INAUGURAL MEETING

NATIONAL BIOETHICS ADVISORY COMMISSION

October 4, 1996
8:39 a.m.

National Institutes of Health
9000 Rockville Pike
Building 31
Conference Room 10
Bethesda, Maryland

EBERLIN REPORTING SERVICE
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Silver Spring, Maryland 20906

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I N D E X

P R O C E E D I N G S

CALL TO ORDER, OPENING REMARKS AND INTRODUCTIONS

DR. SHAPIRO: Colleagues, let me turn to Ms. Rachel Levinson, who is the Designated Federal Official, to open today's meeting.

MS. RACHEL E. LEVINSON

DESIGNATED FEDERAL OFFICIAL

MS. LEVINSON: Good morning and welcome to the inaugural meeting of the National Bioethics Advisory Commission. My name is Rachel Levinson and I am the Assistant Director for Life Sciences at the Office of Research, Technology and Policy in the Executive Office of the President.

As Dr. Shapiro mentioned, I will serve as the Designated Federal Official for this commission for today. That means that I carry out certain administrative duties under the Federal Advisory Committee Act.

President Clinton established the National Bioethics Advisory Commission on October 3rd, 1995, by virtue of Executive Order 12975. In that order he designated Secretary Shalala of the Department of Health and Human Services to carry out administrative duties under the Advisory Committee Act.

There are also, I should mention, several other executive branch agencies that worked very hard on behalf of the President in making the commission a reality today.

Those include the Department of Energy, the Department of Defense, NASA, Veteran's Administration, National Science Foundation, Department of Justice, and others who have worked very hard to support this organization.

I should also mention the fact, very important fact, that this commission would not be a reality without the support and commitment of several members of Congress, particularly Senator Mark Hatfield, who will be missed very greatly in Washington; Senator Kennedy; Senator Moynihan; Senator Glenn; Senator Stevens; and Congressman Markey.

Dr. Gibbons will be here later this morning and he will give you a great deal more information about the background on the National Bioethics Advisory Commission.

I just want to say that this is personally a great day. I am sure it is for many people who helped to work to make this come to pass. And I am very pleased to turn the meeting over at this point to the Chairman of the National Bioethics Advisory Commission, Dr. Harold Shapiro.

DR. HAROLD T. SHAPIRO

NBAC CHAIR

DR. SHAPIRO: Thank you very much. We will be introducing ourselves in just a few moments, but let me introduce myself to begin with. I am Harold Shapiro, President of Princeton University, and it is a very exciting moment for me to serve as chair of this committee and to start off this inaugural meeting.

One of the great things about beginnings is that everything seems possible. That is why I always like the beginning of each academic year. It seems that all the things we failed to do last year could easily be done this year. We, of course, as Dr. Gibbons will talk about later on this morning, stand in a long stream of groups that have gotten together to focus on these issues, and of course our own work will depend an enormous amount on the scholarship that has gone on throughout this decade, a good deal of it, by members who are sitting around this table. So it is always great to be somewhere at the beginning and I am very pleased to be here today.

I, also, like the idea of these types of commissions because they seem to me to be both very old and very new at the same time and I am always attracted to the things that have that kind of mixture to them. They are very new for all the obvious reasons that all of us talk about each day, namely science and technology is rapidly advancing and opening new ethical horizons for us all to deal with and so on. Our moral sensibilities are changing and redefining themselves day by day, week by week, and so on. Those issues, of course, are very critical for us to deal with and will be the center, I presume, of much of our work.

But they are very old in another way. In the sense that societies have worried from the very beginning

how to deal with new knowledge and what it meant. I do not know how many other members of the commission have spent a small part of their lives, as I have, studying Greek myth. But if you look at the very earliest Greek myths, it deals in many ways with the exact same problem we are going to deal with here if you at least take a broad enough perspective on it.

Namely I will just give you one example. For those of you who are interested in this arcane subject I will talk to you some other time about it. But if you remember the myth about the Greek ship Argo, the first boat, and people wondered as these wonderful new horizons were opening up, new interactions between people that were not possible are not possible, when at the very same moment, the very same breath, they worried about the trees that had to be cut down to build the ship and wondering whether these new horizons would take away the moral limits that people accepted for so long in the nature of their community and so on. And there are many other Greek myths which have similar stories.

So the work of this commission really fits into that model at least in my own way of thinking about it. These are very old problems, very new problems and I hope, of course, that our own deliberations will make an important contribution to the continuing national discourse on the issues that we will be discussing.

We will have an opportunity later on this morning for commission members to address directly what they feel should be the agenda of the commission, the kind of approach we should have to particular problems, and what issues we may want to take on as we begin our work. We can all talk at that time, those of us who wish to who have an opinion on that issue, about what kind of structure and ideas should give light to our work. So I will not speak about those issues now. I will wait to discuss that with my colleagues later on this morning.

I thought it would be helpful if we began our session simply by introducing ourselves both to each other, although I know many of you are very good friends and long time colleagues, and to others who may want to know who these commissioners are. Now in introducing ourselves, we ought to strike some nice balance between excess modesty and long speeches. I think it is important to use a few sentences at least to describe your interest and your backgrounds in a way that is informative. Of course, our CVs are available for those who want more detail about just who we are and what we are like.

I noticed in this morning's paper something very directly related to CVs that came from a rather surprising source. I do not know how many of you have seen this morning's Washington Post, but somehow they put the Nobel Prize in Literature in the "Style" section.

(Laughter.)

Now those of you who are Washington natives may have some comment about this, if this is typical. But as you know, a Polish poet won it and they spend the first part of this article helping me, which was very helpful incidentally, learning how to pronounce her name, which I did not know how to -- which I did not know how to pronounce. Szymborska. Szymborska. But they quote a poem about CVs. I do not know why they picked out this poem but I just want to give you a few lines from the poem that is quoted in the Washington Post today. She is talking about CVs.

It says, "Landscapes are a place by addresses. Shaky memories give way to unshakable dates. All of your loves mention only the marriage. Of all your children, only those who were born."

And so as you think about what you might say in a few minutes, you might keep some of those ideas in mind.

What struck me also as funny -- not funny, but just wonderful about this report, I do not know how many of you know that the Nobel Prize in literature is given by the group in -- I believe a permanent group in Stockholm. The Academy, who numbers perhaps 15 members in the Academy, their Academy there. And I have often thought how wonderful people -- 15 people think they can choose this every year who keep on having confidence in themselves, and

I thought that was wonderful. But in describing the winner, they described her as the Mozart of poetry, elegance of language with the fury of Beethoven. So, I guess, they think they are just as good in music as they are in poetry.

(Laughter.)

But in any case, with all that advice, why don't -- I will skip Dr. Gibbons, who I will introduce in just a moment, but why don't we introduce ourselves starting with Rhetaugh Dumas, a former colleague of mine at the University of Michigan.

DR. DUMAS: I am Rhetaugh Dumas. I am currently the Vice Provost for Health Affairs at the University of Michigan where I served 13 years as Dean of the School of Nursing. I also had a period here in government at the National Institute of Mental Health where I was the Deputy Director for a while. I am very pleased to have been chosen for this very important task and I am looking forward to working with all of my colleagues around the table here and others that will join in this work.

DR. SHAPIRO: Thank you.

DR. EMANUEL: I am Ezekial Emanuel. I am currently an Associate Professor of Social Medicine and Medicine at Harvard Medical School. I am a medical oncologist and I work on breast cancer but most of my research is related to ethical issues. I work on "end-of-

life" care issues, issues related to allocation of resources and managed care. I am also looking forward to this with a number of colleagues I know and getting to know new people as friends.

DR. FLYNN: I am Laurie Flynn. I am the Executive Director of the National Alliance for the Mentally Ill. We are a grassroots family and patient organization. We are very supportive and very interested in research issues and hundreds -- hundreds of our members are, in fact, research subjects in a variety of medical centers and research facilities around the country.

I am also the mother of a young woman with a severe psychiatric disorder who has participated in several clinical trials. So this is an issue of both professional and personal interest to me and I am delighted to be able to participate in this challenging task.

DR. SHAPIRO: Thank you. Steve?

MR. HOLTZMAN: Good morning. I am Steven Holtzman and I am currently the Chief Business Officer of Millennium Pharmaceuticals in Cambridge, Massachusetts, a genetics genomics company, where I have been for about two-and-a-half years. Previous to Millennium, I was a founder of a company called GMX, another biotechnology company engaged in transgenic animal research where I was President of GMX biotherapeutics. I am trained neither as a scientist nor as a businessman but, in fact, as a

philosopher in both undergraduate and graduate training, and it is a delight to be here.

DR. SHAPIRO: Thank you very much. Ms. Kramer?

MS. KRAMER: I am Bette Kramer. I am from Richmond, Virginia. I was the founding -- the founder and the first President of the Richmond Bioethics Consortium, which is a citizen based group seeking to expand the education in the field of bioethics. We work primarily with health care institutions helping them establish their ethics programs and educate their ethics committees, and with the general public hoping to provide education and the issues for them. I am delighted to be here.

DR. SHAPIRO: Bernard?

DR. LO: I am Bernard Lo. I am also delighted to be here. My son thinks I work for United Airlines, Seat 7A.

(Laughter.)

DR. LO: I am Professor of Medicine at the University of California, San Francisco, where I practice internal medicine and I direct the program on medical ethics there. A lot of my work has been on end-of-life decision making and ethical issues regarding HIV infection.

DR. SHAPIRO: If I could just interrupt here, so we can treat these meetings as informally as possible, I would prefer, if people do not object, to referring -- to refer to each other by first names. So if you have any

preference for how we do that, whether we use Bernard or Bernie --

DR. LO: Bernie.

DR. SHAPIRO: Bernie. I guess we can find out Lawrence and Larry in a minute, but that would be helpful for you to say so.

DR. MIIKE: I am Larry Miike, currently Director of Health for the State of Hawaii. Unlike Dr. Lo who flies -- it sounds like it is kind of sort of first class, my seat is 26H.

(Laughter.)

DR. MIIKE: So clearly I represent the common people.

(Laughter.)

DR. LO: No, this is just frequent flier miles.

(Laughter.)

DR. MIIKE: I used to be the Scientific Director of ALGEN (?) and a bureaucrat. I am actually a long time policy analyst in disguise. I spent 17 years in Washington at CDC, most of it working for Jack when he was at OTA. I still have a house on Capitol Hill and a farm in Berkeley Springs, West Virginia, so I have not lost my ties. I am basically a policy analyst but right now I am enjoying myself in the worst budget crisis in Hawaii, but dealing with health issues in Hawaii.

And I should say that when I first came to

Washington in 1972 for the old National Center for Health Services Research and Development I went off to a meeting at Hastings-on-Hudson, which turned out to be one of the very first meetings of the bioethics community, and I remember the most inspirational speech was by Andre Helliger (?), who told the group how to get federal funds, and look at this.

(Laughter.)

DR. MURRAY: That is a tough act to follow. I am Tom Murray. I am the Director of the Center for Biomedical Ethics at the School of Medicine at Case Western Reserve University in Cleveland, Ohio.

My training actually was as a experimental social psychologist but I got interested in the ethics of human subjects research. My interests have broadened considerably since then and I have written about a lot of areas but lately I have been writing a good deal about genetics and am very interested in the ethical implications of the Human Genome Project and modern genetics more broadly. Also, parents and children are an issue that interest me very much and having four children of my own I have a lot of personal experience with relationships between parents and children.

DR. SCOTT-JONES: I am Diane Scott-Jones. I am a Professor of Psychology at Temple University. I am a Developmental Psychologist by training and unlike many of

my colleagues here I have not undertaken a study of ethics as separate from my own conducted research. So my interest in ethics is in the way we incorporate it into our every day research activities and into the training of our graduate students.

I am editor of the Journal of Research on Adolescents so I am concerned about ethics as it has been conducted in research that we publish in the journal. I recently participated in the revision of the "Ethical Principles" for the American Psychological Association and the American Psychological Society. So I am interested in how we use ethics in research on an every day regular basis and I am delighted to be here and be a part of the commission.

PROF. BACKLAR: I am Patricia Backlar and only my mother calls me Patricia. Everybody else calls me Trish. I am a Senior Scholar at the Center for Ethics in Health Care and a Senior Instructor in the Department of Psychiatry at Oregon Health Sciences University. I am the editor of the "Ethics Section" of Community Mental Health Journal and write a great deal about ethical issues concerning persons who have serious mental disorders and am particularly interested in families and patients, and my recent book is The Family Case of Schizophrenia.

I am hoping that this commission will be as useful as it promises to be and I am very honored to be

able to participate in this work.

DR. BRITO: I am Arturo Brito. I am Assistant Professor of Pediatrics at the University of Pediatrics at the University of Miami School of Medicine. The majority of my time is consumed by directing and also being the pediatrician on the mobile clinic where we serve the under served children of Dade County, meaning children who do not have health care, which is a growing number on a daily basis. And I, also, educate and train medical students and residents in working in primary care and pediatrics with the under served out in the community.

Currently my interests are working particularly with the sickest of those sick children, the HIV infected children, in the community that are not receiving the services they need to be receiving. And I am, also, involved in an NIH sponsored asthma study in the provision of preventive asthma care to under served asthmatic children in the community.

I am very pleased and excited about being on this committee. I have not had a lot of experience with the research aspect of the ethical -- the ethic aspect in the research area, but I feel I have a lot to offer because I am out there in the community on a daily basis. I, also, feel that working with the under served really gives me an idea of where some of the areas we need to head in terms of providing care in the appropriate manner and doing things

in an ethical manner in the research area.

DR. CASSELL: I am Eric Cassell. I am a Professor of Public Health at Cornell and I am in the 36th year of a practicing internist, which I think is really long enough, and your offer set me free.

I like the first name thing. It is going to be a group therapy session and no matter how upset we get we will always use our first names.

I was practicing for ten years before I went to the Hastings Center for the first time 25 years ago, which transformed my life, and I have been a fellow and a member of the Board of Directors almost ever since then. I am primarily concerned with the care of the dying, the problem with suffering, and the evolution of our notion of the patient and the person, who is that sick person. And I think that that is what we are going to be facing always, is the idea of the evolution of everything, but this is where everything is in process and always in process, and we are a part of that process, and we have a chance to not only be part of the process, but have a big effect on it.

PROF. CAPRON: I am Alex Capron from the University of Southern California, and my first wish is that whoever is controlling our sound system will eliminate the echo that we seem to be boomed.

Coming over here this morning, I guess it was either Eric or Alta asked me if I had a sense of deja vu.

I have been involved with these efforts of public bioethics for 20 some years. I was a consultant to the National Commission for the Protection of Human Subjects of Biomedical Behavioral Research, which operated under an act of Congress from '74 to '78, and was based in the Department of Health, Education and Welfare.

I served as the Executive Director of its successor body, the President's Commission for the Study of Ethical Problems in Medicine and Biomedical Behavioral Research. I must say that when Congress names things they tend to be longer names than Executive Orders.

And then served as Chair of the successor body, the Biomedical Ethics Advisory Committee to the United States Congress, which spent its life as an embryo and then in a deep freeze when the board to which we reported fell to disarray and loggerheads, and our statute lasted a lot longer than our meetings.

I have been very concerned as a person, who believes that these efforts can be worthwhile, to see that something else happened and I am pleased to have the privilege of serving with all of you.

PROF. CHARO: I am Robin Alta Charo. Only my mother calls me Robin. I hope you will call me Alta. By way of minor correction, I am merely Associate Professor of Law and Medical Ethics at the University of Wisconsin with appointments at the Schools of Biomedicine.

I have worked previously with the Federal Government. Most recently on the NIH embryo panel with Bernie Lo and Tom Murray. I also had the opportunity to spend a year with AID learning about international family planning and two years with the late great Congressional Office of Technology Assessment.

The areas I have focused on so far in my academic life beyond the environmental material I worked on early has really been in the area of reproductive health and genetics with a substantial interest in the politics of biomedical research and biomedical ethics. The emphasis continues to be on international issues and currently I am working on transitional health systems, particularly in Cuba.

And to beat Larry Miike in his representation of the common people, I worked my way through college half time cleaning bathrooms, but half time being a research subject in just about every science experiment that went on between 1975 and '79, so do not trust the data from those years.

(Laughter.)

DR. CHILDRESS: I am Jim Childress from the University of Virginia where I teach in the Department of Religious Studies in the Medical School and co-direct the Virginia Health Policy Research Center. Much of my writing has been in the area of biomedical ethics where I have

emphasized theory and method as well as covering several practical areas.

I approach this committee with a great deal of anticipation and hope and having served as Alex only on the last committee that did not go very far, I have a great deal of confidence that this one will. I look forward to working with all of you.

DR. COX: I am David Cox. I am Professor of Genetics and Pediatrics at Stanford University School of Medicine and I am co-director of the Stanford Human Genome Center there.

What gets me out of bed in the morning is figuring out how to apply genetic knowledge to the human condition and, in particular, to apply it to human health. So I have been doing that for a long time and I will teach genetics to anybody who will listen to me or try to at least share genetic information.

But over the past three or four years in terms of trying to do this with respect to human health, I have realized that genetics can really be a double edged sword. So I have gotten particularly interested in the so-called ethical issues of genetics but it is really how genetics interfaces with society. So I am particularly interested in that. I am interested in how genetics interfaces with all the other aspects of society. So society not circulating around genetics but genetics circulating around

society.

I am real interested in this commission and real interested in being able to, as some people have said, be successful and get some practical product.

DR. SHAPIRO: Okay. Thank you very much. Well, once again let me just express my own gratitude to everyone for agreeing to serve. I consider each person's decision to say yes when asked an act of generosity for which we should all be grateful and I am certainly very grateful to all of you.

Before once again I turn to Dr. Gibbons, let me just introduce some members of the staff who are here and perhaps they could raise their hands as I introduce them.

First of all, our Acting Executive Director, Bill Dommel, who is sitting on my right. That is Bill.

Pat Norris, who is --

MS. NORRIS: I am here.

DR. SHAPIRO: -- over here is our Communications Director.

Margaret Quinlan is our Program Administrator. She has probably been in touch with all of you regarding various kinds of arrangements. Margaret is also sitting here.

Michael Nguyen is Administrative Officer. Michael is sitting over in the corner there.

And, of course, Randy Hull and Mariann Rapp,

you may have met in the hallway and wing today, are helping with a number of the administrative tasks.

So today let me also express my thanks to the staff, who at least during the last few months had to work some considerable uncertainty about just how thing would settle down here and I really appreciate their continued devotion to this task.

So now it is my great pleasure to turn to Dr. Gibbons. I think everybody around this table either knows Jack well or knows about him. I am not going to spend a lot of time introducing him. Sometimes in introducing someone as well known as Jack I think it is only -- it is not left to the human imagination to add any more superlatives to what has already -- only God so to speak can add to what has already been said about your work here.

But let me say in a personal sense that the last four years have been years of great challenge in the Congress in the area of support for science and technology, broadly speaking more challenges in some areas than others, but Jack has been a great source of support for all of us and for all of the programs that we care about in those areas and we are very grateful to you and thank you very much for coming here this morning. Thank you.

Jack Gibbons

CHARGE TO THE COMMISSION

DR. JOHN H. GIBBONS

ASSISTANT TO THE PRESIDENT FOR SCIENCE AND TECHNOLOGY

DR. GIBBONS: Thank you, Harold.

My name is Jack Gibbons and I have worked for several people around this table, Larry Miike and Alta Charo and others in their past incarnation, which brought me to Washington, called the Office of Technology Assessment, which was conveniently eliminated by the 104th Congress. And it reminded me that in Washington you can go from "Who's Who" to "Who's That" very quickly.

(Laughter.)

I also come from Virginia where a sense of place is important as well as family lines and the Virginia aristocracy is known as a family that has been descending a long time. I will not comment further on my background, but I have been descending now for enough years to have a sense of joy to see some of my colleagues from the past reassembled in this activity and, also, to find new colleagues that I have known and worked with, and those that I am meeting today. And I cannot tell you how much joy I have in the kind of quality that comes to this table in response to the President's concern about establishing this commission and how much weight now in a sense comes on your shoulders much to the benefit, I think, of the American people in the years to come.

This is a long awaited establishment. It has had a gestation period that I think reflects the

seriousness given to the effort. It builds on a past of a number of activities. I would remind you that it was in the '70s that the Department of Health, Education and Welfare housed the Commission on the Protection of Human Subjects of Biomedical and Behavioral Research, and it also at that time had an internal Ethics Advisory Board.

In the late '70s and in the early '80s there was an important work of the President's Commission on the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research.

Both of those committees and commissions contributed, I think, greatly to our knowledge of both biomedical and ethical issues and raised the national consciousness and even the national consensus about some of the thorniest issues of the day including defining death, the splicing of life and other things. And we still benefit from that path breaking work that was done.

I think, for example, if we had not come to grips with the notion of defining death, where would we be now in terms of bringing the issues faced by families and the medical community?

In 1989, Larry remembers well and I think Alta also, the OTA hosted for Congress a single meeting of the Biomedical Ethics Advisory Committee, which was established by Congress, but it sadly failed because of ideological struggles both within the Congress and between various

stakeholders that were involved.

We hope that in creating this commission we have learned from those experiences. I think it is Confucius that once said, "The wise person learns from experience, the wiser from someone else's experience." And we hope that the integration of that past experience will enable this commission to have an even better opportunity to contribute to the nation's needs here.

We do envisage the NBAC, as it is called -- that is not a first name, but a short name, Harold -- as the bioethics body of the '90s that can carry us in and across the millennium assured that we are aware of and adhering to the highest possible standards for the conduct of human, biomedical and behavioral research. The commission has not only the strong support of the administration, but also, I am very pleased, the bipartisan support of congressional leaders. This is important and somewhat unusual in recent times.

Now I would like to read a message from the Vice-President, and it goes as follows:

He unfortunately could not be with us, but you know that his own background both in the House and particularly in the Senate was one of great concern about bioethics and retains that concern as does the President. So the Vice-President is going to be particularly interested in following this work, Harold, and checking

with us at a later time.

He said as follows:

"The inaugural meeting of the National Bioethics Advisory Commission is, indeed, a momentous occasion and one that the President and I have both looked forward to with great anticipation. As you know, the ethical conduct of research is an issue that has concerned me deeply from my earliest days in Congress and the President's leadership and support for this commission reflects his commitment to the issue.

"We have not been alone in bringing this commission to birth since the day one year ago that the President called for its creation. The time and dedicated efforts of many people have helped us reach this day and lead us forward into an era in which justifiable pride in our scientific achievements is not over shadowed by public concerns about unethical research. We must be certain that our ethics are as good as our science and your mission is to ensure that we hear and understand what is necessary to conduct biological and behavioral research in an ethically sound manner.

"We are most grateful to have such a highly esteemed group of experts and community representatives to embark on what will be a challenging endeavor. On behalf of the President and the American people I want to thank you for your generous commitment to public service as

members of the National Bioethics Advisory Commission."

Now I would like to add my special thanks to those of the Vice-President to Harold Shapiro for agreeing to serve as the first chairperson of the commission and I also want to thank the members of NBAC for whom I know this is an invaluable personal commitment and one that we will all benefit from. But it is also important, I think, in looking ahead to also look back and I should tell you just a few things about the path that led to the creation of NBAC.

In the fall of 1993 the Office of Science and Technology Policy, which I also direct, was approached by the National Institutes of Health and also the Department of Energy and later other agencies, to consider the establishing of a standing expert commission on bioethics. In other words, a common need that spread across agency jurisdictions. This proposal stemmed in part from a congressional request that the NIH and the Department of Energy establish some kind of an advisory capability on genetic privacy.

We felt the need for a high level group to serve as a shared resource to address broad issues and to compliment the more specialized committees and boards that are supported by the various mission agencies. So beginning at that point I held conversations with other agencies within the administration, with others in the

White House, and also with key members on both sides of the aisle in the House and Senate, especially the Senate.

In August 1994 we published a draft NBAC charter and called for public comment. This evoked at least 80 responses. Of course many of the responders were interested in serving as members of the commission. We could have easily had a 300 member commission. But those responses, I think, evidenced the continued active interest of the American people that together we resolve -- we address, anticipate and resolve bioethics questions.

The comments that we received were integrated into the final charter for NBAC, which I signed this summer at the same time the President announced his choice of the members for NBAC. I cannot over emphasize the point that the establishment of NBAC throughout this course of time has been a fully bipartisan effort. Over these three years I have had many conversations with colleagues on Capitol Hill and I want to acknowledge their work and their collegial spirit in bringing us together today, and their continued avid interest in the procedure as it goes forward.

In particular, though, Senator Hatfield, Senator Kennedy, Senator Glenn, Senator Moynihan, Senator Stevens, and Congressman Markey have particularly shown long-standing interest and commitment to the concept of a National Bioethics Board and they have shown great patience

in helping us work through the process.

I spoke with Senator Hatfield yesterday as he was departing to go back to Oregon and he expressed his great gratification at the occasion of this first meeting and his interest in continuing to stay with us. We could not have achieved this time today without that kind of long-term support.

Now during the months over which the mission was refined by a variety of dialogues that went on two events stand out in my mind that sort of put the commission on the front burner of timeliness. One was reports of experiments in human cloning, embryo cloning, and also there was this Department of Energy's revelation of the post World War II human radiation experiments and the succeeding special commission that addressed those questions since that time. Those events and some others, but particularly those two, I think, underscored the need for the administration and for the Congress to have advice and recommendations concerning ethical conduct of human, biological and behavioral research.

The President then decided that the issues could not be resolved on an ad hoc basis, that we needed an effective forum for open and informed discussion on the sensitive issues that face the American people.

For example, questions such as how do we ensure the well-being, the autonomy and the privacy of those

individuals who are first to undergo the newest forms of medical treatment?

What, for instance, is the appropriate use of genetic information? An issue that many of you have wrestled with extensively.

How do we know when it is the right time to administer genetic tests?

Who should be allowed access to the results of such tests?

These were the first two classes of issues that the President has charged NBAC to take up. It is important to note incidentally that the commission has been granted considerable leeway in determining its own agenda, taking into account suggestions submitted by the executive branch agencies, by the Congress and by the public-at-large, and I think this is another mechanism by which we can strengthen the commission's role as a forum for gathering and exploring a wide variety of perspectives.

Then in announcing the establishment of NBAC about a year ago today the President also charged the executive branch agencies that are involved in the conduct of human subject research to review their ongoing activities and to identify gaps or weak points in the system for protecting the rights and the well-being of research subjects. The results of those reviews are to be delivered to Chairman Shapiro today for your examination.

We certainly see the commission as a forward thinking body looking at current and also anticipating the kinds of future research to be supported or conducted by the Federal Government. I hope you will also serve as a forum in which individual voices can be heard, the government and the public can be better informed, and our policy choices from that will be better defined.

One thing occurred to me on the way over this morning that I had not really thought about but it seems to me may well be a question you want to address, we are now trying to balance the Federal Budget over a period of time much shorter than the time it took us to triple the national debt in the last dozen or so years. But we are trying to balance the budget by taking funds from only 18 percent of that budget and that 18 percent includes all federal research and development. And it seems to me that there well may be ethical issues about the choice of the use of these resources as we have an increasingly difficult time in making ends meet across these.

Of course, NBAC is not a regulatory committee and it will not review or approve individual research projects. Rather it will define and identify broad over arching principles to govern ethical conduct of research. And, as I mentioned a while ago, we can learn from experience but preferably someone else's experience. But we can learn from past experience how to avoid mistakes and

abuses.

One example I think I mentioned earlier was that on the work on human radiation experiments. I worked with the President to establish his advisory committee on human radiation experiments early in 1995 and we are in debt to that commission for the enormous efforts that they made in examining the record and making recommendations to the President. I cannot and do not propose to review all the actions today that have been taken or will be taken as a part of that process, but let me underscore that the key departments, that is Department of Defense, Department of Energy, and HHS, have made great strides in uncovering and declassifying the historical record of those events.

Now that committee raised certain broad issues about the ethical conduct of human subject research and the effective oversight of that research and I think these are issues that hopefully NBAC may wish to respond to. I would only mention three of those issues.

First, the commission calls for a continuing public forum on the interpretation and application of ethics rules and principles for the conduct of human subject research. We would like to see NBAC play a role in fulfilling that need. That is clearly part of your charter.

Second, the commission recommended that efforts be undertaken on a national scale to ensure the centrality

of ethics in the conduct of human subjects research. It is my understanding that 19 federal agencies and departments have submitted reports to you for your review or will be today. That is an extraordinary number of departments. It shows in a sense the ubiquitous nature of these issues and the need for a central intelligence about this question that you constitute. I would encourage you to engage those 19 agencies individually as well as in a group to help ensure that we meet uniformly high ethical standards for human subjects research across the Federal Government.

And the third is that the commission recommends changes to the Institutional Review Board, the IRB system, that helps ensure protection of human subjects in federally sponsored research. We would hope that NBAC will examine the issue of IRBs and advise the administration on possible improvements that can be made to that system. I can assure you that you are going to have the full support of government agencies involved in human subjects research as reflected, I think, in today's agenda with presentations by Francis Collins and Gary Ellis.

Well, finally, I think you have embarked on a mission of the utmost importance to the President and to the country. To me, this is democracy at work. We are maintaining our ideals of research for a more perfect union in an age that is dominated by science and technology. The issues that you face will be difficult. They are worthy of

your wisdom. Especially because we will be dealing with values as well as hard facts, opinions, various opinions here will undoubtedly differ. That is expected and it can be a sure sign of health.

In borrowing from Thomas Jefferson, I would say that in the right forum, the right context and the right spirit, "Freedom rings where opinions play." And I want to add my gratitude to that expressed by the Vice-President and thank you for accepting this challenge. I also want to thank the members of the public so broadly represented here this morning -- I do not think we have a seat left in the house here -- for your participation and encourage you to remain involved in this commission's activities.

Thank you very much. I am delighted to be with you.

DR. SHAPIRO: Well, thank you very much. I think that Dr. Gibbons can stay at least a little while for any questions that the members might have.

Let me just say a bit of logistical advice. Apparently we also have people in an over flow room. So if you could speak as close to the microphone as possible it would make it somewhat easier for them to hear our proceedings here. So if you do wish to speak, and I will open the floor in a second, just try to pull that -- grab the microphone and pull it closer to you.

Are there any questions for Dr. Gibbons from

members?

DR. MURRAY: I have one.

DR. SHAPIRO: Yes.

DR. MURRAY: Jack, there is -- thanks by the way, that was eloquent and left me feeling both -- mainly awed, but we will do our best.

There is an ambiguity in our charge that I think I -- I know -- but I think there is also a resolution for it in the charge. The ambiguity is that there is an emphasis on the ethics of human subjects research which is -- which comes up repeatedly and it was in the Vice-President's statement as well -- yet our charge, I think, while it includes that as a major portion, it seems significantly broader than that. And, in fact, quite open as to the implications of biomedical research.

So I would like to take it in that broader sense. Am I taking correctly if I do so?

DR. GIBBONS: Tom, I think the ambiguity is purposeful. We did not want to give a charge to the commission that would be so broad that you would be totally swamped by the issues brought before you. We tried to help define a space that was manageable and yet at the same time we wanted to bow to the wisdom that we know is imbedded in this group. So we provided words that give you the option, if not the implicit charge, to go where the important issues take you. We would hope that that combination of a

focus on human subject research, but the broader -- but taken in a broader context of biomedical ethics would allow you the freedom to move where you need to move.

DR. SHAPIRO: Thank you.

Any other questions this morning for Dr. Gibbons?

Jack, let me thank you very much for coming. We appreciate all of your own work in helping get NBAC established. We know it would not have happened without your efforts and the efforts of your colleagues. So we do want to thank you. Thank you very, very much.

DR. GIBBONS: I also hope that your laryngitis does not consume you, but --

DR. SHAPIRO: There are enough doctors around this table and maybe I can get some advice. It is not an ethical issue.

(Laughter.)

Any final questions, comments?

Okay. Let's turn to the next item on our agenda. We have some presentations from the Congress from a number of staff members who are here.

I believe Aaron Menikoff is here from Senator Hatfield's office.

MR. MENIKOFF: Yes.

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PRESENTATIONS FROM THE CONGRESS

DR. SHAPIRO: Aaron, welcome. It is very nice to have you.

MR. AARON MENIKOFF

LEGISLATIVE ASSISTANT TO SENATOR MARK O. HATFIELD

MR. MENIKOFF: Thank you. Well, it is an honor to be here this morning. I know that Senator Hatfield is certainly rejoicing and breathing a sigh of relief right now. He is rejoicing because you are meeting and I think he is breathing a sigh of relief because you are meeting before he is retired.

(Laughter.)

So he sends his greetings. He is sorry he cannot be here but he wishes you all well.

I would like to thank Dr. Gibbons and Dr. Shapiro, and you, commissioners, for allowing me to be here today.

I see Patricia Backlar, who I had the opportunity to meet in Oregon a few weeks ago and it was a pleasure.

I know that there is going to be a bright and productive future for the National Bioethics Advisory Commission and I am just here to try, I think, and give you a little bit of a picture of what Senator Hatfield has been thinking about over the course of the last several years as he has been longing for this commission.

It was in the first session of the 103rd Congress that Senator Hatfield, along with Senator Kennedy, introduced a bill to establish the National Bioethics Advisory Commission legislatively very similar to the one you are now representing. At the time several issues were brought up that it was thought could be tackled:

Health care reform, the whole idea of scarce resources and federal dollars, that was an ethical issue.

Genetic privacy and issues of nondiscrimination, that was an issue several years ago as well.

Human growth hormones, an example of something that NIH is doing research on. That reached the Hill, that was an example of one of these issues that had been brought up.

Surrogate motherhood, the Supreme Court refused to hear the case of a surrogate mother who sought to maintain the custody of the child that she had carried for nine months. So that decision went to a lower body and there were some ethical issues about how something like that is being decided at that level.

Gene therapy protocols, with the RAC changing that has become very public this year, but the issues surrounding genetic -- gene therapy protocols has been around certainly.

And then something new and dear to Senator

Hatfield's heart, patenting life, human and animal patents. There are currently 27 animal patents in existence in the United States and 511 animal patents pending. And one of the reasons Senator Hatfield has been pushing for a National Bioethics Advisory Commission is to be able to look into that and have some of these decisions or have some of these thoughts not completely made at the Patent and Trademark Office, but let's have somebody think about it and see if it is the right thing to do.

So those are just a few of the issues that Senator Hatfield was thinking of and I think that some congressional members were thinking of a few years ago. And I think it was the existence of those issues that got into play the desire to look into it more with this report. I think you all have this Office of Technology Assessment, Biomedical Ethics and U.S. Public Policy, and it was a background paper that Senators Hatfield and Kennedy both asked to look into the history of the National Bioethics Advisory Commissions that we have had that Dr. Gibbons touched upon. It is a wonderful history and I certainly hope that everyone has read it. It is out of print so save your copy.

In this report there are six suggestions, six issues, six concepts that the writers of this report were concerned that a National Bioethics Advisory Commission, if we are to have another, must somehow address if it is to be

successful or at least if it is to be more successful than the commissions that we have had in the past. And I would like to share what I think would be Senator Hatfield's three most important and pertinent of these suggestions with you now and certainly the remaining are certainly not important.

The first I would bring up would be the mandate of NBAC and the second would be the targeted client of your work, and the third would be the budget.

Well, first the mandate, and that is something that was brought up in a question by Dr. Murray right before I came up. NBAC cannot be charged to address every issue that is out there, every ethical issue that is out there, and if you choose to address issues surrounding health care reform with the 105th Congress you might be spending every hour of the day thinking about health care reform. I do not know if that is what you want to do.

Senator Hatfield is strongly supportive of NBAC carefully addressing human subject research, genetic privacy and nondiscrimination, and gene patenting. So clearly these are the mandates that you have already been given, but I think the OTA report and Senator Hatfield's interest would both say, 'You can only do so much with what you have, do it well,' and the way to do that would be to limit the issues that you cover.

The second issue, the targeted client. I think

the targeted client of the National Bioethics Advisory Commission by very definition is broad. It is the National Bioethics Advisory Commission. It is not held in Portland, Oregon. It is not held overseas. It is here in Washington, D.C. And so I would think that the targeted client would be the nation. Now clearly you all have been deposited in the Department of Health and Human Services, but you do have bipartisan support from the United States Congress and so the United States Congress should be a targeted client.

I think perhaps more importantly when thinking about the targeted client is thinking about all the commissioners we have here. I do not know if we have the eighteenth, I know of seventeen commissioners. Each of you and those ten, twenty, thirty, forty, fifty other individuals who have a passion for the things that you are going to be talking about for at least the next two years, the whole purpose behind Senator Hatfield introducing legislation was the fact that there was not a dialogue.

There was just not a dialogue into the issue of whether or not we should patent animal genes and whether or not genetic privacy was an issue. There was no dialogue. So to his mind bringing you together here is not to select seventeen of these 300 individuals to come and gather together, you know, and make recommendations, but it is rather, as important as the recommendations are, to go back

to your communities and go back to your professionals and spread that dialogue out everywhere so someone in Portland, Oregon is talking about the things that you are bringing up. Someone in France is reliving the meetings that you might have held.

I think that is extremely important and I think when we do not know what the future is going to hold -- we have four or five ethics advisory commissions that have not continued -- we do not know what the future is so that is to make sure as many people as possible are able to share in what you are doing, especially the professionals who will continue that discussion.

Well, finally, the budget. Dr. Gibbons is just -- is extremely right. I think balancing the budget on 18 percent of our federal budget is -- and trying to reduce the deficit on that 18 percent is not a wise thing and I say that on behalf of Senator Hatfield who has said it many times. Senator Hatfield would also underscore that 18 percent does not include the defense portion of the appropriations budget. So to the extent that the Department of Defense participates in human subject research and other areas of ethical concern, as we think about limited resources, please know that that hit is not going on and that is something that Senator Hatfield has brought up.

With regard to the budget again I was listening

to NPR this morning. Most of you were probably already in this meeting. But that issue was brought up on national radio that the budget is very important. If you do not have adequate resources, you know, why continue to meet? And you were referred to as a "Yugo," not exactly perhaps the best analogy.

Well, one thing that Senator Hatfield has tried to do and has succeeded in this past few weeks is to enable this body to draw upon the resources of other federal agencies. Every agency or at least most agencies have an interest and probably an investment in some of the topics that you are going to discuss. So it is not out of the realm that they should contribute to these discussions financially. So I think by having the other executive agencies do that this Yugo can clearly be a Corvette but it is certainly in the hands of the other agencies.

Well, that is all I wanted to cover for Senator Hatfield. It is certainly his hope that, whether it is through subcommittee meetings as many dream of the whole, that the mandate that you do have that is clear you are able to address expeditiously and that whether or not NBAC is able to continue into the future a dialogue is promoted here that is going to last for a long time.

Thank you.

DR. SHAPIRO: Thank you very much. Thank you very much for being here this morning and please send our

thanks to the Senator for his work on our behalf. We want to thank you personally for all the help you have been in the last few months getting this together so thank you very much.

MR. MENIKOFF: It has been my pleasure.

DR. SHAPIRO: Let me now call on Dr. Leonard Weiss, who is right here, who is here to speak to us. He is Minority Staff Director of the Senate Committee on Governmental Affairs.

DR. LEONARD WEISS

MINORITY STAFF DIRECTOR, U.S. SENATE COMMITTEE ON GOVERNMENTAL AFFAIRS

DR. WEISS: Thank you very much, Dr. Shapiro. Let me begin by saying first I have a theory about how the Polish poet ended up in the Style Section of the Post. In this rather interminable election season many people are treating the political news with a great deal of disdain so they turn to the Style Section now for substance.

(Laughter.)

So putting the Nobel Prize for literature in the Style Section is a strategy for maximizing the exposure of the Washington community to high culture. It is, therefore, a good thing.

(Laughter.)

DR. SHAPIRO: If I may just interrupt a moment. There was a piece, I think, yesterday in the New York Times

saying the trouble with this age is image has replaced substance. The Washington Post apparently has married them.

(Laughter.)

DR. WEISS: That is right.

First, let me say I am -- as Dr. Shapiro said, I am the Minority Staff Director for the U.S. Senate Committee on Governmental Affairs whose ranking member is Senator Glenn. I have worked for Senator Glenn for nearly twenty years on a variety of issues and I am appearing before you today on his behalf. He regrets that he is unable to be here himself today, but I can assure you he has a keen interest in your mission and is very supportive and was very supportive of the creation of this body.

I appreciate the opportunity to appear before you and to provide some background and suggestions for further inquiry on one of your priority missions, the consideration of the rights and welfare of human subjects. At the outset I want to thank you for the work you will be doing in advance. This work will have an impact on policy debate and formulation of some very important issues for the United States.

While I understand that your primary customers are the President, the Cabinet Secretaries, and their respective advisors, I would note that your charter provides that you may accept suggestions from Congress on

issues to study. Your charter also requires that any reports you make be provided to Congress and I would expect that some time within the next two years our committee, the Governmental Affairs Committee, will convene a hearing to learn of the progress you have made in addressing these important issues.

Our committee under Senator Glenn's leadership has had a long-standing interest in this subject. In 1979 we held our first hearing on a bioethics related issue when we examined the provisions for radiation protection of U.S. residents by the Federal Government and the states.

Among the issues discussed in that hearing was whether American soldiers were given adequate information on the consequences of their purposeful exposure to radiation stemming from atmospheric nuclear tests detonated as part of a military exercise. As we have learned since then, the risks that those soldiers incurred were higher than what they were told and the U.S. Government has a compensation program in place for those who suffered illnesses that are deemed radiation induced.

An area of current interest for the committee and to Senator Glenn is addressing the problems facing the nation as a result of the end of the Cold War. For example, over the last ten years the committee has held dozens of hearings on the environmental safety and health problems associated with the nuclear weapons complex. When

the Cold War radiation experiments began to receive renewed attention the committee's previous work and experience made this a natural one to investigate.

Since November of 1993 the committee has held three hearings and commissioned three separate General Accounting Office reports on issues associated with the Cold War radiation experiments and the protection of human research subjects. I will not go into detail on these hearings and reports, but if you are interested we can brief you on them at your pleasure.

The committee closely followed the deliberations of the President's Advisory Committee on Human Radiation Experiments and continues to track the administration's implementation of the ACHRE recommendations. As you may know, several recommendations by this previous advisory committee have been forwarded to you for deliberation and action, and I am sure you will take that seriously and examine it with dispatch.

Beginning with the first hearing that Senator Glenn chaired on the civilian radiation experiments in January of 1994 he expressed his concern about whether such experiments could still happen today and whether experimenting on someone without their informed consent was "against the law." The answer, as you all probably know, is "no, it is not against the law." The question of

whether the concept of informed consent should in some way be codified in law is still very much open to debate and I believe this issue is one in which you could play a key role.

To help us address this question we asked the General Accounting Office to examine the current framework for protecting human research subjects. GAO reported their findings to us in March of 1996 and the ACHRE also examined this issue. While everyone agrees that the system is much better than at any time in the past, both GAO and the Advisory Committee on Human Radiation Experiments identified weaknesses. In fact, the ACHRE report states, "Our review suggests that there are significant deficiencies in some aspects of the current system for the protection of human subjects."

For example, not every agency has adopted the common rule which requires informed consent and IRB oversight. Research that does not receive federal funding is not necessarily covered by this rule. The GAO found that insufficient resources may be threatening the integrity of the system.

Other weaknesses identified by the GAO include time constraints and conflicts of interest within the IRBs, the near absence of follow-up reviews by the IRBs, problems associated with IRB oversight of multi-institution trials, lack of resources for the Department of Health and Human

Services Office of Protection of Research Risks, OPRR's placement within NIH's own bureaucracy, and finally gaps that exist in the FDA's inspection of IRBs.

I have provided copies of the GAO report as well as an article by Joseph Palka which appeared in the Hastings Center report in May 1996 for your review. And in addition the committee has queried four federal agencies who have not adopted the common rule concerning their reasons for not adopting the rule. The committee's letters and the agency responses have also been provided to you.

While the GAO report and the ACHRE study provided some helpful insights into the current framework for protecting human research subjects there is still much that is not known. At the heart of the matter is whether the current system of ensuring informed consent is adequate enough to deter abuse.

If abuse occurs is there a sufficient mechanism for punishing the abuser?

What about the adequacy of oversight by IRBs to ensure that inappropriate research is not going on, particularly if it is done within the context of government sponsored projects that are classified?

And what about inappropriate procedures carried out with an approved protocol? Just recently in New York a young woman died from an overdose of lidocaine delivered

during a bronchoscopy in a medical experiment she volunteered for and which was approved by the institution's IRB.

Your committee could also be helpful to Congress by analyzing the human subject research that occurs outside the purview of the common rule. Such research may include experiments that are sponsored solely by the private sector. How expensive is this research? Does it involve more than minimal risk?

As I mentioned earlier, some federal agencies, including some that sponsor human subject research, have not formally adopted the common rule. What would be the cost and benefits of requiring all agencies to adopt the rule and is cost/benefit analysis appropriate in this context?

Another area of concern identified by our committee is research involving persons with mental illness. Medical ethicists and doctors agree that this group of people deserve special attention beyond that governed by the common rule. However, unlike other vulnerable groups, including children, prisoners and pregnant women, research on the mentally ill does not have additional specific safeguards spelled out in the common rule. For these vulnerable groups NIH promulgated additional rules in the late 1980's. However, because of opposition by at least some doctors and advocates of the

mentally ill that group did not receive additional regulatory protection. Testimony presented to our committee earlier this year raised a number of concerns indicating that it may be necessary to revisit this decision.

Finally, it goes without saying that legislation, regulations and procedures can only take you so far in protecting human research subjects. Ultimately there must be a sense of responsibility on the part of the researcher for the ethical treatment of research subjects. Our universities, medical schools and teaching hospitals have made strides in instilling this personal responsibility through education but much more needs to be done.

Your commission's input, advice and research into all these questions, as well as the issues raised by the Advisory Committee on Human Radiation Experiments and the GAO, will be extremely helpful. As you begin your work I believe it would be helpful to involve in your deliberations those people who have been the subjects of research without their informed consent like the subjects of the radiation experiments. Their stories are a sobering reminder that this is not an abstract issue.

I thank you for your time and I would be glad to answer any questions you might have.

DR. SHAPIRO: Thank you very much for those

very thoughtful and very helpful remarks.

Are there any questions from members of the commission for Dr. Weiss?

Excuse me. Just jump in if I do not see your hand.

PROF. CHARO: Dr. Weiss, given the number of items that you have identified that might be worth some attention, I wonder if you would feel comfortable giving any kind of rough prioritization to that list?

DR. WEISS: I would hate to try to do that off the top of my head but I would be glad to provide a prioritization for you in writing in the next day or two.

PROF. CHARO: That is more than I asked for. Thank you.

DR. SHAPIRO: Thank you. That would be very helpful and we would certainly all look forward to that.

Any other questions?

Well, once again let me thank you very much. We appreciate you taking the time and please send our thanks also to Senator Glenn for his continued interest in this area. We appreciate it very much.

Okay. The next item on our agenda is a presentation from Michelle Russell-Einhorn on issues of conflict of interest. She has not yet arrived so we will proceed and then turn to her when she does arrive. My understanding is that she will be here in just a few

moments.

Let me begin with what obviously is a miscellaneous item but something which I would appreciate some help or any advice that the members of the commission might have. We will be establishing shortly a web site for the commission. It could, of course, have many functions and it could serve as a communication device amongst us. It could serve as a way of broadcasting information. It could serve all kinds of functions as you all know since that is, you know, what the flexibility of that kind of technology really is. Tom has his own site, which I have used, that people use quite a bit.

I really would like some advice from the commission. It does not have to come right now. But I am going to be thinking about that some in the next week or ten days or so, and so any thoughts you might have as to the kind of functions we should really focus on of a web site I really would appreciate it.

It is something obviously we can change as we go along. It is not set in stone in some way. But any thoughts you have please let Bill know or myself know in the next weeks. If anybody has any thoughts right now that is fine, but this is really not an item for discussion that has been scheduled, but it was a conversation that came up this morning as I was talking to somebody from staff.

Does anybody have any immediate advice on this

issue?

Okay. For those of you who care about that or look forward to it, let me know. You might be helpful in designing this site. I may be a little bit optimistic but I am hoping that we can get that up in the next few weeks. I am told here at NIH there is some kind of czar in charge of web sites which we have to go through. My only counter threat is I will establish it myself at Princeton if we do not get it done.

(Laughter.)

So we will have to see what happens.

Ms. Russell-Einhorn is here. Thank you very much for coming this morning. We appreciate it very much. Perhaps you could introduce yourself to the committee and then we can proceed.

PRESENTATION ON ETHICS IN GOVERNMENT

MS. MICHELLE RUSSELL-EINHORN

ASSISTANT SPECIAL COUNSEL FOR ETHICS

MS. RUSSELL-EINHORN: Well, good morning. Can everybody hear me all right?

First of all, let me introduce myself. I am Michelle Russell-Einhorn and I am the legal ethics attorney for the National Institutes of Health. I am actually a member of the Office of the General Counsel, like Bob Lanman, and I am based downtown in the Humphrey Building, but I am here at NIH to work with the NIH community on

ethics issues.

I always think that it helps people to have a general overview of how ethics in government works. The Federal Government has a lot of statutes and regulations that control ethics for Federal Government employees. In the White House there is an attorney who is dedicated to working on ethics issues and we deal with that person quite frequently. There is also a separate government agency called the Office of Government Ethics. A lot of people think that I work for the Office of Government Ethics, but I do not. I work for the Office of the General Counsel. They are two different things, two different agencies.

The purpose of the Office of Government Ethics is to administer and implement ethics in government to the executive branch of the government, not the legislative or the judicial side, but the executive branch of the government. We work very closely with the Office of Government Ethics.

Every agency, every executive branch agency is required by statute to have an individual appointed as the designated agency ethics official. We call that person a DEO, like that song, you know, "De-O, de-O." And our DEO for DHHS is Jack Kress and Jack Kress is downtown, and he is my supervisor, and there are other ethics attorneys in the downtown office, some who work primarily with other components of DHHS, like the Center for Disease Control and

Food and Drug Administration. Because it is not a huge community of people who do government ethics we are in very close contact with our counterparts at the Interior Department or the Commerce Department, or what have you. Again I just think it is helpful to have a sense of how ethics in government works.

Now why does this pertain to you? Because when you come here and you serve as advisory council members, we are very pleased that you have all agreed to do so, you are what are called "special government employees." And that means that for certain purposes you are government employees. Many of the conflict of interest statutes and regulations apply to you. They apply differently than they would to me because I am what is called a "regular federal government employee." But some of them still do apply to you and they do have consequences, and it is very important for you to understand what these restrictions are.

Let me start by giving you a little background on the criminal statutes.

Bill, you can tell me if I am talking too long.

There is a set of criminal statutes --

DR. SHAPIRO: You are starting there just to make us all feel relaxed.

(Laughter.)

MS. RUSSELL-EINHORN: There is a set of criminal statutes that go back to the 1800's that we

commonly call the "Criminal Conflict of Interest Statutes" and I will not go into specific detail except to just cite a few of them.

One of them is the Criminal Conflict of Interest Statute. Basically what this statute says is if you work for the government and you work on something in your capacity as a government employee you should not have an outside financial interest in the same thing you are working on for the government. So let me give you a concrete example of how this affects our scientists.

If we have a scientist working on a collaborative research agreement with Bristol-Myers, and for some reason I always love to malign Bristol-Myers, and that person owns stock in Bristol-Myers at the same time that they are working here on a collaboration with Bristol-Myers, you run into a problem with that criminal conflict of interest statute.

Now how does that affect you? It affects you in this way: You as special government employees are also covered by this statute. If you have a spouse who works for Bristol-Myers or a pension plan with Bristol-Myers, or stockholdings from Bristol-Myers, and anything you do here in your capacity as advisory council members might have an impact on Bristol-Myers, you run up against that statute.

So what do we do? Well, that statute actually allows us to issue something called a "waiver" and some of

you may have already seen your waivers.

Let me digress for a minute. You all filled out something called a "financial disclosure" form. This financial disclosure form is something that has to be filled out by every special government employee who serves in an advisory council capacity throughout the executive branch. So everybody has to do these. These are actually created by the Office of Government Ethics and approved by OPM.

What these forms do is they tell us what your situation is so we can look at your financial situation and see if you are going to run up against one of these statutes like the Criminal Conflict of Interest Statute.

If it does, then we have a couple of choices.

We can issue you something called a "waiver" and that waiver will say, "Well, so and so works for Yale University and Yale University has an interest in what this committee is working on." We will give this person a general waiver which means they can work in any general matter that might affect Yale University, but we are going to disqualify them from anything that specifically and uniquely affects Yale University. That is what those waivers are about and we get our information for those waivers from your financial disclosure forms.

It is very rare that we have come up against financial interests that we have not been able to resolve.

I do not know that we have ever asked somebody to leave an advisory council because we could not resolve a financial interest. There is always some way to work it out, but I think it helps if you understand why you are filling out these forms, what we do with the information that you give us, and what the waivers are that you are getting.

In addition, we also have a requirement that thirty days before each meeting you will be sent an addendum, something where you are going to have to clarify whether your financial interests have changed. Now this may seem onerous, but let me explain to you the real issue here. You come in to a meeting and you own stock in Merck and to your knowledge Merck has nothing to do with anything that this committee is working on.

But let's say your Merck -- let's say you have sold your Merck yesterday, right, and you decided you did not want it anymore, you went and bought a different stock, and that stock happened to be something that would be affected by something you are dealing with, but we do not know about it because it happened the day before the meeting.

Well, as a practical matter we cannot keep track of all your financial interests up to the minute. The best we can do is thirty days before a meeting and that is why we have that restriction because you may have new financial interests on January 1st and they may change on

March 1st, and they may change on June 1st, and that is why it is very difficult to only deal with these issues one time a year instead of before each meeting.

Anyway, that is a little bit about these financial disclosure forms and the criminal statute.

Let me just also mention there is another criminal statute which is commonly called the "Supplementation of Salary Statute." What it basically means is that if you work for the government only the government pays you for what you do. So this relates back to the 1920's when government did not have a lot of money and big companies would send people to Washington and they would pay for these people to work for the government. The government would basically pay them one dollar a year. You ran into a lot of questions of divided loyalties and things of that sort.

So now there is a statute that says you cannot do that. You can only get paid by the government for what you do. So if Dr. Fauci says, "Gosh, you know, I think I want to leave, they are not paying me enough here" and some outside organization says, "We really want you to stay at the NIH and we are going to give you an extra $50,000 a year just so you will stay in your position there," that would be called supplementing his government salary.

Now why do you have to be careful of this? Because you are here as special government employees. You

are here dealing with specific matters. Okay. You have to be careful. If somebody outside, because you have your personal lives, wants to hire you and pay you an honorarium or have you do something on something you are doing here, all right, you need to be careful about that. You all have a much broader expertise than what you are doing for this committee, but you have to keep in mind that what you are doing for this committee is just what you are doing for this committee and that needs to be kept separate from what you do in your outside lives.

Let me just also mention that there is other criminal statutes. There is also something called the "Standards of Ethical Conduct for Employees of the Executive Branch." These are issued by the Office of Government Ethics. They apply to everybody in the executive branch. They contain restrictions on teaching, speaking and writing. There actually are some restrictions in here that apply to you as special government employees specifically.

But let me just reiterate that it actually makes sense. If you are working on something here and there is an identifiable outside party, and somebody says to you, "Would you do something for me about that thing, about that thing you are working on here, with that identifiable outside party," please call Bill Dommel because it is likely there is a problem. We may well be

able to resolve it but that is the kind of thing we need to know about.

Like I said, I do not think it is too difficult to put together because if what you are doing here for the government and there is an identifiable outside party then that should have a light bulb go off that there might be an issue.

There are some post-employment issues that come up as special government employees if you work on something specifically here. I mean, if you were a council giving grants, for example, if you gave a grant to, you know, Yale University, you could then become their person to represent Yale back to the NIH on that exact same grant. It does not apply to any other grant, but only applies to that particular thing you worked on when you were here. So you need to keep that in mind. Something particular that you work on here involving outside specific parties could have some post-employment repercussions.

Anyway, that is basically a general overview of ethics in government. It is not as onerous as what people think it is. There usually are ways to resolve problems that come up. I am always available to talk to people privately about any situation that raises a concern. I know Bill will give you all a break now.

DR. SHAPIRO: Thank you very much. We will have an opportunity later today and later this afternoon to

discuss individual issues together, that is if there are any conflicts any of us perceive or want other committee members to know about. That is something we will address together later on this afternoon. I think you are going to be here at that time to help us if we need any help in that area.

MS. RUSSELL-EINHORN: I will be back.

DR. SHAPIRO: Are there any particular questions right now?

Jim?

DR. CHILDRESS: Could I just ask for a clarification? You said that we should be careful, for instance, about accepting honorarium to give a lecture on something related to the work of this group. Obviously a lot of us give lectures that touch on the topic such as ethics in clinical policy and health care where we might well use this as a major portion of the talk. You said be careful about that. Could you be more specific?

MS. RUSSELL-EINHORN: If you go out and give a talk on what this committee is doing and get paid for it, it begins to look like you are going out there as a representative of the committee. You are there in your capacity as a committee member. I mean, this is another issue that is very important, which is you have to separate what capacity are you in. Are you in your capacity as a private citizen with your other credentials or are you

there representing your government office?

If you give a lecture and you say, "This is what the National Bioethics Advisory Council is doing," you may well not be able to accept compensation for that because it may well be perceived to be too related to your official duties. On the other hand, if you give a general talk about what is going on in bioethics generally and you talk a little bit about what is going on here, that is not necessarily going to be perceived as focusing on what you are doing here.

DR. SHAPIRO: Yes?

DR. BRITO: That is a little confusing to me because part -- it was mentioned earlier that part of the reason of bringing the seventeen of us together is not just to draw on our ideas, but ideas nationally from the people we come in contact with, and part of that contact and influence, and other ideas can come from giving these talks and discussing particularly the university -- well, from my point of view from my university and speaking with the bioethics groups there and getting feedback.

So am I understanding that we cannot -- we can only utilize general ideas, but we cannot specifically say that the National Bioethics Advisory Commission has recommended such and such or is contemplating doing such and such?

MS. RUSSELL-EINHORN: Okay. Compensation is

the issue. If you are not getting any money for what you are doing you still need to be worried about it in the sense that, you know, if you are going to give a lecture and you are not going to get compensation and you are going to talk about what the Bioethics Committee is doing, are you trying to make a statement on behalf of the entire committee? That is a different issue. But in the context of ethics issues you can do that. Okay. You are not accepting compensation.

On the other hand you are offered money for what you are going to do and if you are offered money then we do need to make an assessment about whether what you are going to talk about is just so closely related to what you are doing here that it might raise a problem.

Yes?

DR. SHAPIRO: Alex?

PROF. CAPRON: Well, I thought that Jack Kress' memorandum on this, which is not to us but was just a standing statement of these ethics rules, there was a fairly clear differentiation which we may all want to look back at. It says that the statute does not preclude special government employees from receiving compensation for teaching, speaking or writing on a subject within the employee's discipline or generic area of expertise based on the employee's educational background or experience even though the teaching, speaking or writing deals generally

with a subject within the agency's area of responsibility.

That is differentiated from a situation in which an invitation is issued and circumstances would indicate that the inviter expected you to come and speak on behalf of the, in this case, NBAC. In my experience as a long time special government employee this does not raise real issues for us. I mean, if any people here are being invited because of their expertise it is not an issue that you along the way mention the activities of a group in which you are a member. Being a special government employee does not extinguish the First Amendment.

MS. RUSSELL-EINHORN: That is right.

DR. SHAPIRO: Alta?

PROF. CHARO: Okay. First to follow-up just briefly on a couple of these picky things. Compensation, definition of? Okay. Also, I have -- I waive honoraria and ask that they make a contribution to one of several charities that I identify for them. Is that considered compensation?

MS. RUSSELL-EINHORN: Well --

PROF. CHARO: It does not go to me. I do not take a tax deduction.

MS. RUSSELL-EINHORN: Yes. The definitions of compensation is frequently derived from IRS regulations. We do not have any control over them. Usually they are defined as saying if you suggest a charity, that is okay.

If you direct a charity, then it is construed that you have received it even if you really have not.

PROF. CHARO: Good. That is clear. Thank you.

Reimbursement for travel expenses, dollar for dollar.

PROF. CAPRON: It counts as compensation.

PROF. CHARO: Excuse me?

PROF. CAPRON: It is in the definition of compensation.

MS. RUSSELL-EINHORN: There is actually a legal battle about that right now. I would, to be on the safe side, assume that it is compensation, but it may change.

PROF. CHARO: I wish I really were all that compensated.

(Laughter.)

PROF. CHARO: And supplemental income. Now my understanding is that we are not getting anything other than per diem to cover our costs while we are here and my university does not consider this to be away from work. It is part of my work. But are you suggesting that we need to take leave days so that we are being paid by our home institution?

MS. RUSSELL-EINHORN: No, no, no. These are different rules for government employees.

PROF. CHARO: Okay.

MS. RUSSELL-EINHORN: These are very different.

You will find that there are very different rules for academic institutions and government in certain cases.

Let me also just make one other point. Under the Hatch Act, which is the statute that governs political activities for special government employees, you only need to be concerned about the time that you are actually serving as a government employee. Okay. When you come to Washington and you want to do something else, you want to go up on the Hill, I would not suggest that you come here from 9:00 to 12:00, go up to the Hill, and then come back here from 2:00 to 4:00. You need to be able to delineate when your service as a government employee ended and so long as you do that you will have no trouble.

I will be back again.

DR. SHAPIRO: I want to ask a question.

MS. RUSSELL-EINHORN: Sure.

DR. SHAPIRO: I think it has already been asked and I just did not focus on the right answer to that. I am chairman of the committee so I have already been asked by many professional organizations, academic organizations, to come and talk about the work of the committee. There is no honoraria involved or anything like that, but there is travel expenses involved and what you are telling me is that travel expenses are compensation.

MS. RUSSELL-EINHORN: The Office of Government Ethics put out a regulation that said that you cannot do

teaching, speaking and writing activities if you get compensation for that and this regulation affects you as special government employees. They defined compensation for the first time as including travel. Okay. Basically the regulation says if you want to teach, write, speak about what you do for the government, relates to what you do for the government, so long as you do not take compensation for it, it is okay, but then they included travel.

Now what happened was that somebody went and sued. Two people from EPA. And these two people from EPA said, "This is a violation of our First Amendment rights." Just for your information, the Department feels that way too. We do not believe that travel should be defined -- it should be included in the definition of compensation.

The U.S. District Court agreed and said, "You are wrong, OGE, the Office of Government Ethics. You cannot include travel as compensation under this regulation because you are violating the First Amendment rights of these two individuals from EPA."

But then the most bizarre thing happened, which is that the Department of Justice came out and said, "Well, we think this case only applies to the two people who sued." And this was a very interesting interpretation.

There is -- so what they have said is, "You are at risk here. We think it is only the two people at EPA

who can get travel and nobody else."

Apparently there is --

MR. HOLTZMAN: Bill it to them.

(Laughter.)

MS. RUSSELL-EINHORN: There is an attempt in progress to amend these regulations and take away this problem in total. So my answer to you is that I think a U.S. Attorney would be hard pressed to say that travel is compensation and would be hard pressed to say that the Santor case does not apply across the board to all federal employees, and that the department is behind you all one-hundred percent in the sense that travel is not compensation. But I cannot ignore the fact that this little tip is out there and so that is my answer.

PROF. CAPRON: I mean it is not a totally unreasonable position. After all it, I think, aims at people who hold meetings in very comfortable surroundings and bring government employees who have an interest in the area there, and the travel is, in effect, a perk.

The flip side of that is that those people can go to those meetings and the government can pay for them to be there if it is considered a legitimate thing. I would assume that if our chairman is being asked to go places and this rule applied that we ought to pay for him to go there and give that talk on our behalf. So it is not that special government employees are put -- to expend these

funds themselves.

If I have a federal, as I say, grant officer that is involved in a grant we have comes to a meeting, with all the rules that he or she has to be on government travel and so forth to that meeting if it is important to them to be there monitoring what is going on. It is just that I should not be paying them because then it looks as though I am trying to influence their attitude towards the project.

MS. RUSSELL-EINHORN: All right. Let me just add something. You know, I am not involved in the administrative day-to-day work of the Institutes. So sometimes my knowledge stops here. But there is a process where if you were on official travel you can get sponsored travel where the organization reimburses the government to pay for the travel so long as there is no conflict.

Now I have to say I have not been consulted too much about using that for special government employees but it is certainly there. In other words, instead of you going to the professional association on your own and not taking honorarium and, you know, worrying about how you are going to deal with the travel, you make it an official activity in your capacity as chair of this committee or in your capacity as a member of this committee. The money gets funneled through a 348, the legitimate travel process.

DR. SHAPIRO: Thank you. Any of you with

continuing questions as it evolves can speak to Bill or we can get in touch with you.

Thank you very much.

PROF. CAPRON: Could I ask --

DR. SHAPIRO: Yes.

PROF. CAPRON: -- another question?

DR. SHAPIRO: Yes.

PROF. CAPRON: I am curious in part because of the way my own thing is handled, do you have a separate category for something that in the academy complex, we have talked in the National Academy, we have talked about, which is the conflicts of commitment?

In other words, you seemed to focus so much on the notion that it is one's financial interests that are most important and for many of us, who are academics we do not have any business connections and do not own a lot of things, money is perhaps less important than our conflicts of commitment to certain activities, certain conclusions and so forth. And in a scientific process that is considered something that is important that has to be known by people.

Do you do any work like that or you are just looking at --

MS. RUSSELL-EINHORN: No, that is part of a policy matter because when you are talking about laws and regulations you need something specific. That is why it

focuses in on something that is identifiable. Some kind of an asset. We focus in on financial assets. Even the appearance standard, you know, where it is not -- you cannot just say the situation does not feel good or look good and so, therefore, there is an appearance of conflict of interest, you have got to meet certain legal standards before you can say that that happens. So commitment, conflict of commitment is much more of a policy issue.

DR. SHAPIRO: Any other questions just before you go? Any other questions?

All right. Thank you very much. We will see you later on today. Thank you.

One last item before we break. I think it is a very brief item but it is important for us to discuss it and see how the commission feels about it. It is a little bit late into this last issue. That is who is it that represents the commission to the press, and particularly the media, broadly speaking? I think Alex said in conjunction with another comment this morning that we do not want to hold back the First Amendment rights anybody has and, of course, all of us are free to speak about the work of the commission in any way that you feel like speaking about to anyone you want to speak to about it.

However, it seems to me it would be somewhat more orderly and help us if I handled speaking for the commission itself through our office here in Washington.

If that is satisfactory to people we will just proceed on that basis and if anyone has an issue with it or wants to clarify it that is available any time. I am available any time to anyone on the commission.

So this is really not meant to discourage discussion or to talk about the committee's work, which really I encourage every commission member to do, but simply in question more formally speaking for the committee and whatever conclusions that we might reach and recommendations that we will make over time.

Does that seem sensible to members of the commission?

DR. DUMAS: Sure.

DR. SHAPIRO: Okay. We will proceed with that. If issues come up we can always discuss it at any time.

All right. Let's take a 15 minute break and be back here at 10:30. Thank you.

(Whereupon, a break was taken from 10:20 a.m. until 10:45 a.m.)

VISIONS FOR THE COMMISSION

CHAIR AND MEMBERS

DR. SHAPIRO: Okay. Colleagues, let's call the meeting to order. Can I have your attention please?

There are deadlines and there are deadlines. We have an important one in front of us. Namely I am told that if we do not break at 11:45 for lunch we may have a

very long line to stand in. So we are going to break promptly at 11 -- no later than 11:45 so that you can take some reasonable amount of time for lunch without any undue inconvenience.

So we do have an hour and we will have more time later today to talk about the future of our role. This is the first time we have had a time -- a moment to talk together about it, although I have talked individually to some members of the commission before now. And it really is an appropriate moment to speak either to the broad role of the commission as you see it or to specific tactics we might pursue, i.e. which agenda items should we take on at the moment and how should we deal with them.

There are two activities which I would like to bring you up-to-date on very, very briefly. First of all, as you know, there is the World Congress, I guess the Third World Congress.

Is that right, Alex?

PROF. CAPRON: Yes.

DR. SHAPIRO: The Third World Congress on Bioethics which will be held out in San Francisco in the end of November. I think it begins November 22nd if I remember correctly. That one begins the 22nd.

Really Alex made what I thought was a very good suggestion that we try to assemble the day before the Congress starts in San Francisco not only ourselves, those

of us with an interest to be in such a meeting, but members of various types of bioethical commissions from around the world who could share their experiences with us not only in terms of the recommendations that they may have come up with, with respect to issues of concern to both us and them, but also their views on what it took to make commission activities, using the word "commission" just in the generic sense, successful.

I thought that was really an excellent idea to take advantage of both the fact that we are just starting and the Congress meeting to do that. So we have scheduled a meeting to which you have all been invited, which takes place in San Francisco on the 21st. I think it is officially a subcommittee meeting as a way this shall happen. It is a panel that is meeting. But we have invited all members of the commission to be members of this panel if they choose and if their schedules allow.

So just before we begin a more general discussion let me turn to Alex to update you on where those plans are now and to express my gratitude to him for taking initiative to get this meeting going.

Alex?

PROF. CAPRON: Thank you. The office has done a superb job of contacting hundreds of people around the world and issuing invitations. One of the things about our commission starting so much later than, I guess, some of us

had hoped when the initial process began was that letters of invitation to go out in August and September to invite people to a meeting in November from around the world meet with conflicts in their schedules and difficulties of organizing their own official process of getting approvals and so forth.

We have had 22 affirmative responses. They represent actually a very excellent cross selection of the people from around the world. I am pleased to see that they include people such as Jean Pierre Changeux, who is the President, the Chairman of the French Consultative Committee which has been in operation for about a decade, people from China, from a number of the Asian and Latin American countries, and from the international bodies that have shown a strong interest.

I expect that we will have substantially more people than that by the time we gather. In some ways it will be advantageous that the group will not be too unwieldy and I hope that we get the kind of advice that the chairman has indicated we are seeking, as well as the free exchange of ideas both during the session and for those people who are staying longer over the next couple of days.

We have -- Harold and I had worked out kind of a rough agenda for the meeting which is included in the brochure that is going out about the whole Congress and the Associated -- American Association of Bioethics annual

meeting on the 20th and 22nd, and a number of other sub -- post Congress sessions.

And I have for anyone who would like a couple of copies I brought along of the entire document. I think that one of the things Harold would like to do during the meeting now, not at this moment necessarily but at some time today, is to get reactions to the kind of rough agenda that has been established.

We are extremely fortunate that Professor Amy Gutmann (?) has agreed to give a luncheon address. Amy and Dennis Thompson are working on a book about deliberation in democracy.

Excuse me?

DR. EMANUEL: It is already out.

PROF. CAPRON: It is out. It is out. Have worked on.

DR. SHAPIRO: And reviewed in the Post already.

DR. EMANUEL: Right.

PROF. CAPRON: And some of her comments about the role of ethics deliberation will be, I am sure, based on that work with Dennis. I think it is not a conflict of interest that she happens to come from Princeton University where I guess she is now the dean of the faculty.

Perhaps I could give the staff the one page out of this document which sketches the tentative agenda. The fact that it is going to be published in the brochure,

unlike the Federal Government, which once it publishes what the agenda is in the Federal Register gets subject to all sorts of problems if it tries in any way to rearrange things, I think we at this point from this brochure that is published have a good deal of liberality.

The idea was simply to indicate to people who might be interested in coming to the meeting obviously that portion of the Congress was open to the public because it is a -- because we are gathered there in observer status. Just to indicate the kinds of topics that would be talked about.

So I will give that one page and then be happy to share with all of you, anyone who would like to look during the lunch hour or whatever, the full agenda for the other -- the Congress if you are making up your own mind as to whether or not there will be things there that interest you enough to attend.

DR. COX: Alex?

DR. SHAPIRO: Do you have a question?

DR. COX: Yes. What is the time on that? Was that all day the 21st?

PROF. CAPRON: It is set up to be a basically all day discussion.

DR. MURRAY: On the 21st, not the 20th?

PROF. CAPRON: The 21st. That is correct. The day before, the Thursday.

DR. EMANUEL: The 20th is the start of the American Association of Bioethics annual meeting.

DR. SHAPIRO: Any questions regarding that particular meeting which will take place late in November?

Again, if any of you have any questions, Alex is the best person to address them to, although if you would call me I will try to answer them if I can.

Okay. Thank you very much.

Now I would like to open the floor for a formal discussion amongst the commissioners regarding, as I said a few moments ago, their perspectives, both short-term and long-term, regarding the work of the commission. I sent everybody a note saying we would have such a discussion at this meeting and that will take place now and again later this afternoon after we hear from Dr. Collins. Indeed, encourage anybody who thought that they might want to commit their thoughts to writing to do so.

I have received -- we have received I should say -- some remarks from Bernie Lo, from Alta Charo, and Patricia Backlar, and that you should all have copies of those at your place. I will leave it to them to characterize these notes. Some are rhetorical questions, some are observations and so on. But I am really very appreciative. It really does help a lot for people to submit things in writing and we can share them amongst each other in ways that are very difficult otherwise.

So rather than turn specifically to any one of those, let me just see which commissioner would like to speak.

Yes?

PROF. CAPRON: I do not know if it is appropriate. I did not -- this is not an arranged colloquy and I may be out of order, but my own thinking about what kinds of things we should be dealing with is affected by what ability we have to deal with them. And is that something that you are in a position to share or not?

DR. SHAPIRO: I think I am in a position to share that since it is not a deep dark secret as far as I am aware.

As you know, the Executive Order or at least one of the pieces of paper that came through the official channels mentioned a project of $500,000. More than a few members of the commission asked me what on earth I expect to accomplish with that amount of money. As you know, from what I said to some of you last night that our real wealth is the intellectually endowment of the commission members, but that is hardly an answer to that question as true as that might be.

I expect that our final budget will settle down somewhere between three and four times that amount per year and that is the basis on which we ought to be planning. I do not expect more than that, although I think that that is

-- that may, in fact, occur. But what I expect is to meet the requirements set down in that report that someone referred to as now out of print that we all have in the back of our book which suggests that that is an appropriate budget target for a commission such as these and that is what we are planning and as we all ought to plan.

So is that responsive to your question?

PROF. CAPRON: Precisely. Thank you.

DR. SHAPIRO: Thank you.

Yes, Larry?

DR. MIIKE: I am more interested in short-term productions since I am a short-term member. I have a two-year term. So I am not worried about the long-term.

We have two specific charges and I guess we will have to wait for Dr. Collins to talk about the work in the genetic area that is already being done and what we can add to it or leave it up to other people. It seems that in a subject area we can do one of several things. One is simply try to strengthen the current system that if people have identified short-comings among specific population groups, as Dr. Lo has mentioned, improving and setting the process of review like the IRB.

I would add another thing since I am supposed to be here representing a particular ethnic side or whatever you want to look at it, is I think there is more increasing research among communities. The curious phrase

that the Canadian study mentions is "collectivities." Interestingly enough a little community in Hawaii has done exactly what the Canadian group has mentioned as collectivities.

But I only raise that in a sense that so much of what the focus is on human research is the protection of the individual in the research, but we are moving much more toward communities or groups. And I think there is much more awareness now about the rights and responsibilities and the protection of whatever the communities that those people come from. So I think that is an issue worth -- I think it is realistic to address that.

Researchers will not like what comes out of that, but I do not think researchers liked at least in the initial stages what came out of this whole field of protection.

DR. SHAPIRO: Bernie?

DR. LO: Let me try and follow with what Larry said. I had a number of episodes happen to me just this past fall which really struck home that there may be some real problems with the way research is carried out in an institution like mine which supposedly has a good review process.

About three weeks ago, if I could just tell a brief story, one of my clinic patients came in very, very upset saying that she had volunteered to be a subject in a

big NIH funded study and at her initial intake interview there were three other prospective subjects in the room and the researcher started to ask her fairly personal questions and she said, "I do not think we should be doing this with the other people here," and the research assistant said, "Oh, that is okay, we will just go right ahead."

I worked out by calling the principal investigator who was shocked that this happened and said that was a problem with sort of the training. But it really struck -- my patient really had her confidence in the whole research process undermined.

Now this may be just an isolated event that will never happen again, but I think it struck home to me that we have a model for regulating research in this country. It is really a decentralized IRB type model. The assumption is that this will take care of the salient problems. And a number of you in your other statements point out that we have had some episodes over the past couple of years where perhaps the IRB was not doing its job.

I would stress that maybe we want to reconsider whether the IRB model really is up to the task. I think there are some real pressures that might lead one to question how -- whether it is set up to do what it is supposed to do.

First, there are so many studies that IRBs

review. Our IRB averaged about seven minutes per study. If you average the meeting times versus the number of protocols that is about what it comes out to. Real disincentives to top rate scientists to serve on these committee. It is a time statement and lots of controversy in the areas of research.

I am very concerned about researchers that have a financial stake in the outcome of research in equity or consultantships or whatever. Also, just the lack of ongoing monitoring of these processes, which is what I think happened to the situation I alluded to.

So, I think, I liked very much as we went around the table the sort of practical vent people have echoed people's concerns that I would like this to be a productive committee and that it does something that is going to have an impact. Maybe it is not on regulations but at least on standards of practice among researchers.

I outlined a couple of things we might want to look at. Should IRB membership be enlarged to include community representatives, representatives of the subjects for the research to go back to Larry's sort of community theme? Should IRB members have some training? Should there be some sort of standard expectation of expertise? Should potential participants in research be routinely informed of any financial stake either of the institution or the individual researchers have in the research? Does

it matter to a potential subject what financial profits might go to the investigator institution?

Finally, I think I have some real concerns about ongoing monitoring especially of complex controversial studies. I sit on a couple of data safety monitoring boards which have maybe sometimes a conflict of interest. But the themes that we see on data safety monitoring boards remind us that -- that if there is not a procedure in place to identify issues as they come up after the initial IRB approval, that will not be picked up in the yearly review. There may be problems that go unaddressed.

So these are just issues to think about and it may be a way of starting a broader discussion of sort of our public policy towards human subjects research.

DR. SHAPIRO: Thank you very much. There are quite a few members that want to speak. I have Zeke and Diane. Trish, I think you wanted --

PROF. BACKLAR: I just wanted to make one point addressing that.

DR. SHAPIRO: All right. Let's just keep in order here because that is the way I can recognize you. If I am not seeing your hands let me know. Okay.

Zeke?

DR. EMANUEL: I just wanted to pick up on some of the things mentioned and really put my comments into three areas. One is the sort of moral issues we were

charged by Dr. Gibbons with sort of outlining moral principles or identifying them.

I guess my feeling is, and it really goes back to the issue that Larry mentioned about community, it is less a matter for us of identifying than of balancing all the different values we have. I think many of the interest in values and principles we know. It is not a problem of the fact that we do not -- cannot identify them or know them. It is really a problem of balancing them in this complex, ever changing world. And that is going to require a lot of judgment. Unfortunately, that does get us into sometimes politically very controversial areas.

But one of the values which I think has sort of evolved over time and maybe has not received as much attention is the one Larry mentioned. A lot of the focus of bioethics has been autonomy, individuals and much less has been our focus on community or what some people call solidarity. That balance arises a lot in the very issues that we have been charged with. The issue of research and the issue of genetics very much impinge not just the individual but the family and beyond the family, ethnic and racial groups, and beyond that the community at large.

I think that balance between the individual and community is something that this committee really does need to look at in these particular areas that I do not think has been well looked at, but certainly in the bioethics

community, which I know better than others, that balance -- a lot of people are upset about the over emphasis of autonomy and the under emphasis of community, and I would suggest that would be important.

The second point I wanted to make just to pick up something about the individual research topics we would address, and I would, I guess, make my comments in the following order: One of the experiences I have recently had is running a multi-institutional research project. It is enormously difficult. I have been through 40 IRBs now and I will only say that the review process is vastly different in places. The concerns are vastly different and the judgments are vastly different.

My protocol has been approved and rejected at many different places and it is, I think -- my own experience is that when you do multi-institutional research, and that is increasingly becoming the norm, it is too haphazard in this country. I am not sure a national board is the answer, but I think some other process than you have to go through 40 needs to be thought about.

The second area I would suggest is conflict of interest. Not that we need again to identify the principles, but we need a bit of a better balance. The commercialization of medicine, of research raises a lot of issues and I think my own experience and probably the discussion this morning raised it clearly. We have a lot

of different intuitions and rules about it. The government has different rules than academic. Having a sort of broad, but useful comment by the committee I think would be helpful.

Finally, I would suggest the issue of confidentiality and privacy. It has been raised and I am sure Dr. Collins is going to raise it. I think this is a prime subject for the moment. This committee is primed to do it. It impinges on the issue of research and genetics, as well as many others.

Finally, if I could conclude these comments -- I am sorry they are too long -- just about certain procedural issues. I am a practical guy. I like to get things done and I think regulations are important. But I would also urge this committee, some of the concerns that are raised, some of the reasons that we have been brought into existence, I think, go beyond the practical and changing regulations. You might call them, as Steve Holtzman did in our cab ride over here, metaphysical, spiritual, whatever, going to the soul as it were.

They certainly -- if we ignore those and only focus on what is practical we may do a disservice and many people may feel short-changed by what we do, especially in the area of genetics. I think the questions, while poorly articulated, really go to who we are in a spiritual metaphysical way. And I think that is as important for us

to wrestle with and if we cannot say anything meaningful then that is also an important conclusion.

Finally, I would say something about our meetings. We are meeting here at the NIH, a wonderful institution. We are a national commission and not just -- I think we will have profound effect if we direct ourselves not just to the federal government, but to the whole country. Our other meetings are scheduled for Washington, D.C., I would -- a road show would be useful.

DR. SHAPIRO: Thank you.

DR. EMANUEL: As much as I hate traveling.

(Laughter.)

DR. SHAPIRO: Diane?

DR. SCOTT-JONES: I am glad to hear the comments that have proceeded mine because one thing that I think about being in a forum like this is that our entering ideas get enriched by the exchange that we have among ourselves. So some of the things that I think about and am concerned about I am glad to hear reflected in the comments that have already been made so I will be brief.

Bernie Lo's comments about the incident in which a person was talked to in the presence of others rather than in a private setting led him to talk about the role of the IRB and I think that is important. But I think it also highlights for us the importance of training and monitoring ourselves as researchers and how we can do

something to encourage that process.

I think that we have a reverence for science in our society and that when we train students we encourage them to have that reverence for science and some of us may think a lot less about the role of the participants in research. So I think the IRB cannot do it alone. We somehow have to have a greater sense of responsibility in individual research projects because the IRB cannot really monitor the day-to-day doings of a project and they could not really prevent the incident that you described.

I also am glad to hear the concern about communities and not just concern about individuals. I think often of an incident that happened to me when I started a research project at a university where I worked before my present position. I had to go into the community and ask for permission to work in a child care center that was near the university I worked and the child care center for a time enjoyed the support of the university.

When I spoke to the person who was in a position to give me permission to work there, he pointed out to me that the building built most recently at the university where I worked had no doors and no windows on the side of it that faced the African American community. And as we sat in his office I could see this building across the street and in the distance a bit, and he was exactly right but I had never thought about it.

I think what he pointed out to me was a metaphor for the way that we do science. We set up barriers between ourselves and the communities that we should serve and I think that is an ethical issue because it prevents communities from benefiting from the research in the way that they should. It also penalizes us as researchers because we have a situation where persons who we want to participate in our research are wary of us, they are suspicious of us, and so I think we lose on both sides when we set up barriers or divisions between ourselves and the communities we want to study.

So I think although, you know, some reverence for science is perhaps appropriate, I think we should aim more for a model where science is seen as part of person's everyday lives and as a vehicle that they can use for improvement rather than something that stands apart from them. So those are some of the issues that I think we should deal with.

Also the issue of informed consent. Others have made mention. I think that is one that we need to do more with because IRB regulations are sometimes so involved that we end up with a consent letter that parents often do not read. It causes people to question us more than it causes people to want to participate in the study. So we need to find a way to take a prospective look at what we are studying when we are going about doing our research.

DR. SHAPIRO: On the issue of informed consent a lot of people have written me since my appointment was announced. The single most common item I have received comes from physicians engaged in clinical research and deals with the issue of informed consent and whether we are handling that right. So we will certainly come back to that.

Patricia?

PROF. BACKLAR: I feel that much of what I was going to say has been said.

DR. SHAPIRO: It is possible to pass.

PROF. BACKLAR: Right. I think there is one aspect of the IRB that Bernie was talking about that I do want to get back to and people have also mentioned, and that is some elements of conflict of interest that just innately lie within the IRB process, and that is a considerable concern.

The rest of the issues you can read in my piece that I passed out, but I want to say out loud that we do need to balance the need to develop the specific policies and standards and procedures with the need to maintain an evaluative system that is flexible and open to the particulars of research projects. That is what we have to do with our collectives and individuals as well.

DR. SHAPIRO: Thank you very much.

Eric?

DR. CASSELL: Well, like all clinicians no matter how long they have been working or how fancy they are, they take care of common colds. We -- certain gut issues, the conflict of interest and so forth, will never go away and have been, in fact, in ethical boards forever.

However, in the generation since all this really started a lot of things have changed in this country around those same gut issues. One of them is that we have a lot of experts on ethics in the world. As a matter of fact, as everybody knows, everybody knows everything. And ethics is one of the things everybody knows everything about.

It is my hope that as we work along that we begin to move that community into a more sophisticated understanding. Zeke pointed out what Dan Callahan called the desert of paternalism and autonomy and we move past that concept. One of our functions, I think, is an educational function in which people see a more sophisticated understanding.

The second thing that has happened in all this generation is that we are now firmly in a technological era. We are not in the beginning of one. And as such there was a sort of antiscience bias in the early ethics time and that just will not do now.

On the other hand, scientists have a certain vaulting optimism sometimes and blinders that keep them

from seeing distress in their fields, although as David pointed out that is not always the case. We are obligated in part to educate our colleagues and scientists. We also have to understand why Aristotle said in the beginning of metaphysics, "All men by nature desire to know. The pressure to know is irresistible," and we have to be a part of that.

Finally, the other thing that has happened in the same era is there has -- somebody said that in the beginning of this century that it was going to be the century of over-simplification. So it certainly happened.

(Laughter.)

It certainly has been that in relationship to understanding human beings. In the last generation the increasing complexity and what it means when you say somebody is a person is becoming apparent and the same thing about the collectivities and communities. We are just beginning to know what persons are, what families are, what relationships are, and it is this interaction of these trends that I think we sit right in the middle of. It is our function that when we do a simple thing like a conflict of interest question or informed consent, it is always with this philosophical background. We have moved ahead a whole new generation and we have to keep it in mind.

DR. SHAPIRO: Thank you.

Alta?

PROF. CHARO: I think I will let the written piece, and I again apologize for having done it with handwriting, speak for itself.

PROF. CAPRON: But you write so neatly, Alta.

PROF. CHARO: Especially when I am trying to make it legible. I will let it speak for itself with regard to the generic points about uniformity of coverage of human subjects research guidelines or regulations, specific populations are omitted from the regs, and these are the types of protocols involving human tissue and genetic information.

But I would like to add to it because I did not have enough coffee when I wrote this to have remembered to add to it. Number one, a hearty endorsement of all of these things circling around having to do with multicultural issues and I am embarrassed that I only refer to it indirectly in transnational context, which is really horrific.

I think we need probably to take notice specifically of the existence of the Tuskegee Project which is still working to get an apology and the lessons that can be learned from that experience and the radiation experience, et cetera, not only in the context of how people are treated, not only, I think, implicit in Larry's comments about how people want to be approached. But also with regard to an issue that I think really goes to what

Bernie has been focusing on and that is kind of structural incentives that drive things regardless of these specific choices.

What I mean is the following: I have a feeling that no matter what you choose as specific policy that it will be overwhelmed by driving forces like the scientific imperative which will always give incentives for people to go out and say there is a good reason to want to know something, that is one of the very important lessons of Tuskegee, which leads to really over arching decisions about whether the overall thrust of the approach at the federal level ought to be one that is protectionist and always on the side of protectionism or is one that tries to get a more kind of nuanced balance between research that offers an opportunity to subjects versus research that does not.

I think that those questions cannot be answered in a vacuum, but have to be answered against these kind of structural forces.

Second, a more nuanced attention to the actual uses of information. For example, in the area of genetics a lot of concern is focused on health insurance. Alex, I will defer to for sure because he has been working on this issue for a long time. But it strikes me that the existence of large population based programs in which people are automatically entered through their employer, et

cetera, to the extent that they grow really changes the nature of the potential for use of individualized genetic information as opposed to the continuing kind of demographic epidemiological based stuff.

Paying attention to the structure of things out there may make it easier to identify the real trends that may drive things so that you might want to have some kind of counterbalancing force via regulation.

And finally on that list would be a genuine -- I am sorry, I also left off this paper -- the way in which we approach not only the researcher's financial and professional interests in pursuing their research and obtaining subjects, but in the whole phenomenon of compensation for subjects, both financial inducements as well as compensation in the event of injury.

The Canadian report comes out very strongly suggesting that compensation should not be very high for people that do not have high incomes because you do not want to induce them to become subjects. On the other hand, it seems like therefore you pay poor people less to take the same bodily risk as rich people.

You know, as a professor who teaches torts and all the questions around damages, I am familiar with the fact that this is insoluble. But I think a much closer look at this whole phenomenon might pay off in helping to balance that and whatever decisions you make there against

how protectionist your whole approach is going to be when it comes to which kinds of subjects you enroll.

DR. SHAPIRO: Thank you.

Jim?

DR. CHILDRESS: My comments will echo and build on the important points that my colleagues have already made. I would start from one of Zeke Emanuel's comments about we already know the over arching principles.

I believe the language that appears in the charter or in the authorizing document along those lines, Congress meant really to distinguish our enterprise from regulation from making judgments about specific protocols because it seems to me -- and we heard Dr. Gibbons say today -- that really the task to a great extent is that of interpretation. But interpretation of those broad over arching principles, if we assume that we have some consensus in the society about those, involves at least two things.

Zeke mentioned balancing and that is certainly an important one. But also making these principles more concrete and specific for particular areas. Areas that we may not have covered as well in the past such as, something that several on the committee have a particular interest in this area, contemplating paired subjects. But one might also add areas that we have not covered such as a lot that is going on in the area of research involving

collectivities. I would say particularly health services research, outcomes research, an area that we are really not paying that much attention to from the standpoint of evaluation.

Several colleagues have also mentioned, and I would strongly affirm the need to pay attention to structures, and by this I mean first of all the structure of IRB and its role in the overall system of evaluation, approval and monitoring of research involving human subjects, but we really do not know a lot about how that works in practice. Just glancing over the GAO report I am not sure how far this takes us. It may well be this is an area where we will need to commission some research in order to become really very learned to know what kinds of changes perhaps should be recommended. And to attend to the competing structures that may well be at work also.

And I would suggest that structural point comes into play in the area of genetics as well where at NIH and the Human Genome Project there is reconsideration now of the role of the RAC, the role of the Ethics Working Group, and without in any way suggesting how I think those things ought to come out, it seems to me that we ought to look very carefully at this process evaluation and determine whether some alternative structures may be needed to make sure that some of the legitimate concerns are met such as public participation, accountability and the like.

DR. SHAPIRO: Thank you very much.

Tom?

MR. HOLTZMAN: Rhetaugh Dumas has been trying to get on your list for quite a while.

DR. SHAPIRO: I am sorry. I will call on you in a second. I am sorry.

DR. DUMAS: Thank you.

DR. SHAPIRO: Tom?

DR. MURRAY: Thank you. First about research ethics. I have been trying to listen carefully to the remarks of my fellow commissioners and see if I can categorize what strikes me as the central issues that we probably ought to have on our agenda and you can tell me if I have got it wrong or if I am at least close to the mark.

I have put it in four categories. One is community involvement, involvement generally of communities and relationship with communities to researchers and the scientific enterprise. I agree that has been insufficiently discussed.

The NIH Task Force which had a very long name that was essentially looking at research on violence tried to give emphasis to this, a piece of what we thought was important. Communities do care about research on violence in communities.

The second category has to do with adequacies or inadequacies of the current IRB system and we have had a

long list of possible deficiencies and worries about IRBs.

Third, and I say this with great caution in the year of the 50th anniversary of the Nuremberg trials, which those of you who are in ethics will remember that the first sentence of the first principle of the Nuremberg Code says, "The consent of the human subject of research is absolutely essential." Nonetheless it is not the whole story.

There are large classes of human beings, persons, who cannot give their consent because they are too young, too demented, too mentally ill, or otherwise not in the position to have -- to give an informed consent in a way that we regard as knowingly meaningful. And I think that the -- our discussions and perhaps also our IRB rules have not always done the best job of sort of understanding what is morally significant about those kinds of research relationships.

So, I think, a look at informed consent. Not to dislodge it where, in fact, it is an absolute requirement, that is with competent subjects, but in places and for groups where it simply cannot be the whole story we need to take another look.

And the fourth category under research ethics is at this point a miscellaneous category. Alta mentioned compensation and issues of equity and also noncoercive compensation. There have been some other issues as well.

I am going to speak a bit about genetics

although I suppose some of that conversation will also be looked at by Francis in Francis Collins' participation this afternoon.

Genetic information is a part of our mandate. I hope that we will tackle some questions that are, I think, just beginning to be addressed and those questions like is genetic information genuinely distinctive and different from other kinds of information related to health. Should we treat it as different from those other kinds of information? Does treating it differently have generally overall good results or is it, in fact, a contribution to what I take it sometimes to be an overselling of the importance of genetics and human life and welfare? Does it contribute to such things as genetic reductionism and genetic determinance?

There continues to be concern about genetics discrimination. Is it appropriate that a woman who happens to have a mutated form of the BRCA-1 gene, a gene that predisposes to breast cancer -- if you have a mutation in it you have about an 85 to 90 percent lifetime risk of breast cancer -- should a woman who has that gene, therefore, have difficulties getting health insurance coverage because of that? There have been concerns about genetic privacy and, in part, that question is subsumed, I think, under the first set of questions I have asked, that is are genetics different. But clearly many people find

possible release of information about genetics information about them especially threatening.

And I also note that in our mandate the issue of gene patenting came up. I think that might be a particularly good issue for us to take on because I suspect there is a lot of opinion out there about gene patenting. But I suspect it is also fairly thick as people have thought a great deal about what is good or bad about the patenting of genes.

The last word about our mission, as I conceive of what we can do, I want to be very practical about it so I endorse everybody who I think has spoken so far who has also said we ought to do something and not just talk. I want to say in the course of that doing I think our job -- I would urge that we not think of our job as simply contributing to the government decision making. But rather as promoting a dialogue among the broader public about these issues. If all we do is even provide very sage counsel to Congress and the executive branch then that is a good thing, but that is only part of what I hope we will do. We will, in fact, encourage a very broad public debate, an informed public debate about the issues we take on.

Thank you.

DR. SHAPIRO: Thank you. Alex?

PROF. CAPRON: The comments that I want to make

will go over some ground, but it maybe useful just because it gives an indication of those areas which, independent of the comments of fellow commissioners, I regarded as being important.

I want to frame this by saying I think we need to figure out, both because our life is of indefinite duration and because our budget is -- although not inconsequential -- not enough to do everything that we might want to do. How we are going to do what we do, that is to say by having research projects or investigators or calling witnesses, or whatever, that will issue from this report of this commission, and what are the things that we see the need for others to do that they have a potential capacity for doing but maybe are not doing it at a sufficient level in our view, both within the government and without.

On the immediate agenda I suppose I would agree with several of the comments that have been made today. I think the persistent issue of compensation of subjects is something that has been around -- for injuries is something that has been around as a topic for a long time and there have been a number of reports on it. I am not even quite clear where we are in the status of that beyond the published rule and how much is going on, on the subject.

The failure of the adoption of the National Commission's recommendations vis-a-vis research on the

mentally ill and institutionalized. The need for careful consideration of different rules that may apply in epidemiological research and the grave under representation of research in that area which has hampered the development of a real understanding of issues that arise out of the work place and the environment, and so forth.

Changes in the paradigm of research. We used to think primarily of the need to protect people from being in research projects in which they would be harmed. The HIV epidemic has changed the view of potential research subjects to claims about the right to be a research subject and the right to access the untested means. And it has really caused a C change in some ways at least in the way some research is conducted, and I think a way to evaluate it by OPRR and FDA. And yet we have not really talked about what difference that should make for the paradigm that we are employing.

The quality of the IRB process has been mentioned and I have always been curious by our absence of a real definition of why we have diversity in those committees. Is it a representative function? I mean, should the person who happens to be a noninstitutional person think of all the communities? If it is a woman, if it is a minority, if it is a person of particular religious views, is that person a representative of those views at the table or are they a committee member like the

scientists or physicians who happen to sit on the committee? Or do those people represent the interests of science or medicine there as opposed to applying judgment?

But we have never really explained why it is we have this group of people. Therefore, I would expect that the kinds of differences that Zeke has experienced in the multi-institutional world of multi-institutional studies can look as though we have a lot of chaos going on because different committees see their roles differently. Is that good or bad? I mean, I do not know that we know. Maybe it was good that some of those committees rejected you and some accepted. It may have reflected legitimate factors as opposed to just arbitrariness.

Our expectations of the oversight by OPRR and its sister bodies and other agencies. How well is the common rule working? People talked this morning. I think we had several comments suggesting there was a need for somebody to be looking at the whole thing. Well, there is supposedly some interagency coordination on that which I think OPRR is taking the lead. I would like to know more about that. That might be an example of something that is really happening or it could happen at a greater level. We do not have to take that on necessarily, but we would need some assurance that it is happening.

In the genetics area I think the gene patenting issue is absolutely one we have to talk about, not only the

patenting of animals, but of human genes. This is something where I think that the patent trademark office has felt itself constrained by the statutory language and not in a position to make policy, although in effect they have made policy.

We need to talk more about the means of and reasonable expectations for privacy about genetic data and to ask the question that Tom Murray just mentioned. Is genetic information that different? There have been a number of attempts and there is a model bill to protect genetic information very differently. Perhaps all that does is give people a false sense of this being something different.

I mean, there is a lot of genetic information that has been collected. It just has not been labeled genetic along the way. I mean, family histories are a form of genetic information. They have not excited quite the same concerns, but perhaps the molecular based information ought to be different. That is something that needs further thought.

If those are the most immediate things I think we need also a process for figuring out how new topics will come to our agenda and be prepared for us so that we do not just start at the beginning of a topic where there is a little bit of prior work where we could get up to speed more readily.

Mention was made by Jack, I was interested about the ethics of the allocation of federal research dollars, how decisions are made, and the way in which -- I mean, a decent economist will tell you that the allocation of funds is a set of implicit ethical judgments. One could say also the ethics of health care reform, and I would think both of those would be good topics to have.

The reproductive developments have been an area which interestingly none of the past commissions have dealt with. The group -- the congressional body was starting off by looking at some of those and perhaps that was one of the reasons for its demise.

The issues of organ and tissue transplantation, an area which has sort of slid into the background of people's thinking. There remain marked racial disparities in the rate of organ transplantation and in the rate of organ donation. The whole set of rules which are full of ethical judgments behind the way in which potential recipients are graded and so forth are largely in the hands of the experts who are engaged.

There is an active process which is very broadly based in that community of setting those rules and these issues are debated, but I do not think they have had very much public attention of late. And within that there is also this emerging issue of the new technology of the transplantation of human stem cells from cord blood and the

potential interest which has generated already extensive commercial activity. And in some ways that is an example that may offer us an opportunity to get into concerns which I think the public has about the ways in which basic scientific discoveries are so quickly commercialized to the apparent financial advantage of a few people.

So I hope that we make some decisions both about how we will figure out those things which we want to focus on and those things which we may not be capable of, but we do not want to push off our table and we want to say let's find out what is happening here. And if we do not think the efforts are all that they could be, recommend ways in which these other structures can deal with it.

DR. SHAPIRO: Thank you very much.

David, then Rhetaugh and Laurie.

DR. COX: The first thing I would like to do is just make a comment about genetics. Many people have brought up the point about genetics. I think that I share some of Tom Murray's concerns that the great interest in genetics in our society is a plus and a minus. The plus is it gives you an opportunity to get people's attention. The minus is people look at genetics in a very deterministic way and it will make things simpler. So I would like to be aware of both of those on our commission and I would like to use genetics in the plus way.

The plus way is a specific starting point for

more general problems. Zeke said this very nicely I thought. He said that you do not want to get rid of the bigger philosophical, bigger picture, but yet you have to have some specific place to start. And I think genetics gives us that. It is just a starting place for some specific things that we can get our teeth into. But I would like to say that I would only like to consider those that have broader implications outside of genetics.

So one of those areas is in the area of informed consent let's say. We have already heard informed consent goes extremely broadly in many different areas, but there is some pertinent issues with respect to informed consent in genetics. So that may be a place to get started.

As an example, stored tissue samples in terms of tissue banks, it really has people's attention because it is a practical problem. It has real genetic implications, but it has broader implications for informed consent. So I am not saying, you know, stored tissue is a specific thing we should do, but it is an example of a process.

The second point I would like to make, particularly after the past three years dealing with ethical, legal and social issues in genetics in the Genome Project, is that we are not at a loss of facts on these various issues. There are more statements published on

each of these areas that we could all read. Every society has their statement and their point of view. Zeke brought this up in the context of IRBs, how do you adjudicate how you put this together?

You cannot have -- well, actually Alex brought this up, too. You can, in fact, have 200 different points of view and maybe they are all valid. That is one thing. Or you could try and adjudicate them into one point of view. I would just say my personal observations are these individual statements that are made by the individual groups. I do not have to have the name of the group that wrote the statement. It is implicit in their recommendations. So there are stakeholders' aspect of this are all over the recommendations.

I think this commission has a special opportunity to be able to take all these facts the different groups have put together and say should there be 40 things or can we as a -- we each have our own stakes, but as a commission can we put this together in a straight forward set of recommendations that people can follow so we do not have to get it from the IRB.

The final thing that I would like to say is this issue about an IRB. Every -- the different groups I have been involved with in genetics, all the solutions end up being and the IRB will be the one that adjudicates them. I am extremely concerned about this because -- not because

I do not think IRBs can do it, but I do not think -- I think we have to pay a lot of attention if all of our implementation is through IRBs then we better pay a lot of attention to can they do it or helping them do it better. Or even come up with a different model, which I do not have in mind, and I would really like to hear people's views of what other models there are besides IRBs.

DR. SHAPIRO: Thank you.

I would just make one comment on the stored tissue issue because I expect that Dr. Collins will talk directly about that issue. It is a very interesting issue and I expect he will talk more about that this afternoon and we can have some discussion with him.

David, that is a question at that time.

Rhetaugh?

DR. DUMAS: Yes. I certainly share many of the concerns that have been voiced already and I would like to urge that we find ways to tease out in our considerations ethical issues that are related to who gets chosen to participate in the research and who are the major beneficiaries of the outcome of these studies. I think that has been alluded to in many of the comments that I have heard.

But I believe that it is very important to consider who is -- what kind of decisions really influence the opportunities that are available to become a part of

the subjects -- to become a subject in the research, or the kind of decisions that influence what the subject of the research is going to be and who will benefit, as well as the measures to protect their rights and their welfare.

DR. SHAPIRO: Thank you.

Laurie?

MS. FLYNN: I will not restate the views of the others because I certainly endorse them. I think we have identified a series of topics that are very important and I look forward to participating in them.

I want to try to represent perhaps a little bit more of a lay oriented response to the discussion and acknowledge that we are operating at a time when our public out there, our general public, those individuals who are not trained as ethicists, those individuals who are not trained as scientists, who do not know what IRB stands for, and who are generally not in touch with the language and the issues that have been on discussion in this room.

There has been over the last some years, I think, a disturbing loss of competence in our ability to make these tough decisions. A sense that there is no value based well understood moral framework that undergirds what it is that we are about. I think that is a significant issue. I think it is significant if the general public has both an enormous hope for research and yet a deep suspicion about the research process.

I think it is more troubling when organizations and patients who have been traditionally strong supporters of research find themselves less than totally confident that these issues are being well and substantively addressed. Some of that lack of competence is because those of us who represent the patient and family concern have not been well and substantively represented in the dialogue.

So as we look at our work and we have identified some critically important issues, I certainly agree with the shape of the agenda that has been articulated, I would ask that we think about not just perfunctorily, but meaningfully and specifically, seeking ways to engage those who are the subjects of research, to engage those who are most impacted by some of the moral dilemmas in research difficulties that we have addressed, and really use this commission as an opportunity to do some of the education beyond our own community research advocates and ethicists, but some education of the public.

The public, who all at some point in their life will be touched by these issues and we do not know when that will be. We do not know how that will occur, but one would like to think that folks at that point would feel both capable of making good decisions and confident that the establishment supports wise choices.

I would, I guess, close by reminding us that if

we do not find ways to do this job well and meaningfully, and substantively involve those whose lives are affected by these decisions, we may find that some of our friends in the political arena will, in fact, take this task from us. I think none of us would see that as the preferred outcome.

DR. SHAPIRO: Thank you.

Steve?

MR. HOLTZMAN: Thank you. I would like to start off with just some sort of primary pragmatic thoughts about how do we do whatever it is that we want to do and how are we going to get it done. People at this table have said they want to accomplish something. We have an incredibly broad agenda since it also includes the meta-agenda of take on anything you think is important. But getting a little more pragmatic, the charge to us seems to me to have two major elements right in front of us, protection of research subjects is one, genetics is another.

If you take that on its face, I do not think necessarily the idea of using genetics as an exemplar of protection of research subjects is necessarily the best way at it. So how does the committee go about asking the question of what are we going to do if we want to take on both of these pragmatically? Do we set up two working groups? I would be interested in a discussion by the committee of how to get the job done and, for example, if

we want to take on these two that we want to focus.

DR. SHAPIRO: Let me -- you have other things to say so let me just apologize.

MR. HOLTZMAN: Okay. So that was just one. In that context, given that I come from a genetics genomics company, I want to put forth a plea for keeping genetics on the table as an important subject and not just focusing on the protection of research subjects. And maybe in the spirit of Alex's statement that maybe you should -- this is an opportunity to introduce everyone to you. I wrote some thoughts this morning about why I felt it was important to be sitting here and if I can read them -- and it has to do with why genetics, I think, is very important to this commission.

It is that the explosion of knowledge of the biological underpinning of ourselves arising from the Human Genome Project and the biotechnology evolution holds enormous promise for the new practice of medicine. However these same technologies pose the potential undoubtedly for misuse, to stigmatize, to terminate, or to promote social agendas for human improvement as conceived by this or that group.

These technologies as they provide us with a new understanding of the basis of ourselves as physical beings also challenge our concepts of ourselves as self-determining beings and, indeed, as spiritual beings.

Respecting the profundity of these challenges, acknowledging and addressing the deepest platitude that this technological evolution occasions, and providing safeguards against the misuse of guidelines for the social responsible use of the biology are to my mind the preconditions of our societies realizing the benefits of the biology evolution.

Particularly for those of us who would seek to profit financially from the new biology we have a special responsibility to the public to participate and encourage more enlightened discourse on the implications of the new genetics.

The lesson of the new genetics is not the differences that should set us apart, but rather the diversity that should be the cause for our celebration. And the lesson of the new genetics is not that genes are destiny, but rather the profoundly complex interaction of our underlying biological selves with the environment, including our social environment.

What I would like to see this commission do is somehow play a role in moving the discourse forward so that we can have the new terms of debate which will allow us to have an underlying social policy.

DR. SHAPIRO: Thank you very much.

Let me just make one brief comment before we allow people to break for lunch and it has to do with an

issue which has come up in a number of different comments, that is, you know, people's expressions let's do something, let's not just talk, or other versions of that plea, of course, which I think is really extremely important to the point.

Let me remind the commission that we have one very specific task, which is essentially mandated before us, and that is to review the status of the work in the various agencies regarding human subject protection. Each agency has made a report and we have that report. Those reports need to be evaluated and that is a very simple task. But it seems to me that within that task we will have a capacity then to, one, evaluate the status quo, but then to ask ourselves a question. Is the status quo working and how should it be altered? In what way should we try to sculpt the future in this area?

So that is a task which is right before us. It incorporates many of the issues brought up today regarding human subject protection within it because, for example, how do you deal with dependent populations, however those are defined, and so on. It does not deal directly with the genetics issue, but certainly it has come up that genetics also has a version in here which might be helpful.

I just wanted to tell the commission that I have asked Jim if he would head a subcommittee of this commission in order to draw out and articulate a thoughtful

agenda of how we would approach that general area. The staff very early on, i.e. beginning Monday, will be looking at all these reports and do the staff work necessary to evaluate those in a manner that can help the subcommittee and any other member of the commission that is interested in seeing exactly where we are now.

That would be the first stage. The second stage would be, of course, to develop an agenda which takes us forward from whatever the status quo is now.

So it seems to me that is, relatively speaking, an easily defined project. We will find some mechanism as we go along and as both the staff and Jim makes some progress to keep each other informed so we can have some interaction regarding how this agenda gets formed, evaluation and so on, so that by the next time we meet we have a really pretty good work product before us.

One intention is for the committee to have a report each year. It does not matter, that is my intention, not we are required to have a report each year, so that is not an innovation I am making in some sense. But it seems to me that we need to know fairly soon, no later than next month or two, just what in a general way is going to be in that report. But I very much hope at the current time the human subject protection will receive a big part of the attention in that report.

In that connection I would like to know from

members of the commission, I am not going to ask you to raise hands now, whether in the two areas we are certainly going to have to identify an agenda right away -- one is human subjects protection I have already talked about. The other is the genetics area. We have not yet focused and we do not have articulated for us quite so neat a program. We will have to do that ourselves. I would like to know which commission members really have a preference for working in one area or the other as we begin to put these subcommittees together.

I have to tell that I will treat silence as an indication you do not mind which one you are assigned to since I think all members ought to participate in these ongoing developments. So we will have more time this afternoon to talk about these issues and hear your response to what I have just said and talk more on the genetics issue.

Just before we break I think Pat wanted to make an announcement.

MS. NORRIS: This announcement is for the press. I believe we have about 15 members of the press with us today. Once we break, Dr. Shapiro will be available to answer your questions only for about 15 minutes because he has to have lunch, too. We invite you to join us down in Conference Room 6.

PROF. CAPRON: What is happening with our

photograph?

DR. SHAPIRO: That is what I will mention right now. For those of you who are particularly photogenic there is a -- we hope that includes all of you --

(Laughter.)

DR. SHAPIRO: -- photographer and he would like to take a photograph of the commission and he will do so at 12:50 in Room 6, which is right at the other end of this hall. Conference Room 6.

So enjoy your lunch and be back there by 12:50. Thank you.

(Whereupon, a luncheon recess was taken at 11:50 a.m.)

* * * * *

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

(1:09 p.m.)

DR. SHAPIRO: Colleagues, if I could have your attention, please.

I just told Dr. Collins that perhaps our commission has had a hard time recovering from the photograph we just took.

(Laughter.)

In which case he wanted to know if we had the informed consent of all those involved for this particular piece of work.

Well, needless to say it is a great personal pleasure to welcome Dr. Francis Collins, as you know, Director of the National Center for Human Genome Research, here to our first meeting.

I knew Dr. Collins first when he and I were both at the University of Michigan. But I think all of us know him from the work that he has done both prior to becoming director of this important project, and now certainly as director of this project.

So I have asked Francis to come here this afternoon to share some observations that he might have, some ideas he might have, and then we will follow that with discussion both amongst ourselves and with Dr. Collins.

Francis, thank you very much for being here today.

PERSPECTIVES

DR. FRANCIS S. COLLINS

DIRECTOR, NATIONAL CENTER ON HUMAN GENOME RESEARCH

DR. COLLINS: Well, I must say I am really very happy and honored to have a chance to come and speak to this group on its first meeting and to be given such a generous allocation of time which I will try not to abuse.

I would certainly like to extend my personal thanks to Harold Shapiro for the way in which he has pulled this group together for this first meeting and the open way in which he is organizing the dialogue, the multilogue, that we are all being part of here today.

It is interesting, October 4th seems to be an ELSI extravaganza because half a mile from here in the Holiday Inn in Bethesda we are in the middle of a very intense meeting talking about employment and genetic information, and the possibility for discrimination in the work place based upon what people find out about your genes. Out of that meeting we hope will come some interesting recommendations about protections that are beginning to emerge in some states, but certainly have not emerged at the federal level.

So I apologize that on account of that meeting I was not able to be with you this morning and I will also have to dash back over there this afternoon to help lead the final discussion, which we hope will produce some results,

but that does not reflect in any way my enthusiasm for what you are doing, which is enormous.

Many times I have been asked over the course of the last year-and-a-half what was the view of the Director of the National Center for Human Genome Research in having a commission that was going to be looking at genetics. After all isn't that what the ELSI Working Group, the Ethical, Legal and Social Issues Working Group of the Genome Project, is already doing? I must say from the very beginning my answer to that has been this is a wonderful idea. This is a wonderful potential for a partnership.

The ELSI Working Group, some of whose past and present members are on this commission, has been, I think, a wonderful think tank, a way of looking in very significant detail at genetic issues. But perhaps what that group has lacked in some circumstances is a higher location in the scheme of things and having a commission whose members are appointed by the President who has the kind of visibility that this group has and will have is to my view a wonderful development and I certainly am delighted to see that it has come to pass.

And from my own personal vantage point I would like to say how grateful I am particularly to Senator Hatfield for the way in which he helped keep this idea alive and to the Administration, the President, for seeing the wisdom of this and putting together this very remarkable group of

participants.

I do want to mention there are some ELSI alumni in the room and I may have mentioned them as we go along, particularly perhaps Tom Murray and David Cox. Tom has been on the ELSI Working Group and David Cox currently is. But there is much to be done.

I am not going to talk about topics outside of genetics. You will probably be glad about that. You have enough other items on your agenda. But I am going to try to do a couple of things. One is I want to give you a brief snapshot of where the Human Genome Project is because I am not sure that is something which has been explained to everybody in this group in the last month. And if it was a month ago that you heard about it, it might now be out-of-date because that is the way this project has been moving really at quite a dizzying pace.

I want to then put a human face on that in terms of what does this mean for patients and families who are facing the prospect of illness as a consequence of genetics. Then I want to review what the ELSI Program has considered to be the major issues and I will break them down slightly differently perhaps than they have been before.

And along the way I am going to suggest from this rather humble view of the Director of the Genome Project not expecting really that you would necessarily share all

these views that there are perhaps three areas that this commission might consider becoming involved in a significant way, and I will suggest two projects which are perhaps more short-term and one which is more challenging and more long-term, and I will identify those as we go along, and hopefully we can have some discussion about them.

So that is what you are in for here and I guess I need to have the -- the slide is already on. All I have to do is push the button and maybe the lights down a little bit in the front.

(Slide.)

Just to remind you, those of you who have not been part of a government commission, I do not know if you have seen this cartoon in the New Yorker. If you cannot read the caption, there are these two folks wandering around through hell with various awful things happening in the background and one of them is saying to the other, "On the other hand it is great to be out of Washington." So imagine what you have walked into by joining this commission. Welcome to wherever it is that we are here.

(Slide.)

Now what I am going to talk about is much discussed in the media, of course. Genetics is everywhere around this. This recent issue of Time magazine focused on genetics pointing out that the future is now and you might say that

that is a bit overstated and perhaps it is a little bit. But the way that things are going it is hard to imagine where we may be in a few years considering the discoveries that are going on in genetics.

Notice, however, there is a subtext to this cover, "New breakthroughs can cure diseases and save lives, but how much should nature be engineered?"

I think it has been one of the more positive things about the Genome Project, was the incorporation of considerations about the ethical, legal and social implications along with the scientific effort, which was something that was decided at the beginning, and that is what the ELSI Program is about.

I think at this point we have made considerable progress. In your briefing books there is a five-year report on the progress of the ELSI Program which goes through a number of the research projects that have been funded and deliberations that have been carried out. I think that is well worth having a look at as a summary of this first five years of the ELSI experiment.

(Slide.)

Now the fuss about genetics relates to the fact that virtually every disease can be thought of as having some genetic component. I think until fairly recently genetics in clinical medicine was that subspecialty devoted to the study of relatively rare conditions caused by single genes

gone awry. But that is really much too narrow a view and the advances in the Genome Projects and gene discovery are making it ever more practical to identify the risks that we all carry.

It is estimated that we all have four or five genes that are seriously misspelled and perhaps another ten or twenty, or more that have variant sequences that might have been advantageous in some past environment but are not deleterious and, therefore, places us at risk for things like diabetes or hypertension, and a long list of others.

So, in fact, while virtually every disease has a genetic component one needs to be careful not to, therefore, say that all diseases are purely genetic. That is not the intention of the analysis, but rather to point out that every disease is an interaction between some environmental contribution and genetics.

Even AIDS we have learned in the last few months is in some sense predicated upon host factors that are genetically inherited. We know now that one percent roughly of the caucasian population is immune to HIV infection on the basis of a genetic inherited alteration in a cell surface protein. If you are missing that protein the virus is unable to get inside your cells. So even an environmental disease like AIDS has a genetic contribution.

The point of this slide really is to say what we are talking about when it comes to genetics is not about some

subset of the population. It is really all of us. We all have these risks. There are no perfect genetic specimens. We are hurdling towards a time where individual susceptibilities will be determinable on the basis of technologies that allow your DNA sequence to be sampled and statistical predictions to be made about your future risk of illness.

That is both an enormously exciting paradigm for preventive medicine and potentially a very worrisome situation where the fact that that information might be misused rather than used for your benefit tends to cloud the optimism about the future and I think this commission will clearly spend a good deal of time worrying about those clouds and how perhaps to take care of them.

Now the reason it is an optimistic view is that by identifying individual predispositions it should then become possible to practice the kind of preventive medicine that we could have only dreamed of in the recent past where you focus your efforts on the actual disorders that that individual is at risk for as opposed to doing sort of one size fits all preventive medicine recommending the same thing to everybody, which is currently largely what we do. Obviously we are not at that point for many diseases, but we are getting close to that for, for instance, breast cancer, ovarian cancer, colon cancer, and a number of others as I will perhaps touch on as we go along.

(Slide.)

Now if a disease has a genetic component that means that somewhere written within the DNA sequence there must be some difference in the people who are predisposed as opposed to those who are not. This is basically the justification for putting our energies into doing the Human Genome Project, is to try to uncover the genetic basis of virtually all diseases, the code for which is going to be written into the three billion base pairs of a human genome.

(Slide.)

The Human Genome Project, started in 1990, had the audacious goal of finding the entire blueprint, reading out all those three billion base pairs in a 15 year period, that is by the year 2005. And as I am about to explain to you that is actually going somewhat ahead of schedule despite the fact that the budget for this has never reached the levels that were initially thought to be necessary. So we do have a federally funded project that is ahead of schedule and under budget which astonishes many people.

(Slide.)

Now what were the goals of the Genome Project? They were actually rather simple. It is helpful to think of the project itself as sort of building infrastructure which the entire biomedical research community then has the ability to use and is using at a vigorous rate. The infrastructure

that the Genome Project is trying to produce comes in three sort of flavors. There is a genetic map part and a physical map part in the DNA sequence. Let me just quickly explain each and tell you how we are doing.

What do you need genetic maps for?

I cannot seem to focus that from up here so if somebody was sitting near there who could touch the focus button that would be very nice. If not, we can manage, I guess.

The genetic maps are collections of markers, here labeled A through G, which vary a little bit from one individual to the next. So that means that you can track their inheritance through a family. Now if that happens to be a family that has a disorder such as diabetes or schizophrenia, or a susceptibility to cancer, and you find one of these markers that tends to successfully predict who has the disorder, that tells you that the gene or genes that confer susceptibility to that disease must include at least one that is close to this marker that you are following. That is the strategy called linkage. What is linked is your piece of DNA which you possess and which you followed in this family with the disease gene that is causing the susceptibility.

Now that is a very powerful concept. It is a concept that is really only about 16 years old and when it was first put forward in 1980 I think most people thought it

would take decades, maybe a century, before you could actually apply it to human diseases. And yet that concept has allowed us to map hundreds of human conditions and to actually find the precise gene involved in more than 60 of them. Conditions where we previously had no clue of what the biological basis of a disease might be.

So these genetic markers, which in order to be useful have to be scattered over all of the human chromosomes, because you do not know when you start where the disease gene is going to be, are the first step in getting a disease gene identified.

(Slide.)

We thought, well, we would need perhaps 1,500 of these in order to have a pretty good splattering across all the chromosomes and we thought that would take us until the end of '95. And as you can see, that goal was exceeded clear back in 1993 and now in 1996 with over 10,000 of these in hand it is fair to say we really have an excellent genetic map.

There is no reason you cannot map a particular susceptibility if you have collected the families and you have this set of markers which are all easily and freely available because they are basically available over the Internet. The kinds of markers that are being currently supplied do not require you to mail around clones to each other, which is a wonderful assistance in getting things

done.

(Slide.)

Now once you have identified a region say between marker C and D where your gene is, you then want to sift through that DNA which may still be a few million base pairs to try to find the gene that is actually responsible. For that you need a physical map and ideally you would like that map to be annotated with the locations of specific genes. That is also coming along very well. Without going into great detail I will show you an illegible slide which means that it is going really well because the more data you have the harder it is to read the slides.

(Slide.)

This is the long arm of chromosome 14. Each one of these little horizontal bars here is a yeast artificial chromosome which is a cloned fragment of human DNA which has been isolated and is being propagated in a fashion to allow you to study it in pure form. The point of the slide is to say there is a lot of those and they are all arranged in order and we know there are overlaps. In fact, 96 percent of the human genome now exists in well validated physical maps thanks to the efforts of various genome centers, particularly the one at Whitehead Institute of MIT. Major efforts also in physical maps have been carried out by other groups including David Cox's group at Stanford.

(Slide.)

The hardest part is the sequence. Three billion base pairs no matter how you cut it is a lot of DNA. If we tried to start doing this back in 1990 we would really, I think, have been making a mistake because the technology was not up to it and you really need the maps before you can attempt to accomplish sequence in a rational fashion.

(Slide.)

That, in fact, has also been coming along quite well, although most of the sequencing that has been done up until about now has been on model organisms. And these five, in particular the so-called Security Council of the Genome Project, have been particularly focused on. And some of them have made substantial progress.

Yeast, for instance, had its genome completely sequenced by last April. A eukaryote that has a nucleus and goes through the cell cycle and does a lot of things that human beings do in their cells, and this is an enormously valuable storehouse of information. C. elegans, a more complicated organism in the round worm will have its sequence done by the end of next year. And drosophila probably a year or two after that.

The mouse, we have never actually said we are going to do the sequence of because it depends on whether the price comes down and we can afford to for the budget that is available. But obviously many people would love to see

that done because the comparison with human sequences will be enormously valuable in telling us what the human sequence is all about.

(Slide.)

Now in order to achieve this kind of sequencing throughput that we are now anticipating, that is to get the human done, technology really has to be pushed. The human sequence of three billion base pairs was initiated in some earnest here last spring by the funding of six genome centers around the country, again one of them is the Cox and Meyers Center in Stanford, which in the aggregate should produce about 100 million base pairs of sequence by the end of next year largely using instruments like this one, which is a promotionally available automated sequencer.

But I think the real future of DNA sequencing is likely to be in advances in the technology that allow you to go from an instrument like this, which while very elegant and very efficient by the standards compared to say five years ago, is not the ultimate answer.

(Slide.)

And perhaps we can look forward to instruments like this one which is an experimental apparatus built by David Burke at the University of Michigan where all of the components of a sequencing machine in terms of doing the reactions and running the electrophoresis have been put

onto a silicon chip borrowing technology from the computer industry which has been so successful in making integrated circuits.

The idea of scaling everything down is enormously appealing because it cuts down on volumes and allows you to automate steps that currently you cannot. I think that is where sequencing is going in the long term. You should think of DNA sequencing -- and this is relevant to this group, this is not just a "techy" statement, this is really a medical statement -- sequencing is having almost unlimited potential for increasing the throughput and decreasing the cost so that the notion of being able to collect very large quantities of information about an individual's DNA in the coming decade or so is really not a notion that is science fiction. It is quite conceivable that that will be possible in a medical setting. How will we be sure that that is used to benefit patients rather than to injure them?

(Slide.)

So just to summarize the report card part of this here, the Genome Project is, I think, going extremely well as far as achieving these goals. The genetic maps are essentially done. The physical maps are very close to done. DNA sequencing has just become to ramp up in earnest, but when one goes through the estimations of where we will be two or three years from now or six or seven

years from now it is hard to find people who are not pretty confident that the sequence will, in fact, be completed by the year 2005.

I should have said at the beginning this is not just the National Center for Human Genome Research, this is the Department of Energy here in the U.S. which is a cosponsor of the Genome Project, and also the rest of the world with significant contributions in the Genome Project coming from the United Kingdom, from Germany, from France and from Japan.

PROF. CAPRON: Before you change the slide, Francis, what is the significance of the mathematical statement that it makes that we are going to get beyond 100 percent?

DR. COLLINS: For these two --

PROF. CAPRON: Yes. These little rocket ships there.

DR. COLLINS: Yes. Maps can be defined sort of by what density of mile markers do you want on the map. And those were very carefully defined by the originators of the project and then redefined in 1993. But once you have an acceptable map and a 100 percent map you can still make it denser.

So even though we exceeded the goals for genetic markers back in 1993 we keep adding more markers to the map because more is still better than what we have. But as far as saying what was the minimum that we had to achieve for that goal to basically not hold up the rest of it, that

would be accomplished. Physical maps can still get denser, too.

The sequence at some level when you have got it, you have got it at least for a reference sequence, and obviously that raises the question but what about all the variability which is what makes human biology interesting. And that is, in effect, sort of the next stage. That is genome phase II of whatever you want to call it where you take that reference sequence and really begin to take apart what are the things that are responsible for differences between individuals.

Obviously that is already happening. Once you have identified a gene that you think may be interesting in a disease the first thing you do is to sequence that in large numbers of affecteds and unaffecteds to see what the variability is.

To look at variability on the whole genome scale is not unimaginable. I think many of us look forward once we have that first reference sequence to say, well, that was good practice, now let's go on and do another few hundred carefully chosen DNA samples and see what we can learn about variability and population relatedness.

Remember 99.9 percent roughly of our DNA is all the same. So having that reference sequence tells you an awful lot about the normal human biology. But it does not tell you a thing about that .1 percent of very interesting stuff

that accounts for the fact that we are all quite different. That will be obviously an interesting topic under its own.

(Slide.)

So the flow of molecular medicine and the consequences of this are obviously all around us and it will be, I think, both stimulating and bedeviling. This commission can be conceived of as this kind of flow chart. You want to understand a disease these days, you would like to identify the genes that contribute to susceptibility to that disease, and that involves first mapping and then cloning. And the Genome Project has telescoped that time interval which used to be ten years down to a year or two and, as things go on and the sequence gets completed, to a month or two. So clearly this kind of thing is going to be happening in great perfusion and already is for large numbers of diseases.

But then what? It is a research activity essentially until you get to that point, but what are the consequences for the public? How does it spill out into the practice of clinical medicine?

Well, it spills first over here into diagnostics because having found a gene, you have found alterations in that gene that occur in people who have a disease and not in people who do not. That is part of the process of proving you have got the right thing. And that means, like it or not, you have in your hands the potential of offering

a diagnostic test to individuals to predict who is at risk or whose children are at risk and that obviously has potential benefits in situations where effective interventions are available, say colon cancer where knowing you are at high risk might allow you to have a colonoscopy beginning at age 35 instead of waiting until much later and finding out that you have got a polyp which can be removed easily without eventuating into a metastatic colon cancer years down the road. That is a very appealing concept.

But not all of the diagnostics allow you an effective preventive medicine strategy. Alzheimer's disease is the sort of classic example. We know now how to make predictions about individual risk for Alzheimer's disease. It is not perfect, but it certainly has scientific validity. But is it clinically useful? Is it the kind of information that people want given that the diagnostics do not suggest a way of reducing your risk? It only provides you with information about which you cannot do very much.

Now let's not forget, however, during all these discussions and during all of the concerns that we have about dealing with this arm of the diagram that also down here there is the enormous potential to see these gene discoveries become ever more therapeutically useful, but however time is over here and you are going to have to deal with this interval, this window, in between good diagnostic capability and not so great therapeutic capability for a

lot of diseases. There is nothing we can do about that. You cannot speed this up other than stimulating research even more than is currently being done. You cannot just skip over this step and pretend it is not there. It is going to be haunting us for many conditions.

I think that diagram actually sort of is a useful way to see how we got into the pickle that we are in for a number of conditions because of this discrepancy between diagnostic brilliance and therapeutic brilliance.

(Slide.)

Well, let's put a human face on all of this infrastructure and basic science. This is a very powerful magazine cover from Newsweek a couple of years ago before this gene was found. It now has been. But look at this three generation pedigree and then read the caption. This woman has had breast cancer, her daughter at the age of 29 has undergone a prophylactic bilateral mastectomy because of her concerns about her very high risk of developing breast cancer as a consequence of having inherited an alteration in the gene called BRCA-1. The cover is asking the question, "Will we have better things to offer the next generation?"

BRCA-1 is a very interesting paradigm because it raises many of the issues that this commission will probably be struggling with all the way from patenting to privacy issues, to concerns about informed consent for

participants in research protocols, or even for participants in a possible testing situation who need to have information about benefits and risks before the test is done, and certainly should not have the test done on them without their consent. Almost all of the concerns that one has can be perhaps thought of in this particular situation.

(Slide.)

I will just quickly tell you about a woman recently seen here at the NIH as part of a research protocol studying BRCA-1 because I think it does sort of make the case. Here is a woman over here marked with the arrow who came in not because she is ill. She is perfectly fine. She is a federal employee, aged 40, about ready to leave the government and start her own consulting business. But came in because she got a phone call from her cousin over here who she had not seen in some years and the cousin said, "I want you to know that I have breast cancer, my mother died of ovarian cancer."

She had not even realized that. This is not a close knit family. And she said, "I have been involved in a research protocol that those people at the NIH are carrying out and as part of that research protocol they have discovered that I have an alteration in this gene called BRCA-1 and so I am concerned that other family members might be at risk which is why I am calling you up and maybe

you would like to contact those folks and hear what this means."

Now imagine what kind of a phone call that was for this individual to receive not having really realized that there was much of a family history of cancer and then learning not only there was a family history of cancer, but there might be a very specific way of finding out her own risk.

Now the geneticists in the room will have figured out that her risk of having the BRCA-1 mutation is 25 percent based on this pedigree. But obviously with a known mutation in this woman, which was also identified in stored tissue samples on this woman, another issue that I want to come back to, it is possible to take a DNA sample from that person and look very quickly and precisely to see whether that same misspelling exists in her. And that would tell her whether her risk is the same as everybody else if the test is negative or very high, although we do not know exactly how high for both breast and ovarian cancer, but probably substantially elevated, perhaps as much as 85 percent.

What did she decide to do? Well, she was actually very interested in knowing the information. She was troubled by the fact that we could not tell her what interventions would be ideally carried out by someone in her circumstance if she were found to have this mutation

because we do not know whether mammograms started at an earlier than usual age, in this case age 40, and done very faithfully would definitely reduce her risk of dying of metastatic breast cancer.

We would like to think that is the case but we do not know that for this highly specific genetic risk population. We do not know what the value of interventions of a more drastic sort like mastectomy or ovariectomy might be. We think that those should reduce risk, but there are troubling anecdotes of women who went through those procedures and still developed cancer.

So she was bothered by that. But she said, "You know, I guess all things considered I would still like to know my situation because it probably would influence the kind of care that I would get."

However, she eventually decided not to be tested and the reason was, as I mentioned, her intent to go out of the federal employment and to get her own consulting position which means she would have to get her own health insurance. And after hearing our explanations of the lack of certainty that she could count on being able to get adequate insurance without paying exorbitant premiums she decided this just was not a good equation and she declined to be tested.

So here we have a situation where there is complicated benefits and risks, but the decision was based largely on a

discrimination possibility rather than on the sort of personal medical benefits and risks that one would like to think somebody could decide based upon. This is not an unusual situation. This is a significant cause of people deciding that they do not want the information. There are other causes of course.

(Slide.)

Well, that leads me into talking about the ELSI program and perhaps suggesting some areas where I believe this commission could make a very important impact. The ELSI program at NCHGR is often sort of confused so let me just take a minute to explain that it is not one thing. It is really now four things. It used to be two things and we have added a couple in the last couple of years and maybe it is helpful to try to explain this.

It is a research program on which we spend five percent of our budget and DOE spends three percent of their's. This has funded a large number of investigators all over the country studying everything from philosophical implications to legal concerns, to actual clinical studies to try to see what genetic testing leads to for cystic fibrosis or for cancer. So that is a very significant investment. The largest investment ever in ethical research coming out of this research program of the ELSI portfolio and there are several grantees in the room.

The ELSI Working Group, which was started back in

1989, is a deliberative body composed of experts from a wide variety of points of view, from science to law, to ethics, to sort of social science and policy, who have been charged with trying to take the issues, wrestle with them and come up with policy options that might be considered by decision makers. And I will come back to the ELSI Working Group a couple of times and again Tom Murray is a former member and David Cox is a member. So this commission is nicely connected with that deliberative body which has been meeting now for about six years and met most recently yesterday.

The Office of Policy Coordination is a relatively new arrival on the scene. This is located within the Director's office at NCHGR. Kathy Hudson, who is sitting in the back row, is the Director of this office. This office tries to interact productively and effectively with a whole host of individuals who come to us seeking information about the Genome Project and its policy implications. Some of them being legislators. I think that has been a very helpful rapid response situation when something is about to happen on Capitol Hill or somewhere in this town and also to help us think through where we should be going.

The most recent addition is an Intramural Office of Genome Ethics, which has been directed in an acting capacity by Ron Green, an ethicist that many of you know

from Dartmouth who has been on loan to us for the last six months, and has been working with the intramural scientists, most of whom are over here in Building 49, who are on the cutting edge of genetic research trying to help them wrestle with some of the consequences of their own personal research interests. That has been a very interesting addition to this. So the ELSI Program is all four of these things.

(Slide.)

Now ELSI priorities can be divided in various ways. You have in your briefing book the five year review of the ELSI program which breaks it down into four categories. I am going to break it down into five because I want to make a particular point here today. So I have split out one of them into two different ones and do not be alarmed if they do not seem to be a perfect one on one match. We are still talking about the same issues here.

I want to briefly go through each one of these and sort of say what progress has been made and also what serious challenges still remain, and there are plenty of challenges here, believe me.

But first these priorities and you could certainly say there are things left off here and there are, and we will probably want to add others as we go along. But in the first six years of the ELSI Program these have been the major areas of interest. And I will maybe go through them

one at a time.

(Slide.)

I should also point out that in the back of your briefing book is this document or the abstract of it from the Institute of Medicine's study called "Assessing genetic risks," which was funded by the ELSI Program, which is I think a very good starting point for almost any discussion in the policy consequences and the societal consequences of genetic research. And many of the points that are made there are the right points and the ones which need to be deliberated about.

That group met for a period of almost two-and-a-half years and produced this document, but then of course as happens with IOM studies they went out of business and many of the recommendations and suggestions they made still are remaining to be followed up on. This, I think, would be a very useful starting point for many of the discussions of this group.

(Slide.)

Now let me highlight a little bit about what is going on in specific areas beginning with clinical integration of new technologies. This is the whole question of who decides when a test is ready to leave research and move into clinical medicine and how do you make sure that the laboratories that are doing this are maintaining adequate quality control? This is a topic which is really quite

complex and is hard to get your mind completely around.

As part of this effort we have been funding research projects to look at CF carrier testing, to look at cancer susceptibility testing, and I think we have learned a lot through those research projects.

(Slide.)

But I think the most important sort of policy efforts in clinical integration of test is the Task Force on Genetic Testing which was spun off of the ELSI Working Group. So this is a subgroup of the ELSI Working Group. It is chaired by Tony Holtzman of Johns Hopkins University. And it has these objectives and it has a clear mission statement. It has been meeting now for a year-and-a-half and expects to be completed with its work by next spring.

Its objectives were to review the state-of-the-art of genetic testing, to examine current policies and practices, and if necessary, and it looks like it is going to be necessary, recommend changes or policy options that will assure protection of the public. This task force has membership from a broad group of potential stakeholders in this, including companies, health care providers, geneticists, health care insurers, consumers and a list of government agencies that have potential authorities in this area, including AHCPR, CDC, FDA, HCFA and HRSA.

(Slide.)

This group I would say has developed a very vigorous

effort and has good chemistry between all of these folks who might not necessarily be on the same side of the issue, and have come forward already last March with a document, which is not in your briefing books but which certainly we could provide to the members of the commission if you would like to look through it because I think it is in many ways relevant to the possible topics you might take up.

This set of interim principles was put together by this group and endorsed by all of them unanimously and basically aims to set out what should be achieved or achievable in the field of clinical applications of genetics testing. It is a document that I think is full of thoughtful points and some very specific principles, but it does not seek in this iteration to suggest how those principles might be implemented, although I think in some instances the principles are themselves sort of action statements that imply a certain implementation.

The task force is now wrestling with the implementation part of this and expects to put out its draft principles in that regard by the end of this year. They will be published in the Federal Register as will these and comments will be received. The final version of this task force's output should be coming out in about March.

I would think that it would be very useful for the commission to stay abreast of what is coming out of this

because the big question here, and it is not going to be an easy question to answer, is who decides when a test is ready to leave research and move into more general medical practice. That debate is raging right now for BRCA-1, for instance. You may have seen earlier this week in the newspapers the publication of a study that suggests that one in fifty Ashkenazi Jewish men and women are carrying a BRCA-1 or BRCA-2 mutation that may place them at very high risk for developing breast cancer, the women that is, and ovarian cancer as well.

(Slide.)

So is it appropriate to begin to market that kind of testing specifically to Jewish individuals? Such marketing is happening whether you think it is appropriate or not. This is clipped from the Washington Jewish Weekly and such advertisements have appeared in multiple other newspapers around the country basically offering analysis for a particular mutation in BRCA-1 by a company in the Washington area.

Is that something which the public as a whole has a stake in weighing in on, whether this is a good thing or not? Or is it the case that this kind of testing is already appropriately enough overseen by professional practice guidelines and no special regulatory interventions are necessary? Those are the kinds of things the task force is wrestling with.

By the way the FDA has authority to regulate genetic testing of this sort, but it has chosen not to exercise it thus far. These tests are done in-house by laboratories. If they were kits that were being sent out to other laboratories then they would be regulated by the FDA. But because they are home brews done inside a particular highly specialized laboratory they are at the present time not subject to FDA oversight. The laboratories are inspected through CLIA regulations, but those inspections are largely on sort of good record keeping and not necessarily on the specifics of DNA testing about which the inspectors have relatively little experience.

(Slide.)

So one of the very important things to watch is to sort of see what does the task force say about the oversight of the introduction of a test such as BRCA-1 into clinical practice. A very critical issue because if we do this wrong, if we get too many horror stories of people who are tested without even knowing it and then had information dumped in their laps that they were unprepared to deal with and wished they did not have, the public will quickly get disillusioned with this new brand of genetics and decide they do not want anything to do with it. And it might take us decades to recover from that. That would be truly unfortunate.

Even though I stand up in many settings and say we

have to be really thoughtful about this and cautious about how genetics get introduced into practice, I believe and I think almost anybody working in the field of medical genetics believes that this is an advance, a set of advances that have enormous promise to benefit people, to alleviate suffering, to eliminate unnecessary deaths, and to have that sort of stillborn because of a too rapid introduction in too thoughtless a way of a new technology would be truly sad.

(Slide.)

So this is sort of one of the ELSI priorities and again I think the most appropriate tact perhaps for the commission is to stay very tightly abreast of this. And David Cox, he is not only a member of the ELSI Working Group, he is a member of this task force and will be in a position to keep you well informed about what is going on. And it may well be that some weighing in by the commission now or later will turn out to be very useful.

(Slide.)

A second topic which everybody agrees is important and almost nobody seems to know how we are going to do is it health professional and public education about genetics. I have just made this strong statement about the value of this information for advancing medicine, but it will only do so if the health care providers and the people listening to the information are prepared to receive it. Let's be

honest we are not there yet.

(Slide.)

This is many people's idea of gene therapy here.

(Laughter.)

You can buy this stuff in the health food store for a rather exorbitant price and pop your tablets of RNA and DNA. It does not even say on the label what organism this is. I hesitate to speculate. But if that is, in fact, a hot seller item in the health food store it means we have got a bit of a problem here. It is not just the general public that I think has not received much information, most physicians have had no exposure to genetics as part of their formal training and are, therefore, going to be in a tough spot when a patient is sitting across from them asking what does this particular genetic test result mean.

(Slide.)

We have recently helped to catalyze, although we are not running, the National Coalition for Health Professional Education in Genetics, which is an attempt to bring together specialty and general practice organizations that represent health care providers, not just physicians, but also nurses, social workers, a broad range of health care providers, to work together to develop materials to educate their members about genetics as quickly as possible, and perhaps to try to influence board exams and license exams as well to make genetics more significant in that kind of

evaluation than it currently is.

(Slide.)

The ethical conduct of genetics research. Obviously very central in the charter that this commission has received and let me just make a couple of comments. I think the current regulations, which you are all familiar with, perhaps do a pretty good job of protecting against harms, but emphasize physical harms certainly more so than the psychosocial harms which can come about as a consequence of genetic research projects that involve testing and prediction of future risk.

The other consequence that is perhaps not as well attended to as it might be is the fact that a genetic analysis reaches a conclusion with implications that are broader than just that individual but also for their family, and how do you balance those things.

I want to highlight, however, and this is sort of my first suggestion of a specific project, an area within this ethical conduct which I think is ripe for a group such as this to deliberate about and to produce a set of consensus guidelines. That is the appropriate oversight of a use of archive tissue samples for DNA testing. This is a very significant topic. There are hundreds of thousands of tissue samples, most of them are sitting in paraffin blocks in hospital pathology laboratories that have been collected over decades and which are a gold mine of useful

information when it comes to research projects that would like to understand those diseases better.

There are tens of thousands of DNA samples that have been collected on individuals enrolled in prospective studies like N-HANES, for instance, to try to understand what risk factors contribute to what disease and DNA samples are available but consent has not necessarily been obtained in the way that you would hope for to allow a broad testing of those. So what are the restrictions on carrying out such testing?

We have a real issue here between what might be best for the public and society as far as allowing research that is going to give very important answers to go forward in as unfettered a way as possible and at the same time the likelihood that somebody will have something determined about them and that information find its way back to them that they did not consent for and wish subsequently that had not been obtained.

I have heard at least one horror story of a pathologist in a major eastern city who was looking for the presence of mutations in the BRCA-1 gene in tumors that had been taken from patients over the preceding five or ten years. And what he thought he was looking for were mutations in that gene that were somatic, that is were acquired during life. Well, he found one, but then when he looked in the normal tissue adjacent to the tumor the

mutation was there, too. So this was not a somatic mutation. It was an inherited mutation.

This pathologist with good intent felt that he then needed to warn that individual of her risk of getting a future breast cancer because individuals in this situation are at risk for bilateral disease and also the risk of ovarian cancer. So he contacted her and gave her this information.

Now imagine her puzzlement and dismay at getting this sort of unexpected phone call about a situation which she thought was over having been operated on for breast cancer four or five years earlier and being apparently cured of her disease.

She was unable based on the information he gave her over the telephone to really quite figure out what this meant and sought advice from her own physician who was similarly confused about what this meant. This woman subsequently attempted suicide. That kind of situation I think brings into sort of stark belief the possibilities here of damage being done by completely unrestricted testing of archive samples of this sort.

(Slide.)

Now there have been a number of groups that have looked at this area. Certainly this is not one that needs to be started from scratch. In fact, as of yesterday I counted five different statements that have been made on

informed consent in genetic analyses of archived tissue samples.

There is one in your briefing book, the first one, which was the result of about a year-and-a-half of deliberations of a group that was convened by NIH and CDC. Ellen Wright-Clayton is the first author on that article and I think it is a thoughtful analysis. An independent group from the American College of Medical Genetics produced a statement which is also published. The American Society of Human Genetics has recently published a statement as well. The ELSI Working Group has a draft statement which we discussed yesterday at their meeting. And very recently in the last week the College of American Pathologists, but actually in concert with fifteen other pathology organizations, has put together their statement about this which differs in some significant ways from the other four. Although I would say there is more in common than there is in difference between these five statements.

The problem is what happens now? We have got five different points of view. Clearly this is an issue of, I think, fairly significant urgency in my view. But again I hesitate to be too strong about this. In my view this would be a very appropriate topic for this commission to take up early.

It is a topic which I think could in a matter of a few months be reduced to some consensus view and you could make

recommendations perhaps to OPRR about how to move this forward. This is clearly a topic that affects more than one agency. It crosses a lot of boundaries and is well within the mandate that the commission was given in its charter. So that is sort of suggestion number one.

(Slide.)

Moving along here, the fair use of genetic information is obviously a topic very much on the public's mind. This is one where I think the complexities of this are considerable, but perhaps also there is a very strong moral basis for taking a particular point of view. The strong moral basis in my sort of nonethicist view goes like this: You did not get to pick your DNA. I did not get to pick mine. Policies that allow that information to be used to discriminate against you are unjust and we should not all them. That is the strongest statement.

So this is a civil rights issue essentially. I do not think it is extreme to use that kind of terminology. Genetic information about you should not be used to deny you basic things like health care or a job. In fact, those are the two areas where I think the greatest interest has been devoted and rightfully so.

(Slide.)

Now why is genetic information so special? That is often a question that people ask. Well, yes, that is fine, but what is special about this as compared to other medical

or personal information? I have been assembling a list. Karen Rothenberg is responsible for most of these. A growing list of words that begin with "p" that sort of remind us of what is special about genetic information. It is "personal." It is about you.

It is "predictive." A very significant part of this, I think the greatest concerns often arise not when you are talking about somebody who already has an illness and you are trying to make the diagnosis, but when somebody is entirely well and you are predicting something about their future. The potential for mischief there is considerable.

It is "powerful" in that way that it may be able to make predictions about your future.

It is "private" or it should be. At the moment it is not.

It is "pedigree" sensitive. That is a little bit of a push there trying to turn the fact that it is familial into a word that begins with "p" but that is what I am saying here. That information about the "person" also may reveal information about their relatives.

It is "permanent." It is not going to change, which is one of the reasons you better not make a mistake when you analyze it.

And it is "potentially prejudicial." It may be, in fact, used in ways to prejudice people against you.

No single one of those characteristics about genetic

information would distinguish it from other kinds of medical information. But taken together I think they justify considering this in a very special way.

(Slide.)

Now the public is worried about this as I said a minute ago. A much quoted Harris poll from last year, 86 percent of people asked said they were worried about health and life insurance companies or employers using genetic information against them. A rather significant figure to say the least.

(Slide.)

Now going to health insurance. The first major effort in this regard by the ELSI Working Group culminated in this particular document and the chair of the group that put this together is none other than Tom Murray who is now on this commission. This document called, "Genetic Information and Health Insurance," put forward a set of recommendations which basically underlined the notion that genetic information should not be used to deny coverage or to set exorbitant premiums or to in other ways discriminate against people in the health insurance arena arguing that health -- the access to health care is not a privilege, but a right.

(Slide.)

Subsequent to that about a year ago a coalition effort between the ELSI Working Group and the National Action Plan

on Breast Cancer met and put together a set of recommendations which were published in Science magazine on the 20th of October, 1995. This is in your briefing book.

(Slide.)

That particular piece of work, which was the sort of policy recommendations of this collection of the ELSI Working Group and a very vigorous group of consumer activists in the breast cancer community included the following:

Insurance providers should be prohibited from using genetic information to limit any coverage or establish eligibility, continuation, enrollment or contribution requirements. Every word was carefully chosen here.

(Slide.)

Affordability: Insurance providers should be prohibited from establishing differential rates or premium payments based on genetic information.

(Slide.)

And privacy: Insurance providers should be prohibited from requesting or requiring collection of genetic information and they should be prohibited from releasing it without prior written authorization of the individual.

There are other recommendations, but I highlight these there in particular.

Now it has been a very interesting year in the federal legislative process because in the last year after very

little activity in the area of genetic discrimination at all a series of bills were introduced.

(Slide.)

And one of them, the Health Insurance Reportability and Accountability Act, often known as the Kasselbaum-Kennedy Act, was passed and signed by the President just about six weeks ago.

These other bills which focus more specifically on genetics and many of which cover more than discrimination and also cover privacy received, I think, some attention and some good discussion, but did not succeed in generating something that would actually be approved by even one House and one will have to wait and see what happens in the subsequent Congress.

Let me just say this bill, which is the Kasselbaum-Kennedy Bill, does specifically mention genetic information as one of the things that a health insurer must not use in discriminating against individuals, that is must not use to deny them coverage. But what it does not say is anything very comforting about what can be done about setting premiums.

So while this bill was a good step, I would say a very significant step because it sets a precedent that genetics ought not to be used in discriminatory ways, it does not close the door on that in health insurance in the way that one might like. The recommendations, therefore, that I

showed you a minute ago have only been met in sort of one out of three.

So here comes the sort of second suggestion. I think it would be very appropriate and helpful for the NBAC to consider this issue and to look at the recommendations which the ELSI Working Group and the Action Plan on Breast Cancer put together, and if you see fit even to endorse them as a way of perhaps moving this process along and perhaps reminding the public and the Congress that this issue has not been resolved to anything except sort of a very incremental step in anticipation, one hopes, of being able to do better the next time around.

(Slide.)

So this cartoon reminds us that we have not solved this problem. The quote is, "Apparently I am genetically disposed to pay very high premiums." That is still true if you happen to have a genetic predisposition.

(Slide.)

Now employment I am not going to say much about because that is the subject of today's meeting. Wendy, maybe you could focus this one slightly better for us here. The quote here is, "Very nice resume. Leave a sample of your DNA with my secretary." It is very nice to get cartoons from the New Yorker. I recommend it to commissioners. If you want to be giving public talks on this issue that is a good source of material.

(Slide.)

Let me, however, spend the rest of the time talking about privacy because here is my third topic that I would like to perhaps urge some significant effort by this commission. A very thorny one and a difficult one, but one where I think the potential is ripe for a serious effort to try to take care of what is currently a large problem.

First of all, let me say that even if we are so lucky as to solve the discrimination issues in health insurance and employment, the ones that I think are most on people's mind, that will really not take care of the misuses of genetic information.

It is helpful to sort of think of this building as having two pillars and one is to try to do something about discrimination and the other is to do something to protect privacy. For instance, even if those two issues of insurance discrimination and employment were taken care of, and you find out that you are at risk for colon cancer, do you really want everybody else to have access to that information? Do you really believe that there will not be ways covertly for such discrimination to go on in employment or in health insurance if the information is available?

What about other settings, education, the armed services? Adoption agencies, will they decide you are not a good candidate because they learn you have genetic risks.

In this particular season I have to say about what about running for election? Will everybody who is running for election have their genetic risks divulged? Will there be any protection against that? Who will want to run for office if that happens?

So it is not enough to do something about discrimination in the areas of greatest concern. You really have to side-by-side do something about privacy. We have not, I am afraid, got a lot to show for the concerns about that, although they have been around for a while.

(Slide.)

They have been around, in fact, since about the time of this quote which says -- I will not read it for you, I will just read the last part of it here, "Recent inventions in business methods call attention to the next step which must be taken for the protection of the person, the right to be left alone." Essentially one of the first statements of what a privacy right might be. This is from 1890. The writers are Samuel Warren and Louis Brandeis in the Harvard Law Review.

And this kind of thinking then led to some efforts in privacy which were particularly vigorous, in fact, in the early 1970's in the wake of Watergate. With the anticipated power of new computer technologies Washington got much more focused on this issue and there was a committee --

(Slide.)

-- advisory to the Secretary of HEW, as that department was called at that point, which looked at automated data systems. And as a consequence of that the Federal Privacy Act of 1974 came out which had some good things in it and a commission was set up to look at privacy protection which President Carter was very interested in. That commission made 172 recommendations, none of which were implemented because administrations changed and this interest rather faded.

I think it is fair to say there has not been a lot of progress in the area of privacy at least as it regards medical information, which is my major topic with you today. There have been a few bills that have been passed about privacy. I will not go into them here. I probably could not. You can see what they are. And you might think that something good has happened if you read a statement such as this:

(Slide.)

This comes from one of those bills. "A provider may disclose personally identifiable information concerning any consumer only --" it says, "-- to the consumer, to any person with the informed written consent of the consumer --" that sounds good, "-- to a law enforcement agency pursuant to a warrant --" well, yes, "-- or pursuant to a Court order." And there are even penalties provided here

liable to the aggrieved person if you do this without permission. So that sounds pretty good.

(Slide.)

What do you think they are writing about here? Video records. See this is the response to the attempt to find out what videos Judge Bork was watching. This is certainly an important issue but it is sort of ironic that this much attention was paid to that and nothing similar was done about medical information.

Now is that a concern? I recently was shown a study which is not yet published of Fortune 500 companies. In that study 35 percent of those companies said they use medical records in making employment related decisions. 35 percent of Fortune 500 companies. That is a significant concern.

(Slide.)

A Harris poll in 1993. People, in fact, believe that. 25 percent of the people they talked to believe that their own medical information had been improperly disclosed and, in fact, 34 percent of health care professionals said, "Well, yes, they are right." So these are not 25 percent of the world that is paranoid. They may be the ones that are paying attention.

(Laughter.)

So it is certainly the case that there is a problem. I think it is fair to say there has not been meaningful

federal legislation enacted on this topic in about the last 22 years.

(Slide.)

Now there has been an effort, however, in the recent year or two, or three to deal with this issue. In the current Congress there were three bills that were particularly focused on privacy as well as some of the genetic discrimination bills that I showed you earlier which had privacy provisions.

The ones that were most heavily discussed this year include the Bennett Bill, which went through several drafts and was felt by many people to have a lot of the right features. The McDermott Bill in the House also much discussed with lots of interest in it. And the Condit Bill, which has come back now a couple of years, the Fair Health Information Practices Act.

They have different approaches to the problem and I think it is fair to say that perhaps none of them received broad support from all possible stakeholders. But the sad thing is that not much headway was made in getting these actually taken really seriously by the leadership in that none of them received the blessing to reach the likelihood of actually being discussed and potentially passed.

So there is plenty of opportunity here. Now I might say some of these bills, and I will not name names, have been more effective than others in trying to protect

research at the same time they are protecting privacy. There is a real issue here. If you write a sloppy privacy bill you could destroy medical research in one stroke.

If you simply decided that no use of any tissue samples of any sort, I mean under any circumstances, could be done without going back and getting informed consent from individuals who may have given those samples five or ten years earlier, if you decide that is the case and that there is no such thing as anonymizing samples, you could destroy the field of research pathology for instance. Thought needs to be given to that.

(Slide.)

So what could NBAC do about this? Just a few points here. Genetic, and I am going to say genetics/health information because I do not see how you can separate out the genetic part of the medical record from the rest of it. It might be politically easier to get something done if we could do it that way, but I do not think that is viable.

I cannot imagine a record keeping system that is able to keep these things apart because they are changing every day anyway and things that we thought were not genetic all of a sudden are becoming so. Look at APO/EPO testing which we used to do for cardiovascular disease and now, oh, my goodness, it is a risk factor for Alzheimer's.

So genetic health information is sensitive and it can be used and is being used to stigmatize, discriminate and

arm individuals. New genetic technologies will increase the amount of information that may be determined in dizzying ways. New computer technologies will increase the ability to collect that and transform it ever more easily. It is currently already accessible to many who have no need for the information and often without individual consent.

(Slide.)

Individuals will be deterred from participating in research as a consequence of this and that is already happening because of fear the information will be accessed by others who should not see it. There is little federal protection for this kind of information and state protections which I did not get into are quite nonuniform and certainly inadequate. So I would like to make the case that this is a high priority issue. There is a critical need right now to define and enforce conditions for access to and use of genetic health information. I will not be so bold as to suggest exactly how that should be done, but it certainly seems as if this is an issue whose time has come.

(Slide.)

This is a group that has the expertise and the drive and the position in the scheme of things to perhaps make a very significant impact on this. I, for one, would love to see that taken up and would volunteer that the National Center for Human Genome Research would do everything we could to work with you to pursue that agenda.

So, to summarize, if I could have the lights up, basically I welcome the chance to come and go through these suggestions. I know you have many other things on your table. I guess, I think of this group, who by the way, I guess, celebrated their first anniversary of existing simultaneously with starting to exist because the President announced his Executive Order on October 3rd, 1995. So one year ago and now here you are initiating your efforts.

I would think it would optimum, therefore, to take on a couple of things that have fairly short time lines where products could be reasonably expected to come forward, but not to shy also to wrestle with a tougher, higher risk, longer term effort. Just as when you are starting out a research laboratory, you know, you do not want to put all of your eggs in one research project. I suppose that applies to commissions as well.

So I appreciate your attention in this description of what ELSI is all about and the Genome Project. I would be happy for some discussion. Thank you very much.

DR. SHAPIRO: Francis, thank you very much. Would you like to join us here or do you prefer too --

DR. COLLINS: I will come down there.

DR. SHAPIRO: Alex?

PROF. CAPRON: I am curious, Francis, on the issue of the archived tissue samples. Your eagerness to see that issue from ELSI, which has been working on it and has not

yet finished its work, to us, that has two sides. One your own disabilities to play the consensus role. I wonder whether those are part of the terrain or peculiar to ELSI. And, two, what special capabilities you think we would bring to the topic?

DR. COLLINS: Yes. I think that is maybe a specific example of a general issue. What kinds of issues are particularly appropriate for ELSI Working Group to hand off to the commission. I think this is a good example because it does have implications that are pretty broad. If the ELSI Working Group comes forward with a statement about what they think the synthesis should be of all of these circumstances, is anybody really going to alter their behavior as a consequence of that or will that be one more statement out of what are now five statements on this topic?

There is some significant disagreement on some parts of this and I think one of the great advantages of a commission such as this is your broader representation, your more authoritative position in the scheme of things, and I think that is the major reason to ask this commission to take it on.

As I say, it seems like an ideal circumstance where a lot of the state work has been done, but the synthesis needs to be occur in a way that once it is synthesized people will pay attention.

DR. SHAPIRO: Eric?

DR. CASSELL: Well, I want to pick up on the privacy issue because I think most people do not realize that the ordinary medical record that sits in their doctor's office has no privacy or confidentiality whatsoever anymore and there are two consequences of that. One is that people's privacy is broken and the second is that the record has no value. That really is kept in the head of the practitioner, most of us lie constantly in order to protect people and that is inherently failed. That is on the one hand.

On the other hand the issue is so difficult a resolution that it is hard to see a commission getting into something that there is almost no way to get back out of. Even -- just to give one specific example, even HIV information in the State of New York, which is protected by criminal law, except for third party payers, insurers, and so forth so that you cannot tell the wife, but you can tell the insurance company.

DR. SHAPIRO: Alta?

PROF. CHARO: Just by way of warning, I do not want this to come out sounding disrespectful in any way. But I am really constantly frustrated by the shifting grounds about whether the focus is on the genes themselves or on their expression. Let me give you some perhaps counter examples to show you why I am confused.

It seems to me that one of the most powerful genetic predictors is the presence or absence of the Y chromosome and that sex is, in fact, highly genetic determined. There are a minority of people for whom it is not tremendously determinative, but it is for most. And it is, you know, obviously linked to significant physiological differences. It is the cause of fifty percent of the population being disabled and constitutionally unable to carry a pregnancy. And, you know, those guys just have to live with that.

(Laughter.)

Why do you laugh? They are unable to do something.

And that is obviously genetic information that is revealed every time I have to check off "M or F" on one of those little forms. Similarly height, although not completely determined by genetics, we know this from the effect of dietary changes, have an extraordinarily strong genetic component and so you can tell just by looking at somebody an awful lot about certain aspects of their genetics. And obviously then in certain diseases you can look and see if somebody is expressing a disease that they obviously must have one or another mutations even if you have not identified specifically all mutations that could account for it.

So I am not sure if the focus is on only things that are latent and have not yet been expressed so that you are getting at the predictive phenomenon of genetics. But then

in light of multigenic and multifactorial conditions, whether it is only on latent and highly determined conditions, and I ask this because some of these problems occur because of the way the ground keeps shifting in the conversation to whether it is because you are going to test people for predictive purposes or because there is information that is going to confirm existing things or it is going to reveal relationships among people.

I just wonder if you all have like focused in on any aspect of this because if it is about genes themselves what you have really done is you have given us the Equal Rights Amendment for which I would thank you, but I do not know that is what you are aiming at.

DR. COLLINS: Yes. This is obviously an area where the boundaries are always a little tough to define. I guess most of what I was talking about I was relating to the consequences of genetics that involve disease and I recognize that the borderline between a disease and a trait is not something that many of us could precisely draw.

I think when we talk about genetic information it is helpful to break it down if it is related to a disease that everybody would agree, yes, that is a disease, to the circumstance of are you talking about an individual who already has the illness and you are trying to determine precisely what the molecular level -- what the alternation is because that might make some prediction about what they

are going to respond to. We do not have a lot of good examples of that, but there will be more.

Are you talking about a situation where they are a carrier and it is their children who are at risk. The sort of CF situation. Are you talking about a situation where they are at risk but they are currently healthy?

I think it is that latter category that is the newest arrival on the scene. It is the one where I think there is the least protection in place for people against discrimination and misuse, and violations of privacy. So much of what I was talking about relates to that circumstance and I probably should have defined it more narrowly to begin with. But obviously one should not limit the conversation to that. There are many other opportunities for mischief in other circumstances. But I think that is the most troubling one.

And the one which is coming down the tracks most quickly right now is this business of predicted information about currently healthy people based on an analysis of their DNA combined with their family history and saying that they are a highly unusual risk of this disease and somebody wanting to use that to deny them something that they ought to have a right to.

DR. SHAPIRO: Tom?

DR. MURRAY: Thanks. First of all, Francis, congratulations to the project for being ahead of schedule

and under budget. We should do as well on the commission.

DR. COLLINS: It is going to be hard to be under your budget.

(Laughter.)

DR. MURRAY: I have the same problem at home. It seems congenital. Not genetic, just congenital. Thanks for the warm words about the insurance task force and the work of the ELSI group more broadly.

I want to add a couple of comments about the insurance task force and then tell a quick story. The comments are, first of all, we -- I think if you read the report very carefully you will never see the phrase "right to health care." And that is interesting not because we were trying to avoid something political, but we could not have gotten an agreement among all the members of the task force that there was such a thing as a right to health care.

We could, however, get unanimous agreement that everybody ought to have access to health care that they need and that in any event genetic information along with other information about likelihood of illness or actual illness should not impair that access to health care. Now you might say, well, isn't that the right to health care? But I will leave that up to others who are concerned with such discussions.

I was at first not sure what you were saying. I thought you were saying that genetics was, in fact,

different from other things and rather dramatically so. But in the end you said at least in the case of say health records, practically genetic information is there along with everything else. And that was a part of our reason for rejecting this idea of what we have called genetic exceptions and that genetics ought to be distinguished and treated differently.

We also thought it was conceptually difficult to distinguish genetics from nongenetic information. Not in some cases. The HD gene is pretty clearly genetic, but lots of other things seem to be on the borderline. We also could not find a good ethical reason for distinguishing between genetic health risks and other kinds of risk to health. Most risk to health has at least as little to do with the events of interest to health insurance, that is episodes of illness, especially expensive episodes of illness, as do nongenetic factors.

I mean, getting run over by a truck can lead you to need health care and you may be as little responsible for that as you are for something that your genes did to you. So I want to thank you for all that. I thought you said that very eloquently at the end.

Now the story. I will be quick. I was at a genome conference a couple, two, three, four years ago. I do not remember the exact date, but I guess both I and the person behind me were not as interested in the speaker or equally

uninterested in what the speaker was saying at the moment. I do not remember who was talking. But it was the head -- the guy behind me was the head of the FBI laboratories.

He tapped me on the shoulder and I leaned back and he said, "Well, we have done the analysis on the samples from the World Trade Center bombing. We have a letter that was sent claiming credit for the bombing. We are analyzing the DNA on the back of the stamp. We have, in fact, identified one of the suspects." He said, "We also know that the person who licked the envelop was a different person." That is how hard or not hard it is to get at least certain kinds of genetic information.

It also led me to the fanciful conclusion that one of the largest identifiable collections of DNA samples belongs to Publisher's Clearing House.

(Laughter.)

You know, you even sign it. You even wrote the stuff inside.

It is not hard to get genetic samples.

DR. SHAPIRO: Thank you.

Zeke?

DR. EMANUEL: I wanted to push hard on something that Tom had commented. You seem to be sliding between genetic exceptionalism as Tom has put it and genetics is like other aspects of health care. And this morning we have talked and David Cox has said that he thought of genetics -- I am

putting words in his mouth, but I think the spirit is right -- that genetics should be a wedge to other health care issues and research issues that should not be treated all that different.

You know my own inclination and I just want to be a little clearer because when you talk about archival tissue for DNA testing, that could look like it is very exceptional. I mean, to me it seems part and parcel of a broader issue, access to medical records for research. While you are not looking at a tissue sample, you are looking at other relevant health information, lab tests, et cetera, outcomes. So it may be part and parcel of a bigger outcomes question that we are presenting about genetic discrimination. You know, it could be genetic and it could be health related in a more broad based sense.

My own bias is that, you know, genetics is a good wedge, but not unique either morally or should not probably be unique in most policy implications. I wanted to hear more about your views. Can I just tag on you mentioned three, I think, suggestions to us and we actually have a -- part of the charge is about the patenting. You did not say anything about that and I was wondering if that silence was pregnant or just time constraints.

DR. COLLINS: Let me quickly respond to both questions. I guess, now I have been inside the Beltway for about three years and I have become a bit of pragmatist. I

guess my own personal sort of philosophical view is very much that genetics is part of the tapestry of medical information, that it is often difficult to decide whether you are looking at something that is genetic or is not, and that therefore it might make the most sense to deal with the whole thing as a package.

But realistically when it comes to health insurance discrimination and employment discrimination when you look at what has been done say in some of the states, the effort to sort of make an omnibus bill that covers generic as opposed to genetic discrimination has often floundered because it produced too many complexities, too many enemies and nothing happened.

I think it is possible, practical and achievable to produce something in the way of legislation that protects against health insurance discrimination and employment discrimination based on genetic information. I think that is a viable strategy. It does not solve the whole problem, but it is, as you quoted David may be saying, sort of a wedge to get into a larger issue.

With privacy, however, it is not -- that is the problem. I mean, it would be a great strategy, but how are you going to take a medical record and separate it out into its various components and say, "Well, that lab test was not genetic and this one was," when we all understand that they are all interconnected. There I think it would be

rather self-defeating to try to have a specific effort and genetic information as deserving some sort of special protection and, therefore, just demanding some sort of special system of record keeping. There you sort of have to do it all which is one of the reasons that it is really hard.

With regard to patenting very quickly, I did not bring up patenting although I was pretty sure somebody would ask. I think the discussions about patenting have matured a good deal over the course of the last five or six years since this has been around when it came to specifically very high intensity discussions about DNA fragments. I am not going to say anything about animal patenting.

I think many of the discussions that used to be sort of based on moral arguments, people have sort of come around to the idea that that does not necessarily serve the needs of an issue which is largely a legal issue. Does patenting serve the public or not?

When the founding fathers came up with their schemes for allowing patent protection for inventions so that an inventor would be motivated to develop something into a useful product, were they thinking of something that DNA sort of represents? Well, sometimes yes and sometimes no.

My own sense is there are circumstances where a DNA fragment that codes for a useful protein -- I am sure Steve Holtzman would be happy to endorse this view -- are

appropriate for patent protection because they inspire the development of a very useful product like erythropoietin, for instance. There are other circumstances where there is no sort of utility being met and you do not know what the sequence does and it seems almost ludicrous. The real question is where in between should one draw that boundary and boundaries like that are always hard to draw.

Is patenting a gene like BRCA-1 for purely diagnostic purposes? Does that serve the public interest? I think we do not have enough experience yet to know.

But my sense was this is an area where the changes -- what the PTO is going to say is still not clear. Whether the PTO will listen to anybody, including this commission, is not clear. Whether legislation in the patent area is ever a good idea is not clear. It sort of seemed like a less fertile field. That is my own sort of personal private view.

DR. SHAPIRO: Thank you. I have three more members of the commission who want to speak and then Francis, I know, has got some time constraints and we also have to get on with other agenda items.

Bernie?

DR. LO: I want to thank you for coming and laying out so nicely sort of what ELSI has done. As I was listening to your three suggestions for us it struck me that the audience for those three suggestions was going to be

legislators or regulators. As I was listening to you the answer to these would be some sort of omnibus law on privacy of medical information and so forth.

We were talking earlier about sort of trying to, you know, produce a product and be pragmatic and everything. And I just -- there could be several concerns raised about trying to think that what we will do will sort of inspire a legislator or Congress to act. One is it is always a role of the dice as to what gets passed and what does not.

And certainly there is clearly sort of an antiregulatory sentiment certainly in parts of Congress and parts of our country. Even though there may be a need for regulation I can imagine people lining up to say, "Well, if you regulate it, it is going to be over regulation, burdensome, et cetera, et cetera."

Again, following your sort of suggestion you do not want to put all your eggs in one basket when you are just sort of starting out in an endeavor, are there ways in which we could address these very important topics and not fall in the trap of just making recommendations that other people do not turn to? Is there a way of sort of enlarging the audience to try and work for voluntary guidelines by professional organizations, health care service, integrated systems? I mean, some way that some of this could be done without having to depend on legislation and regulation.

I guess that is a general topic for us because there

may be some things that, you know, are uniquely within the providence of government to pass laws on. But we do not have the power to pass the laws directly and that leap between our recommendation and their enactment can be pretty tough.

DR. COLLINS: Yes. I think of the three topics I suggested certainly one of them does not require legislation. The archive tissue sample example I think really requires a thoughtful look at the recommendations that other groups have put together trying to figure out where is the appropriate balance between the various needs and then a recommendation which I think could be made directly to OPRR and other parts of other agencies that are responsible for human subjects oversight. I think the time is right for that.

Much of probably what needs to be done is at least imaginable when you look at the existing guidelines like 45 CFR 46. But it needs some clarification. IRBs will probably need some instruction. While this may seem sort of a narrow issue in some ways, I think it is a very achievable one and it does not require you to have an audience that is sort of unpredictable like the members of the Congress.

The other two issues I honestly am not sure how you can make much progress in medical record privacy or in health insurance discrimination without legislation. I

mean I would hate to go back and say there ought to be a law that in this situation it sort of seems as if that is the most likely way to get a solution because there are strong motivating factors not to necessarily adhere to these principles which I think all of us around the table would like to think we stand for that are driven by other forces. And even if you can get some part of the equation to behave properly the other parts may not.

I understand what you are saying and I am concerned as well about what is this commission's audience most effectively going to be and are you in a situation where you can expect to have an impact of that sort. But I would certainly encourage trying.

DR. SHAPIRO: Arturo?

DR. BRITO: Kind of along those lines and about this commission and what our role is, and I am not sure my question or my point has to do with what our role is. But it is interesting because during your talk and any of these readings and most readings, whether it is the lay journals or scientific journals, there is a lot of concern, the big focus is on the health insurance and employment coverage, et cetera. But it is exciting to know that there is a potential preventive measure about finding out somebody's genetic predisposition to a certain disease.

But I had not heard mentioned or talked about people that are in the latent stage of this potentially fatal

disease genetically predisposed to it and what about the right to know that you have this potentially fatal disease and what is going to be done and what guarantees are there for the people in this country that -- first of all, will they be able to find out that they have this disease?

And, second of all, will there be any preventive measures or any means for providing those preventive measures? Because if we start providing the ability for only a certain segment of our population to receive screening and further to receive the preventive measures so they do not develop these diseases, what about the rest of the public?

So I do not know if this is something -- I think it is definitely an important issue and it is going to become even more important as more and more diseases are defined in this way. I am just -- I am not sure how far this commission can take a big interest in this because we already see it with something that is -- mammography screening, for instance. This is not available to everyone in the population and when it is available there is a delay in getting appropriate care.

DR. COLLINS: That is a very serious issue. Genetic interventions and testing are going to be expensive. Who will have access to those services and it will be the same problem that we have with medical care in general only maybe even particularly so here because of expense and

because of complexity and the need for sophisticated health care providers that you often do not find except in tertiary care centers. It is a very serious issue. How will we engineer the delivery of medical services so that this technology does not end up being even less fairly distributed?

DR. BRITO: And along those lines, the reason I bring that up, too, is that from my point of view and the point of view of a lot of people, and statistically too, preventive care is more cost effective than reactive care or waiting until the disease develops. So that is just something that maybe from the beginning, not wait to find this out. Particularly in genetics if you could do preventive care early on even though it is costly it is definitely going to be less costly than waiting until down the road.

DR. COLLINS: That is a very good point.

PROF. CAPRON: Didn't your insurance task force say exactly that?

DR. COLLINS: Tom Murray's task force talked about access, indeed. And it is also mentioned in the ELSI Working Group Action Plan. It is one of those things that you cannot be -- you can hardly disagree with. I mean the question is how do you make that happen in a medical care system which is currently very unfair.

DR. SHAPIRO: The last question and then we have got

to let Francis go and get on with our agenda.

David?

DR. COX: This is the issue with respect to privacy. We heard Eric basically say that right now medical records are not private and they are out there. We heard you say, and it is my prejudice also, that it is not smart sort of -- and actually what Eric implied, it is a very hard problem. So we clearly want to fix it, but it is a very tough nut to crack.

So the question would be then, well, one way to crack a tough nut is break it down and make it more narrow. But you said, and I agree, that it is a wise move right now at least with respect to privacy to put genetics off.

So there is another potential tact that people have thought about and that is instead of trying to close the barn door when the horse is already out, is to do it a different way and deal with the issue of informed consent. Now some people do not see informed consent as privacy, but in fact that is another way -- a potential way to get at this.

So do you then given that the privacy issue with medical records is going to be very difficult that we should proceed with that? Do you see that tackling informed consent is a way of perhaps getting around it is a possibility and/or should we be doing both? This is in the context of this commission and, you know, real time and

real money.

DR. COLLINS: That is a very tough question . I think informed consent has to be part of any meaningful privacy legislation or policy because you must have situations where the information can be given out for that person's benefit because they want to know that. So under what circumstances? Well, you always come back to informed consent.

But is that sufficient? I guess it is hard for me to imagine a circumstance where you would not find multiple ways of getting around that by accidental determination or simply by volunteering of that information without intending to.

DR. COX: But I will make it even harder, Francis. If you had a choice, I am only giving -- you have to pick one or the other. Okay. Where should we focus? I know that that is totally unfair because we would like to have -- I think we need the two.

DR. COLLINS: I think you have to come up with very strict regulations that limit access with really muscular provisions to punish those who break those rules. I think informed consent alone will not.

DR. CASSELL: No, but with informed consent if people give consent they are informed and then that consent acts not at the time of disclosure, but at the time later on when you are getting their insurance company consent. They

have no idea what is in their record and then they are shocked to discover they have now consented to knowledge about their childhood behavior.

DR. COLLINS: The paradox we heard yesterday about informed consent is that the more you depend on it the less it means because people are signing and signing and signing, and after a while they are not reading what they are signing at all.

DR. COX: And so the conclusion, which is actually my own and it is quite worrisome, is that there is no easy way out of this particular privacy issue with respect to medical records?

DR. COLLINS: That is correct.

DR. SHAPIRO: Well, let me thank Francis very much for your very thoughtful and stimulating remarks. Thank you for taking the time to come today. It is a pleasure to have you here.

We will break for about ten minutes. We have just given away five minutes of our break. Let's try to get back here in ten minutes.

Thank you very, very much.

(Whereupon, a break was taken from 2:42 p.m. until 2:59 p.m.)

DR. SHAPIRO: I would like now to move on to the next item on our agenda if I could have your attention, please.

I would like to introduce Dr. Gary Ellis, the Chair of

the Human Subjects Research Subcommittee.

Gary, I do not know what to entitle your remarks.

But he is going to give us an assessment, I believe, of human subject protection as it is working today. Of course, Gary is, as you know, out of OPRR and has been very active in this area and he is very central to it.

Gary, thank you very much for coming.

RESEARCH INVOLVING HUMAN SUBJECTS

DR. GARY B. ELLIS

CHAIRMAN, HUMAN SUBJECTS RESEARCH SUBCOMMITTEE,

COMMITTEE ON HEALTH, SAFETY, AND FOOD,

NATIONAL SCIENCE AND TECHNOLOGY COUNCIL

DR. ELLIS: Thank you, Harold.

In my bland way I have titled my remarks "remarks."

(Laughter.)

I appreciate the opportunity to speak to the commission and it is a privilege.

(Slide.)

The Subcommittee on Human Subjects Research is the interagency body that oversees the uniform implementation of the "Federal Policy for the Protection of Human Subjects," you have a copy of that in your briefing book, among 17 adherent federal departments and agencies.

This interagency group of federal officials has met regularly for more than 13 years without interruption. Yesterday the subcommittee met for the 19th time during my

tenure as chairman which began in 1993. Subcommittee members asked me yesterday to emphasize today both their willingness and their strong desire to work with the NBAC in any way that will assist the commission in its consideration of protecting the rights and welfare of human research subjects. To that end most of the department and agency human subject representatives are present this afternoon at this inaugural meeting.

(Slide.)

Well, it is ironic to note as we consider human subject protections in 1996 that more than 30 years ago Congress conferred certain protections on laboratory animals. In August 1966 the President signed the Animal Welfare Act into law. It has been amended four times since.

(Slide.)

The Animal Welfare Act states that when research involves any live or dead dog, cat, monkey, guinea pig, hamster or rabbit the research facility must, among other things --

(Slide.)

-- register annually with the U.S. Department of Agriculture, provide an annual census of animals used in research to USDA, and report annually on animals and procedures that involved pain or distress, alleviation of pain or distress, or no pain or distress. Violations of

the Animal Welfare Act carry civil penalties and in certain instances prison terms.

(Slide.)

What I am about to say may be surprising to some. With regard to human subjects there is no law that confers upon all individuals who may be research subjects the twin protections of institutional review board review and informed consent. There is no annual registration of all research sites, no annual census, and no reporting of pain or distress.

Please do not interpret me as being an alarmist. Indeed, as a general statement --

(Slide.)

-- human research subjects have never been more well protected than they are at this moment. But this commission's analyses need go beyond generality. Let me describe the system of protections in place today.

(Slide.)

The Federal Policy for the Protection of Human Subjects, also known as the Common Rule, applies to human subjects research conducted or supported by 17 different federal departments and agencies.

(Slide.)

A copy of this policy, as I said, is in your briefing book.

(Slide.)

The Food and Drug Administration has human subject protection regulations that apply to research involving products regulated by FDA, such as drugs, biologics and medical devices. And FDA concurs with the Federal Policy for the Protection of Human Subjects.

(Slide.)

It is noteworthy, too, that the regulations of the Department of Health and Human Services, Title 45 Code of Federal Regulations Part 46, a copy is included in your briefing book, go beyond the Federal Policy for the Protection of Human Subjects by including additional protections when research involves certain vulnerable subjects. For example, pregnant women, prisoners and children. Several departments and agencies beyond HHS have embraced these additional HHS protections.

(Slide.)

Many biomedical or behavioral research institutions that receive HHS support for human subjects research have elected on a voluntary basis to pledge all human subjects research conducted under their auspices irrespective of funding to the HHS Human Subject Regulations at 45 CFR Part 46.

(Slide.)

Now human subjects involved in research beyond the perimeter of the preceding protections that I have described are protected only by occasional state or local

law or regulation, or at the discretion of the individuals or institutions undertaking the research.

Now let me put it another way. We know that there is human subjects research that is not conducted or supported by any of 17 federal departments or agencies that adhere to the common rule, not regulated by the Food and Drug Administration, and not voluntarily pledged to HHS regulations at 45 CFR 46.

(Slide.)

In one department, HHS, the Office for Protection from Research Risks, which I direct, receives a number of inquiries involving human subjects research over which it has no jurisdiction. Most are informal inquiries received over the telephone and are never pursued by OPRR. A few such complaints are presented to OPRR in writing and are reviewed in sufficient depth to confirm OPRR's lack of jurisdiction.

(Slide.)

Let me describe some examples drawn from OPRR files. The parents of a young child who underwent experimental bone marrow transplantation alleged that they were not adequately informed about the procedure's reasonably foreseeable risks, including the severe brain damage which their child suffered.

A second example, it was alleged that women who had experienced multiple miscarriages were misled about the

substantial financial costs of participating in research to enhance pregnancy.

A third example involved a mid-level state university where there was a considerable controversy about appropriate confidentiality protections for subjects involved in the study of adult literacy as well as charges of conflict of interest among members of the university's institutional review board.

A fourth example, a woman who had been treated for breast cancer alleged that identifiable private information from her medical record had been placed in a registry and made available to research investigators without her consent.

In each of these examples OPRR was unable to pursue the allegations because the research was neither supported by the Federal Government, nor voluntarily pledged to HHS regulations under an institutional assurance of compliance submitted to OPRR.

(Slide.)

OPRR believes that the overwhelming majority of human subjects research outside of its purview never comes to its attention. Some months back, for example, the New York Times reported two examples of human subjects research done apparently outside of the scope of current protections.

One involved 126 pregnant patients of a New York City doctor. The other involved an unknown number of North

Carolina school children and their families.

These research subjects are real people. They are our fellow Americans. In 1996 we do not have the tools necessary to ensure that they and all human subjects are protected by first initial and continuing IRB review and, secondly, legally effective informed consent.

As you proceed with your consideration of protecting the rights and welfare of human subjects, please do not advance beyond what I would call square one without articulating a meaningful standard of protection for all individuals who may be research subjects. If as you reach conclusion you find it somehow appropriate to stop short of conferring upon all individuals who may be research subjects the twin protections of IRB review and informed consent, please ask yourselves why is that acceptable? I have no answer to that question.

(Slide.)

With respect to research conducted, supported or regulated by the Federal Government, the President's October 3rd, 1995, Executive Order mandated that departments and agencies report to the commission regarding existing policies and procedures related to human subject research. All member departments and agencies of the Subcommittee on Human Subjects Research have conveyed reports to your chairman.

In reviewing these reports you will find that across

the board the Federal Government is employing its most powerful tool, education. This is our best and most effective instrument to enhance the protection of human subjects. Education is preventive maintenance for our dynamic and ever evolving system of protecting human research subjects.

(Slide.)

Already today you have discussed informed consent. We put great stock in a structured informed consent process and in a written informed consent document that embodies certain required elements of informed consent.

(Slide.)

The informed consent process is an information exchange that includes subject recruitment materials, oral instructions, written information, question and answer sessions, voluntary agreement and continuing understanding or agreement.

(Slide.)

Federal regulations specify 14 potential elements of informed consent. Eight of which are required.

(Slide.)

First, a statement that the study involves research. An explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.

(Slide.)

Second, a description of any reasonably foreseeable risks or discomforts to the subject.

(Slide.)

Third, a description of any benefits to the subject or to others which may reasonably be expected from the research.

(Slide.)

Fourth, a disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.

(Slide.)

Fifth, a statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.

(Slide.)

Sixth, for research involving more than minimal risk an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of or where further information may be obtained.

(Slide.)

Seventh, an explanation of whom to contact for answers to pertinent questions about the research and research subject's rights and whom to contact in the event of a research related injury to the subject.

(Slide.)

Eighth, a statement that participation is voluntary. Refusal to participate will involve no penalty or loss of benefits to which a subject is otherwise entitled and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

(Slide.)

A researcher who seeks to recruit an individual for research without conveying these elements of information in language understandable to the potential subject is not obtaining informed consent. The specificity of this federal regulatory language, its endurance through many years, and the enthusiasm with which we all adhere to it belie the fact that little empirical work exists to document the degree of understanding achieved by research participants.

There is a scarcity of data that bear upon, for example, research subject's comprehension of a study's methods and procedures; research subject's understanding of relative risks and benefits of participation; subject's understanding of confidentiality and any exceptions to confidentiality; and subject's understanding of the implications of withdrawal from a study.

Such data are needed to aid in designing informed consent procedures that are readily comprehended by

prospective participants and at the same time impart all critical information.

(Slide.)

In this vein I am delighted to see a newly minted request for applications from the National Institutes of Health for original research proposals in the area of informed consent in research involving human participants. NIH, the Department of Energy, and the Department of Veterans Affairs will make available fiscal year 1997 research funds for investigations into the informed consent process in biomedical and behavioral research.

This is an exciting investment by funders in the development of new knowledge relating to informed consent. These three agencies are igniting the engine of research in an area that has for too long been under explored. I understand that two additional agencies, the National Science Foundation and the Department of Defense, are strongly committed to joining this effort. The notice about this RFA is available in the room this afternoon.

(Slide.)

A few words about institutional review boards.

(Slide.)

The IRB is by federal regulation to be established at the local level and has a minimum of five people, including at least one scientist, one nonscientist, and one person not otherwise affiliated with that institution. The

nonscientist must be present at IRB meetings.

(Slide.)

IRB review is a local review by individuals who are in the best position to know the resources of the institution, the capabilities and reputations of the investigators and staff, and the prevailing values and ethics of the community and likely subject population.

(Slide.)

Federal regulations invest IRBs with specific responsibilities.

(Slide.)

IRB review assures that risks are minimized, that risks are reasonable in relation to anticipated benefits, that selection of subjects is equitable, that there is proper informed consent, and that the rights and welfare of subjects are maintained in other ways as well. This is particularly important when subjects are likely to be vulnerable to coercion or to undue influence.

With an estimated 3,500 IRBs operating today in the United States the local IRB at the research site is the cornerstone of our American system of protection of research subjects.

(Slide.)

The March 1996 report by Congress' General Accounting Office, "Scientific Research: Continued Vigilance Critical to Protecting Human Subjects," acknowledged what GAO termed

"the conspicuous activity of local institutional review boards." GAO noted "the struggle to balance two sometimes competing objectives, the need to protect research subjects from avoidable harm and the desire to minimize regulatory burden on research institutions and their individual scientists."

(Slide.)

In the final analysis the member department and agencies of the Subcommittee on Human Subjects Research along with research institutions, IRBs and investigators are the stewards of a trust agreement with the people, both patients and healthy individuals, who volunteer to be research subjects.

(Slide.)

We have a system in place that to the greatest degree possible first minimizes the potential for harm; second, enables and protects individual autonomous choice; and, third, promotes the pursuit of new knowledge. By doing so we protect the rights and welfare of our fellow citizens who make a remarkable contribution to the common good by electing to volunteer for research studies. We owe them our best effort.

(Slide.)

Please let that effort begin anew with your completing the unfinished business of extending the existing umbrellas of protection to cover all Americans who may be involved in

research.

(Slide.)

Let me make just a few comments based on some discussion earlier. Alta Charo asked Leonard Weiss if he could prioritize his list of items that he presented to the committee. Let me offer two priorities based on his remarks and my own remarks.

I see two categories of general activity for the commission. First, to extend the protections that exist, and a second priority behind that first priority, to enhance existing protections. First, extend; then enhance what is in place.

(Slide.)

We heard discussion this morning about the fundamental principles underlying our human subject protections and in your briefing book is a copy of the Belmont Report, so named after a Maryland Conference Center. This is the single most enduring product of a very productive commission, the National Commission. OPRR prints and distributes about 10,000 copies of this brochure every year. It is used by many target audiences ranging from lay people to IRB members, to research investigators, administrators and so on.

The Belmont Report describes three principles. You know these principles. Respect for persons.

(Slide.)

Beneficence. Literally some good must come of the research. And justice.

The discussion this morning, which I endorse and I believe is right on target, suggests that in the intervening years since 1978 a fourth principle may be evolving.

(Slide.)

I will label that principle "community," but I ask you as a commission to flush out what this principle means and to afford IRBs, research investigators, and others the opportunity to factor this into the formal mix of principles as they weigh those principles in reviewing and approving research.

Put simply, it may be that during your tenure you will pass the 20 year anniversary of the Belmont Report and you may wish to revisit it and update it.

(Slide.)

Finally, again Alta Charo mentioned Tuskegee. We have heard one mention of it only today and I do not think that we would want to go by with so brief a mention as we had.

(Slide.)

In fiscal year 1995 the Department of Health and Human Services spent $2.7 million dollars for the medical expenses, burial expenses and other expenses of the survivors of the Tuskegee Syphilis Study. I will update this slide for the fiscal year that ended last Monday

night.

(Slide.)

There are alive today 12 participants, 12 men who were in the Tuskegee Syphilis Study. Their average is 89 years. There are 23 of their wives and widows and 18 offspring. The government, society, can never really repay the debt owed to these individuals for the harm that was done to them. But we will service that debt for as long as it takes.

And I close with this as a reminder of the cost of missteps in our work. I hope that I and my successors will not be able to show slides like this ever again. The work that you begin today can help ensure that that is the case.

Thank you very much.

DR. SHAPIRO: Gary, thank you very much. I also want to extend our gratitude to your colleagues you work with and other agencies who work with you.

DR. ELLIS: They are here.

DR. SHAPIRO: Let me thank them for being here today.

Let me now turn to the commission for questions they might have. Alex, then Alta, then Jim.

PROF. CAPRON: Gary, one cannot help but be moved by your question about why is it acceptable to have some research subjects not protected by an IRB and legally effective informed consent. As I understand the terrain, research is conducted in two sets of institutions. Those

which receive federal funds and those that do not. As to the latter some of the researcher's research is sponsored by people who have an intention of taking something to the FDA and so that research is covered by the same set of protections. So there is the subset of research that is carried on privately that is not ever going to go to the FDA and so it is not covered.

Within the institutions that are recipients of federal funds, as I understand it, those institutions in their assurance can voluntarily choose to agree that they will review all research. Is that right?

DR. ELLIS: That is correct.

PROF. CAPRON: Your proposal to us then addresses what should happen as to research conducted at institutions that have federal assurances but do not make that promise and research not conducted at federal institutions that is not covered by the FDA, is that correct?

DR. ELLIS: The only thing I would add to that, Alex, is you might want to consider the strength of the foundation of a system that relies on a voluntary commitment of those major biomedical research institutions to follow the rules.

We are very proud that we have been able to extract that promise from about 450 -- in other words, all the major biomedical research institutions commit, 99 percent of them commit all research, irrespective of funding, to

our rules. But we are well aware that that is a voluntary elective step on their part.

PROF. CAPRON: Since we are not the Congress of the United States, what has kept you in your own regulations from requiring that all institutions that want to receive federal funds for their research agree to review all research that will be conducted at the institution?

DR. ELLIS: I am not certain, and the Council for the Department of Health and Human Services representative, I am not certain that the department has that authority at all. As it stands now the regulations across 17 agencies follow the federal funds for human subjects research. And not being a lawyer I yield to you and others. It is not clear where the authority would come from to requiring institutions that receive money for this project to apply the rule to that project.

PROF. CAPRON: What I am saying -- I guess my question is an oblique one. If the Grove City case, the Supreme Court case, suggests that you cannot do that, you cannot tie to federal funds requirements about how they conduct themselves outside of federal funds, I am not sure what you think we could do about that.

I mean, if you have been unable to do it, what are we supposed to do about it? And so I mean -- I say I was moved by your plea, but it is certainly something which you, yourselves, could have acted on if all it took was

saying so it should be. If the Federal Government does not have that authority or -- I am just puzzled what you are asking us to do.

As to those institutions -- and as someone who is conducting research at a private hospital or a doctor's office, doctors doing research or one of these in vitro operations that is doing research. Because the techniques are not very well proven and it really ought to be called research, but the patients are paying for it.

What is -- if we have a handle, why don't you have a handle?

DR. ELLIS: Well, let's suppose that the government were to pursue your first course of action and to cover those institutions receiving federal funds. The frontier protector would have been extended that far and we would still have those individual research subjects who are outside of that --

PROF. CAPRON: Well, I agree. But I am saying as to either one, I do not know the hook to hang my hat on that you would not already have to hang your hat on.

DR. ELLIS: I am suggesting if we were to begin anew today and create a system for protection of research subjects, we would not proceed in a patchwork fashion. I do not use that term pejoratively, just descriptively, in a patchwork fashion as it stands now. We might say that any research subject in the United States deserves these

protections. So the discussion you and I are having right now is whether to proceed and add another patch to the patchwork system to extend the frontier or to step back and say let's build the system correctly from the start.

DR. SHAPIRO: I guess the question is who would have the legal capacity to do that?

PROF. CAPRON: I mean, we have -- it is not as though the issue is not arcane in that you cited examples of people who have been injured. You are an existing office. You have a consortium of all the federal departments and agencies, a couple of dozen of them that sponsor and conduct research.

DR. ELLIS: We have no authority over those agencies. We work together collaboratively.

PROF. CAPRON: I know. I know. But, I mean, if this were the kind of thing that was an important issue -- I guess, I am asking are you asking us to tell you that you should do the right thing? Are you asking us to tell Congress that Congress should let you do the right thing?

DR. ELLIS: I am asking you to consider whether it is important that every research subject in the United States should have these protections.

PROF. CAPRON: Of course.

(Simultaneous discussion.)

PROF. CHARO: Alex, before you have a stroke --

DR. MIIKE: I think this discussion is going on too

long. Can we move on?

DR. SHAPIRO: It is unresolved, Alex. We are short of --

PROF. CAPRON: I think we need to schedule then at one of our meetings a chance where the discussion will not be regarded as going on too long. If we are going to raise these issues we have got to have a day or so to hear in detail about them.

DR. SHAPIRO: I agree to that.

PROF. CHARO: Without losing the chance to ask you specifically about the task force's work on some of those vulnerable populations because I know about some efforts for a long time to revise some of them for pregnant women and I was not sure if it also applied to prisoners, et cetera. So, please, keep that in mind to just give us an update.

I have just got to add two things here. There are other approaches besides going at it through federal funding and ties. You could look at the international documents we have signed having to do with human rights and see whether or not they give authority to the U.S. Congress to implement them on a national level. You could also check under the interstate commerce clause whether or not we would be able to get away with saying no product can be put into commerce if it was developed or if its components were developed using research that does not meet certain

standards. That would also be possible.

So there are other avenues for going at this and I agree that a more leisurely discussion for strategies could be arranged.

DR. ELLIS: And you might add the National Conference of Commissioners to Uniform State Laws. That is another avenue.

PROF. CHARO: It is another avenue although much more complicated.

DR. ELLIS: Be creative. That is all I am asking.

PROF. CHARO: And for the vulnerable population stuff, just an update?

DR. ELLIS: Well, you mentioned pregnant women. The Public Health Service Working Group on Human Subject regulations completed a revision of what we call Subpart B, Additional Protections for Research Involving Pregnant Women, Fetuses, and In Vitro Fertilization, in summer of 1995, and it has been forward to the Secretary of Health and Human Services for her consideration to put out a proposed revision. That part of the human subject regulations is the most dated. It was last revised in 1978. So the proposed rule is under consideration by the Secretary.

If the commission has a special interest in seeing the revision or proposed revision to Subpart B of the HHS regulations, the commission certainly could make that

interest known to the Secretary. I am sure she would be interested in this.

DR. SHAPIRO: Jim?

DR. CHILDRESS: Thank you very much for that clear and helpful presentation. Let me ask three questions. One, you suggested the addition of community, that falls in line with the humanitarian thrust into our discussions. But I guess I am curious about what you think it adds to what is already present in beneficence. Is it something new or does it simply add additional weight?

I will just go ahead and give you all three and then you can respond to them.

Second, you have talked about extending protections but also enhancing protections and I was less clear really what you had included under enhancing protections.

And then third you emphasized the protective role of IRB review and the importance of having access to that protective role. And yet you mentioned the GAO report which does raise some problems with that IRB review and we have talked about that some already today. Are there other studies that we should look at that would help us get some -- a good sense of what is going on in IRBs, what kinds of problems are there?

I just had -- we just got the GAO report today so I only had a chance to glance at it and I do not know whether you think it is sufficient or whether you think more needs

to be done, or whether other stuff is available.

DR. ELLIS: Well, answering the last question first, I thought the GAO report was very good. We worked with the GAO for a year-and-a-half and these were very bright auditors and they got the point and they expressed it well in their report. I cannot give any higher praise to my fellow government workers.

The first point, community, I am taking note that Francis Collins' presentation, for example, in the area of genetic research. But the research subject may not be an individual anymore, but an individual plus those blood relatives.

And beyond that, particularly Dr. Miike mentioned in minority communities, not just blood relatives, but neighbors and friends may be so closely apposed, not opposed, but apposed to the research subject to be considered in the calculation of respect for persons, the weighing of risk and benefits, the equitable selection of subjects, and then interests of individuals other than the research subject, as we have classically thought of that individual, whose interests may need to be factored in.

I know that IRBs are already factoring in community interest and it might be time to expand and explicate this principle and put it into the existing dogma formally.

The second question you had, enhancement of existing protections, I am considering additional elements of

informed consent that might be judged to be required, changes in composition of the IRB. The skeleton IRB of five individuals with one nonaffiliated member, one nonscientist member, a gender balance that requires at least one member of the opposite sex, whatever the majority sex is on the board.

Those may be assumptions that need to be revisited. So the core elements of what makes an IRB, what means an IRB, and the elements of informed consent. That is what I was referring to.

DR. CHILDRESS: Thank you.

DR. SHAPIRO: Diane?

DR. SCOTT-JONES: I was going to ask about community, but it has already been asked and answered.

DR. SHAPIRO: Thank you for your thoughtfulness.

David?

DR. COX: I have a question about IRBs and it is really a sort of structural process question. Given all the things -- you laid out, I think, very beautifully the advantages of having IRB, you know, local knowledge, all that good stuff. But given what is coming down on them right now in terms of all the things that they have to do, both in terms of breadth of knowledge, as well as ensure massive stuff that has to happen, is it your view that IRBs are viable? So that -- I mean, is that the process from your point of view that we should focus on and, if so, is

that because there is no other process you can see or because you believe that that is, in fact, the best process?

DR. ELLIS: Well, I think that they are viable. We fault institutions for not making available to IRBs the training. We heard a statement this morning that IRB members ought to be trained. Hear, hear. The resources in terms of staff support.

You might wonder why would I introduce the concept of annual census of laboratory animals and imply that an annual census of research subjects might be useful. It is not that I am interested in the number of research subjects, but that is a very useful predictor of the resources necessary at the institution. I would like that predictor as a federal regulator to see if the resources match the volume of subjects.

I have lost my train of thought, but if that did not answer let me know.

DR. COX: But it did, in fact, because what you are saying then is that you believe this is a viable process that we should work through to beef up rather than change the process?

DR. ELLIS: It would be hard to bring to bear this much time, effort and dedication for the relatively low cost. Remember IRBs are largely volunteer effort. They get by on the dedication and it is sincere dedication. We

go out to institutions and we are always impressed by the dedication of the individuals at the table. They may not know the regulations cold. In fact, they do not. But they bring good sense, common sense on a volunteer basis to the table and they do the right thing. I could not duplicate that in any other way right now.

DR. SHAPIRO: Zeke?

DR. EMANUEL: I guess my question is a follow up really Dr. Cox's. You were here for the morning and you heard some of the comments by myself and others about the possibility of thinking about moving a national IRB -- I actually do not like that idea, but some other framework to bolster possibly the local IRB. I know you have thought about the IRB issue long and hard, probably longer and harder than most of us. What is your reaction to supplementing, not supplanting, but supplementing the IRB process for particular, either complex research or research that is multi-institutional or research that is with particularly vulnerable subjects, et cetera?

DR. ELLIS: We endorse the maintenance of local governments. The response to your interest is education. There is no upper limit to the amount of education on a national scale and a local scale that can be done. It is a function of the resources committed to it. It works. It is relatively cheap, effective.

DR. SHAPIRO: Any other comments?

Yes, Bernie. I am sorry. I had your name down. I am sorry.

DR. LO: Gary, thanks for your presentation. Can I ask you to think along with us about the problem of conflict of interest? The Canadian report we got a copy of, but you elevated that to sort of principle status almost. And clearly if enhancing informed consent is one way to deal with that, let the potential research subject know if there is an apparent or potential actual conflict of interest. But are there also some situations which are so treacherous that they ought to be regulated or prohibited as opposed to just relying on informing the subject as the way to resolve it?

DR. ELLIS: No doubt there are situations that are so treacherous that they must be addressed. But at the other end of the spectrum even a simple financial conflict of interest, how would it play out? Regulations could dictate that the subject be told that the physician researcher owned stock in the company that is developing the device. So now that is revealed.

What is the subject to do with that information? We have gone around and around on this in our office. I do not have a clean answer. It is not that we are not interested in pursuing this, but that opens a can of worms that we may not have fully thought through. What is the subject to do with that piece of information?

DR. LO: It probably depends on the subject. Some may find it very pertinent to their decision to participate and others may not.

DR. SHAPIRO: Tom? And then Eric. Then we are going to have go on.

DR. MURRAY: Gary, you closed your talk by urging us in priorities to extend, then enhance. I am a little worried about that order because if we take seriously the criticisms we have heard of the IRB system it is -- we are in a difficult position telling other people, well, we have this horribly flawed system that we think we really need to revamp in a major way, but you want it now.

DR. ELLIS: I am not sure you have heard anyone say it was horribly flawed. I did not.

DR. MURRAY: Yes. I have extended it a bit, haven't I?

(Laughter.)

DR. MURRAY: How about significantly flawed? That would still be enough to alert me. I would guess -- I guess what I want to say is there seems to be two fronts and maybe we ought to work on them simultaneously.

DR. ELLIS: That is your question.

DR. SHAPIRO: Eric?

DR. CASSELL: Well, in regard to the disclosing your financial conflict of interest, for example. I mean many times people have argued about informed consent. Well, the

subject cannot understand this. The subject, we all know, goes away without remembering, da, da, da. All those things have been said about it 15 years ago and which I am sure are still true. But the subject brings one thing to it that nobody else brings to it, their knowledge of their own interest. The fact that you do not know what that interest is, is irrelevant. Or what that person might do is irrelevant. The question is not do you know, it is does the subject know.

DR. ELLIS: I am not opposed to the conveying of the information. I just posed the question. I think this is a fertile area for research. We know very little about the informed consent process as I said.

DR. CASSELL: Well, I mean, there were a number of studies about 15 or 20 years ago and they all stopped dead because of what they showed and so maybe the new crop will show something entirely new about informed consent. It is not as if nobody ever tried.

DR. SHAPIRO: Okay. Well, thank you all very much. I regret that we do not have more time to pursue these issues. We will have them in front of us at future meetings. We will take careful note of the interest of the commissioners and particular aspects of them.

Gary, thank you very much. We appreciate it very much.

DISCUSSION OF CONFLICT OF INTEREST GUIDELINES

CHAIR, MEMBERS AND MS. RUSSELL-EINHORN

DR. SHAPIRO: We will return now to the conflict of interest discussion.

Again, Ms. Russell-Einhorn, thank you very much for coming back.

As I understand it, the purpose of this session is for those commissioners who think it is helpful for the commissioners themselves to discuss something about their own particular sense of any conflicts they may have. Normally conflicts of interest or conflicts of commitment, I guess, is what Alex talked about earlier today, personal experience and other biases that we all had. We all have some subset of biases. If you think it is helpful to share that with your fellow committee members this, I believe, is the time to do so.

I will start off the discussion by being the first to go on this round, but is there anything further you want to tell us?

MS. RUSSELL-EINHORN: No. I think it is a great idea, but just let me caution you all that the forms you fill out, the financial disclosure forms, are confidential financial disclosure forms. You need to be careful about how much you disclose that is on there so that we do not lose the confidentiality of those forms.

I just want to remind you, also, that --

DR. EMANUEL: It is our confidentiality, right?

MS. RUSSELL-EINHORN: Okay. I just want -- but I want to make you -- but you need to be aware of that. That is all. Okay. And I just want to also mention that we have gone through the forms. We have identified what are conflicts under the relevant regulations and laws. And where we have found problems you have been given waivers or advice that you need to be disqualified. So I just wanted to add that.

DR. SHAPIRO: Well, I presume that anything that any one of us wants to say here is no longer deemed confidential by then. What we are -- what you are saying is that what we may say here may open up those forms as well. Is that what you are saying?

MS. RUSSELL-EINHORN: It is a possibility.

DR. SHAPIRO: Well, everyone can think about that in their own way and decide what it is they would like to do, but in any case let me begin the discussion. It need not be overly long and, of course, it is totally voluntary as I said in my note to you.

As I thought about my own situation I think there are various issues that could come up in this area at least along a number of different dimensions. Of course, as you all know, I am president of a university which is a -- not super major, but major performer of research, a good deal of it going on with human subjects and so that obviously is an interest of mine and I will have various commitments

that come up in that connection. We will just have to see how that goes along depending on what we -- how we pursue.

I also have, I should tell you, two daughters whose own research takes them into dealing with very large subject populations. One of them is in general medicine and the other is in psychology and social work, both of whom, however, have gotten themselves involved in studying very large samples of human subjects. So obviously that is an interest I have in another dimension.

Finally, the only other thing I would like to mention is I have been a long time director of the Dow Chemical Corporation. They have all kinds of research projects going on, none of which at the moment, I think, involve anything related to human subjects. But nevertheless there is all kinds of issues that come up in that respect and I think it is just helpful to me if the fellow commissioners know about that.

I think that is all I want to say and I will go around this way. But again, please, if you prefer not to say something now that is fine, too.

DR. EMANUEL: I think I have three potential issues that I think the committee should know about. The first and probably most important is that I have been retained by the NIH here, Building 10, the Clinical Center, on a professional services contract to do bioethics work for them. Immediately upon hearing my appointment here I

notified our chairman who kicked it up to the general counsel's office and they have ruled on it. But I think everyone should know about that and that is an arrangement which is ongoing.

Second, I am a researcher. I do a lot of research with human subjects and in particular terminally ill patients facing life-threatening illnesses. I do a lot of interviews with them and participate in research in that regard.

I think, third, I should let everyone know that my wife is a vice-president of the AMA for ethics and also does research. So I have that, I guess, interest as well.

No financial that I can think of.

MS. FLYNN: Similarly, I have no financial potential conflicts. I think the most significant commitment I have already addressed. I have a personal interest in these issues because of a daughter with a serious mental illness.

As I think I also mentioned, more than one member of my family has participated in various research trials. I do not believe I mentioned that my organization supports a research program in which I have some responsibility, although it is not direct, in approving the research. But we do have some ongoing involvement at about the rate of $10 to $12 million dollars a year in research on psychiatric disorders.

DR. SHAPIRO: Thank you. Steve?

MR. HOLTZMAN: I am an officer and a significant shareholder in a biotechnology company that conducts genetics and genomics research. We conduct a significant amount of human genetics research inside and outside of the United States involving the collection of DNA samples. Under my direction we license and file patent applications which include composition of matter frames, preparation of genetic material and uses of the same. This bad enough yet?

(Laughter.)

MR. HOLTZMAN: And I co-chair the Biotechnology Industry Organization's Bioethics Committee.

DR. SHAPIRO: Thank you.

Bette?

MS. KRAMER: Nothing.

DR. SHAPIRO: All right. Thank you. Bernie?

DR. LO: I carry out research primarily on patients towards the end-of-life, but also on physicians as well just to give equal time to them.

In my other professional work I am on the Data Safety Monitoring Board for the AIDS Clinical Trials Group and for two for profit companies, GenenTech and Chiron, that involves looking over interim analyses of clinical trials.

My parents gave me some shares of stock in Abbott Laboratories, a tiny amount. I assume they are doing some research somewhere on some people.

(Laughter.)

DR. SHAPIRO: Larry?

DR. MIIKE: I am Director of Health for the State of Hawaii so I doubt very much that there would be real conflicts arising from any kind of the federal grants that we get. While I am Director of Health I am refusing any other kinds of outside resources.

I am more worried about my Playtex stock. Is that going to brand me as somebody?

MS. RUSSELL-EINHORN: We waived it.

DR. MIIKE: Okay.

DR. SHAPIRO: Thank you.

Tom?

DR. MURRAY: I do not own any stock except through mutual funds connected to retirement. I do not do any human subjects research. I research ideas and I guess informed consent has never been an issue here. I am on the Board of Directors of two professional associations, both of them not for profit. The American Society for Law Medicine and Ethics and I am on the Board of Directors. The title of the other organization is Executive Committee member and that is the Association for Practical and Professional Ethics. As you know, these are the sorts of boards with which it costs money to be on the board rather than is remunerative. I guess I have received waivers for those.

DR. SHAPIRO: Diane?

DR. SCOTT-JONES: I do not think I have anything at all that is a financial conflict of interest. I do research myself with children, teenagers and families. The research currently now is funded by the MacArthur Foundation, but I cannot imagine there is any real conflict.

DR. SHAPIRO: Pat?

PROF. BACKLAR: I think that my outstanding conflict is that I am an advocate for families and patients, but I actually also do, do some research on human subjects. Currently I am primary investigator for a small survey that is going on about supported housing services and does it address the needs of people with schizophrenia, their families and their communities, and that was funded by Portland State University in a faculty development program grant.

I am the primary investigator of a pending research to be funded -- it will be funded by NIH, which is a state survey of families and mental health providers to determine usage of Oregon's advanced declaration for mental health treatment. I am a co-investigator on another study which is pending at SAMHSA to examine the impact of managed care on seriously ill Medicaid patients.

DR. SHAPIRO: Thank you.

Arturo?

DR. BRITO: I do not have any financial interest or investments that would conflict. The research I am currently involved in is NIH sponsored. I am a co-investigator in an NIH sponsored asthma study. I am involved in several current grant writing for research of proposals that are from charitable contributions such as March of Dimes and Robert Wood Johnson Foundation, et cetera. So I do not think they will conflict and as they come along we will address them.

DR. CASSELL: My retirement funds, I think, have already been ruled on and, unfortunately for my future, I have no control over them.

(Laughter.)

DR. CASSELL: And then, of course, there is the inevitable conflicts that come from being of two minds about a lot of things.

(Laughter.)

DR. SHAPIRO: Only two minds.

Alex?

PROF. CAPRON: Well, I have no financial conflicts, although the waivers I got involved a lot of organizations like the Hastings Center whose board I serve, which I guess you deemed as a financial conflict. As Tom comments, that is the kind of organization where you end up losing money. My center and I personally conduct a certain amount of human subjects research involving ethics issues.

DR. SHAPIRO: Thank you.

Alta?

PROF. CHARO: Like Alex and Tom, I do not have any financial conflicts. I wish I had enough money to have those kinds of problems. Consider donating and divesting to me if you must.

(Laughter.)

PROF. CHARO: I serve on some boards like they do for which waivers had to be obtained. The American Association of Bioethics and the Alan Guttmacher institute. I think on a more pragmatic level the -- and this may not be limited to me, I do not know, I have served for many years off and on at various levels having to do with the oversight of research at the University of Wisconsin and on the All Campus Committee that has to help respond each year to the Multiple Insurance Agreement. I will assume unless there is a problem that I will be rotated back onto our local IRB.

There is one open investigation at our university for which I am both a witness and part of the team that is responding to OPRR inquiries following a scandal at another university that peripherally dragged in a whole bunch of universities around the country. So that I have also been on the receiving of OPRR's enforcement action in the form of trying to respond to it on behalf of an institution.

DR. SHAPIRO: Thank you.

Jim?

DR. CHILDRESS: I have no financial conflicts of interest. I did receive a waiver as a fellow at the Hastings Center. I have been a participant in a grant that is running out from a study, the education of professionals and the ELSI issues.

DR. SHAPIRO: Thank you.

Dave?

DR. COX: So I will put these in the order that I think are the highest potential for conflict and let's do the intellectual first. It is my interest in genetics in case you have not guessed. I mean, I am involved in the National Center for Human Genome Research up to my ears.

So the things that pertain particularly to this is being a member of the ELSI Working Group, being a member of the Genetics Testing Task Force. I am on the Council of National Center for Human Genome Research and I think that that could be -- might be perceived by some as a conflict. So I just want to mention it now. But, you know, that was not perceived in terms of having to get a waiver for it, but that is the one I would like you to know about. I do research that involves large scale human subjects and it is multicenter research collecting patient samples for hypertension. So that is a potential intellectual conflict.

I also have a financial situation and that is I am a

director and founder of a biotechnology company called Mercator Genetics, Inc. and although I do not -- there is not a lot of money involved there, but in particular because that is the company that recently discovered the chromatosis gene. We may be particularly talking about that particular disease here if that comes up. So that is one thing I would particularly like people to know about. And then I have a small amount of Genzyme stock.

DR. SHAPIRO: Okay. Thank you very much. Do you have anything you want to add, or say, or comment on?

MS. RUSSELL-EINHORN: No. Just let me add that do not put it past these statutes -- the Criminal Conflict of Interest Statute actually makes uncompensated service as a board member a conflict of interest. So just because something is not compensated does not necessarily mean that it falls outside of the guidelines. And we have particular trouble with that statute because it talks about being a board member or a partner, or a trustee and it is your status, not the fact that you are compensated or uncompensated.

DR. SHAPIRO: Tom, I think that includes negative pay as well.

(Laughter.)

MS. RUSSELL-EINHORN: That is right.

(Laughter.)

MS. RUSSELL-EINHORN: Anyway, I am always available

again if any specific situation comes up and someone wants to discuss it.

DR. SHAPIRO: Thank you. Any comments or questions from other members?

(No response.)

DISCUSSION OF FUTURE PLANS

CHAIR, MEMBERS AND STAFF

We have really just, unfortunately, a few minutes left this afternoon because at 4:00 o'clock we do have our public comment session and some people have been patiently waiting for that and we want to start it promptly at 4:00. It will be an important feature of all of our meetings and I think it is something which all commission members will benefit from as we hear from various people over each of our meetings.

But let me say something -- let me use a few minutes at least to say something about logistics. I have had a number of requests to meet at least once in a while on the West Coast and not all the jet lag on the shoulders of a small number, not so small, a minority shall I say, of our committee members. We will give that some considerations.

Yes, Tom?

DR. MURRAY: May I --

DR. SHAPIRO: Yes.

DR. MURRAY: -- I was talking with some members last night at the reception and my proposal -- I have a proposal.

DR. SHAPIRO: Yes.

DR. MURRAY: My proposal would be to do every second meeting in Washington, in the Washington area, and to do the alternate meetings some on the West Coast and some in

the middle of the country.

DR. SHAPIRO: We are going to give that very careful consideration as we look over our financial situation now that we have got that somewhat clarified. And we also, as Rachel reminded me earlier today, we have been invited or at least a number of universities have indicated they would like to invite us to their locations and some of that -- that might be a very useful way to do it depending on what the arrangements are and so on. So we will give this every consideration.

I have also had a request from the delegation from the West Coast, I guess I could call it, if we could start our meetings much earlier in the morning. In particular, start them 7:00-7:30 because that enables people like David, who do not seem -- and Bernie to fly in, arrive here at 5:00 and come to a meeting at 7:00, and then go back that night, which is a very economical use of their time. I hope they sleep on the planes well. But in any case that is something we are also going to consider.

I know for those of us on the East Coast at least broadly speaking 7:00 might mean coming the night before rather than that morning because we cannot get down, I guess, from Boston and come to a meeting at 8:00 o'clock or 7:30. But we will take a look at all of those issues and try to arrange something that both is reasonably equitable for members of the committee and meet some more

programmatic objectives such as meeting at different places and giving people in different parts of the country a chance to speak to the commission rather than simply always doing it here in Washington. So we will do that very quickly.

Secondly, we will in the next week-and-a-half to two weeks identify some working groups and proposed topics. We will consult with members of the commission probably largely through e-mail regarding some proposals in this regard. As soon as we settle down we will ask each of you to join on one or the other of these working groups because I hope our time at our next meeting that we will be able to hear back from these working groups some of the substantive issues. There are a lot of issues that have come up today for us to address. We obviously cannot do them all in the next six or eight months, but I think there have been some interesting possibilities.

I think that we can converge on at least a small subset which we all might agree or at least most of us would agree would be a useful number of first steps. So we do not have time to discuss that further, but you will hear very shortly from myself and the staff on some proposals. What I would ask from you is that you respond as quickly as possible because we really will need your input. Given the technology question response that is available these days we can really do this in a joint way even though we are not

meeting face-to-face.

We will very shortly, quite aside from our web site, will have some kind of capacity so that we can communicate easily with each other and I hope everybody's touch typing is up to par so that you can use these kinds of facilities easily. So you will hear quickly from us.

Are there any questions along those lines? Yes, Alta?

PROF. CHARO: Could you update us on the status of staffing and plans now that we have had a chance to find out about the money? I do not know if you have had a chance to think about --

DR. SHAPIRO: Well, no --

PROF. CHARO: -- what you could do with the money.

(Simultaneous discussion and laughter.)

DR. SHAPIRO: So the answer is no. It is not a good time to respond. However, as I have told other members of the commission today that is an issue which we had put on the back burner in part in order to see what our situation really was before making those kinds of plans.

I feel very fortunate with the staff we already have who have been working very hard and very effectively with us and hopefully will continue to work with us. But now that we do have this clarified over the next weeks we will lay some more definite plans. I appreciate the suggestions I have gotten in that regard from those members of the commission who wrote me on that particular subject.

Yes, I am sorry.

MS. KRAMER: Are these firm dates on the future meetings?

DR. SHAPIRO: Well, yes. They are firm dates. That is it is very hard to find dates for all people. We passed that out to everyone today. There should be a -- we will perhaps look at that once again, but we know we cannot find dates which everybody can come to. We know that from surveying. We have tried to make a fair distribution of that. That is we do not have -- we were not trying to satisfy some members and not others. We were just trying to do something that seemed reasonable in terms of what was available.

It is -- I can say something right now is apparent, there is not a date in which all members are going to be able to come. I was astonished that everyone came today because when we set this date it appeared that it was really not possible for many of the members.

Have people found that sheet of paper? That is available obviously from the staff. As soon as we get our web page up, of course, they will be available there for everyone who wants them.

Other questions?

Yes, I am sorry.

MS. FLYNN: I have a question that may be better answered by the staff. I know that we are wanting to have

a process that engages and involves a variety of people who may be considering these issues but were not able to sit at this table or sit in the rooms we will meet in. Is it your preference that those who would ask of us how do I share my views communicate directly in writing to the Office of the Commission or communicate to whomever they may know who are members of the commission? What would be the most efficient way to have that -- a dialogue that may be largely through e-mail or postal service?

DR. SHAPIRO: Thank you very much. I think the most effective way is to write directly to the staff who can respond most expeditiously to people's concerns. I am sure each of our subcommittees is going to have some set of meetings in which interested parties will be able to address issues of concern to them and as soon as we have established these subcommittees that will be, of course, public and widely known so people with specific interests can know who it is they might want to speak to.

MS. FLYNN: Thank you.

DR. SHAPIRO: Other questions?

DR. SCOTT-JONES: I have a quick question --

DR. SHAPIRO: Yes, I am sorry.

DR. SCOTT-JONES: -- about the meeting dates. Should we allow two full days then, the night before, or will we have to wait to find out?

DR. SHAPIRO: We are trying to get people to hold that

much time. We have not got the detailed schedule yet and until we make a little more progress we do not know how much business that we can productively do. So it is hard to answer that fully at the moment. We are hoping most people will try to keep those dates open. We may not use it fully. But I know if we do not start reserving dates it is impossible later to expand on them.

Other questions?

All right.

PUBLIC COMMENT

DR. SHAPIRO: There are a number of people who have written and wanted to talk to the commission. Let me tell you what the ground rules are. We have a half hour for this. We have approximately -- we have not approximately, I think we have six people signed up. That means between four and five minutes for each person. I hope they will not consider it impolite, at the time it reaches four minutes I am going to tell them they have to start winding up just in deference to others who want to also be heard by the commission.

Needless to say we are glad to receive written documents of any length from people who would like to address the commission in our ongoing proceedings.

So let me see, is Gwendon Plair here?

DR. PLAIR: Yes.

DR. SHAPIRO: Perhaps -- is that convenient for you to

sit? Either end would be fine.

MR. PLAIR: Thank you very much for this opportunity to speak here today. As I said before, because of the length of time I gave Ms. Norris a copy of my statement and what have you. But when I talked to you, Dr. Shapiro, you said it was a small group so I was looking for a real small group, so I made 10 copies, so she said she would make you some copies.

DR. SHAPIRO: We will produce copies for all of the members.

MR. PLAIR: Okay. I would like to spend my short time briefly giving you, hopefully, the highlights of what I would like to say to you specifically in two parts. One is speaking on behalf of the Task Force of which I am an executive member, the Radiation -- the Task Force on Radiation and Human Rights, here in Washington, D.C. It has members around the country, 34 member groups, and also as a son of a radiation experiment victim in Cincinnati, Ohio. I am speaking for those people.

Let me first say good afternoon to you, to Mr. Chairman, and also to the members here, and visitors.

My name is Gwendon Plair. I am the son of Ms. Beatrice Plair, Experiment Victim Number 044 at Cincinnati General hospital, which is now known as the University of Cincinnati.

Mr. Chairman, I would like to thank the NBAC Committee

for giving me this opportunity to speak on behalf of radiation victims and survivors of Cincinnati General hospital, the factory workers at nuclear plants, and the victims of radiation experiments around the country. I also wish to extend our thanks to Senator Glenn, who is not here, but we feel -- we thank him for his efforts, and also to the chairman of the NBAC, Dr. Shapiro, for his ongoing support on these issues. We met with him early and we really thank you for that opportunity.

I would just say that the statements that I have entailed in my presentation give an overview and background on how I came to be involved in this matter. The evolution of CRCSPCO, which is Concerned Relatives of Cancer Study Patients in Cincinnati, Ohio, of which I founded and developed as a grassroots organization supporting radiation victims around the country, also recommendations to the NBAC committee and also a closing statement.

First of all, I would like to just address very briefly remarks from the Task Force on Radiation and Human Rights. It is very important as you look at the relevance of radiation experiments to NBAC -- two, I will just approach -- there are three highlight areas. One is notification. There is a great need for the right to know before and after the fact if you are involved in radiation experiments.

As in my mother's case and other victims, we were not

aware that we were involved in radiation experiments before and after the fact. The other part that was mentioned in the advisory report is that of "no harm done." And definitely there was serious harm done. Death is harm done. Or the shortening of one's life is harm done.

Looking at remedies that we looked at, we look in terms of -- we focus you towards the bill, House Bill 3946, that also looks at government leaving the past issues unresolved, that is important that the families and victims around the country and plants, and even including our small children are looking towards this committee to review research and give input for resolution to this issue never happening again, to assure against more experiments' victims in the future.

The Advisory Committee on Radiation -- Human Radiation Experiments did not really get into prevention. You might look very closely at Katz, Dr. Jay Katz, who is on the President's Cancer Advisory Committee on Radiation and Human Rights, who gave an opposing view on human research and look at his views on that. I think that kind of points out exactly what we are talking about here.

We do not want to spend a lot of time talking about being not involved in this process in the past. Our understanding is that this group here of esteemed individuals has an opportunity to set precedence. As I told Dr. Shapiro in our brief meeting a short time ago it

is imperative that the victim survivors around this country be participatory not only in this opportunity speaking in the public in hearings such as this here, but it is very important that we be on the inside of this situation in your meetings, to have the public input.

Certainly if you look at the various comments made at the national conventions being an election year, inclusion is a very important part of what the public is asking at this point. We are asking you that we be included inside the doors at these meetings and we review suggestions and recommendations. We said this -- the same thing to the advisory committee and it did not happen. We are saying it to you again. We need to be on the inside of the doors in this process.

My colleague, Mr. Acie Byrd, will talk more about the national security issue as related to experiments a little bit further.

I would like to --

DR. SHAPIRO: Will you try to bring your remarks to a close? We are running out of time and there are a lot of other people who want to speak.

MR. PLAIR: Okay. All right. Okay.

I would like to close my remarks by saying this here, that there are several esteemed persons that I would like to cite here.

"The constitution is an important parchment that

protects all of us. It says, 'For the people and by the people.' Barbara Jordan told this to her colleagues on Capitol Hill. "All the people are important regardless to whom they are and where they came from.

Hillary Clinton said this at the Democratic Convention in Chicago: "We must do everything we can to make sure this never happens again."

President Clinton upon receiving the October 3rd release of the Advisory Committee's Final Report on Human Rights made the statement, "We must as a nation include all people in making this country great and problem solving rather than excluding some of our people in the process."

General Colin Powell at the Republican National Convention made the statement that basically says what we want to say, "We want to be inclusion, not exclusion in this process," ladies and gentlemen, if you really want to make an outstanding move forward in what happens next.

Thank you very much.

DR. SHAPIRO: Thank you.

Is Mr. Cossman here?

Mr. Cossman is from the College of American Pathologists. Welcome to our meeting.

DR. COSSMAN: Thank you. Thank you very much. Mr. Chairman, I am Jeffrey Cossman, M.D., Chairman of the Department of Pathology, Georgetown University Medical Center.

Today I have been asked to represent the College of American Pathologists, a medical specialty society representing more than 15,000 board certified physicians who oversee most of the patient laboratory testing that is performed in the United States. The College of American Pathologists accredits more than 2,000 clinical laboratories in America and is authorized to do that by the Federal Government.

We commend the commission for its attention to the bioethical issues that have arisen from medical research and genetic testing. My comments today will focus on just two areas specifically involving protection of patient rights with respect to laboratory information, particularly with regard to patient care and, second, research.

The College of American Pathologists supports the efforts to assure the privacy of medical information and the protection of both the public and the individual patient. The principle of confidentiality is a cornerstone of the patient-physician relationship and it is important to recognize for those of you who are not involved in patient care that information generated within the departments of pathology is often the most sensitive and personal in the patient record. Accordingly, pathologists have long held the tradition of developing and implementing procedures to guard the release of clinical laboratory information.

And why we bring this up at bioethics hearing, that is because retaining diagnostic specimens is essential for patient care and research. However, several proposed regulations have put this at risk. All tissues removed from patients undergoing diagnostic or therapeutic medical procedures are examined and interpreted by pathologists. However, only a portion of the tissue is usually needed for diagnosis. The rest is stored while maintaining confidentiality. This is the key issue. The pathologist is responsible for ensuring that the stored tissue is available for future diagnostic tests for future patient needs.

However, some recent proposals intending to protect patient privacy dictate that tissue cannot be stored with a patient identifier. It either must be discarded or anonymized. Under these restrictive conditions it would not be possible for the pathologist to determine whether a patient has come back to the patient with a second new cancer after having been treated for another or has an old cancer which has broken through previous therapy. Also, you would not be able to have your slides reviewed by a second expert consultant.

With regard to genetic testing, which is where these regulations arose from, pathologists are concerned that restrictions related specifically to genetic information are not applied so broadly that they encumber all of

medical care. Indeed, in the hope of protecting privacy for genetic testing, the public debate has grown to encompass far more than just genetics. We are now faced with constraints in all tests to the extreme that they could go even so far to disable the microscopic review of stored histologic slides as I just mentioned.

A detailed complex system for obtaining informed consent for each tissue sample for every prospective research protocol which has been proposed would be impossible to administer. These onerous regulations would create an overwhelming obstacle for medical research for patient care as we know it and would be a disservice to the benefit of the patient.

The development of new tests evolves continuously. For this reason the College of American Pathologists together with a consortium of 17 pathology societies have issued a signed document that supports the policy of existing standards for the protection of rights, including privacy, that can be extended to genetic testing. You have a copy of that which has been given to you at lunch time.

I will finish in the next twenty seconds.

DR. SHAPIRO: Thank you.

DR. COSSMAN: It is our opinion that federal regulatory agencies working together with professional societies can broaden the existing regulatory mechanisms which work and that these can now be used to encompass

genetic tests.

The community of research scientists, physicians and professional organizations will work with the regulatory agencies as they have in the past to develop the necessary guidelines to ensure the safety and privacy of the American public.

Thank you.

DR. SHAPIRO: Thank you for your remarks and thank you for providing us with a written version of your remarks. Thank you very much for being here today.

Mr. Charles McKay?

MR. McKAY: I have some materials for commissioners.

DR. SHAPIRO: Thank you.

MR. McKAY: At the suggestion of Dr. Gary Ellis I agreed to come and make a brief presentation to you today about a study that is about to go into the field sponsored by NIH. It is a study of the IRB system nationally that has been several years in planning.

I thought of developing slides for it but since I have been a bureaucrat so long I thought a thousand words would do better than a picture to describe it.

(Laughter.)

MR. McKAY: The materials will illustrate to you the scope of the study. We will do a census of all the extramural IRBs, nonfederal IRBs, in the country and that will cover some 445 institutions. Subsequent to that a

subset of the chairs and then a smaller subset of members, and then of investigators at each of these institutions will also be surveyed. We will also have some on site document extraction.

The method of the study will be to look at the IRB system as a system. The input, the throughput or output, the outcome and some of the questions of process. The materials I have for you have a detailed crosswalk table in matrix form that show you some of the 200 items we hope to identify in studying and translating the responses from the questionnaire and the document extraction to do confirmation and evidence of just what IRBs are effectively doing in their review of human subjects protocols.

I think it is important for you to understand something of the timing of this study so that you can make some plans with respect to your agenda. We anticipate the study will be completed and the results in, in spring of 1997. It may then be useful to discuss with you some preliminary findings before then, but we would hope to make available to you the results of the study at that time so that you could see what light they would shed on your own deliberations about any enhancement, or changes, or modifications in the IRB system.

We have been delayed in getting this study off the ground, but I think it is serendipitous because the hope I once had of somehow from within NIH erecting some sort of

august body is this, to be able to deliberate and make recommendations with some clout. Obviously we can get so far from where I was perched in the bureaucracy. You will have that opportunity and I hope you will find the findings useful.

One of the other documents I have taken the liberty to distribute to you is a brief study of the evolution of IRBs from the early stage of their endorsement by a lot of bodies through their actual being enfranchised in the Public Health Service Policy of 1966 and regulations of '74 to what is I have termed their empowerment through the latest version of the regulations that have been published and continued in the federal common policy.

The one thing I find absent in there that I would ask you to consider is I think it is imperative to make a translation not only of consent documents in understandable language, but I think the regulations themselves should be translated into layperson's language, made available to them so that they can understand what it is that is being asked of them, the mechanism, the protections. In other words, kind of a subject's bill of rights.

Some states have anticipated that. California for one has a bill of rights which is required to be distributed to any research subject under their jurisdiction. You may not be able to change the laws Professor Capron has indicated, but certainly you could endorse making this available as

part of OPRR's very widespread and important educational effort.

I thank you for your time. I will continue to be available to the staff should you have any further questions. Thank you.

DR. SHAPIRO: Thank you and thank you very much for bringing the materials with you. I will certainly distribute that to the members of the commission.

DR. SHAPIRO: Yes. Can someone just pass those along, sort of take one and pass it on kind of procedure here?

Now let me call on Suzanne Thomlinson.

MS. THOMLINSON: Right here.

DR. SHAPIRO: Oh, there you are. I am sorry. From the Biotechnology Industry Organization.

MS. THOMLINSON: Thank you very much, Dr. Shapiro.

I am here today on behalf of the Biotechnology Industry Organization, what we call BIO for short. I would like to offer the services of our organization as the commission's work proceeds. I would also like to share with you some of my personal experiences as a patient with cystic fibrosis taking a biotechnology drug and participating in clinical research.

First of all, BIO represents 680 biotechnology companies, academic institutions, state biotechnology centers, and related organizations around the U.S. and in 20 nations.

BIO companies are leaders in identifying the genes that cause disease and developing diagnostics and therapeutics for these conditions.

Today over 85 million people have been helped by biotech drugs, products and vaccines. Forty-two biotech drugs, products and vaccines have been approved in the United States. Biotech drugs help people who were suffering from once fatal heart attacks, kidney cancer and leukemia. And biotech diagnostic tests now keep the blood supply safe from AIDS. Other tests identify many diseases early enough for people to obtain more effective treatment. There are many more biotech drugs, vaccines and diagnostic tests in the pipeline.

Before discussing some of our specific concerns I would like to share with you my experience in living with cystic fibrosis. I was diagnosed with the disease in 1964. At the time little was known about the disease and how to safe a child's life. My parents were told that I might not live long enough to attend kindergarten. But thanks to medical advances in the last 30 years I have lived a very full life and achieved many goals, including obtaining a law degree.

I am now taking a biotech drug called Pulmozyme. It enables me to clear the mucus from my lungs more easily and to avoid hospitalizations for treatment of potential fatal lung infections. I started taking Pulmozyme in a clinical

trial in the spring of '92 when I was attending law school and working. Immediately upon taking the first dose of the drug I found I could breathe much easier. Because I coughed less frequently I had more energy for my schoolwork. In essence, it gave me a new lease on life. With Pulmozyme I was able to finish graduate school and to plan for a much greater future.

I have long been committed to medical research and I have personally benefited from it obviously. I have been a patient actually at the NIH for 15 years and I have participated in a variety of clinical research studies. I recently participated in a study up at Hopkins last April.

I have sought employment with the biotech industry because I believe in the promise of research. I believe the biotech industry is the cornerstone for today's research for tomorrow's cures. My life was lengthened by medical technology in the '60s and by biotechnology in the 1990's. I want to help others who are not as fortunate by encouraging the development of this technology to treat and cure cystic fibrosis and other diseases.

We believe the biotech industry plays a critical role in the debate on bioethics. We are committed to speed the development of new therapies and cures. We are well aware of the need for public education to address some of the suspicion and distrust of science and scientists. We have conducted focus groups around the country to gain insight

into people's thoughts on this technology and its potential uses.

As a bioethics counselor for BIO I work closely with the co-chairs of our Bioethics Committee, Elliot Novac of Genzyme Genetics and Steve Holtzman of Millennium Pharmaceuticals. We are pleased that Steve serves on this commission. We believe his sensitivity and practical knowledge of bioethics issues will contribute greatly to the work of this commission.

Our Bioethics Committee is fashioning guidelines concerning the ethical implications of our work. We have three task forces actively working in the areas of gene patenting, genetic information and responsibilities of biotechnology.

We are pleased to note that our Board of Directors recently adopted a statement on the need for medical privacy. Our statement calls for strong protections against the misuse of all personal medical information, including data derived from genetic diagnostic tests. We agree with Dr. Collins on the need to address the privacy of all medical information because genetics is a part of the statute of medical information.

We plan to work with the next Congress on a comprehensive medical privacy bill to include genetic privacy as a subset of that. We also believe that there needs to be standards to protect confidentiality of medical

information that should ensure that legitimate and vital medical research will continue and is facilitated.

We supported the provisions in the Health Insurance Act that was recently passed to protect against misuse of genetic information for insurance.

We are concerned about the issue of gene patenting. We believe this is an economic issue and not a bioethics issue.

We support the continuation of the current law to allow patenting of human genes if the applicant meets the necessary criteria for securing patents. We do not believe exceptions should be made for patents on genes, life forms or other subject matter.

We are committed to our work in bioethics and we want to set exemplary standards while ensuring our nation's biomedical research continues and we look forward to working with the commission as we delve into these issues.

Thank you very much.

DR. SHAPIRO: Thank you very much. Thank you very much for being with us today. We appreciate it very much.

Let me now call on Lisa Angerame if I have pronounced her name correctly. If I mispronounced it, I apologize.

Is Lisa here?

Okay. I assume the answer to that is no.

Mr. Byrd? Mr. Byrd?

Incidentally, the beeps that the speakers hear are not

someone's pager going off, but that means time is up.

MR. BYRD: Thank you very much for inviting us here and I appreciate this opportunity for the Atomic Veterans to have a chance to speak to you today.

I have some copies here if I can pass them around.

DR. SHAPIRO: Sure, absolutely. We will pass them around for you.

MR. BYRD: Okay.

DR. SHAPIRO: Do you want to just pass them up this side? Thank you very much. People just take a copy and pass it around.

MR. BYRD: The final report of the President's Advisory Committee on Human Radiation Experiments provides dramatic insight into the lengths to which the Federal Government went during the Cold War era to justify its use of innocent unsuspecting citizens in the name of "national security." Nowhere during these years was the conflict between national security and the right of individuals more prevalent than in the conduct of the nuclear weapons testing program, particularly in the military treatment of its soldiers, the "Atomic Veterans."

Obviously there are a number of issues that emanating from the Advisory Committee's investigation of the radiation experiments that deserves NBAC's attention. We submit to this commission the most profound among them and the ones which will ultimately determine the commission's

relevance to the charge that has been handed to you by President Clinton, is that of the right of the individual, particularly those in the military, versus the perceived needs of national security in the area of experimentation and human research.

Let there be no doubt about it, that is not a historical issue, but one with which the present administration wrestles even as we meet here today. The best example of this point we made was aired just this last Sunday on the CBS show, 60 Minutes. The subjection of the Gulf War military personnel to experimental vaccines and drugs without their informed consent.

Now as mentioned in the conclusion to that show and as evidenced by the attached article which appeared in the Detroit Free Press earlier this year, the Food and Drug Administration is now under pressure from the Pentagon to make permanent an FDA interim ruling that allow the military to use biological and chemical investigation products on troops without their knowledge or informed consent.

The justification is the very same that was used to justify injecting plutonium into the veins of unsuspecting patients at Rochester, New York, during the Manhattan Project years, and to justify subjecting testicles of prisoners at Oregon State Prisoner to radiation during the '60s, and to justify subjecting Black patients in

Cincinnati to whole body radiation in the early 1970's, and to justify exposing those who fought in the Gulf War in the '80s to experimental products. All with the need of national security.

Those of us who were at the front lines of democracy during the Cold War years submit to you that Atomic Veterans are not a historical curiosity, but a living testament to the challenges that now confront you, the National Commission. And I think that is one of the main issues we would like to have this body examine very closely since you have just -- it has just been revealed and now the numbers of Gulf War veterans has been extended from 15 to possibly 100,000.

I think this is the characteristics of what -- characterizes I should say of what has taken place historically with veterans and we think that there is a definite need to be more precise on setting some guidelines and standards that respects the constitutional guarantees of citizens, as well as the human rights guarantees that are available to all citizens with regard to this.

DR. SHAPIRO: Thank you very much. Thank you for your remarks and thank you very much for bringing copies of your testimony which has now been passed around to all members.

MR. BYRD: Thank you.

DR. SHAPIRO: Thank you.

Mr. Robert McMurrough?

MR. McMURROUGH: Thank you. Good afternoon. Thank you, Mr. Chairman, for the opportunity to talk today. This is on the subject and in support of the Executive Order 12975.

My name is Robert McMurrough and I am currently the Committee Chairman for CDC HIV/AIDS Prevention and Community Planning; and HRSA Title 124, Patient Care for the State of Florida, Office of Disease Intervention, a statewide group. I am a member of the FDA AIDS Health Task Force specializing in harmful treatments and therapies that are geared towards people living with AIDS and educating the HIV/AIDS community on fraud.

The ultimate priority in my life at this time is living with HIV/AIDS. I have been a clinical AIDS drug trial patient here -- subject at NIH since 1992 at NIAID taking the chance to further research. In the last past year I have participated in a private trial by Merck Corporation receiving the protease inhibitor Tryptophan Inhibitor Sulfate. My participation proved to be a tremendous turnaround in my life and I continue today.

This was through a national IRB and my doctor had to do this all on her own to get me to participated in this with Merck's supervision.

Currently I am on a treatment IND for the mammalian recombinant growth hormone, Serostem (?), which was released by the FDA for wasting syndrome, which causes

26 percent of all deaths of people who live with HIV.

In all cases I have signed informed consent and I am educated and I know my choices of risk when I participate. This is not always the same for others.

My concerns are that with the wave of the new drugs and the quick approval that we seem to be having. I applaud the efforts of this Executive Order and that the Bioethics Commission will place the highest priority on the rights and welfare of human research subjects, as myself. And the current situation allows any person to participate if they are qualified but that does not always mean that they have PAR, which is "parody, inclusiveness and representation," in knowing what they are getting into.

I urge the commission to promote education on choices and empowerment to the subjects, to continue to work with researchers in response to any risk that might be incurred. Researchers doing it outside our system or guidance is detrimental and destroys credibility.

Your new commission can take leadership, because of its expertise that it has at this table, and strive towards a level of safety to all of us that participate and deserve confidentiality, choice, education of subjects and research is ensured. Our research is the best in the world here at NIH and around and our subjects are our greatest assets.

Congratulations on your new commission, its diversity of its staff. My life and lives of others alike will look

to you for our protection to be evaluated and ensured giving us long-term survivorship with HIV/AIDS along with medical research superiority, along with that with our working with other countries to make this international disease pandemic come to an end.

I offer my own support and consultancy to this commission at any time free of charge with no conflict of interest to ensure that there is always a person who is living with this disease, which of course NIAID spends a great deal of money on research on for that.

So as a person living with HIV I commend the President of the United States for putting this commission together. Thank you.

DR. SHAPIRO: Thank you. Thank you very much for your comments.

Unless there is further business to come before us today, I am about to adjourn this meeting.

We are adjourned. Thank you very much.

(Whereupon, the proceedings were adjourned at 4:37 p.m.)

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