed so far this morning, that is an evaluation and assessment of how the IRBs are doing and what changes might be necessary to make the system more coherent or at least more satisfactory from our perspective is an important thing. That is what Jonathan and others are leading us on.

Of course, how the federal agencies operate within the system and what problems they find with it and, therefore, what changes we might wish to make or we might wish to suggest I should say is a second important aspect of it. And that is what Kathi and others are leading us through.

Then we have, of course, the broader issue or set of issues which keeps popping up even when you discuss these particular components. Namely how do we think about this whole system and its adequacies and its inadequacies and what broader set of changes might be appropriate.

Whether something like the Common Rule, the focus as it is, with its various subparts is really an adequate structure or is no longer adequate or needs to be changed or adapted in some way is going to be extremely important. To say nothing of the issue which we have talked about many times here, that is our wish
to get all human subjects or human participants, depending what the right vocabulary is here, covered. Not just those that are -- come through sponsored federal projects or require FDA approval or otherwise fall under the existing set of regulations.

We have often expressed our view that everyone deserves the so-called twin protections in some appropriate manner. So that is really the job of the broader issue which Eric and Marjorie are going to lead us in that area.

So let me now turn to Eric first to begin some of our discussions in that area.

REVIEW OF REVISED OUTLINE

ERIC M. MESLIN, Ph.D.

DR. MESLIN: Jonathan and Rob, you are welcome to --

DR. SHAPIRO: They are more comfortable back there.

DR. MESLIN: Or be wherever you --

DR. SHAPIRO: Lean against the wall.

DR. MESLIN: Kathi needs company.

Or you can come up here if you want.

The -- as I mentioned a moment ago, the draft outline that you have in your books is the second version of this document but to be quite honest about
it, it is probably the ninth version of an outline that
the commission has seen over the last couple of years
that has attempted to weld or meld together a number of
disparate topics, including the IRB structure and
function, the oversight process, the adequacy of the
Common Rule, et cetera.

I will ask you to suspend your -- either
critique about whether this is the eighth, the ninth,
the third or the first outline and just keep in mind
that this is organized really as a scope document. One
that is attempting to capture as many of the issues
phrased as questions as we essentially could come up
with that attempted to address these two or three major
domains of work.

I will just mention briefly what some of the
ideas were that informed this quasi outline and we are
hoping that you will be able to both provide us some
feedback about the scope question knowing that this is a
promissory note for a work plan which will be more
substantive within the next ten days or so. But
certainly -- and we promise -- well in advance of the
next meeting so that you will have had a chance over the
E-mail list to give some comments.

The first point relates to the Common Rule
issue. Rachel has alluded to this and so has Harold.
It is fairly clear to us as we have been working our through the outline that the approach that would be of greatest use in response to Dr. Lane's charge to us is to keep in mind that the Common Rule is only subpart A of the federal policy for the protection of human subjects. It is only one of many parts of a federal regulatory structure that we think it is now important to address from a so to speak top down.

There are a number of imbedded questions in that first section which begins on page 3 and goes on for several more pages. No, there was not a particular organizing principle for why we clustered the questions in paragraph form in the way that we did although they do have some thematic similarity.

I think the most important thing to take away from those sets of questions is not whether you like them all or you do not like some of them but whether you think that they adequately capture the kinds of questions that NBAC would be able to respond to, gain information on, and more relevantly write recommendations for.

So this, I think, we took very seriously Dr. Lane's question and challenge that this is an opportunity for NBAC, whether it is following Jonathan's point that every 10 or 12 years a federal commission
gets a chance to take a big picture look and this is our or your chance. But I think it is important to keep in mind that unlike past advisory groups I think this group may now have a chance to look beyond just the Common Rule and beyond the biomedical paradigm that the Common Rule seems to have incorporated.

The only other thing I will say, and then let Marjorie offer some comments, is that methodologically -

DR. SHAPIRO: Eric, how often do we get a phone call? It must be for you?

(Laughter.)

DR. MESLIN: Telepathically.

Methodologically this -- or chronologically this is not set out as the Common Rule project first, the IRB project second, et cetera. This is something that we believe ought to go on contemporaneously, that there will be a set of discussions, commissioned papers and testimony that we will hope to get on this project or on this component I should say of the project while at the same time pursuing some of the IRB questions.

I would rather not go over much more of it and then let Marjorie offer some comments, with the following exception:

I think it will be most helpful to staff if
you can for a moment think as creatively as you can about this entire report, that unlike the past reports which have been topic based and, therefore, almost served as case studies, and the logically anterior questions to be answered before we got to this one, this is now the report where you can ask some of the big questions.

It is not that I am staring at Larry because he wonders if big questions will take forever. We want to get this report done, you know, in a reasonable amount of time so it can be reviewed and made use of. Clearly this could be a 20 year project. It is not going to be a 20 year project. It is going to be far less than a 20 year project.

So we would be very interested in hearing not only your ideas about the scope of either -- any of these sections but ways that we can pursue this above and beyond the usual and customary ways that we always have, which is commissioning papers, as we will, hearing expert testimony, as we will. You have already heard about the PRIM&R idea and other national meetings that we can go to.

We sent a note around to you on e-mail and Bernie Lo responded a few days ago with some conversations that he had had with his own IRB chair and
we hope that all of you who are on IRBs or who have experience with IRBs or with regulation can start to spread the word.

Maybe I will ask Marjorie maybe just to make a couple of other comments about our process or what she may want to do next before we open it up for commission discussion.

DR. SPEERS: Thank you. I just will make a few comments to reinforce what Eric has said.

As we put this outline together, it is -- in some ways it is divided into two parts. It is divided into a conceptual part, which is to weigh the number of questions about the Common Rule in the regulatory framework and then the other part is to look at the IRB system and some of the more process and less involved types of questions.

What would be most useful for us to move this to the next stage is, as Eric said, to get two types of comments or feedback from you. One is on the scope. Do we seem to have the right questions here? And we tried to frame these questions in a very neutral way, not leaning them either way. I hope that that is obvious to you.

Some of these questions as well appear very
obvious in what the answer may be and so some of these questions can be answered, I think, fairly quickly or easily and some are much more deliberate.

And then the second piece of information this morning is to help us -- give us some feedback on the work plan, which you see as the next step being, and we have discussed that this morning so we will continue that discussion.

While we want to pursue both of these two components simultaneously, they are deliberately ordered that we would discuss the Common Rule or the regulatory framework first, followed by the IRB system, only in the sense that, as Eric said, we want to at least begin by thinking very broadly and, therefore, one thing that could come out of the discussion when you talk about the regulatory framework is whether the IRB system is the appropriate system for review and monitoring of research.

And if we started with that discussion first then it would perhaps put some limits on the discussion about the Common Rule. So we felt we needed to start with the broader discussion and then move more to the discussion on the institutional review system.

If -- I would rather at this point open it for discussion. If you have questions about any of the
particular questions we can certainly answer those.

DR. SHAPIRO: Thank you very much.

Larry, and then Bernie?

DR. MIKE: Well, first in response to Eric, large does not mean a whole lot of activities. I think to me that is the trap we always fall into.

One of the things that we face in this is the biomedical paradigm but I think the larger issue is the definition of human subjects and I think that we should look in this study and not rule out the fact about cutting out some of the things that are currently under human subjects protection and looking at other laws like the confidentiality types of information to see whether those provide adequate protection so that we can say -- well, for example, when we listened to the agencies, I think the DOE especially, a whole lot of survey research and try to shoe horn those kinds of things into something in the biomedical paradigm.

So besides looking at -- I would like to see within the scope of this project whether there might be some things that we might exclude from human subjects protection which would fall under other areas of the law, whether they exist or whether we propose other ways of protecting human subjects, trying to shoe horn everything under it.
DR. SHAPIRO: That is helpful.

Bernie?

DR. LO: First, I want to welcome Marjorie and say that we are all looking forward to working with her on the project.

As I think about the issues that we have talked about and that I hear from investigators and IRB members, I am concerned the current outline may not enable us to sort of get prominence to some of the issues which I think may be really important. Let me just suggest what some of them are.

One is the issue of informed consent and the difficulty ascertaining whether the patient really understood as opposed to they got a piece of paper with a lot of disclosure on it and how you can better present information to patients and how you might start to assess whether patients really comprehended that information. So to sort of shift away from looking at the consent forms and looking to an interaction between an investigator and a potential participant.

Secondly is the issue of education which we have talked a lot about and that you do have some material to educate the IRB members but not only -- I think we should put in a section on education to investigators.
And I think really give it more prominence because it is the sort of thing that in the long run has to happen and most reports like this have as recommendation, you know, the last from the end there should be increased education for IRB members and scientists and very little on, you know, how you would actually do it, what resources do you need, et cetera.

We know how to do it.

Another issue is just funding for IRBs and what should be an adequate level of staff support, whose responsibility is it, how is it now being paid for, and is that adequate.

I mean, again I am impressed when I talk to IRB members and chairs they just -- they are doing this, you know, in their spare time, which they do not have any of. I think it sort of gives the wrong message that we pay for statisticians. We pay for people to process the grants to get the money but we do not pay for people to review human subjects protection.

And a final issue is sort of what, if anything, can we take away from IRBs. I think certainly a lot of investigators and IRB members feel there is a lot of sort of paperwork bureaucracy they do which seems to be very important from the point of view of the federal oversight agencies. It sort of misses the
point of that is not -- is that really the crucial issue in protecting human subjects? I think there is a concern that every time they get asked to sort of take on yet another responsibility is there going to be anything taken away from their responsibilities or at least made more streamlined.

Someone talked earlier about efficiency in these private IRBs. I think when you talk to university IRB members they will admit that they get asked to do -- and they spend a lot of time doing things which to them seem just like bean counting and paper pushing, not real protection issues.

So if we could sort of highlight those I think that might be useful.

DR. SHAPIRO: Just to comment a little bit on that before turning to Eric, I think if we can in this report come up with some ideas about making the system more effective from everybody's perspective, not simply from one perspective, then we will not have any credibility. So -- it is not possible for me to believe that after all this time we have not accumulated in the system things which are no longer performing any function at all except taking up people's time and filing cabinets.

So I think that is -- I do not know what they
are yet. I am not in a position to say but it seems to me that if we cannot find that we have not done very much work and I do not think we will have much credibility in the community.

Eric?

DR. CASSELL: Well, as I think about the subject, I think one thing, almost everybody around this table has served on an IRB and lots of times for a lot of years so it has gotten sort of fixed in there as the way we do things.

I am sort of interested if we could lay out a flow diagram of how do we protect human subjects. What, in fact, are the protections of human subjects that we have created apart from the institutional form that they take and then put back in so we can see whether, in fact, we are still doing what we meant to do in the first place.

I would like to see that.

DR. SHAPIRO: Okay.

Other comments and questions?

Yes, Laurie?

MS. FLYNN: I did not study your -- I confess -- your outline as carefully as I might but I heard an allusion to the issues around confidentiality and wondered if we will be careful to give emphasis to the
impact of the sort of exploding information technology on this issue. There is certainly a lot of concern in some areas of research about how one conducts research while providing appropriate confidentiality. It bleeds over into concerns about health services research in particular.

There are also opportunities that the internet revolution, as they call it, provide us in terms of protections and again some of us are talking about ways to provide sort of on line classes for people ongoing in research to help them understand what research is, to help them be partners in research, to continue to expand the realm of participation for human subjects as they go forward in research.

So I just think there is a whole area that is perhaps ripe for partnership if we look at information technology and its impact.

DR. SHAPIRO: Thank you.

Tom?

DISCUSSION WITH COMMISSIONERS

DR. MURRAY: Well, I want to congratulate the preparers of this report. It is very thoughtful and very thorough.

Let me just mention two things briefly which I think might be added.
There is at least one family of research paradigms which seems to fly in the face of the requirement -- the central requirement of informed consent and those are the various conceptive research paradigms which are still permitted and which I was familiar with 30 years ago more so than I am now but it is always rather bothered me that they seem to have escaped scrutiny.

The second issue is although we do refer to federal infrastructure to support IRBs, we do not say anything about the resources that an IRB might need more broadly and from within say their own institution. I think it would be -- it would just be a terrible oversight on our part.

DR. SHAPIRO: One of the -- I was talking to Eric and others earlier this morning about this project and it is an issue one of -- in my mind one of the big issues in here relates both to an issue that Larry raised earlier and others have raised regarding is there anything less that we can do or more than we can do.

And that is how -- what it is we call research and that is really central to this whole system of making sure that the decision -- with some easy decision to decide what is research and what is not research, therefore what should fall on one side. I am not for
the moment occupying a position either way. We put too
much or too little in that category. But rethinking the
definition of what we call research and seeing if we
have it right or not.

I think it is an important exercise for us all
as we go through the next few months because that really
starts everything off. If it is research you go down
this line, if it is not you are out in some other world.

There are a number of those things and I think perhaps
someone suggested this morning that we want to have a
decision tree or a flow diagram, which is what someone
suggested yesterday. And the one that is very easy --

(Simultaneous discussion.)

DR. SHAPIRO: -- is often the most critical
and gets the least attention. Like what is research?
That is sort of at the top of this. The investigator is
also near the top. It is essentially investigator
initiated activity. And education and things like that.

So there is some really critical big things here that
we need to think through as we get -- at least that is
how -- I do not know the answer to that.

Eric?

DR. MESLIN: I just wanted to remind
commissioners of another issue that we discussed -- you
have discussed before related to, in a sense,
nonregulatory mechanisms of oversight. There has been 
discussion around this table about accreditation and 
auditing and other institutional mechanisms. It has 
been in two of your previous reports as those 
mechanisms.

I know that there are groups, PRIM&R being one 
of them that is interested in following up on this. And 
like the IOM and other groups that are working on things 
that we might be able to take advantage of, obviously 
staff will pursue that, but again it is buried in the 
set of questions. I wanted to just draw to your 
attention that the interest is not simply being 
presented to you. It is not simply as regulatory 
solutions plus or minus but what other nonregulatory 
opportunities are there for ensuring adequate oversight 
and protection.

I only raised the audit, accreditation, 
disclosure policy issue as one of those categories, and 
it is an enormous category obviously. But if you have 
other suggestions that you would like us to follow up on 
or would like to share with us ideas about even that 
suggestion we would be grateful.

DR. SHAPIRO: Jonathan?

DR. MORENO: This goes to comments that Bernie 
and Laurie made about informed consent and real
Something I did not mention earlier because it really was not appropriate was that one continues to hear, of course all of us do, from investigator colleagues a level of cynicism in some quarters about informed consent and so I simply want to address that problem for just a moment.

When the Advisory Committee on Human Radiation Experiments did its subject interview study and they were interviewing 1,900 subjects around the country in medical oncology, radiation oncology and cardiology research, they also did focus groups with a selective number of those people.

And in discussion with people who have often been in protocols for a while, studies for a while, they found people saying things like when asked, "Did you understand the consent form when you signed it?" They said, "Well, I really did not."

But they would pull it out of their purse or their briefcase and said, "But, you know, I have reread it and I do not -- and sometimes -- and I showed it to my wife and we talked about it or I showed it to my Uncle Fred, who was a medic in the war or something, and got some questions answered."

And they really did learn about the study as they were going through it. As the textbooks say,
informed consent is not an event, it is a process if it really works.

I think it would be very useful for the NBAC to think about a way of encouraging -- this is not possible in all kinds of research, of course, but in some research, particularly Phase I research it may be possible, encouraging and finding mechanisms for doing what often times is in gerontology settings where there is reconsenting in a way that is at minimally burdensome but nonetheless gives people the sense that they really are involved in an educational process.

It would be wonderful, I think, if the commission could find a way of encouraging institutions to see that that happens when it can happen.

DR. SHAPIRO: Just to pick up on a comment that has already been made by -- I just want to -- I think myself that should be part of what we do, and that is the comment was made before by some that we ought to find parts of the system that really are traditions we can now do without because there undoubtedly are some.

At the same time someone mentioned the education done by -- I think it was University of California, Irvine, and Rochester and Minnesota, I guess, were three examples that Jonathan mentioned. I do not know if -- there are some terrific IRBs around
the country who really do a very good job, at least my belief, and they are the kind of models that we would hope would happen.

And it seems to me it might be helpful if we could identify some of those, both as examples and as acknowledging our own or others appreciation for the fact that even with all of these different -- some people have really done an interestingly good job. I do not know if that is most of the people or half of the people or ten percent. I have no idea what the percentage is.

But I do know just in conversations there are some that are really -- really did work well and that might be helpful also for us to understand what they did, how they did it, how they got that tradition going, and why it seems to work in those particular places and not so well elsewhere.

So I hope we will be able to find some maybe in our attempts, both at the current meeting and other places, and have people help us identify some of those institutions, which have done particularly well.

Yes, Marjorie?

DR. SPEERS: Harold, your comment is moving us into the next issue, which is fine, because I think the group is ready to go there but I did want to ask one
more question about scope.

We have got a number of comments from you of things to think about and to add. The flip side of that is, is there anything in the scope now that should not be in here that we do not need to address? Are there any questions that we should be dropping? Is it too broad? Or is there an area that you want to drop?

DR. CASSELL: Well, I mean, for myself, one of the reasons I asked the question about one of the things to go into the protection of human subjects, when I look at that again I am going to get an idea of what, in fact, has accreted to this thing that could be dropped because it is no longer doing what we thought it was doing and so forth. We just have not gotten basic enough for me at least to know.

DR. SHAPIRO: Steve?

DR. HOLTZMAN: This ties, I think, to Eric's point and it is going to take the form of a really strong endorsement of Harold's suggestion, and that is I think you have to start at the top with what are the different kinds of research that are now falling under the rubric of human subjects because all of these questions about appropriate education, appropriate regulation, the role of the IRB, what is the nature of consent, what is the motivation and the role of consent
versus protection, it has been accreting and that I think is a large part of the issue.

And I think when I look at how we took on the human biological materials, from my personal perspective it started with the assumption this is human subjects research, and as a result we found ourselves trying to deal with things in a way that did not for me really work. Whereas, if we had gone right to the top and said, "How is this different in human subjects research?", it could have given a whole different approach.

Another example in the field of genetic testing, though we have not been dealing with it, the whole tradition of genetic counseling arose around the fact that those genetic tests for monogenic disorders, highly penetrant that affected reproductive decisions. A genetic test is the moral equivalent of a cholesterol test. Do you really start to talk about the need for genetic testing or genetic counseling? And yet because it is called that you start to lay all of this stuff on it.

I think that is where we could make the most salient contributions by going back and saying what are the different forms of research and what is appropriate in terms of the goal.
DR. SHAPIRO: Thank you.
Bernie?

DR. LO: I am going to say something which may be very heretical and may get me thrown out of the meeting.

(Laughter.)

DR. LO: The outline is very heavily weighted towards the Common Rule and sort of how different agencies have different needs and different interpretations and stuff. And understanding that this is important to the administration and this is important to Dr. Lane, but I just wonder if that is really where the money is in terms of what our task and strengths are.

What I hear going around the table are issues that really have to deal with conceptualization of issues and clarification of issues, not so much kind of applying them to different agencies which we do not very much about and which have their own special needs.

I am just wondering if -- you know, certainly in the outline when you look at the number of lines devoted to different things, there seem to be a lot of material in that and relatively little on some of the topics that catch our interest like, you know, education, the consent process, what can we take away,
how do we address them as fundamental issues.

So I would make a plea for our hitting the big picture issues and maybe saying, look, somebody needs to look at how different agencies may want to deal with these topics but maybe that is not where our biggest contribution is.

DR. SHAPIRO: You cannot get thrown out for something -- it is not heretical enough --

DR. LO: Okay.

(Laughter.)

DR. SHAPIRO: -- to get bounced off the wall here. It sounds like that is --

DR. LO: Have all the meetings in San Francisco.

(Simultaneous discussion.)

DR. SHAPIRO: I mean, it is logical. Steve said, I think --

(Simultaneous discussion.)

DR. SHAPIRO: -- and I quite agree with you but I do not think at the moment yet it is one way or the other but I quite agree with the thrust of your remarks.

David?

DR. COX: So I do not think it has to be one way or the other because what Steve was saying if I
heard him right and I think what you were saying, Bernie, is that as long as we start at the top then that will inform how you implement it but if you do not clearly define what it is you are trying to implement then you spend all your time dealing with stuff that you really do not care about because you will not know what it is you are trying to implement.

In my view that is the primary problem at the local level and that is what I was saying to Jonathan. With the human subjects, everyone is there well-meaning and trying to get stuff done but they are not quite sure, you know, what the principles are. I know that sounds silly but it did not sound so silly when Jim pointed out that, you know, some people do not even -- have never heard of the Belmont report. So, you know, at that level we can certainly do that.

DR. SHAPIRO: Thank you.

Other comments or questions?

Eric?

DR. MESLIN: I just wanted to push Bernie a bit so I made sure that we understood well what his question was because as you were making your comment I certainly was nodding that what was the outline was supposed to be doing, taking the larger picture rather than the smaller ones. But I am wondering whether you
were -- not that I doubt that you were -- serious about
the issue of the micromanagement of informed consent as
appropriate for this report because in some ways it is
obviously a very important issue that goes without
saying.

I thought when you were going to make your
heretical comment it might have been something on the
order of do we really believe the 1997 resolution that
the commission adopted that the twin protections are
informed consent and IRB review. Maybe there are other
protections. Maybe those are insufficient.

I am not wanting to put words in your mouth
but were you really asking for more detailed thought
about issues like informed consent in this outline or
was it a broader conceptual question about these things?

DR. LO: I am certainly not going to
challenge, you know, apple pie and parenthood in terms
of the twin protections for human subjects but, I mean,
one of the things you hear over and over again is the
IRB cares about my consent form. They do not care about
all kinds of other issues like conflicts of interest or
the consent process.

They just want to make sure I have got the
right language and, you know, my IRB, among others, has
sort of model consent forms. You take paragraph A from
here and paragraph B, cobble it together.

And I think, you know, what Jonathan was saying, you know, consent is a process. It is an interaction. It is an educational thing. And just to sort of say to people that is what really counts and here is some innovative ways to do that well, do not get scared by consent monitors, here is some situations where it has really worked well and the researchers thought it was a good idea, it seems to me that would go a long way towards changing the view that, you know, what we are doing here is getting the consent form to rewrite.

I think that would have a lot more impact on sort of day-to-day research that is done in institutions like mine.

DR. SHAPIRO: Larry?

DR. MIIKE: I do not see any conflict in the big picture but we are stuck with the fact that we make recommendations on large policies that get implemented but the poor IRB is the one that has got do the detail part so that is the balance that we have got to find here.

And I would guess that -- and I agree with Steve, I mean, you know, we were saying the same thing. I said take a look at the definition of human subjects.
You are saying take a look at the definition of research. And the trick here is to see how it filters down to the federal agencies and to the local IRBs just to get all those people that have got to the day-to-day stuff that they have got to do.

DR. SHAPIRO: Any other comments or questions?

Eric?

DR. MESLIN: Well, there are a couple of next steps that would be helpful to us so that we do not just belabor the point.

One is if there are individuals that you think would be most helpful to have the commission hear from soon, or sooner rather than later, we need to know that. I am talking about the January meeting that is coming up in about six weeks. So we would really want to know sooner rather than later.

Secondly, I would very much like to know whether you think there are folks that can provide us with substantive assistance in terms of commission paper writing or on any of the topics that we have just mentioned. We will send back to you a list of action items of which there are many.

The third item is whether or not commissioners themselves want to become more or less engaged in some of these meetings that we are planning on attending that
fall outside of NBAC meetings, going either around the
country to various places, you need to let us know that.

And I guess fourth and final is really
repeating something that Marjorie has just said about
whether there are things that are missing from this that
should be there or things that are in here that should
not be.

I want to reemphasize one of the items that
was mentioned only as a passing note by the independent
IRBs, and it is the question of the -- we will call it
the Common Rule for the moment, but the extension of
federal protections to the private section.

This is a topic that we have talked -- you
have talked about on a number of occasions. The
independent IRB is not the same issue. That is one
example of how there are different types of protections
in place. But the commission has discussed on many
occasions whether to go outward and get all the agencies
complying with one set of regulations and outwards until
you have one federal system or one other system.

I mentioned before that there are other
countries that do have one system that covers both
publicly funded and privately funded research. We will
share with you the analysis of those countries but I
think we would be grateful to know what kind of remit --
what kind of license you would like the staff to
exercise in developing the next outline and work plan
regarding the private sector or the public-private
split.

DR. SHAPIRO: Bette?

MS. KRAMER: Eric, do we have any idea of the
scope of the research, the number of subjects that are
involved on these independent IRBs?

DR. MESLIN: I would say no. I do not know if
there are folks around the table. I do not know if John
or Kathi or Bob knows but I -- we do not know but I
think we can make a good faith effort to find out.

MS. KRAMER: Right. I think that would be a
question that we ought to pursue.

DR. SHAPIRO: Well, it seems to me, this is my
own particular opinion and I think it is shared, that
the commission has a desire to at least make an effort
to see if we cannot develop a reasonable system where we
can feel that all human subjects will get appropriate
protections irrespective of the level of -- or the
source of the financing of a particular experiment.

That would mean extending it into the private
sector in additional ways. It already extends there
along certain dimensions as we all know. Now desiring
that and being able to design a sensible and thoughtful
way of doing it is a separate issue but the latter is a challenge. I do not have a system to recommend but it seems to me that we have an obligation to at least try to think that through the best way we can.

So if you are asking should we pay attention to that issue and try to challenge ourselves to find a way to deal with it, my answer to that is yes. We cannot let this opportunity go by us.

Now whether we will find something we can feel good about or not, that is another issue. But it should not -- to me it does not seem like an overwhelming problem. Other countries have done it and we may not be able to do it or even want to do it the same way but it does not seem to be an overwhelming challenge.

Steve?

DR. HOLTZMAN: Again, I think where the private sector --

DR. SHAPIRO: Yes.

DR. HOLTZMAN: -- to the extent there is one would come from on that, it comes back to the original question.

DR. SHAPIRO: Right. Exactly.

DR. HOLTZMAN: Right. It is what are you attempting to extend it to?
DR. SHAPIRO: Right.

DR. HOLTZMAN: Right. I think that is one point.

I think the second point to recognize is to be very clear about this issue of independent IRBs. All right. They arise primarily out of the need and the desire to comply with the Common Rule when you are doing human subjects research that would be subject to FDA and hence is subject to the Common Rule but you are dealing with sources and subjects and investigators who are not part of institutions that have IRBs.

DR. SHAPIRO: Yes.

DR. HOLTZMAN: So it -- somehow we are rhetoric here with let's get around the system and, in fact, it is --

DR. SHAPIRO: No, it is --

DR. HOLTZMAN: -- that may be true in some instances for all I know but it is not to get around the system, it is to comply with the system.

DR. SHAPIRO: My only item -- and I agree with what you say, Steve, I think my view is that I would like to feel good about all human subjects without prejudice one way or another as to whether existing initiatives are either adequate or inadequate but I do not -- my guess is that they are not at least fully --
not widespread enough in some sense.

Now it is really quite interesting how listening around the table on the issue of conflicts of interest which Trish raised and other people have responded to, and one of the examples given was the fact that some IRBs are now selling their services in some sense or charging for their services. Maybe that is a pejorative way to say it. And the example was given of $500 or $1,000 or some figure like that.

I actually first heard about this attending the conference of the Veterans Administration Research Group and heard about their desire to do this mainly to provide support for the IRBs as a way of building up the resource base of the IRBs. They would sort of do this. And my -- I have been smiling all morning because my reaction was the opposite of what I heard. My reaction was how do they dare sell those services, as valuable as they are, for such a low amount per month.

(Laughter.)

DR. SHAPIRO: That was my initial response. They just do not understand what -- how valuable this service is. I understand that sort of increases the incentive the other way around. There is another side to that. I certainly understand that. But it seems to me that this is one of the most valuable services any
group could put together and to -- but anyhow that is just a side issue.

(Simultaneous discussion.)

DR. SHAPIRO: Bernie?

DR. LO: But I think it is really a crucial issue. I mean we have been saying here the IRBs are under staffed, they do not have the resources, they need somebody to give them full-time staff and time for the chair at least.

But how you provide that support in ways that create perverse incentives is very tricky. I mean, look at what is happening with --

DR. SHAPIRO: I think it is important.

DR. LO: -- financial incentives to doctors. I mean, we do not know how to pay -- doctors have to be paid but we do not know how to pay them in ways that does not create more problems or a procession of problems. So I think we need to tackle both issues together otherwise we are sort of asking for pie in the sky without attention to the real tough details of how we are going to do it.

DR. SHAPIRO: Trish?

DR. BACKLAR: Actually that makes the conflict of interest worse as people will talk around and pay for the IRB which will pass the protocol. There is another
issue here and I am wondering if --

(Simultaneous discussion.)

DR. BACKLAR: -- it is a little obscure. I am very interested in the problem of when one is on one side wanting to protect the subjects and then when one is on the other side as a researcher, and one's experience with an IRB, and I am wondering if it would be very useful, in fact, to also go back to researchers to find out what are the things that they find are useless that the IRB does with them as opposed to things that are efficient in terms of protecting the subjects. We are getting a few hints of that, Bernie, and other people who do research here.

DR. SHAPIRO: Well, I think it is essential that we ask investigators both what they like and dislike about the system and that would be one of our primary sources of information.

DR. BACKLAR: I did not want to leave those out --

DR. SHAPIRO: Yes. I think -- and we ought to have -- in my view we ought to have at one of our regular meetings some investigators come and talk to us as a commission about it so we can question them and see whatever questions are on people's minds.

DR. BACKLAR: And I think it was important
what Bette brought up and that Jonathan had mentioned about not knowing how many subjects when what one wants to do to know also what Jonathan brought up is how many subjects do this on a regular basis.

It is not just how many subjects generally but how many subjects may be -- may use this on a regular basis.

DR. SHAPIRO: Other comments and questions, issues?

Okay. Is there anything else on this project? Not necessarily to go on because we have got lots to do here. Okay.

Let me just say a word. There has, of course, been some e-mail traffic on other topics, topics we are not spending time on today -- of course, people are interested and are very interested, and I am interested in as well in patents and other kinds of issues dealing with various genetic issues.

On the one hand I am sympathetic to trying -- wanting to do something in that area. On the other hand I remain quite determined that we focus our resources on these two main projects until I feel quite comfortable that we really have those underway and in hand and just as a matter of conservation of our resources. I do not want to discourage ongoing conversation but I do not
think we have the resources to really attack them at this time so I mentioned that at our last meeting.

And I think maybe by our January meeting we will know more about just what our work plan is and see what leeway we have to possibly take on some other issues but I do not feel comfortable doing that just yet until we have our work plans on all these projects in better shape and we know exactly what resources are going to be necessary in order to carry them out.

So we will return in the future to some of these, whether it be January meeting or perhaps the meeting after that. I am not sure. So we will return to that at that time.

So I do not mean this in any way to discourage our ongoing discussion of these issues. It is just to say that at least for some period of time we just do not have the resources to devote to it other than our ongoing conversations amongst ourselves, which we are keeping very close track of and will pursue at some time at our next meeting or the meeting after that depending on how the work is going.

Any other issues to come before us?

Okay. I am threatening to adjourn this meeting.

DR. BACKLAR: Are you?
(Simultaneous discussion.)

DR. SHAPIRO: We are adjourned.

(Whereupon, the proceedings were adjourned at 10:12 a.m.)

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