



CENTER FOR BIOMEDICAL ETHICS

School of Medicine
Case Western Reserve University
2119 Abington Road
Cleveland, Ohio 44106

THOMAS H. MURRAY
Director

file ethics

3/8/89

Dear Elke,

I have 3 lists that might be useful for you: a list of Ethics Centers/Programs; the list of people attending the last Society for Health and Human Values meeting; and the list of adjunct associates and Fellows of the Hastings Center. (I got Sam Callahan's permission to send the last item.)

There are some foreign addresses and others you may not want. But these are a good starting place.

Call me if you want to discuss any of this.

Best,

Tom

ST. CLOUD STATE UNIVERSITY



College of Social Sciences

Office of the Dean
St. Cloud, Minnesota 56301
612/255-4790

January 27, 1989

Dear Colleague,

Enclosed is a copy of the ethics centers list which I promised you earlier. This version reflects the changes you sent and, in some cases, phone inquiries.

I recognize that many of you have specialized interests, but a general list seemed to be a more practical alternative for me. I hope that the list will enable you to maintain contact with others in the field.

If you wish to make further corrections, please write. I will endeavor to keep the list current and up-to-date.

Cordially yours,

A handwritten signature in cursive script that reads "David L. Carr".

David L. Carr
Assistant Dean

file ethics

College of Physicians & Surgeons of Columbia University | New York, N.Y. 10032

DEPARTMENT OF PSYCHIATRY

722 West 168th Street

May 4, 1989

Dr. James Watson
Cold Spring Harbor Laboratory
P.O. Box 100
Cold Spring Harbor, NY 11724

Dear Jim,

I am pleased to tell you that Jon Beckwith has accepted to be a member of the Ethics Working Group and is looking forward to being part of the discussions. We hope to have the first interdisciplinary workshop in the Fall, October or November. This workshop would set the research agenda for the critical issues which need to be first addressed by the Ethics Working Group.

I had a talk with Eric Lander recently who told me of his involvement in testifying against Life Codes. Eric feels there are at least two people in jail erroneously because of shoddy interpretation of gels. There are no standards, no quality control and no accountability. With the increasing penchant of this country toward the death sentence, mistakes are even more hazardous.

It may be that standards could be set by courts through common practice, without lengthy legislation. Once one court has adopted rules, the others can follow suit through precedence. This is apparently the way standards were set for the use of voice prints in trials, according to Eric. The Ethics Working Committee might want to consider a special workshop in this area, explicitly to set standards in the forensic use of DNA technology. This could be one concrete way of rising to a perceived need created by DNA mapping. We are being proactive in responding to what could be deleterious legal consequences.

If we do not take the lead in this effort, I am certain that others will and should. It is too important to lie fallow. There also may be reasonably straight forward ways of insuring quality control, such as requiring more than one individual to read an autorad, taking steps to insure that a DNA sample is actually from the person in question, etc.

I would be interested in hearing your thoughts as to whether the forensic use of DNA technology should be within our purview.

Sincerely,

Nancy
Nancy S. Wexler, Ph.D.
Associate Professor of Clinical Neuropsychology

Columbia University
College of Physicians and Surgeons

DEPARTMENTS OF NEUROLOGY
AND PSYCHIATRY

To: ~~Betty Graham Elke~~

From: Nancy S. Wexler, Ph.D.

Date: 10-3-89

I also
have a
copy
Betty

- Noted
- For your file
- For your information
- Please note and return
- Please give appropriate attention
- I'd like to talk this over with you
- Please advise and comments
- Please handle
- Please reply with copy to me

* Will FAX the list
you need next Monday
or Tuesday when
Dr. Wexler returns.

Judy Forner

CALIFORNIA INSTITUTE OF TECHNOLOGY

DIVISION OF THE HUMANITIES AND SOCIAL SCIENCES 228-77

March 30, 1989

Nancy S. Wexler, Ph.D.
Associate Professor of Clinical Neuropsychology
Department of Psychiatry
College of Physicians & Surgeons of Columbia University
722 West 168th Street
New York, New York 10032

Dear Dr. Wexler:

I am responding to your letter of 9 March 1989 asking for proposals for the Ethics Subcommittee of the Advisory Committee to the Office of Human Genome Research. As you can see, I am a visitor at Caltech for the spring term, so my first inclination was to go speak with Dan Kevles whose office is across the hall from mine. I was gratified to find that he and I agreed in large measure about the basic questions that could be usefully explored at this time. I expect that he has already written you, in far greater detail based on his own knowledge and research.

Like many historians it occurs to me first to ask in what way today's conflicts are connected to conflicts of earlier periods? And if these connections do exist, in what way the associations between past and present are meaningful? Two classes of issues arise from this approach: first, issues associated with new knowledge and techniques and second, issues associated with the structure of conflicts in different social environments.

With respect to new knowledge and techniques, clearly your committee will be concerned with identifying those salient characteristics of power and efficacy that are immediately troubling. I also believe that distinguishing among specific populations and contexts in which new knowledge and technique is different from the past, or similar, would be useful. I found in talking with Dan Kevles, for instance, that he assumes the public and the medical profession agreed about a broad range of medical ineffectuality in the past. As I suggested to him, and as I know you know from your own research, historical and cultural contexts shape both professional and public experience of efficacy. It seems to me that this is a subject that a careful case study might illuminate.

My own view is that the most important research will be in the area of understanding the structure of conflicts and how this has changed over time. I am particularly interested in how the law and public opinion and the law and public policy intersect. My interest begins in vast ignorance, but it occurs to me that understanding the changing role of law and the legal profession is critical for knowing and guiding the implication of genome research. I do not know whether you have made inquiries of scholars in this field. If not, let me recommend Lawrence Friedman, a professor of law and legal history who is a member of the faculty at Stanford. I believe that he is visiting at Princeton this spring and might be more easily consulted as a result.

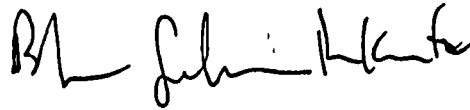
Nancy S. Wexler

2

March 30, 1989

My best wishes to you and your colleagues in this exciting and important project. I look forward to learning more about your plans as they develop.

Sincerely,

A handwritten signature in black ink, appearing to read 'Barbara Gutmann Rosenkrantz', written in a cursive style.

Barbara Gutmann Rosenkrantz
Sherman Fairchild Distinguished Scholar

Enclosure

br/gm

CALIFORNIA INSTITUTE OF TECHNOLOGY

DIVISION OF THE HUMANITIES AND SOCIAL SCIENCES 228-77

April 7, 1989

THE J.O. AND JULIETTE KOEFFLI
PROFESSOR OF THE HUMANITIES

Professor Nancy S. Wexler
Department of Psychiatry
College of Physicians and Surgeons
Columbia University
722 West 168th St.
New York, New York 10032

Dear Professor Wexler:

To respond to the request, in your letter of March 9, for thoughts and suggestions as to what the Ethics Subcommittee of the Genome Advisory Committee might consider doing: First, for an easy recommendation, I would think that the subcommittee ought not to take up questions in gene therapy. The principal product of sequencing the human genome will be information, which by itself raises a broad enough spectrum of difficult issues. Issues arising in connection with gene therapy would seem to fall more in the area of human subject research or medical practice.

I would say that the most important agenda item for your subcommittee should be to try to sort out what may be new, or at least relatively new, about the challenges that analysis of the human genome seems likely to raise from what is not. A good many of the challenges are not sharply new. For example, how to handle information about any individual's genome would seem to fall into the category of how to handle medical information of any kind -- a subject on which there already exists a body of social thought as well as legal precedent and discussion. This body of thought and precedent encompasses both access of employers and insurance companies to private medical information, on the one hand, and, on the other, the obligations of the medical profession to tell patients that they may obtain and use such information about themselves. (I have in mind, with regard to the latter, various court cases that have held physicians liable for not informing women over thirty-five, for example, of their risk for giving birth to Downs syndrome children.)

Information developed from human gene sequencing will no doubt speak to group differences in the human family. Clearly, what data is sought concerning the human genome and how that data is used are questions that need to be examined carefully. Here again, precedent would provide insight. There is considerable historical material concerning the misuses of scientific information to stigmatize, ostracize, and foster discrimination against minority groups as well as women. Much of the "information" proved to be wrong, though it was accepted as sound in its day, often by members of the scientific community.

What may be relatively new about the challenges raised by the human genome project involves diagnosis and prognosis of individual human futures. I have in mind here the likelihood that human gene sequencing will be able to predict a diseased child's -- or a fetus' -- medical fate long before any therapy is available. The availability of this information can produce profound emotional and psychological problems for the individuals concerned. However, I use the phrase "relatively new" in this context because human genetics can already diagnose many more diseases than it can treat. Thus, a good deal of thoughtful discussion has gone to this area, too.

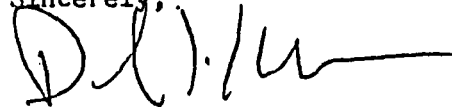
The information that arises from sequencing the human genome will obviously modify the legal and social thinking that has already resulted in these prior areas. My point is that consideration of the ethical issues should pay attention to precedent, while recognizing that precedent will not entirely suffice. This is to say that approaches to the ethical issues would benefit from the input of historians, experts on medical law, ethics, and economics, philosophers, and practitioners of both biology and medicine.

Equally important, I would urge strongly that all attention given to the ethical issues related to the human genome project be tied closely to the scientific realities of what is actually being learned - - and is likely to be learned in the reasonable future -- rather than to fantasies. It would be a waste of time, for example, to put any effort into ethical problems that may arise from our ability to engineer new human beings or modify existing ones in major ways.

It may interest you to know that Lee Hood and I expect to run some informal discussion sessions with interested faculty here at Caltech next academic year on social and ethical issues connected to the genome initiative. We would be very eager to have you participate in one of these sessions. Do let me know if you would be interested. The sessions are intended to be part of a small program in Science, Ethics, and Public Policy that I have started at Caltech, which will have linkages with Lee's NSF Center for sequencing technologies.

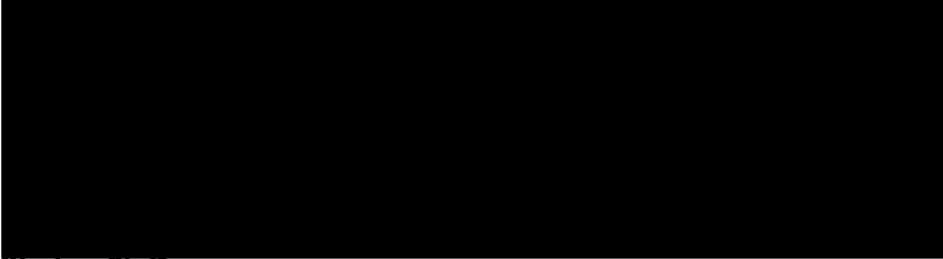
In any case, I hope that you will keep me informed about the activities, programs, and publications of the Ethics Subcommittee.

Sincerely,



Daniel J. Kevles

Robert Muller Cook, D.D., M.D.



Nancy S. Wexler, Ph.D.
Department of Psychiatry
Columbia College of Physicians and Surgeons
722 West 168th Street
New York, NY 10032

Dear Nancy,

This letter is in reply to your letter of 9 March. I apologise for the delay in getting back to you, but the Senate members of the Biomedical Ethics Board met on 8 March and found themselves in deadlock over election of a chairman and appointment of a final member of the Biomedical Ethics Advisory Committee. This has cast the future of both into serious doubt, and I have been trying to keep a low profile. It now appears that the BEB and BEAC may go out of existence via next year's appropriations process. My own future is somewhat unclear. I am not worried about having a job, but I also have no idea what I will be doing come October 1, unless there is progress.

As you know, the BEAC had a legislative mandate to look at the implications of human genetic engineering. We had planned to frame a project around the following areas:

Human Gene Therapy

Somatic cell therapy: to express the consensus among religious groups, governments, and secular groups that treatment of genetic diseases is acceptable in principle, and morally equivalent to using a DNA drug.

Germ line therapy: to express the lack of consensus about its appropriateness. I hoped to focus on four aspects in particular. First, whether germ line therapy would be called for at all, since selection of normal embryos would involve the same technologies but would not involve the added risk of DNA insertion. Second, the need for technical improvements to make transgenic expression reliable enough for clinical application. Third, to raise the issue of deliberately and directly causing inherited change (comparing and contrasting with inadvertent changes such as caused by radiation or chemotherapy on the one hand, and indirect gene pool effects caused by non-DNA treatments of genetic disorders, on the other). Fourth, to note the fact that germ line interventions are most likely at the early embryonic stage, and thus would be impossible under federally funded research until the IVF and fetal research bans are lifted.

I hoped to pose the clinical situation, not unlikely to arise in the future, in which a mother and father both have PKU, sickle cell disease, CF, or some other genetic disorder. (Perhaps they would have fallen in love in a genetics support group.) This would bring the fundamental ethical issues starkly to the fore. Would society ban their marriage (almost certainly not)? Would it circumscribe their choice to have children (probably not)? Would it prevent them from germ line intervention if it were reliable and if it were the only or the most effective treatment? If not, would the child be given access to health care (almost certainly yes)? The last two questions

point out the conflicting values, in that it would make little sense (in my opinion) to permit treatment of a child after born, but disallow the means to prevent disability by the most effectively just because it had to be administered to an embryo and involved DNA rather than a drug or surgery. I do not know where this would have led, but I hoped that it would further the debate by making it a bit more concrete.

Enhancement of desirable characteristics. This seems, according to the OTA poll of several years ago, to be much more important to the general public than the somatic/germ line distinction. People in that survey were overwhelmingly in favor of treating a fatal disorder with DNA, regardless of whether it caused inherited changes or not, but were much less accepting of selection for gender or intelligence or athletic ability. This seems to be the more important moral distinction, but there is no bright line separating disease from genetic character. In extreme cases, the appropriate model (social versus medical) is clear, but there are many cases in which a disease is at least debatably a social construct as much as a medical problem. Yet some of these characteristics may well have genetic components. Alcoholism, short stature, and fragile X syndrome are good examples of difficult cases. Again, I am not sure where the analysis would lead, but I think this is where the debate needs to be made more concrete.

LeRoy Walters had also alerted us to monitor whether conflicts arose in having NIH act both as promoter and regulator of gene therapy research. He raised the issues of whether current review is too cumbersome already, whether the right people are in place to review protocols (he thinks so), and whether the regulatory function shouldn't be moved higher up the ladder within DHHS to avoid conflicts (even though the current system seems to work well for gene therapy, there are troublesome conflicts regarding animal and human subjects research, and regarding research misconduct).

Genetic Testing and Screening

BEAC had already agreed that one likely conclusion of the genetics study would be that the real issues in human genetic engineering are more in the area of testing and screening than gene therapy (particularly regarding enhancement and germ line interventions, which are not even seriously contemplated now). The committee had not framed how to approach testing and screening. The obvious starting point is the debate about mandatory and voluntary testing. The NAS and President's Commission did much good work in this area, and there is even more sophisticated analysis of related issues raised by HIV testing underway now. I think our distinct contribution would have been in a few areas.

First, fairness and privacy issues related to presymptomatic testing. As you know better than I, the impacts of genetic testing are particularly complex for this application. There are issues of technical validity, specificity, and sensitivity of the tests themselves, particularly if they rely on linkage to markers tests rather than allele-specific tests. Second, the linkage of testing to counseling and education is an issue. And finally, the nonmedical uses of tests and test results are potentially controversial -- particularly in light of uncertainty about how information would be used by employers (or prospective employers), insurance companies (long-term care insurance coverage of AD or HD is a particularly interesting example), and the general public (regarding disease stigmata or reinforcement of racial prejudice).

Second, it would be interesting to see how genetic conditions should be handled for purposes of protection under the law. Should they be handled like gender (one can discriminate sometimes, but not always), race (one can rarely discriminate), or disability (with a presumption of nondiscrimination, but criteria for when it is acceptable).

What would be the consequences of adding genetic nondiscrimination clauses to civil rights laws? To the Rehabilitation Act?

Third, is there a need for legislation to regulate dissemination of and access to genetic information? To what degree are results of genetic tests just like other medical information, and to what degree are they different? I have not thought enough about this to reach any conclusions or erect useful conceptual frameworks, but BEAC had begun to discuss these issues.

Eugenics

BEAC heard a lecture from Dan Kevles about the historical roots of eugenics and racial hygiene movements in the United States and Europe earlier this century. The committee had tentatively agreed that this was quite important to keep in mind, but should be analyzed by reference to historical precedents when talking about therapy and diagnosis (testing and screening). There would thus be no separate historical analysis, except perhaps a set of summary points relevant to future policy decisions (e.g., that state intervention in reproductive decisions is highly suspect).

Human Self-Conceptions

The issue here is whether the explosion of knowledge about human genetics, likely to come as a flood of incremental reductionist particles, will reduce conceptions of the sanctity of life. This is really a replay of the Huxley-Wilberforce debate about whether it is an honor or a stigma to have an ape as an ancestor. In Tom Murray's image, does understanding the score of a symphony detract from its beauty as music? People will fundamentally disagree on this, I believe, and this must be directly confronted. New knowledge will doubtless change how we think about ourselves, and new technical opportunities will likely provide means for human "engineering" such as that discussed by Jonathan Glover in his book What Sort of People Should There Be?. I do not know how to frame this issue, however, as attempts to make it more concrete inherently "technicalize" the issue. This leaves out the emotional and cultural factors that are inchoate more than articulated, and thus entirely misses the point. The problem, stated one way, is that a future society may acquire moral values different from currently acceptable ones. Another way to see it is a "ethical drift" propelled by new technical means (e.g., how IVF threatens traditional notions of parenthood). Some people see the resort to such technical means as a loss of fundamental values. Is this good or bad? How can such issues even be framed?

Mapping and Sequencing the Human Genome

BEAC had agreed to wait and see what other groups do on this, but to keep abreast of developments in your NIH subcommittee, the EEC, UNESCO, and other foreign projects.

For purposes of your subcommittee's work, I would suggest that the place to start is genetic testing and screening. First, it is important to establish whether and to what degree mapping and sequencing efforts are likely to accelerate the availability of genetic tests. Second, technical considerations differentiating types of tests are important (RFLP versus allele-specific). Third, some specific issues regarding testing and screening are more pressing than others, and I would suggest addressing pressing matters first. These could be divided into work-related (pre-employment screening, genetic monitoring in the workplace, and linkage to health insurance), civil rights-related, and general (issues of prejudice beyond the law, and impacts of human self-conceptions). I also believe that issues of genetic screening of neonates will come to the fore as states contemplate updating their laws in light of new technologies.

Later on, it would be useful to discuss how medicine will adapt to genetics. Genetics is at the core of human biology, which in turn underpins medicine (although not delivery of health care, which is a social phenomenon). It is my belief, based at this point only on an un-rebuttable intuition, that genetics has to date been conceptualized for purposes of public policy as a problem of reproductive decision making and perinatal care. This is because most "genetic" diseases, as traditionally defined, were pediatric in expression. I believe this will radically change, as the genetic components of other diseases are better understood -- from cancer to Alzheimer's disease to so-called mental disorders. This will likely challenge our way of thinking about medicine, and will expose some underlying inconsistencies (e.g., how "mental health" services are separately organized and financed from "medical" services; also true for "long-term care" services).

Genetic services have always been somewhat distinct from other medical services in taking care to recognize the autonomy of those being counseled or tested. I doubt that this distinction will survive the movement of genetics into mainstream medicine, but perhaps the norms of genetic counseling will drag medicine into its value system rather than the other way around.

Who will be trained to understand the new genetics, and what will happen before physicians and other health professionals begin to learn about genetics routinely in training? As you know, the notions of RFLP testing, interpretation of genetic tests, and projection of their meaning for clinical prediction are difficult to master even for specialists trained recently. What is going to happen when (not if) these methods are made available to practitioners, most of whom never even had a course in genetics (even less, of recombinant DNA)? This is more a health policy than an ethical issue, but it is certainly worth raising.

There are some issues that relate directly to NIH-funded work. These include privacy and information exchange guidelines for the families and others who are the human subjects of the mapping enterprise. The Huntington's group had some specific guidelines for access to the database, but I wonder if these are practical for a much larger effort that involves many cultures and nations. What are the guidelines for use of CEPH families? What will be done to communicate risks of disease to those in the CEPH or other research pedigrees, for example, when new disease markers are discovered? Who will be able to use the data, with what degree of knowledge about the clinical histories of the individuals involved, and under what privacy constraints? The problems are much more complex than for single-disease research, because the number of potential discoveries is much greater, the number of researchers is much greater (complicating the informal lines of communication that regulate so much of research now), and the sharing of information is so important (otherwise maps cannot be constructed or disease linkages identified). This is a set of first-order questions that will have to be addressed even as genetic mapping proceeds.

Prenatal genetic testing raises issues that should be addressed, but I seriously question whether the federal government is the place to do so. Prenatal testing is a small but important part of existing genetic services at many centers, and the practice of abortion following prenatal testing is repugnant to some and ethically wrenching for all. This may vex many scientists, but this is a democracy and all have a vote, especially when the expenditure of federal funds is in question. The issues are real and important, but I do not think that the politics make it possible for a federal agency to deal with them productively. In fact, NIH might put its entire genetics program at risk by trying to do so. The best option for the committee might be to acknowledge the issues, recognize that they are inherently complex and divisive, and use whatever informal means are available to have private groups dedicate their efforts to wrestle with the ethical issues. This might mean informally enticing a university, professional, or foundation group to sponsor activities bearing on the issues.

A few practical suggestions. It was my hope that BEAC would be able to commission a broad public poll that bears specifically on gene therapy, genetic testing, and genetic screening. When we did the OTA survey related to biotechnology, we learned much more than just how the public responded to the questions we posed. The process of convening focus groups, framing questions to get at the issues we wanted to address, and analyzing the results of the survey was extremely instructive. The focus group meetings held as we began to develop an instrument were particularly memorable, and exploded many of our preconceptions about public ignorance and inability to reason through technically complex issues. There are, of course, inconsistencies in the responses, but such inconsistencies are themselves reliable indicators of conflicting values that are likely to emerge as political and social issues. I strongly urge that a major poll be financed early on.

When the poll results are in, then I believe that it would be useful to hold a series of "town meetings" throughout the United States. Some folks at the University of Utah have expressed interest in this idea; a BEAC member, Julianne Beckett, suggested also that arranging some public meetings in coordination with genetics support groups would greatly assist in identifying current issues. It would also go some way to fighting the tendency to "group think" that can so easily intrude on small group deliberations about ethical issues.


I apologise that this letter is so long. I did not have time to make it shorter. Please do feel free to contact me if I have been unclear, or if I can be of help in any of this.

Best wishes and good luck!

Sincerely,



Robert Mullan Cook-Deegan, M.D.

PD: Hope to see you soon!


Biological Laboratories

Harvard University



Dr. Nancy S. Wexler
Department of Psychiatry
College of Physicians and Surgeons
Columbia University
New York, NY 10032

Dear Dr. Wexler:

I am sorry I have been so slow to answer your letter of March 9. I have not found it an easy letter to answer.

As I am sure you know, I have grave misgivings about the ethical and political impacts of the Human Genome Project. One of the principal reasons is that it directs too much attention to what usually can be identified only as genetic correlates of particular traits. Yet these correlations are then promptly treated in the general press (and by some scientists) as though they caused those traits.

Furthermore, to the extent that genetic correlates will be identified with some measure of reliability, diagnoses are bound to precede therapies by years, if information at the level of the gene can lead to therapy at all. Presumably it will do that in some cases, but who knows in how many. I have little confidence that standing conventional genetics (that is, deducing information at the level of the gene from information at the level of traits -- be they anatomical or functions) on its head, by trying to deduce traits from genes, will prove useful or even will work at all.

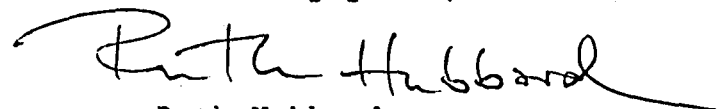
I am sure that, having thought about Huntington's to the extent you have, you must be aware of these problems and I would love an opportunity to talk with you and find out why you continue to be supportive of the Human Genome Project. I have been concerned with similar problems in connection with retinitis pigmentosa, which was something I was very interested in while I was still working in vision. And I should tell you that I resigned from the scientific advisory board of the Retinis Pigmentosa Foundation when they decided to go all out for trying to identify the "RP gene" in the sex-linked form of the disease, with hopes of moving on to the autosomal dominant and recessive forms.

I realize that some people want to know diagnoses even when no treatments are available. But I feel strongly that there has been entirely insufficient discussion and debate about whether it is appropriate to put in this level of effort to generate a whole range of such potential situations, particularly in view of the uncertainties that will inhere in many of the predictions until they have been tested in practice.

For all these reasons, and many more, such as the ones you mention in your letter, I believe that the ethical and political issues are at the core of the Project and that they need to be considered *before* specific projects to identify genetic correlates of particular diseases are launched. I do not think they can be dealt with adequately by relegating one to three percent of the budget to "studies and activities in the area of ethics and society." To my way of thinking the entire Genome Project falls into this area.

I understand that you will participate in the meeting the Genetic Screening Group has put together for April 29 and wonder whether it might be possible for us to meet on that occasion. I watched the Nova program on Huntington's and was very impressed with the entire program as well as with your part in it. I would very much like a chance for us to talk more fully. If before or after that meeting are not good times for you, maybe we could arrange some other time, either here or in New York. I am not teaching this term and am usually working at home. So, if you would like to call me and I am not at my office, please try me at 617-868-7748. In any case, I look forward to hearing you April 29.

Sincerely yours,

A handwritten signature in cursive script that reads "Ruth Hubbard". The signature is written in dark ink and is positioned above the printed name.

Ruth Hubbard



National Institutes of Health
Bethesda, Maryland 20892
Building Shannon
Room 201
(301) 4960844

March 13, 1989

Nancy S. Wexler, Ph.D.
Associate Professor
Department of Neurology and Psychiatry
College of Physicians and Surgeons
Columbia University
722 West 168th Street, Box 58
New York, New York 10032

Dear Nancy

While you are in Venezuela, I want to commit some of my thoughts about the ethics subcommittee to writing. I hope your work is going well.

You have spoken of your desire to have a large and broad group advising us on ethical, legal and social issues. From many points of view this is highly desirable. However there are also drawbacks, and I want to propose an alternate approach that would be more flexible.

Let me first explain the drawbacks. Currently we have no authority to establish standing subcommittees for our Advisory Committee. This authority could perhaps be obtained, but comes with restrictions that may not be advantageous for our needs. First, all subcommittee members would have to be officially appointed through the regular appointment procedures and approved by the Secretary of HHS. This is a lengthy procedure and can run into a number of roadblocks, including the Secretary's desire to appoint people other than those we chose. There are a number of Boards dealing with ethics already and there could be a feeling that we are overlapping with them. We have also just heard that the new administration wants to reduce the number of advisory committees, which may also affect subcommittees. All in all I think the path of a formal subcommittee is fraught with unpredictable problems.

Working groups with limited tenure are much easier to handle. They can draw in other people to work with them on a specific issue for a specified period, basically to get some job done that would then go back to the full committee for action.

My suggestion would be to continue on the path we are on, establishing a temporary working group to get us started with a plan and then call together carefully selected representative groups for various activities such as public hearings, workshops, or whatever else you recommend.

The activities I envision would not involve voting on policy matters, so there really is no need to have a formal committee. Rather what I think we need to do is involve the scientific community and the public in discussion and debate in order to come, if possible, to some consensus.

NIH runs Consensus Development exercises, which perhaps could be a model for us for some of our activities. These always involve matters of clinical practice, but the format lends itself to other issues as well. A committee of experts is brought in and for one or two days they listen to presentations from all the interested investigators and other interested parties. Then they take all the information and withdraw to write a report of their conclusions. Since they are not an advisory committee, they are not chartered and the process of selecting them is faster and more flexible. The final recommendations are then usually published.

We will soon be revising the charter for the Advisory Committee on the Human Genome and it is my plan to add language addressing the fact that the Committee will have working groups from time to time and that the committee, including its working groups, will call in additional expertise for specific issues to advise the committee on technical matters. This kind of change will allow us more flexibility to do our work and should go through smoothly. However, the additional experts called in would not be voting members.

This is a rather rambling description of my concerns about the work of the ethics subcommittee. I would like to discuss them with you when you get back from Venezuela. My specific suggestion right now is to appoint a lawyer, as we discussed, and then use the existing group to develop a plan of things to do to present to the Advisory Committee in June. This plan would include things like:

- o get a group together to design additional program announcements
- o appoint a group to plan a workshop
- o seek someone who will develop a paper on some subject under a contract from the genome office
- o plan to have a public hearing
- o plan to have a consensus exercise to identify the issues of greatest concern and then develop ways to address those

Page 3 - Nancy S. Wexler, Ph.D.

These are just-off-the cuff ideas as illustration. I can see that this working group will need a lot of staff support!!

Sincerely yours,

A handwritten signature in cursive script that reads "Elke".

Elke Jordan

cc:
Dr. Watson
Dr. Zinder



CENTER FOR
BIOMEDICAL
ETHICS

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Thomas H. Murray, Ph.D.
Director

May 16, 1989

Nancy Wexler, Ph.D.
Associate Professor of
Clinical Neuropsychology
Department of Psychiatry
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Dear Nancy:

It was awfully good to see you in Washington. I am specially glad that you were able to meet briefly with the membership thus far of the Ethics Working Group. I think the hour and a half or so we spent was well worth it. The two people we came up with as possible members of the working group make good sense to me. I hope they will agree to serve.

I thought I would take a few moments to respond to the set of letters received in response to yours.

It looks as if at least a couple of the respondents misunderstood the working groups mission. As I understand it at least, we will not be directly sponsoring research. We may sponsor public hearings or research policy oriented symposia with scholars, or we may make suggestions about research funding priorities to the genome advisory committee and NIH.

Let me take the letters one at a time now. First, Barbara Rosenkrantz. Barbara is one of the world's best known historians of public health. Her idea of distinguishing classes and issues into those concerned with new knowledge and techniques and those concerned with the structures of conflicts and different social environments is intriguing, although I don't quite understand what she means by the latter. I am not sure that the genome initiative should be funding more generic research in the relationship between law and public opinion or law and public policy, unless the research was focused quite explicitly on the management of genetic knowledge (or genetic pseudoscience) or the legal and public policy

control of genetic technologies. I don't know Lawrence Friedman, but it certainly seems sensible to send him a copy of your original letter.

Now Dan Kevles. His letter contains much that seems very sensible, although it doesn't have many specific suggestions about directions for research. One that he seems to indicate is the history of the misuse of scientific information against minority groups and women. This is a reasonably well trodden ground I suspect. But I think it is important for us to encourage research on historical perspectives. Genetic pseudoscience, particularly in the form of eugenics, will be an obvious topic if fresh research ideas are forthcoming.

Sissela Bok is a wonderful person and a fine thinker. I hope she follows up on her promise to respond more substantively to your letter in the future.

Paul Billings seems to believe that we can directly fund projects. I have heard him present his preliminary findings. There are certainly some interesting things there. We will have to consider whether the ethics and law aspect of the genome should sponsor such social science research. I have asked him for a copy of his work; if you get anything from him, I would appreciate seeing a copy of it.

Rebecca Dresser seems to call for some very general and very specific, practically oriented legal research. I will look to the lawyers on the working group to respond more directly to Rebecca's suggestions.

Ruth Hubbard's letter. This letter seems to be very generally opposed to proceeding with the scientific aspect of the genome project. I think she seems to agree along with others that there needs to be more study and debate about the wisdom of developing technologies to detect genetic polymorphisms predictive of disease in the absence of any therapeutic measures one can undertake to prevent, manage, or cure the disease. I presume our committee or one or more of the research projects we sponsor will deal with this question.

Last, Bob Cook-Deegan. Bob's letter may be long but it is chock full of substance. It is difficult to pick out one or two important points but I will try, understanding that I am leaving out things just as important as what I am mentioning. First, I think he is right that testing and screening are more likely to be immediately consequential for society than gene therapy. I would like to both encourage the working group to talk about testing and screening and to consider proposing to the full genome advisory committee that research on the ethics and law of testing and screening be a high priority at this time. Second, like Bob, I share an interest in how knowledge in genetics will influence the way we conceive of ourselves. I am not sure that the working group is the proper body to articulate this question. But I would though

like to see us include such questions in any questionnaire that might be done (or at least encourage the body that does the questionnaire to do so); I would also like to see the questions like this raised in some of the public hearings.

Bob's comments on how genetics will "challenge our way of thinking about medicine and ... expose some underlying inconsistencies" is insightful. We could encourage others to do scholarly research on this; we could make recommendations to professional, legislative, and regulatory bodies that they begin to pay immediate attention to the practical consequences Bob outlines. I would say just about exactly the same thing on Bob's point about the relationship of the ideology of the genetic counseling movement and its relationship to mainstream medicine. (By the way, what are CEPH families?) Lastly, we will have to talk more about the notion of a broad public opinion poll. I gather there are some questions about what would be the most effective and sensible way to arrange for such a poll, e.g., whether we should try to do it directly out of the working group through a subcontract or whether we should encourage such polls as a part of the research funding.

I hope this is helpful. Feel free to share it with any other member of the working group or advisory committee that you wish.

Take care and I hope to see you soon.

Best,



Thomas H. Murray, Ph.D.
Professor and Director

THM/bp



TUFTS UNIVERSITY

Department of Urban and
Environmental Policy

May 2, 1989

Professor Nancy S. Wexler
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Dear Dr. Wexler:

Thank you for your letter of March 9 inquiring about my views on the ethical issues that may arise in pursuing the Human Genome Project. It is certainly a laudable idea to prepare for ethical problems that may accompany new technological developments.

The Genome Project is attracting a good deal of attention in the media. Although Congress has entered the arena of discussion and debate, the vast number of people do not have the foggiest idea what is at stake. My first impulse is to recommend projects that prepare society for the types of knowledge, and the social and ethical dimensions of that knowledge, that this research project promises.

Undoubtedly, you will be receiving many taxonomical proposals on how to organize the meta-scientific aspects of this research enterprise. Nevertheless, I shall throw mine into the ring. Please excuse the very sketchy nature of my remarks.

1. Ethics and Quality in Science

Will we get generalizable results? How can society and science protect itself from hasty generalizations that move from sequence to phenotype? What genes are eventually sequenced? A composite; an archetype; a cohort group; a particular racial/ethnic group? Does this have bearing on what the sequenced genes tell us about predictive aspects of medicine? How do we cast issues of "good" and "bad" genes in situations where phenotypes are expressed in a continuum of qualities. Given the nature of polymorphism in the human gene pool, does the sequencing of genes from a few selected individuals produce incomplete and possibly misinformation that correlates the composition of the base-pairs with the gene.

2. Opportunity Costs

To what degree will the Genome Project cause a reconfiguration of public investment in biomedical research; if so what are the opportunity costs? Is it the case that the project will centralize biomedical research and therefore

eliminate the creative aspects of decentralized independent researchers? Even if the Genome Project is advanced in third gear, we can still address the question: Which areas of genetics are being left behind?

3. Hasty Promises

What are the ethical issues in promising the public too much? Will the size of this project lend itself to all types of unsubstantiated promises about new cures for disease? Is that part of the nature of mega-funded efforts of this type? Must they promise more than they can deliver to justify the concentration of funding?

4. Individualized Gene Maps

What will the future be like when, as part of a complete diagnosis, we will be asked to have our individual genome sequenced? Or at least key sites? Who will have access to this information? Who will interpret it for us? What psychological impact will this interpretation have? Presumably, the Genome Project will greatly accelerate the generation of markers-- markers for disease; markers for propensity for disease. People who have G-6-PD are susceptible to adverse effects from a number of environmental factors. How will we process information of this type if each individual is given long lists of markers for abnormalities that are waiting to become actualized? Do we avoid unhealthy air, copper pipes, chlorinated drinking water, industrial chemicals at low exposures, wheat, milk etc. We have entered a period when people have become overwhelmed with health information; some of this information is conflicting. If taken seriously, the information creates narrower and narrower choices. How will the information of the Genome Project add to this existing trend to proliferate information for which people have great difficulty processing. Society will need to learn ways to sort out "health risks." This overdose is already happening with chemicals in the environment. The results are the people react opportunistically in response to media.

5. Social Science and Genetics

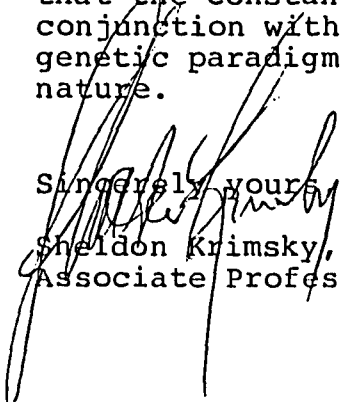
One of the least discussed areas of concern is the impact that genetics will have on sociology. Social deviance is a natural area for genetic reductionism. Sociobiology may be able to realize a more powerful methodology for identifying the genetic basis of social behavior. Instead of extrapolations from animals to humans, I am convinced a new paradigm will emerge. The gene maps of populations with certain personality types, i.e., social deviants, drug users, aggressive males, those with criminal tendencies, can be analyzed for similar "abnormal" sequences. Statistical correlations might be found between the sequences and the behavior. Eventually, sociobiologists will be looking for the intelligence sequences. It will not reveal itself that easily. But there will be hypotheses, conjectures. How will society deal with that? Will the availability of human genome information create a genetic aristocracy?

6. Elevation of Genes

When the atom was split, nuclear energy became a dominant force--political and technological. It displaced other approaches to things. Solar energy was laughable next to nuclear power. Atomic processes became the dominant paradigm within which to organize the world. We lost lots of opportunities as a result.

The Genome Project is placing considerable emphasis, whether intentional or unintentional, on the role genes play in the biological and social life of humans. We have literally been turned into our genes, according to the current metaphors. To know ourselves is to know our genes. Any extreme form of genetic reductionism can have undesirable consequences. First of all, it trivializes what and who we are and how our body works. Secondly, genetic reductionism shuts out other possibilities in medical research. However important genes are, it is possible that the constant publicity about genes in the media in conjunction with the vast funding in sequencing may propel the genetic paradigm beyond a balanced and true understanding of nature.

Sincerely yours,



Sheldon Krinsky, Ph.D.
Associate Professor



University of Pittsburgh

CENTER FOR MEDICAL ETHICS

June 15, 1989

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Dear Dr. Wexler:

I am (somewhat belatedly) writing in response to your letter of March 9th asking for my views about the ethical questions raised by the Human Genome Project. It was good to meet you, even if too briefly, at the "Unlocking Potential" Conference in Washington the month before last.

I view the ethical, social, and legal issues generated by the Human Genome Project as an overlapping combination of short and long term concerns. Thus even though issues associated with genetic discrimination (in both insurance and employment), for example, may be most immediately pressing in the practical sense, I believe that problems involving genetic therapy, along with an appropriate response to concerns about the potential misuse of eugenics, also need to be addressed by your Committee (and subcommittee). I think this is a political necessity as well as being advisable in order to develop an in-depth public discussion of these matters. There are a sufficient number of deep anxieties raised by human genetic research — anxieties that have an almost atavistic force — which continually need to be addressed and answered. These, coupled with the atrocities which have been perpetuated in the name of genetics and eugenics, strongly suggest that attention needs to be paid to such long-term issues, lest the United States project succumbs to the European postponement strategy (as described in the February 3rd issue of Science magazine). Thus I would urge that the Advisory Committee encourage support for appropriate studies in this area as well as more immediate (and realistic) short-term matters.

It would be redundant for me to list a survey of all of the ethical, social, and legal issues generated by the Human Genome Project, a number of which you mention in your letter. It seems to me that the standard sources such as the President's Commission for the Study of Ethical Problems in Medicine... volumes on Screening and Counseling for Genetic Conditions and Splicing Life, as well as the more recent OTA report on Mapping Our Genes (ch. 4) and the IOM/NAS volume by Eve Nichols on Human Gene Therapy (ch. 7) are good overviews of these problems. Also, if you've not yet seen it, Neil Holtzman's quite recent book Proceed With Caution (Johns Hopkins University Press, 1989) has a fine treatment of genetic testing and touches on a number of ethical and legal issues.

I believe that you wrote to me as a philosopher of science with a special interest in the biomedical ethics of genetics, and it is under this rubric that I offer the following more specific comments.

First, it seems to me that a set of significant distinctions in the gene therapy area that were accepted by the President's Commission as well as by the IOM/NAS needs further attention. In Human Gene Therapy there is reference to the "framework" that experts in bioethics have developed over the past ten years. This framework "divides gene therapy into four distinct categories: somatic cell gene therapy, germ line gene therapy, enhancement genetic engineering, and eugenic genetic engineering" (p. 190). It seems to me that more attention needs to be paid to developing a detailed analysis of the distinction between treatment for a (genetic) disease versus treatment to improve or enhance normal characteristics. There exists a small literature on the foundations of "normality" but little that I have been able to find on genetic normality. The recent OTA report also mentions a relative of this distinction in connection with a form of eugenics of which it seems to approve, writing:

The third eugenic use of genetic information would be to insure not merely that a person lacks severe incapacitating genetic conditions, but that each individual has at least a modicum of normal genes....This argument is based on the idea that there can be some consensus about the nature of a normal genetic endowment for different groups of human species. The idea of genetic normalcy, once far-fetched, is drawing closer with the development of a full genetic map and sequence; however, concepts of what is normal will always be influenced by cultural variations and subject to considerable debate. (OTA, p. 85).

There has been a good deal of work in philosophy of medicine on the concepts of health and disease and the difficulties with providing clear definitions of such. As genetics progresses, there will be temptations to extend its power to "improve" individuals, with "normal aging" perhaps the first area to be so targeted. (It was my sense that this was a kind of "hidden agenda" for some at the recent Washington Conference, though I could be wrong on that.) The current consensus suggests that the transition from disease treatment to enhancement therapy is likely to be one where careful ethical analysis and extensive public discussion will be required. In point of fact, the IOM/NAS report argues that "society as a whole must decide whether enhancement of physical traits is an acceptable rationale for medically manipulating human genes" (p. 190).

A more speculative issue (still under the "philosophy of science" perspective) which the Human Genome Project engenders is the twin problem of reductionism and genetic determinism. The IOM/NAS monograph writes that "The fear that gene therapy might "reduce" the human species or "change the meaning of being human" raises many different issues"(p. 163). The OTA report on Mapping Our Genes asks "How will a complete map and sequence of the human genome transform attitudes and perceptions of ourselves and others?" (p. 85) and refers to "the considerable debate in the philosophy of biology" on this question. The issue is linked with genetic determinism and thus with issues of responsibility and culpability (see OTA report, Box 4-B, p. 86). As the

human genome project proceeds, particularly in those areas that identify mental and behavioral diseases and traits, this set of concerns will intensify. Though focussed discussion on these matters may be premature, I would urge that such speculative considerations not be forgotten, and that research and conferences in these areas be encouraged to facilitate what I believe will become a most complex and contentious debate.

I hope these thoughts might be helpful to you. I'm enclosing one of my reprints on "Reduction, Reductionism, Values, and Progress in the Biomedical Sciences" which might be of interest to you.

With very best wishes.

Sincerely,



Kenneth F. Schaffner, M.D., Ph.D.

Co-Director

Professor of History and Philosophy of Science

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Dave Durenberger
Albert Gore
Gordon Humphrey
Edward Kennedy
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Tuesday, June 6, 1989

LeRoy Walters, Ph.D.
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Dear LeRoy,

I am writing in response to your request for specific topics to be addressed in the NIH project proposal that you and Tom Murray put together. I will review the specific topics that I expect BEAC to address, and then make some comments on what you and Tom might consider doing for NIH in light of this. I have enclosed an outline for a talk I gave last week to the National Conference of Lawyers and Scientists at AAAS. I was asked to discuss prospective issues that the Conference might want to address. The outline was for myself, but I send it in hopes that it may clarify some of what follows.

First, as you know, it is not at all clear that BEAC will be able to complete a study of the implications of human genetic engineering as mandated. If it does not, it would be doubly unfortunate. First, because such a study is desired by Congress and it would be a shame not to complete at least the first element of our mandate, but also second because BEAC can do some things that no other organization can. For example, one element that I regard as essential to prudent public policy is a more detailed investigation of what citizens think. A survey of attitudes and reasoning about genetic testing, genetic discrimination, prenatal and postnatal testing and screening, and gene therapy would be of great value to the public debate. I can envision a questionnaire that would allow an dissection of how much discomfiture there is about genetics, and a profile of the sources of anxiety. The questionnaire I propose, however, is extremely unlikely to be undertaken by an executive agency; I believe that your project would also be hard pressed to do it, as even surveys done under grant or contract to agencies, I believe, must come under OMB review. This would make the survey process so protracted and political that it would not be done.

As you know, the first day of the February 17-18 BEAC meeting was focused on human genetics. The main conclusion of that meeting was that gene therapy was less likely to be a vexing ethical question in the near future than genetic testing and screening, with the possible exception of the following questions, many of which you so aptly raised in your presentation:

1. Is the current review process appropriate? Is it too cumbersome? Are review committees properly situated in the bureaucracy, or is there an inherent conflict between NIH promoting research and regulating it (should RAC and its subcommittees be moved into the OASH or another location in HHS, for example, even though there is no indication for now that the review process is "broken").

2. Is there a clinical rationale for germ line therapy? I would propose to address this by asking a small team, including an ethical scholar and a geneticist, to write a short paper on the topic. This might be a topic for your grant proposal, although it does not directly relate to mapping or sequencing. I would propose to ask the team to think about possible clinical scenarios, such as a marriage between two PKU or Sickle Cell homozygotes. All their progeny would have their disease. If a germ line intervention were 1) highly reliable, 2) safe, and 3) the only or the best means to treat the condition; what would be the moral considerations for approving a clinical trial of such therapy? Would reproductive choice be restricted (by banning such marriages or disallowing reproduction within such matings)? Seems unlikely. Would treatment be covered postnatally? Likely yes. Than what would be the rationales for denying coverage prenatally? Would it be acceptable to use the most effective therapy in utero? If so, what can be said about the implications for future generations (both on the gene pool and on the progeny)? If not, what is the justification for denying access to such therapy?

3. What can be done to narrow the gap between discovery of a gene's location (and consequent ability to develop diagnostic tests, at least in some families) and development of an effective treatment? While this question does relate to gene therapy, I think it is best considered as one of many problems related to genetic testing and screening, noted below.

BEAC also concluded at its February meeting that questions related to genetic testing and screening were both more pressing and more difficult than those related to gene therapy; they thus need to be covered in some depth in our report. Beyond the agreement that, for the foreseeable future, genetic diagnosis and screening would have far more impact on more people as "human genetic engineering" than gene therapy, there was less sense of how to deal with the issues. The following comments, therefore, reflect more my personal opinions than those of BEAC or its members. These thoughts will undoubtedly change if BEAC moves on to consider the issues in a report. BEAC came close to agreeing that the most troubling and politically relevant aspect of testing and screening is the potential for discrimination. This is a gray area, fraught with technical complexity and ethical uncertainty, and BEAC could do a great service by covering these issues in some depth, as Congress (especially the judiciary committees) will undoubtedly have to address these issues in the next five to ten years. Even if BEAC addresses these issues, however, I believe they should be included in your proposal, because our report would be out relatively early in the period covered by your grant, and BEAC will certainly not have the last word on any of these questions. There will be plenty of debate on many of these topics, and your group's efforts could build on whatever BEAC produces. The issues are sufficiently complex that it may take many years to reach consensus.

Concern about potential genetic discrimination seems, at first blush, to break down into several component arenas. In considering topics for the NIH grant proposal, each of these would be highly relevant to assessing the social and ethical implications of mapping the genome. The foci of possible inquiry include:

- 1 general social stigma and prejudice (genetic labeling)
- 2 discrimination in getting a job
 because of disability
 because of possible future disability
 because of health care cost (if self-insured company), health
 insurance, or life insurance implications
- 3 discrimination in job placement once hired

- 4 discrimination in coverage or cost of health insurance (other than job-based)
- 5 discrimination in availability or cost of life insurance
- 6 discrimination in coverage or cost of long-term care insurance
- 7 lessons from eugenics laws
 - immigration laws
 - mandatory sterilization laws
 - miscegenation laws

A second set of issues relates to the renewed debate about population screening with genetic tests. This is in large part an extension of the debate from the early 1970s, rekindled by new technologies, but with an interesting twist as regards carrier detection. Discussion of genetic screening is coming to the fore because of advancing technology that makes tests cheaper and more widely available. I am not sure that there is much to add about the ethics of testing and screening that hasn't already been said by the President's Commission or the NAS report, but Ruth and Tom might disagree. One relevant observation here, however, is that dedicated mapping and technology development programs will certainly change the technical feasibility of large-scale screening, and will therefore bring closer the time when the issues must be resolved and will broaden the base of diseases that might be subject to screening. One issue of great interest that has not been as deeply analyzed in previous reports is the proper role of carrier testing. Direct genetic tests differ from biochemical tests by making carrier detection, in most cases, as reliable as homozygote testing. The issues raised specifically by population screening for carriers might be productively studied in some detail under your proposal.

My preliminary thought is that BEAC might let a few contracts with disability law experts, perhaps working with ethicists or geneticists, (1) to think through the proper legal framework for preventing discrimination (e.g., under the Rehabilitation act as a disability; under civil rights laws as a factor analogous to race; or under some other framework), (2) to suggest specific language as amendments to existing statutes (or entirely new statutes) intended to prevent discrimination, (3) to discuss the impact of various options suggested in (2), and (4) to discuss the desirability of preventing genetic discrimination by new legislation compared to application of existing statutes or leaving decisions to case law. One special contract might be an analysis of the consequences of the New Jersey antidiscrimination statute.

For purposes of investigation under the NIH grant, you might want to stake out some territory in which BEAC will probably not tread. First, the inchoate public discomfiture about mapping the genome might be disaggregated into several components. There are those who fear that more gene mapping means more prenatal diagnosis means more abortions of fetuses believed destined to develop genetic diseases. The crucial issues here are twofold: is abortion under any circumstances permissible (which you would likely not want to address, as it is a generic abortion issue) and if it is permissible sometimes, then where do we draw the line? What is a genetic disease, and how do you separate it from a mild disability, or from "normal"? Good examples abound of conditions where the line between a medical condition and a socially valued trait can be difficult to draw. One case that Tom has spoken about in the past is dwarfism versus familial short stature versus "short person." Others might include fragile X or PKU versus normal intelligence. Even more difficult cases will arise in connection with Alzheimer's disease or Huntington's disease, when a diagnostic label relating to behavioral and cognitive factors may be applied in advance of any disabilities. This question also arises in your own writing about treatment of diseases versus enhancement of characteristics in the context of gene therapy.

Second, the disease/social label distinction is especially important, and difficult, in the area of behavioral traits. Examination of this area will of necessity entail a review of the lessons of eugenics, and also a re-examination of the sociobiology-antisociobiology debate. A really good book is waiting to be written on the moral significance of genetic factors underlying cognitive, behavioral, and other socially desirable characteristics. Such a book could easily be much better than either of the ideological poles (Wilson and others on one hand, and Gould, Lewontin, Rose, and the CRG on the other) has managed to put together. A treatment that includes a sophisticated ethical and legal analysis informed by a thorough knowledge of medical genetics has not been done. The strength of the existing works is their understanding of history and genetics of lower organisms, but they are quite weak when it comes to practical matters of medical genetics and social policy. If a multidisciplinary group could respecify the goals of predictive genetics, especially regarding behavioral characters, then it would be a fundamental and lasting contribution. This is a much more substantial effort than BEAC will be able to undertake.

The future of genetic services is a separate topic that may well prove the largest determinant of how tests are used in the future. The issues here center on how the flood of new information about human genetics will enter medical practice -- much of which is poorly adapted to handling the new information -- and whether tests will be linked to appropriate mechanisms to interpret them for patients. The issues here are about training of doctors, nurses, and other health professionals, about reimbursement for tests compared to interpretive services, and about the proper focus of regulation -- whether it should focus only on the technical validity of a test, or should examine also how the tests are likely to be used in practice (i.e., whether genetic tests are likely to be properly understood by health professionals and patients). There is room here for an interesting case study the fate of an oasis of medical practice in which patient autonomy has hitherto reigned supreme -- genetic counseling -- as genetics becomes more a part of mainstream medicine, where more paternalistic norms apply. It would be useful to have an analysis centered on patients and families, rather than providers.

One feature of the political evolution of genome projects is proving even more confusing than I would have predicted -- the different reactions elicited by genome proposals in different cultures. The debate among scientists until recently was largely focused on (1) should genome projects be done, or are they just new ways to boost science budgets? and (2) if they proceed, how can gene maps and analytical technologies be most efficiently completed? What, in a technical sense, will distinguish genome projects from other science?

As the debate has entered the public arena, the focus has shifted. The debate in mainstream politics is: (1) can we trust the scientists to govern themselves? and (2) can we as a society fairly and responsibly handle the new knowledge that arises? A few other elements are also important to politicians and the general public, but less relevant to your grant proposal -- the preservation national prestige by technological and scientific leadership, and the economic spinoff of genomics research.

The debate about scientific elitism is to some extent a replay of the one about the Bomb. In Germany, human genetics research is viewed as highly suspect in the historical shadow of Nazi racial hygiene. You might or might not want to explicitly consider the ethical obligations of scientists to anticipate the uses of new knowledge arising from their efforts. This is becoming more and more an issue as biology becomes more a part of everyone's life. It has surfaced in a renewed debate about biological warfare, and seems to be dominating debate about genomics on the European Continent. Another option would be to examine the political philosophy of elite expert groups in a democracy, in this case molecular biologists.

I find it fascinating that different countries are reacting to genome proposals so differently. The intercultural differences might be an area of study for some group, although the composition of the group under your proposal may not be the proper one to consider such questions (you would need some cultural anthropologists and historians, most likely). I do think, however, that it would be extremely useful for the program to be linked, and formally so, to international efforts to study ethical and social implications of human genetics research. It seems increasingly likely that UNESCO and the EEC will have some specific projects to consider such questions. Could your group serve, along with the NIH subcommittee under Nancy Wexler, as US nodes for information exchange? I wonder if your group might not serve as the scholarly focus to collect information on other US efforts and disseminate it abroad and to collect international information and disseminate it domestically. This would logically be linked to the NRCBL. The NIH genome advisory subcommittee could serve as the more official planning and coordination node in the USA.

A final issue is perhaps the most pressing to be considered under the NIH proposal. It is less sexy, but more immediately relevant. It concerns ethical issues in the mapping efforts themselves. I do not mean the resource allocation issues (e.g., why genome projects versus more general genetics grants or why this chromosome before that), but rather how to promote the usefulness of databases and repositories while protecting the privacy of those family members being studied.

There are inherent conflicting pressures in doing studies involving large pedigrees. Unanticipated and potentially damaging information is inevitably discovered in doing genetics research. Nonpaternity is quite commonly uncovered, for example, and how to handle this when publishing pedigrees and discussing results with family participants is always difficult. Other issues also arise. Those searching for a particular disease gene need extensive clinical background to ensure the homogeneity of the character whose inheritance they are studying. This means access to the individuals' medical histories, and often the individuals themselves, in addition to blood or tissue samples from them. As more and more groups get interested in genetic approaches, some families can be asked to participate in more and more studies. This often becomes a serious problem, and some researchers tightly constrain access to "their" families for fear of overwhelming the families. Scientific competitors often ascribe this reluctance to share "data" as fear of scientific competition, and they are often right. In addition to the issues that arise in studying particular diseases, there are issues of access to patient identity in large materials collections such as maintained by CEPH. As more and more researchers move into the field, and more work becomes critically based on the few widely shared resources, what are the guidelines for linking data to individual persons? Who decides when it is necessary? Who decides what to tell CEPH (or other large pedigree collection) families if a discovery that indicates they may be at risk for a disease? I know of no rules for conduct in large family studies, and yet it is clear that they are going to be more and more common. The group maintaining the Mormon pedigrees and the Huntington's group have developed policies on this, and CEPH has some procedures, but I think it might be extremely useful to produce a document dedicated to this topic. It is important to do this early, as it can promote well-considered policies before ill-considered ones are too far along and become more difficult to change.

To summarize a letter that is much too long, I think that I would rank the possible specific topics, roughly in chronological order (rather than overall importance) as:

- 1 ethical considerations in research involving large pedigrees
- 2 genetic discrimination in making hiring decisions

3 genetic discrimination in insurance (health, life, and long-term care)
4 researchers' obligations to monitor the uses of genetic testing and screening
5 ethical issues in carrier screening
6 the role of genetic factors in cognitive, behavioral, and "desirable" traits
7 information exchange on intercultural differences regarding gene mapping
8 resource allocation issues in genetic services.

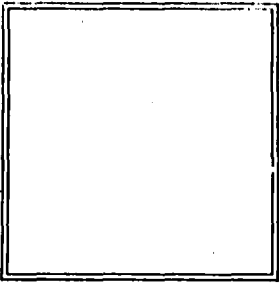
I believe I might concentrate my first efforts on these topics, with some specified schedule and process for doing so.

Sincerely,

Robert Mullan Cook-Deegan, M.D.
Acting Executive Director

cc: Alexander Capron
Nancy Wexler
Tom Murray

encl: Outline of talk for National Conference of Lawyers and Scientists, AAAS/ABA



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722 West 168th Street
New York, NY 10032

March 22, 1989

Dear Dr. Wexler:

Thank you for the opportunity to offer my thoughts on the role of the Ethics Subcommittee of the Advisory Committee to the Genome Project. I must admit to being somewhat at a loss to suggest which of the many complex issues should have priority for discussion. The rapid development of these technologies no doubt will require that guidance be offered on many issues as soon as possible. Fortunately, I expect your call for grant applications will be well received by scholars in many fields so that the pressing questions will get some if not all of the attention they deserve.

I would suggest, therefore, that the first priority of the Subcommittee should be to define how the ethical and social issues should be addressed rather than which issues have priority. There is, of course, a great apprehension in society about these technologies and an undercurrent of mistrust of scientists and the "academic-industrial complex." Academic ethicists have also not been beyond suspicion as hired casuists - critical enough to justify our titles but unwilling to offer fundamental challenges to the system that feeds our own needs. From my perspective, the question is how to involve all segments of society in a constructive discussion and analysis of the issues.

How a consensus is achieved on any specific ethical or social issue will be critical to its perceived value. If there is significant suspicion that these issues have not received an independent, unbiased, and broad based review, then the NIH will find itself fighting a whirlwind and perhaps unable to pursue related work for which little controversy exists. My apologies if these comments are self-evident but some of these issues may create (or exacerbate) a divisiveness in society that will outweigh their medical or social benefits.

I. Bruce Gordon, M.D.
Director, Department of Pediatrics
Cleveland Metropolitan General Hospital
3395 Scranton Road, Cleveland, Ohio 44109
Telephone: (216) 459-4278

School of Medicine
Department of Pediatrics

Obviously this is more than effective public relations for the Genome Project. Genetic technology will be an integral part of our society and the general knowledge of human genetics in the community is low. By fostering input on this issues from the literary community, high schools and colleges, religious organizations, and interested lay organizations, education and community involvement will be enhanced.

Again, thank you for the opportunity to provide my thoughts. I wish you and the Subcommittee success and effectiveness in this fascinating area.

Sincerely,

A handwritten signature in cursive script, appearing to read "Jeffrey R. Botkin". The signature is written in dark ink and is positioned above the printed name.

Jeffrey R. Botkin, MD



Department of the History of Science
Harvard University
Science Center 235, Cambridge, Mass. 02138
617-495-3741

23 March 1989

Professor Nancy S. Wexler
Department of Psychiatry
College of Physicians & Surgeons of Columbia
University
722 West 168th St.
New York, New York 10032

Dear Professor Wexler:

Thank you very much for your letter of late February. I was pleased, of course, to know that the materials used in the PBS program made sense to others like yourself deeply involved in the issues of genetic and medical research.

I am sure you have had lots of advice on how to proceed, but I have found in discussions of these issues with some of my own students and younger colleagues that one very worthwhile procedure is to ask what I have called "the counter-intuitive" questions. This doesn't mean that each of them has to be given the same serious weight, but we ought to try to ask about the things which the system has not yet been thinking about. I have also found that it is very worthwhile to cast some research, and the issues the research raises, in an historical framework. Sometimes we understand the structure of thinking and the potential problems when we recognize the trajectory of research and, indeed, the trajectory of disputed issues. I think this is particularly true in the area of genetic research, since many of our best researchers at the technical level operate outside the context of where their research is coming from and, indeed, where prior people in the area saw it headed.

How to get at issues like this? I like the system of mini-consultations or workshops where people are really free to probe in depth issues which, if raised out loud in public, might be seen to have too much rhetorical content or to represent unnecessary moralising. Small candid workshops often shake

people from conventional positions they have adopted or public stances they have taken. Out of workshops might come a distillation of real questions as compared to what are often pseudo-questions.

I am a real believer in involving the public, particularly in those areas where segments of the public may become the "parties at risk." Certainly failure to develop adequate public involvement will almost certainly lead to increased suspicion and will feed the kind of paranoia and fear which has always been the other half of the public's celebration of science. What are the best means for public involvement? I am not certain, but it might well be worth thinking of some of the forms that we used in countries like Austria, Sweden, and Holland where nuclear issues were being publicly debated. They developed mixed teams of people with different points of view who engaged the public in discussions at various meetings arranged in schools, libraries, etc. Perhaps we also ought to think of today's functional equivalent of the "teach-ins" of the past where we really open up ideas for full and knowledgeable discussion representing the ranges of evaluation that are available in our university communities.

I would love to discuss this further with you, perhaps over the phone or, if our paths cross, in person. I will be traveling from now until the end of the first week in April, but perhaps after that we can have further contact.

Thank you for your letter of inquiry. I look forward to further discussions.

Sincerely,

Everett Mendelsohn
Everett Mendelsohn (rmb)

EM:rmb

The University of Texas
Health Science Center at Houston



Sc [REDACTED]

April 18, 1989

Nancy S. Wexler, Ph.D.
Associate Professor of Clinical Neuropsychology
Department of Psychiatry
College of Physicians & Surgeons of Columbia University
722 West 18th Street
New York, NY 10032

Dear Nancy:

It was a coincidence that your letter arrived asking for suggestions concerning the ethical and legal issues involved in the Genome Project. I had a conversation with Mark Rothstein about this topic last month since he had heard from you before I did.

As you know, Mark is Director of the Health Law Institute (HLI) at the University of Houston Law School where I have been an adjunct faculty member for the past several years. (I am now retired.) The HLI sponsors an annual meeting on a current health law topic (See enclosure for this year's program). Mark and I discussed the possibility of holding next year's meeting on the topic "Legal Issues Surrounding the Human Genome Initiative."

Would your committee be interested in sponsoring or co-sponsoring this meeting with us? Mark thought it might be preferable to hold an invitation-only meeting, limited to approximately 100 people. I can see some advantages in making it broader, trying to reach a larger audience, but have no strong feelings about it. The legal papers (but not the medical papers) of the HLI annual symposium are published in the Houston Law Review.

The HLI needs money to put on the symposium. Tell Mark if you would consider an application for this purpose. I think there would be advantages to having your committee help in the development of the program and the invitation of speakers. There should be a good mix of geneticists, lawyers, ethicists, policy makers, etc. Please let Mark know how to apply.


As for as other suggestions, I think it is quite important to use some of your funds and activities for public education. Possibly a series of articles in the New York Times and/or Wall Street Journal, a half hour on Ted Koppel's "Night Line," a NOVA production or a slot on MacNiell-Lehrer News Hour would be appropriate.

Mark could help you to identify health lawyers around the country who might address the legal issues with commissioned papers. Hastings Center in Georgetown might help you do the same regarding ethicists.

Phil Reilly is chairing an ad hoc Committee of the American Society of Human Genetics on the specific topic of DNA Forensics. I am on his committee and we are drafting a policy statement for adoption by ASHG. Phil could give you further details.

Good luck on your work. I see the Genome Initiative as one of the most significant projects of the 21st century and it will have repercussions throughout the fabric of our society and all over the world.

Sincerely,



Margery W. Shaw, M.D., J.D.
Professor Emeritus

MWS:bg
enclosure



HEALTH LAW INSTITUTE

Mark A. Rothstein
Director

March 15, 1989

Nancy S. Wexler, Ph.D.
Associate Professor of Clinical Neuropsychology
Department of Psychiatry
Columbia University College of Physicians & Surgeons
722 West 168th Street
New York, NY 10032

Dear Dr. Wexler:

Thank you for your recent letter and your invitation to contribute to the Ethics Subcommittee of the Advisory Committee to the Office of Human Genome Research.

I have written a new book, Medical Screening and the Employee Health Cost Crisis, which focuses on the negative consequences of increased medical screening by employers to select employees who are less likely to use health benefits. New genetic technologies could have a major impact on this area and the legal and policy issues raised by genetics are discussed at some length in the book. I will be glad to send you a copy when it is published in May.

I am also working on a project with Arthur Bloom on the legal and ethical issues of genetic testing for predisposition to cancer. My paper addresses issues in clinical medicine, public health, reproduction, insurance, and employment. The entire monograph should be completed this summer, but if you are interested in seeing a draft of my chapter, I can send it to you.


Finally, I would be interested in exploring with you a possible role for the Health Law Institute. For example, each year the Institute sponsors a major, national, interdisciplinary conference on an important health issue. This year's conference, "Health Care for an Aging Society," will be held this week. Our conferences bring together leading experts from science, law, ethics, and policy to address a topic of contemporary concern. With funding from the Genome

Nancy S. Wexler, Ph.D.
March 15, 1989
Page Two

Project we could host a conference to explore some of the numerous legal, ethical, and policy issues raised by mapping the human genome. I am enclosing a copy of this year's conference brochure for your information.

Once again, I'd be happy to assist you in any way you deem appropriate.

Sincerely,



Mark A. Rothstein
Professor of Law
Director

MAR:ldg
Enclosure



New
England
Deaconess
Hospital

Department of Medicine
Section of General Medicine
Deaconess Medicine

110 Francis Street
Boston, MA 02215
(617) 732-9719



Instructor in Pathology

Paul R. Billings, M.D., Ph.D.
Director, Clinic for Inherited Diseases

March 20, 1989

Nancy Wexler, Ph.D.
Department of Psychiatry
Columbia University College of Physicians
and Surgeons
722 West 168th St.
New York City, NY 10032

Dear Nancy,

I have recently seen a letter you authored as representative of the "Human Genome Project." As I understand it, you will be in charge of a subcommittee which will oversee projects of a non-molecular nature. In particular, studies on the efficacy and ethics of human genetic screening will be of interest to your group.

First, I would like to request that my name be placed on the list of recipients of such mailings. Second, as you may remember, I have for the last several months been collecting cases where genetic discrimination may have taken place. To date, I have 36 well documented cases containing multiple incidents of discrimination in the fields of social entitlements and health care delivery. A manuscript, describing these preliminary results, is in preparation. It is tentatively titled "Genetic Discrimination as a Consequence of Genetic Screening: A Preliminary Study."

Our data does not address the issue of the prevalence of genetic discrimination in individuals labeled with genetic conditions. It does begin to characterize some of the forces involved in the stigma associated with genetic labeling. I would like to propose that the Human Genome Project consider funding a study from our unit on the issue of prevalence. Given our preliminary results, we already have a notion as to what kind of condition would be most applicable for this kind of study.

I would be happy to provide you further information concerning our preliminary results and will certainly send you the manuscript when it is available for circulation. On a separate note, I am looking forward to your visit to Boston at the end of April for the conference with the journalists.

Looking forward to hearing from you in the future concerning these and other issues.

Sincerely,

A handwritten signature in cursive script, appearing to read 'Paul'.

Paul R. Billings, M.D., Ph.D.

PRB/lmcd

April 4, 1989

Nancy S. Wexler, Ph.D.
Associate Professor
Department of Psychiatry
College of Physicians and Surgeons
Columbia University
722 West 168th Street
New York, New York 10032

Dear Dr. Wexler:

Thank you for your letter asking for my suggestions on topics of investigation by the Ethics Subcommittee of the Advisory Committee to the Human Genome Project. I have a few general remarks, which I'm happy to share with you.

As a lawyer, I am very aware of how access to information on the genome could affect nearly every area of law. I also know that often the law changes quite slowly, indeed, too slowly to respond optimally to newly-developed technologies. I would support legal research and analysis in general areas of law, including contract, tort, criminal, constitutional, insurance, employment, property, and health care law. The emphasis should be not only on surveying future issues, but also on the specific statutes, regulations, and other procedural and substantive legal revisions that will be needed to address and resolve the particular problems and questions that will arise. A "legal blueprint" for action would be something concrete to guide and stimulate action by future lawmakers and other decision-makers.

I hope this is of some help to you.

Yours sincerely,

Rebecca Dresser
Rebecca Dresser, J.D.
Associate Professor

RD:js

33 ELMWOOD AVENUE
CAMBRIDGE
MASSACHUSETTS 02138

March 30, 1989

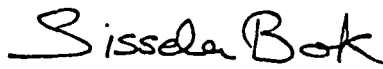
Dear Dr. Wexler,

Many thanks for your letter concerning the new Ethics Subcommittee of the Advisory Committee to the Office of Human Genome Research. I am glad to hear that there will be such a subcommittee and can think of few sets of tasks more challenging than those which its members will confront.

You ask for my thoughts and suggestions. I shall be considering the questions you raised and writing you concerning any ideas that come to mind as the debate on these topics progresses. But at present, I am so immersed in questions of an entirely different nature (having to do with the ethical issues of war and peace that are the topics of my most recent book A Strategy for Peace) that I must wait before I turn to the questions you raise. I shall, however, follow the debate on the issue, and send you my very warmest wishes for your work in heading the new Subcommittee.

With warm regards,

Sincerely,



Sissela Bok

HOWARD UNIVERSITY

WASHINGTON, D.C. 20059

COLLEGE OF MEDICINE
DEPARTMENT OF PEDIATRICS
AND CHILD HEALTH
Division of Medical Genetics

May 26, 1989

Nancy S. Wexler, Ph.D.
Associate Professor of Clinical Neuropsychology
Department of Psychiatry
College of Physicians and Surgeons
Columbia University
722 West 166th Street
New York, N.Y. 10032

Dear Dr. ~~Wexler~~ ^{Nancy}:

I am responding to your letter of March 9, 1989 in which you asked me for my thoughts and suggestions as to how the Ethics Subcommittee of the Advisory Committee to the Genome Project might best function to ensure the most responsible and ethical use of evolving genetic information as it unfolds.

First of all let me extend my congratulations and say how pleased I am that you agreed to chair the Ethics Subcommittee. In my opinion you combine the incisive thinking of a scientist and researcher with the compassion and sensitivity of a humanist, an ideal combination for the person who chairs this important committee.

I am sending along four articles that might help in developing a process by which the benefit of the genetic information developed by the Genome Project can be maximized and the harm can be minimized. Three of these were written to provide guidelines for establishing and operating programs in screening and counseling for genetic disease and prenatal diagnosis. The fourth is a brief article pointing out the special aspects of genetic counseling that ought to be considered if it is to be effective and also consistent with ethical principles.

It might be useful to review the recommendations that were developed in these articles by task forces or working groups that worked for one or two years to develop them and consider and adopt those that are applicable to the issues peculiar to the Genome Project. The article "Ethical and Social Issues in Screening for Genetic Disease" contains points and principles that seem especially appropriate for the genetic

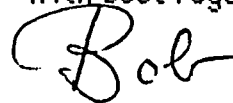
information that will be generated by the Genome Project and its potential uses. There is no need to reinvent the wheel.

Thank you for this opportunity to contribute to the work of a very important part of the Genome Project. As I uncover other articles of interest I'll forward them to you.

I will mention one point in particular. This is the point I made at the recent Genome conference in Washington on the panel on Ethics in which both you and I took part. In the interest of honesty and the ethical principle of truth-telling it is vital that the project begin without making promises for the technology that may not be realized for some time in the future. In particular it is critical that the members of the public be kept aware of the limitations of the genetic information that will be generated.

I look forward to working with you and other members of the subcommittee. Please let me know if I can be of any other assistance.

With best regards,

A handwritten signature in cursive script that reads "Bob".

Robert F. Murray Jr., M.D.
Chief, Division of Medical
Genetics, Department of
Pediatrics and Child Health

file ethics

no standing committee!

Shannon
201
0844

March 13, 1989

Nancy S. Wexler, Ph.D.
Associate Professor
Department of Neurology and Psychiatry
College of Physicians and Surgeons
Columbia University
722 West 168th Street, Box 58
New York, New York 10032

Dear Nancy

While you are in Venezuela, I want to commit some of my thoughts about the ethics subcommittee to writing. I hope your work is going well.

You have spoken of your desire to have a large and broad group advising us on ethical, legal and social issues. From many points of view this is highly desirable. However there are also drawbacks, and I want to propose an alternate approach that would be more flexible.

Let me first explain the drawbacks. Currently we have no authority to establish standing subcommittees for our Advisory Committee. This authority could perhaps be obtained, but comes with restrictions that may not be advantageous for our needs. First, all subcommittee members would have to be officially appointed through the regular appointment procedures and approved by the Secretary of HHS. This is a lengthy procedure and can run into a number of roadblocks, including the Secretary's desire to appoint people other than those we chose. There are a number of Boards dealing with ethics already and there could be a feeling that we are overlapping with them. We have also just heard that the new administration wants to reduce the number of advisory committees, which may also affect subcommittees. All in all I think the path of a formal subcommittee is fraught with unpredictable problems.

Working groups with limited tenure are much easier to handle. They can draw in other people to work with them on a specific issue for a specified period, basically to get some job done that would then go back to the full committee for action.

My suggestion would be to continue on the path we are on, establishing a temporary working group to get us started with a plan and then call together carefully selected representative groups for various activities such as public hearings, workshops, or whatever else you recommend.

Page 2 - Nancy S. Wexler, Ph.D.

The activities I envision would not involve voting on policy matters, so there really is no need to have a formal committee. Rather what I think we need to do is involve the scientific community and the public in discussion and debate in order to come, if possible, to some consensus.

NIH runs Consensus Development exercises, which perhaps could be a model for us for some of our activities. These always involve matters of clinical practice, but the format lends itself to other issues as well. A committee of experts is brought in and for one or two days they listen to presentations from all the interested investigators and other interested parties. Then they take all the information and withdraw to write a report of their conclusions. Since they are not an advisory committee, they are not chartered and the process of selecting them is faster and more flexible. The final recommendations are then usually published.

We will soon be revising the charter for the Advisory Committee on the Human Genome and it is my plan to add language addressing the fact that the Committee will have working groups from time to time and that the committee, including its working groups, will call in additional expertise for specific issues to advise the committee on technical matters. This kind of change will allow us more flexibility to do our work and should go through smoothly. However, the additional experts called in would not be voting members.

This is a rather rambling description of my concerns about the work of the ethics subcommittee. I would like to discuss them with you when you get back from Venezuela. My specific suggestion right now is to appoint a lawyer, as we discussed, and then use the existing group to develop a plan of things to do to present to the Advisory Committee in June. This plan would include things like:

- o get a group together to design additional program announcements
- o appoint a group to plan a workshop
- o seek someone who will develop a paper on some subject under a contract from the genome office
- o plan to have a public hearing
- o plan to have a consensus exercise to identify the issues of greatest concern and then develop ways to address those

Page 2 - Nancy S. Wexler

These are just-off-the cuff ideas as illustration. I can see that this working group will need a lot of staff support!!

Sincerely yours,

Elke Jordan

cc:
Dr. Watson
Dr. Zinder

College of Physicians & Surgeons of Columbia University | New York, N.Y. 10032

DEPARTMENT OF PSYCHIATRY

722 West 168th Street

February 24, 1989

Nancy, with the changes shown, I think this is fine. E. Lee

Dr. Thomas Murray
Director
Case Western Reserve University
School of Medicine
2119 Abington Road
Cleveland, OH 44106

Dear Dr. Thomas Murray,

The National Institutes of Health recently established an Office of Human Genome Research under the directorship of Dr. James Watson. This office will be advising and overseeing the massive and far-reaching project to map and eventually sequence the human genome.

As you know, a major aim of the Genome Project is to alleviate human suffering through the ~~eventual eradication~~ ^{better prevention & treatment} of hereditary disease. It is imperative, in the wake of new knowledge regarding the identification and action of human genes, that individuals or groups not be harmed by our improved capacities to detect deleterious genes. The Office of Human Genome Research is committed to ensuring the most responsible use of evolving genetic information as it unfolds.

I have the privilege to head the ^{Working Group} ~~Ethics Subcommittee~~ ^{on the} of the Advisory Committee ~~to the Office of~~ Human Genome Research, chaired by Dr. Norton Zinder of Rockefeller University. The Advisory Committee and staff of the Office of Human Genome Research are all deeply committed to understanding and planning for the ethical, social and legal ramifications of the Genome Project as well as fostering its scientific base. The Office of Human Genome Research is prepared to commit between 1%-3% of the Genome Project's budget for studies and activities in the area of ethics and society. A Program Announcement ^{will also be} ~~will soon be~~ issued (which you will receive) soliciting grant applications in this area. In addition, the ~~Ethics Subcommittee~~ ^{Working Group} is empowered to hold workshops and conferences, solicit position papers and ~~hold~~ ^{gather} public testimony.

I am writing to you as a leader in your field to ask for your thoughts and suggestions as to how the Office of Human Genome Research and the ~~Ethics Subcommittee~~ ^{Working Group} can best function to explore this matter. What, in your view, are the essential ethical, social and legal questions which should capture our immediate attention? What questions are the most pressing?

*harmful genes carried
by an individual*

Issues that have been raised are legion: How can one best prepare to prevent stigmatization, discrimination, ostracism, psychological trauma, or other potential hazards which may be a consequence of identifying ~~carriers of harmful genes?~~ ~~Should~~ ~~matters pertaining to gene therapy, somatic or germ line, be~~ ~~addressed by this committee?~~ Who "owns" one's genetic information? Should insurance companies or employers be precluded from requiring genetic testing or be barred from learning the results of voluntary testing? How might wrongful birth or medical malpractice suits influence the integration of new genetic knowledge into mainstream medical care? How can patent questions be resolved equitably? There are questions of forensic and work place genetic screening as well as the use of genetic diagnostic tools in the protection of human rights.

I would be appreciative of any thoughts or suggestions you might have regarding subjects to pursue, policy areas to explore and activities to undertake.

Thank you.

Sincerely,

Nancy S. Wexler

Nancy S. Wexler, Ph.D.
Associate Professor of Clinical Neuropsychology

*No, RAC
does that.
I think
we should
try to focus
on other
issues since
this is
well covered.*

Both, Include to list sent to Nancy Wexler

Barbara Rosencrantz, Ph.D.
 Professor of History of Science
 Harvard U.

Marjorie W. Shaw, MD, JD
 Health Law Program
 School of Public Health
 U. TX - Houston

Roger Shinn
 Professor of Social Ethics Emeritus
 Union Theological Seminary

Bernard M. Dickens
 Faculty of Law
 U. of Toronto

Mark Rothstein, JD
 Director, Health Law Center
 U. of Houston

~~Stuart~~
~~Rebecca~~
~~JFB~~
~~Tom~~
~~Stephanie~~
~~David~~
~~David~~

February 4, 1989

Dear Elke,

I didn't have a chance to discuss this with you before leaving for Venezuela this Sunday.

I mentioned when I was in Bethesda that I was thinking first of sending a letter to people soliciting their views. Here is a draft of a letter. I would love to have your opinion. The list of names enclosed in the group associated with Tom Murray & LeRoy Walters grant & others. I have additional names for whom we are seeking addresses. If you could FAX me your comments, they are in favor of the idea, the California office of the Hereditary Disease Foundation

can mail out the letters.

My FAX number at the
Hotel Del Lago in Venezuela is:

country code city code number
58-61-914-551

You can also contact either Ann Copeland
or Edy Shakell at the H.D.F. office at
(813) 458-4183.

If you think this should wait
until we can discuss this - let me
know. I'll be back in LA April
3 and in New York April 11.

Please don't write me in Maracaibo -
will never arrive. But you can try calling -
58-61-912022, room 372 or 374. We're
one hour ahead of Bethesda.

Thanks

Nancy

P.S. I have also sent this to Tom for his review.
Obviously the letters to people I know would be personalized
and appropriate to their activities - i.e. Tom knows about the 3

program announcement, etc. This is just a
sample.

Columbia University
College of Physicians and Surgeons

**DEPARTMENTS OF NEUROLOGY
AND PSYCHIATRY**

To: *Dr. Jordan*

From: Nancy S. Wexler, Ph.D.

Date: *2-22-89*

Noted

For your file

For your information

Please note and return

Please give appropriate attention

I'd like to talk this over with you

Please advise and comments

Please handle

Please reply with copy to me

College of Physicians & Surgeons of Columbia University | *New York, N.Y. 10032*

DEPARTMENT OF PSYCHIATRY

722 West 168th Street

February 21, 1989

Dr. Everett Mendelsohn
Harvard University
Science Center, Room 235
1 Oxford Street
Cambridge, MA 02138

Dear Dr. Mendelsohn,

I recently heard you speak on the PBS program THE WEB OF LIFE. I was impressed by your cogent remarks on the social and ethical ramifications of current plans to map and sequence the human genome. Your warning that we must take heed now and plan to stave off the most dire possible consequences of the advancing knowledge should not fall on deaf ears. (I particularly liked your bringing in Tom Lehrer as an ally. He would have had a fine time with the genome project!)

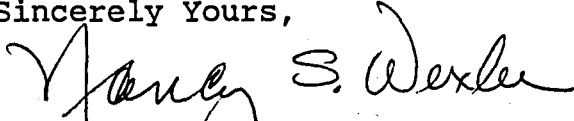
The Office of Human Genome Research at the National Institutes of Health, under the direction of Dr. James Watson, takes seriously the ethical, social and legal implications of the scientific advances of research supported under the genome initiative. Dr. Watson has organized an Advisory Committee, chaired by Dr. Norton Zinder, Rockefeller University. I am a member of the Advisory Committee and have been asked to head an Ethics Subcommittee. Dr. Watson is prepared to dedicate 1%-3% of the monies allocated for the Human Genome Project to high quality research or planning involving the social, legal and ethical issues in this area.

I am writing to ask for your suggestions and thoughts regarding viable activities for the Ethics Subcommittee and for the NIH Office of Human Genome Research. If we are not to be Werner Von Braun, what ought we do to prepare for a new medical and social future? Should position papers be prepared in areas which are presently murky? Should legislation be proposed? Should workshops be held to thrash out what should be done? Should public hearings be held to solicit lay and professional input in these vital areas? Are there individuals or groups that you recommend we contact? I would be very interested and appreciative of your thoughts and suggestions.

Page Two

I am leaving for the month of March for field work in Venezuela where we are working with a very large family with Huntington's disease. I will return the beginning of April and look forward to being in contact with you then.

Sincerely Yours,

A handwritten signature in cursive script that reads "Nancy S. Wexler". The signature is written in dark ink and is positioned above the typed name.

Nancy S. Wexler, Ph.D.
Associate Professor of Clinical Neuropsychology