SCIENCE POLICY IMPLICATIONS OF DNA RECOMBINANT MOLECULE RESEARCH

WEDNESDAY, SEPTEMBER 7, 1977

HOUSE OF REPRESENTATIVES,
COMMITTEE ON SCIENCE AND TECHNOLOGY,
SUBCOMMITTEE ON SCIENCE, RESEARCH AND TECHNOLOGY,
WASHINGTON, D.C.

The subcommittee reconvened, pursuant to adjournment, at 2:08 p.m., in room 2325, Rayburn House Office Building, Hon. Ray Thornton, chairman of the subcommittee, presiding.

Mr. THORNTON. The hearing will come to order.

This afternoon the Subcommittee on Science, Research and Technology continues its series of hearings on the general subject of recombinant DNA molecule research with an accent, however, today on the broader question of the effect of ethics on science policy and how these two dissimilar philosophical concepts may be related to policymakers and used in making decisions.

It is well-known that science, by definition, is a search for truth, and that ethics is a matter of social conscience or transcendent values, or whatever other philosophical definition might be given. But basically it's a judgment which society makes and expresses. And yet the two occasionally bump into each other, and in the search for science truth it is sometimes possible to offend ethical standards, and so in early days the study of cadavers led to very grave problems [laughter] of science research affected with the ethical considerations of the time.

Today, as science pursues ever broadening horizons, the occasion for bumping into problems of ethics would seem to occur more frequently, and certainly in an area which is as vital and fundamental to the question of life itself as recombinant DNA research. However, the question is not limited to that particular aspect of science research, but rather to a way of determining what the impact on science research should be of ethical standards.

We are very fortunate this afternoon in having a distinguished group of witnesses who will discuss the ethical issues in scientific research.

The procedure I would like to follow is to allow each of the witnesses an opportunity to make a brief opening statement and then, hopefully, to open the panel for discussion, which we will try to prod along, hoping to get a good deal of interplay, not only between Congressman Hollenbeck and myself and the panel, but between the various panel members. In pursuing that objective, I propose to ask each of you in the order in which your names appear as witnesses to give us your primary discussion.

Our first witness is Dr. Marc Lappé, who is chief of the office of health, law, and values of the State of California Department of Health.

Dr. Lappé.

[A biographical sketch of Dr. Lappé follows:]

CURRICULUM VITAE

MARC ALAN LAPPE'

Personal History:

Date of Birth: January 14, 1943
Place of Birth: Irvington, New Jersey
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Education:

Undergraduate	1960-1962	Wesleyan University, Middletown, Conn.
	1962-1963	Weizmann Institute, Rehovoth, Israel
	1963-1964	Wesleyan University, Middletown, Conn.
Graduate	1964-1966	University of Washington, Seattle
	1966-1968	University of Pennsylvania, Philadelphia
Postgraduate	1968-1970	University of California, Berkeley

Degrees:

B.A. (Biology) Wesleyan University
Ph.D. (Experimental Pathology) University of Pennsylvania

Honors and Awards:

Warner-Chilcott Scholar	1960-1964
NIH Trainee	1964-1966
Anna Fuller Fund Fellow	1968-1970
Honorary Postdoctoral Fellow University of California	1968-1970

Educational Positions:

1966	Graduate Supervisor of Pre-college Training, The Jackson Laboratory
1965-1967	Teacher, Free University at University of Pennsylvania
1968-1969	Teacher, Free University at Berkeley
1968	Lecturer, University of California, Berkeley
1969-1970	Staff Instructor, University of California Extension, Berkeley
1969-1970	Consultant in Biology to Worth Publishers, New York
1970	Acting Assistant Professor, University of California, Berkeley

1970	Consultant to Senator John A. Nejedly, California Legislator
1971-1974	Adjunct Assistant Professor, State University of NY at Purchase
1971-1976	Associate for the Biological Sciences, Institute of Society, Ethics and the Life Sciences, Hastings-on Hudson, NY
1972-1975	Principal Investigator, NIH Grant to study Social and Legal Aspects of Human Genetic Research
1975	Member, Bioethics Advisory Commission, National Foundation/March of Dimes
1975	Guest Instructor, Sarah Lawrence College program in Human Genetics
1976-present	Chief, Office of Health, Law and Values, Department of Health, California

PUBLICATIONS

M.A. Lappé 1966 "Evidence for the antigenicity of papillomas arising on isografts of initiated skin." Proc. Am. Assoc. Cancer Res. 7:40 (abstract)

M.A. Lappé 1968 "Immune elimination of pre-malignant papillomas in isografts of initiated skin." Proc. Am. Assoc. Cancer Res. 9:39 (abstract of paper presented at 9th annual meeting at AACR)

M.A. Lappé 1968 "Evidence for the antigenicity of papillomas induced by 3-methylcholanthrene." J. Nat. Cancer Inst. 40:823-840.

M.A. Lappé 1968 "The role of immunologic surveillance during skin carcinogenesis in the mouse." Ph.D. Dissertation, University of Pennsylvania, Philadelphia. (LC card. no. Mic. 69-15, 079). Ann Arbor, Michigan, University Microfilms, Inc., 1968, p. 84.

M.A. Lappé, R.J. Graff, and G.D. Snell 1969 "The importance of target size in the destruction of skin grafts with weak incompatibility." Transplantation 7:372-377.

R.J. Graff, M.A. Lappé, and G.D. Snell 1969 "The influence of the gonads and the adrenal glands on the immune response to skin grafts." Transplantation 7:372-377.

M.A. Lappé 1969 "Tumor specific antigens: Possible origin in premalignant lesions." Nature 223:82-84.

M.A. Lappé and R.T. Prehn 1969 "Immunologic surveillance at the macroscopic level: Non-selective elimination of premalignant skin papillomas." Cancer Research 29:2374-2378.

M.A. Lappé and P.B. Blair 1969 "Interference with mammary tumorigenesis by antilymphocyte serum." Proc. Am. Assoc. Cancer Res. 11:47. (abstract of paper presented at 11th annual meeting of AACR).

M.A. Lappé and D.S. Steinmuller 1970 "Depression of weak allograft immunity in the mouse by neonatal or adult exposure to urethan." Cancer Research 30:674-680.

M.A. Lappé 1970 "Chemical and Biological Warfare." In: The Social Responsibility of the Scientist, Martin Brown (ed.), The Free Press, Berkeley

M.A. Lappé and R.T. Prehn 1970 "Predictive value of skin allograft survival during the development of urethan induced lung adenomas in BALB/c mice." Cancer Research 30:1357-1361.

M.A. Lappé 1970 "The ecology of cancer" Contact Point 48:140-146.

M.A. Lappé 1971 "Failure of long-term immunologic control of 3-methycholanthrene-induced skin tumors in the autochtocous host." (Presented at the 7th Annual Meeting of the Reticuloendothelial Society, December 1970). J. Reticuloendothel. Soc. 10:120-130.

M.A. Lappé 1970 "Evidence for immunological surveillance during skin carcinogenesis: Inflammatory foci in immunologically competent mice." Israel J. Med. Sci. 7:52-65.

P.B. Blair, M. Kripke, M.A. Lappé, R.S. Bonhag, and L. Young. 1971 "Immunologic deficiency associated with mammary tumor virus infection. Hemagglutinin production and allograft response." J. Immunol.

M.A. Lappé 1971 "Genetic control." N. Eng. J. Med. 286:49-50. (letter to the editor.)

M.A. Lappé and J. Schalk 1971 "Necessity of the spleen for balanced secondary sex ratiors following maternal immunization with male antigen." Transplantation 11:491-495.

M.A. Lappé 1971 "The Genetic Counselor: Responsible to whom?" The Hastings Center Report 2:2.

R.T. Prehn and M.A. Lappé 1971 "An immunostimulation theory of tumor development." Transplantation Review 7:26-54.

M.A. Lappé 1972 "Risk-taking for the unborn." The Hastings Center Report 1:2.

M. A. Lappé, J.M. Gustafson, R. Roblin, et al. 1972 "Ethical and social issues in screening for genetic disease." N. Eng. J. Med. 286:1129-1132.

M.A. Lappé 1972 "Moral obligations and the fallacies of genetic control." Theological Studies 33:411-427.

M.A. Lappé 1972 "The possible significance of immunological recognition of preneoplastic and neoplastic cell surfaces. National Cancer Institute Monographs 35:49-55.

M. Lappé 1973 "Mass genetic screening programs and human values: Another view." Med. Dimensions 2:2.

M. Lappé 1973 "Allegiances of human geneticists: A preliminary typology." The Hastings Center Studies 1:2.

M. Lappé 1973 "Human Genetics" In: Public policy toward environment: A review and appraisal. Ann. N.Y. Acad. of Sci. 216:152.

M. Lappé 1973 "Genetic knowledge and the concept of health." The Hastings Center Report 3:4.

M. Lappé 1973 "Genetic and biochemical screening: Beyond testing for disability." Lab. Management Vol. 11, No. 11, November 1973.

M. Lappé and J.A. Brody 1974 "Genetic counselling: A psychotherapeutic approach to autonomy in decision making." Birth Defects Original Article Series (in press).

M. Lappé and P. Steinfels, 1974. "Choosing the Sex of our Children." Hastings Center Report 4, February 1974, pp. 3-7.

M. Lappé and R. Roblin, 1974. "Newborn genetic screening as a concept in health care delivery: A critique." Birth Defects Original Article Series. Ethical, Social and Legal Dimensions of Screening for Human Genetic Disease 10:1-23.

L. Ehrman and M. Lappé 1974. "Screening for polygenic disorders." Birth Defects Original Article Series. Ethical, Social and Legal Dimensions of Screening for Human Genetic Disease 10: 102-122.

D. Brower, M. Lappé and J.C. McCurdy, Of All Things Most Yielding. New York: McGraw-Hill, Inc. (book).

M. Lappé 1974. "Censoring the Hereditarians." Commonweal 50: 183-185.

M. Lappé 1974. "What Counts in Deciding to Withhold Treatment from the Defective Newborn?" Tufts Medical Alumni Bulletin 33.

W. Gaylin and M. Lappé 1975. "Fetal Politics." Atlantic 235: 66-71.

M. Lappé 1975. "Moral Claims of the Wanted Fetus." Hastings Center Report 5: 11-13.

M. Lappé 1975. "Putting 'Genetic Engineering' into the Medical Lexicon: Some Technical and Ethical Reservations." Medical Research Engineering (in press).

M. Lappé 1975. "Human Uses of Molecular Genetics." Federation Proceedings 34.

M. Lappé 1975. "Accountability in Science." (Letter to the Ed.) Science 187:696.

M. Lappé 1976. "Abortion and Fetal Research: A Reconsideration." Encyclopaedia Britannica Year Book.

M. Lappé 1976. "Reflections on the Non-Neutrality of Hypothesis Formulation." Clinical Research 24: 56-63.

M. Lappé 1976. "Reflections on the Cost of Doing Science." Annals of the New York Academy of Sciences 265: 102-111, January 23, 1976.

M. Lappé 1976. "What's in the Genes Anyway?" Man and Medicine. In press.

M. Lappé 1976. "Genetic Screening," in Principles of Counseling, (Alan R. Liss, Inc.) (in press).

M. Lappé, Alexander M. Capron, Robert F. Murray, Jr., and Sumner B. Twiss, (eds.) "Genetic Counseling: Facts, Values and Norms," (in press).

STATEMENT OF DR. MARC LAPPÉ, CHIEF, OFFICE OF HEALTH, LAW, AND VALUES, STATE OF CALIFORNIA DEPARTMENT OF HEALTH

Dr. LAPPÉ. Thank you.

Let me preface my remarks by saying that I am, like some recombinant DNA molecules, a kind of unique hybrid, having spent 5 or 6 years doing basic scientific research and an additional 5 years doing bioethical research, primarily at the Institute of Society, Ethics, and the Life Sciences prior to joining the Office of Health, Law, and Values in the California Department of Health.

My purpose in being here today is to offer some very broad observations about ethics and scientific research and to suggest some positive options about how we might link scientific findings to social policy.

It is that linkup which is difficult, as you've emphasized in your introductory remarks. Ethics and science are a bit like oil and water: they don't mix very well. There are some fundamental reasons for that clash of values. Ethics deals with truths which change with the vagaries of the human condition. Because ethics deals in part with the way in which human values should shape decisionmaking, ethics is shaped as much by cultural mores and political forces as by internal rules.

Science, on the other hand, involves the discovery of absolute, unchanging truths. In marked distinction from ethicists, for instance, scientists feel a need to isolate themselves from the daily affairs of humanity. Einstein once wrote of his pronounced lack of need for direct contact with human beings and communities, and commented on how ironic it was for that emotion to be present in someone who was committed in his heart, as Einstein was, to social justice.

Even today, science, remains essentially a solitary activity, ethics a social one. The pressures to drive science into a more public arena have been met with often massive resistance. The National Academy of Sciences recently has seen fit to oppose further public involvement in regulating the conditions under which recombinant DNA are conducted, as if the continued separation of science and the people, like the church and the state, is somehow a desirable state of affairs. In my view, it is not.

Opponents to unfettered and uncontrolled research are legitimately concerned with the protection of societal values in much the same way as opponents to similarily unfettered human experimentation in years past were concerned with protecting the rights of persons who were conscripted as subjects in biomedical research.

Today we have moved from a focus on individuals to a broader focus on society as a whole. Questions of informed consent, which were more or less easily resolved at the level of an individual, on a one-to-one basis with a physician or an experimenter, are now thrown into entirely different perspective when we place whole groups of people against society for consent purposes.

Science is as much a shaper of that society as it is shaped by it. Rene Dubos spoke of the intimacy of this codependency, in his book, Man Adapting. He wrote that it is "probable that the very continuance of science itself depends on the ability of scientists to relate their professional interests to the main currents and aspirations of society," and here is our dilemma.

Scientists are conditioned to follow research leads, not social trends. They are trained in problem solving, not social policy. And the most successful scientists tell us that excellent science simply cannot be done if it must adhere to some arbitrary external standard of behavior or rules. These scientists insist that science's internal conduct rules will make it self-correcting and value-neutral. In my view, nothing could be further from the social and political realities in which science is conducted today.

All of the steps of the scientific process are heavily shaped by political and social forces. Today the choice of an area of interest; the testing methods that are chosen to challenge a hypothesis; and the uses to which early scientific data are put, are all areas that are conditioned by forces which are external to the scientific establishment. What scientists choose to study is as much conditioned by values as by the traditional norms of heuristic appeal or scientific merit. When scientists select an area of interest in research these interests may be piqued as much by political considerations as by the timeliness of discovery. And how scientists go about doing science often involves political judgment as well as abstract, rule-following procedures.

For instance, in the recent past when scientists chose to look for genetic variants in the human population it was both because new tools opened up that area of inquiry and because genetic variation for a key susceptibility to illness might explain away a social failure to cope with a specific problem.

To be more specific, an initial scientific discovery that a genetically determined ability to produce a key enzyme called arylhydrocarbon hydroxylase, apparently necessary in the activation of carcinogens, suggested that the responsible gene might be mixed in varying proportions in the population.

If this were true and if that enzyme were indeed needed for making an agent carcinogenic, it would be of tremendous public health interest. But, prior to verification that there was a causal relationship between the inducibiliy of this enzyme and susceptibility to cancer, major corporations, particularly Dow Chemical in Texas, instituted testing for their employees to determine which had the inducible enzyme at a high level and which didn't.

In nefarious hands that type of example can be used to deflect attention away from environmental causes of cancer and focus attention on individual presumptive genetic variation. The fact that this went to a policy application before verification bespeaks the need for some kind of review at the level of basic scientific research that puts fetters or other constraints on premature application of unproven associations.

Let me suggest a classification scheme for the kind of involvement that public policymakers might have. There are two almost independent questions that are traditionally raised: First, what constraints or controls, if any, should policymakers impose on doing science in the first place? The basic research question. Second: What limits should be placed on what is done with what science produces? The level of application.

I strongly believe that both of these areas are open—and appropriate—for public scrutiny. But, others have argued that regulating research from its inception has to be almost so problematic that wise courses of action appear impossible.

Nevertheless, some kind of regulation at the level of basic research appears to me appropriate. Controlling the inception of an idea or the choices which scientists make admittedly is a knotty problem. It does tread on the prerogatives of persons to make free choices, and opens the door for governmental regulation of basic research, which, by its nature, I am convinced, can only flourish when unregulated. Even saying that, I want to say that I would like that door for public regulation to be left open. Where public health or the rights of persons are potentially compromised by scientific research, or where that research lends itself to abuse, I want the people who may be affected to have recourse either through their representatives or some other course of regulatory activity.

[The arguments for the appropriateness of research unnecessary involvement in basic research are presented in an appendix.]

I would like to propose an avenue of action in an area where public relevance of regulation is much less disputable. The results of some scientific investigations are so provocative that they fairly cry out for application, as, for instance, the case of the discovery of the inducibility of this enzyme I mentioned previously. Little or no public guidance now exists to say when data should be used, or, if timely, how that new and often unproven data or associations should be made into policy. Egregious public policy failures have been made simply because scientists and legislators failed to communicate in the past, or when they did, legislators accepted without question the technological imperative to use scientific data to formulate social policy.

I think I have a simple message for Members of Congress.

First, insist on involvement and education of the public, and, second, where appropriate learn to say "no" to data which implies policy decisions which compromise human values.

Let me be specific, by citing two examples:

First, an instance in the area of public education suggests the pitfalls of inadequately preparing the public: In the 1970's, you are probably well aware, the first genetic screening programs were instituted without prior public involvement or education. Sickle cell anemia, a then incurable and prenatally undiagnosable disease, was selected as the targeted goal. Instead of the primary health care which they needed, members of the black community were seemingly singled out for the labeling and resulting stigma which identifying carriers of a "deleterious gene"—sickle cell trait—entailed. A significant portion of that black population—and the medical profession itself—came to believe that carrying a gene for a harmful disease was somehow culpable behavior or physically harmful.

A second example, more current, centers around the discovery of the possible carcinogenicity of the flame retardant that you know of as "Tris," which is added in large amount to children's clothes. In California we knew about this data long before public policy application was taken by the Federal Government. Had we prepared careful support documents which balanced the grave but indeterminate risks of cancer to a large population against the severe but less awesome appearing risks of childhood burn injuries, we might have staved off a precipitous court order which reversed the ban on Tris and led to a potentially dangerous chemical persisting on the open market unregulated.

How do we avoid similar pitfalls? There seems to me to be at least three possibilities for deciding how to deal with scientific data. These are, by necessity, oversimplifications of the actual intricacies of policymaking.

The first is that the scientific data itself can be taken to dictate policy; second, the data can be used with other nontechnical data to suggest policy; and, third, the data may be taken to be irrelevant to policy. The middle course is familiar to any policymaker. Less often, scientific data give the appearance of being so compelling that in and of themselves they are presented as policy ultimata. For instance, Dr. John Lorber of Sheffield, Scotland, presented his staff's experience in operating on newborn children who had a variably disabling spinal cord defect known as "spina bifida."

After reviewing the experience of operations on each of the first 1,000 patients, Lorber concluded on the basis of the scientific data alone that the medical outcome was so disfavorable as to dictate that some children not be operated on at all. In 1971, he proposed and then used a set of purely medical criteria to sort children into categories of operable and nonoperable. Questions of family acceptance of potential handicaps, availability of supportive services and the possibility of conditioning the societal reception of impaired children were expressly excluded from these considerations. In my judgment, this was a distortion of the role which scientific data should play in making public policy. In my view, technical considerations are virtually never all determining for choices that affect people's lives.

I believe the same maxim should apply equally to recombinant DNA research. Technical assurances of low risk alone appear to me to be insufficient criteria for giving DNA research a green light. Who is to decide what constitutes an acceptable risk? What lines of inquiry are walled off by shunting funds to this area of investigation and not to others? And who shall decide if some research is so potentially harmful in its future applications that restraint should be exercise now? All of these questions, of course, require ethical as well as technological analyses.

Finally, there is the third possibility. Some policy decisions appear to me to be so value laden that scientific data should be given no weight at all. Before a person scientifically determined to have epilepsy is allowed to put an "X" on his voting record, we do not ask if he passed some scientific test to determine his biologic or genetic normalcy. The "fact" that a person is diagnosed as having schizophrenia does not, and in my view should not, constitute grounds in any State for involuntary commitment or drugging. In each instance I believe we should recognize the primacy of autonomy and equal deservedness of persons in our society, to temper our judgment about the use of scientific data.

Scientists, however, will continue to insist that we are somehow obliged to assign more intrinsic value to "hard" data than to the "soft" data generated by the social sciences. They believe that the only realities on which we may base social policy are those provided by science. For instance, if science reports systematic differences in educability and then links those to the genetic makeup of some groups of individuals, it is considered foolhardy not to incorporate those data into public policy. I believe that is simply not so. I believe it is entirely

justifiable to ignore scientific data which indicate group genetic differances in "educability," if by doing so you encourage social values which are higher than those sought by the scientists themselves.

A society might well decide that social cohesiveness, mutual trust and a sense of communality, which might well follow from treating all children alike in one or more of their formative years, would outweight the advantages of special classification schemes which use a genetic criteria for educability. The ethical principle of treating like things alike is an extension, I believe, of a basic conviction in a democratic society that individuals are vested with equal rights, irrespective of any systematic biological or scientific difference.

Finally, the lesson from all this appears to me to be straightforward: sometime scientific data alone do not constitute appropriate grounds for policymaking; and, second, legislators are justified in saying that human values can be allowed to supercede scientific imperatives in some instances.

That completes the formal testimony which I have prepared.

[The complete statement and additional material of Dr. Marc Lappé is as follows:]

Testimony Before the House

Subcommittee on Science, Research and Technology

Marc Lappe' Ph.D., Chief
Office of Health, Law and Values
Department of Health
Sacramento, California

September 7, 1977

Introductory Remarks

My purpose in being here today is to offer some broad observations about ethics and scientific research and to suggest some positive options about integrating scientific findings into social policy.

Linking ethics to science policy is difficult. Ethics and science are like water and oil: they don't mix well. Ethics deals with truths which change with the vagaries of the human condition. Because ethics deals with the way human values should shape decision-making, it is shaped as much by cultural mores and political forces as by rules.

Science involves the discovery of absolute truths. In marked distinction from ethicists, scientists feel a need to isolate themselves from the daily affairs of humanity. Einstein once wrote of his pronounced lack of need for direct contact with human beings and communities, and commented on how ironic that emotion was for someone who was committed in his heart to social justice.

Even today, science is still essentially a solitary activity, ethics a social one. The pressures to drive science into a more public arena have been met with massive resistance. The National Academy of Sciences has seen fit to oppose further public involvement in regulating the conditions under which recombinant DNA are conducted, as if the continued separation of science and the people, like the church and the state, is somehow a desirable state of affairs. It is not. Science is as much

a shaperof society as it is shaped by it. René Dubos spoke of the intimacy of this co-dependency in his book, Man Adapting. He wrote that it is "probable that the very continuance of science depends on the ability of scientists to relate their professional interests to the main currents and aspirations of society."

But scientists are conditioned to follow research leads, not social trends. They are trained in problem solving, not social policy. The most successful scientists tell us that excellent science cannot be done if it must adhere to some arbitrary external standard of behavior. They insist that science's internal conduct rules make it self-correcting and value-neutral. Nothing could be further from the realities in which science is conducted today.

All of the steps of the scientific process are heavily shaped by political and social forces; the choice of an area of interest; the testing methods chosen to challenge an hypothesis; and the uses to which early scientific data are put. What scientists choose to study is conditioned as much by values as by heuristic appeal or scientific merit. When scientists select an area of research, their interests may be piqued as much by political considerations as by the timeliness of discovery. And, How scientists go about doing science involves political judgment as well as abstract, rule-following procedures. When scientists chose to look for genetic variants in the human population, it was because new tools opened that area of inquiry -- but occasionally, because genetic variation for a key susceptibility to illness explained away a social failure to cope with a specific problem. All of these realities justify policy makers getting involved in the conduct of science in society.

Let me suggest a classification scheme for that involvement. The debate on where public policy experts should step into over-sight of scientific research usually centers on two independent questions: 1) What constraints or controls, if any, should policy makers impose on doing science?; and 2) What limits should be placed on what is done with what science produces? I have tried to make the case that both of these areas are open--and appropriate--for public scrutiny. Regulating research from its inception is so problematic that "wise" courses of action appear virtually impossible.

Controlling the inception of an idea or the choices which scientists make is an incredibly knotty problem. It treads on the prerogatives of persons to make free choices, and opens the door for governmental regulation of basic research which by its nature can only flourish when unregulated. Even saying that, I want that door to be left open. Where public health or the rights of persons are potentially compromised by scientific investigation, or where research clearly lends itself to abuse, I want the people who may be affected to have recourse through their representatives. But that is not why I am here today.

I want to propose an avenue of action in an area where public relevance is indisputable. The results of some scientific investigations are so provocative that they fairly cry out for application. Little or no public guidance exists to say when data should be used, or if timely, how new often unproven data or associations should be made into policy. Egregious public policy failures have been made simply because scientists and legislators failed to communicate, or when they did, legislators accepted without question the technological imperative to use scientific data to formulate social policy.

I have a simple message: insist on involvement and education of the public, and learn how to say "no" to data which implies policy decisions which compromise human values. Let me be specific. Here are two examples: Education: In the 1970's, the first genetic screening programs were instituted without public involvement or adequate education. It happened that sickle cell anemia, a then incurable and prenatally undiagnosable disease, was selected as the targetted goal. Instead of the primary health care which they needed, members of the black community were seemingly singled out for the labelling and resulting stigma which identifying carriers of a "deleterious gene" (sickle cell trait) entailed. A significant portion of the black population -- and the medical profession -- came to believe that simply carrying the gene for a harmful disease was somehow culpable behavior or physically harmful. Communication: Health officials in California and elsewhere were unprepared to deal with the necessary balancing of needs when they first learned of the potential carcinogenicity of the flame retardant known as "Tris" which is added to childrens' clothes. Had we prepared careful support documents which balanced the grave but indeterminate risks of cancer to a large population against the severe but less awesome risks of childhood burn injuries, we might have staved off a precipitous court order which allowed this potentially dangerous chemical to persist on the open market. Earlier and more comprehensive contacts with the scientific community would have given us that lead time. How do we avoid similar pitfalls?

Before using scientific data in making policy decisions, a legislator should consider three options: 1) data can be taken to dictate policy; 2) data can be used with other non-technical data to suggest policy; and 3) data may be irrelevant to policy. The middle course is familiar to

any policy maker. Less often, scientific data give the appearance of being so compelling that they are presented as policy ultimata. Dr. John Lorber of Sheffield, Scotland presented his staff's experience in operating on newborn children who had a variably disabling spinal cord defect known as "spina bifida." After reviewing the experience of operating on each of his first 1,000 patients, Lorber concluded that for some patients, the medical outcome was so disfavorable as to dictate that some children not be treated at all. In 1971, he proposed and then used a set of purely medical criteria to sort children into categories of operable and non-operable. Questions of family acceptance of potential handicaps, availability of supportive services and the possibility of conditioning the societal reception of impaired children were expressly excluded from consideration. In my judgment, this was a distortion of the role which scientific data should play. Technical considerations are virtually never all determining for choices which affect peoples' lives.

The same maxim applies equally to recombinant DNA research as to spina bifida. Technical assurance of low risk are insufficient criteria for giving DNA research a green light. Who decides what constitutes an "acceptable" risk? What lines of inquiry are walled off by shunting funds to this area of investigation and not others? And who shall decide if some research is so potentially harmful in its future applications that restraint should be exercised now? All of these questions require ethical as well as technical analyses.

Finally, there are policy decisions which are so value laden that scientific data should be given no weight at all. Before a person scientifically determined to have epilepsy is allowed to put an "X" on a piece of voting

record, we do not ask if his genetic composition meets some test of normalcy. The "fact" that a person is diagnosed as having schizophrenia does not constitute grounds for involuntary commitment or drugging. In each instance we continue to recognize the autonomy and equal deservedness of persons in our society until social criteria, like felonious behavior or dangerousness to others are available to temper our judgment.

Some scientists will continue to insist that we are somehow obliged to assign intrinsic value to "hard" data. They believe that the only realities on which we may base social policy are those provided by science. If science reports systematic differences in educability and genetic makeup of some groups of individuals, it is considered fool-hardy not to incorporate those data into policy. Not so. It is entirely justifiable to ignore scientific data which indicate individual difference in educability if by doing so you encourage social values which are higher than education. A society might well decide that the social cohesiveness, mutual trust and sense of communality which would follow from treating all children alike in one or more of their formative years would outweigh the advantages of special classification schemes which use educability as criteria. The ethical principle or treating like things alike is an extension of a basic conviction in a democratic society that individuals are vested with equal rights irrespective of their systematic biological differences.

The lesson from all this is straightforward: scientific data alone do not constitute sufficient grounds for policy making -- and legislators are justified in saying that human values supercede scientific imperatives.

From Science Ethics and Medicine,

H. Tristram Engelhardt, Jr., and Daniel Callahan, eds.,

The Hastings Center, Hastings-on-Hudson, New York, 1976.

3

The Non-neutrality of Hypothesis Formulation

Marc Lappé

I. Freedom of Inquiry

Critics and proponents of science alike consider hypotheses the free ground upon which scientific inquiry takes place. Hypotheses become the jousting grounds of criticism where ideological adversaries tilt at each other, intent at toppling insecure concepts or weak formulations. The *generation* of a hypothesis is in this view a value-free enterprise; values come into play only after the fact, when hypothesis-testing is conducted according to rules of procedure which demand both intellectual and ethical rigor. Thus for some, the formulation of a hypothesis itself is envisioned as taking place in a quasi-Camelot, where pure ideas spring fully armed from the head of the scientist.

In such an idealized world, hypotheses are seen as being "struck like sparks from unaccountable hunches or quirks of the mind, from an idiosyncratic penchant for the pleasing form or agreeable order."(1) Karl Popper reinforces this value-neutral view in advocating the imperative of freedom of conjecture as part of scientific advance.(2) For Popper, it is only *after* their formulation that hypotheses are to be subjected to normative tests. If we take this view, scientific scrutiny and criticism are essential to the process of justification, not that of discovery.

This view of science conveys a sense of the germinal period of scientific innovation as one in which total abandon is permitted, and even encouraged. As George Wald put it, "The scientist is willing to plunge blindly, the better to plunge. . . . The logic is left to be repaired later."(3) Dangerous stuff that, in a world in which the domination of any one hypothesis can hold sway for decades (or in Copernicus's time, centuries) before illogical or faulty construction becomes apparent. More dangerous still, when expropriation of hypothetical formulations (about presumptive genetic bases of criminality, for example) threaten traditional notions of human autonomy or liberty. However, if the problem of value-laden hypotheses were purely one of misuse, this analysis would stop here—no one questions that ideas can be misappropriated for nefarious purposes. It is rather the stronger claim, that some hypotheses in and of themselves can be inappropriately preferred, that I am addressing here. The source of error to be examined is not one of misuse, but of factors internal to the hypothesis itself—the source of its assumptions, its predictions, its required tests. In sum, the cultural and historical forces which precondition a mind (or an historic period) toward a world view.

At any time, a novel hypothesis poses a risk of dislocating human attention from one set of problems to another. Whether the later appropriation of its verified predictions leads to social decay or flourishing is rarely, if ever, in the hands or mind of the scientist who first formulates his idea. But this first formulation may be laden with cultural and political baggage. The heuristic appeal of a hypothesis all too often capitalizes on a world view which is already socially conditioned—and is thus subject to cultural biasing factors. For instance, the notion that people as well as plants might be perfectable in an inheritable fashion through environmental manipulations was an idea which inevitably linked Marxian ideals to Lamarckian genetics(4)—and thence to Lysenkoism.

II. Disaffection from Science

I would agree that the progress of science requires that hypothesis formulation embody irrational elements to ensure that it goes beyond the bounds of existing knowledge. The

critical question remains whether or not constraints can or should be imposed on this process. Often the claim is made that exercises in creativity should not be subject to the same kind of scrutiny reserved for their products. Even those counted among the most politically radical have tended to concur with this view.

James Shapiro, who with Lawrence Eron, Jonathan Beckwith, and others, isolated a gene (the *lac* operon) for the first time, created a stir in 1969 by announcing that he was leaving science for politics. In a letter to *Nature*, Shapiro, Eron, and Beckwith gave a surprisingly docile view of their scientific work before critiquing the social and political context in which it might be abused. They said, "In and of itself our work is morally neutral; it can lead either to benefits or dangers to mankind. . . ."(5)

Why this reluctance to question the roots of science? The solution to the paradox of political radicalism in the company of scientific conservatism is not hard to find. In a different setting, Shapiro was asked why he did the work in the first place. His answer: "We did this work for scientific reasons, also because it was interesting to do. But scientists generally have the tendency not to think too much about the consequences of their work while doing it. But now that we have, we are not entirely happy with it."(6) It appears that Shapiro, Eron, and Beckwith were scientists first and political radicals a far second. The questioning of fundamental assumptions of freedom of inquiry cannot be done by those who have benefited by that practice.

Some would say that if Shapiro *et al.* truly were concerned with the political implications of their work, they would have questioned their priorities in choosing a genetic system for study which could not foreseeably yield benefits as much as harms. But that view misses the central point of doing science itself. In order for a scientist to question the roots of his own work, he must profess disinterest in the very matter which sets his tasks apart from the purely political: the quest for truth. In this case, Shapiro, Eron, and Beckwith quite understandably subordinated their political ideologies to the sudden accessibility of a "truth" which they found possible through development of a novel technique. They were able to discount any

ethical cost implicit in the work itself, by projecting concern to its probable misuse at some later time. But the very *selection* of a problem raises questions of resource allocation which conflicts strongly with the ideology of free inquiry. A scientist trained in one narrow discipline may not be able to adopt a new priority system to select hypotheses based on moral values.

III. Instability of the Central Dogmas

Surprisingly, Shapiro's disaffection created a major furor. To understand why one member's quitting could cause such a dislocation in the scientific establishment requires an understanding of science as a collective activity. The four norms of scientific activity given by Robert Merton (organized skepticism, universalism, communality, and disinterestedness) have become highly unstable. Israel Sheffler recently observed that:

> The notion of a fixed observational given, of a constant descriptive language, of a shared methodology of investigation, or a rational community advancing its knowledge of the real world—all have been subjected to severe and mounting criticism from a variety of directions.
>
> The overall tendency of such criticism has been to call into question the very conception of scientific thought as a responsible exercise of reasonable men. . . .(7)

An instability of internal structure makes it possible for the "normal" processes of hypothesis formulation to become destabilized. A possible result, already realized in transplantation immunology,(8) is that heuristic but unsubstantiable hypotheses will gain greater currency. More important perhaps, a period of instability affords an opportunity for scientists to inspect their premises and assumptions about the nature of hypothesis formulation.

IV. Descriptive Elements

To analyze the basis for instability, it is useful to bifurcate the scientific enterprise by distinguishing processes unique to the elaboration of scientific hypotheses and those entailed in the process of corroboration or refutation of those hypotheses.

As Stephen Brush has pointed out,(9) the first of these processes comprise the "context of discovery," the second, the "context of justification." Errors and unethical conduct in the latter have been well documented recently(10) and show that errors of judgment persist. But the nature of the errors which might be made in the context of discovery has not, to my knowledge, been systematically explored. Certainly, acts of omission may occur because of human fallibility, so at first examination it appears difficult to define the conditions under which morally responsible errors occur.

Under what circumstances then is hypothesis formulation (as distinct from hypothesis testing) itself appropriately scrutinized for its value content? Since the ordinary process of hypothesis formulation does not embody moral rules, where do value constructs, if any, come from? Does hypothesis formulation include value conditions? The problem is first one of descriptive, rather than normative, ethics. To state the problem in Stephen Toulmin's words:

> Where a dominant direction of variation [in new lines of scientific thought] can be observed within any particular science, or where some particular direction of innovation appears to have been excessively neglected, a new type of issue arises. Within the total volume of intellectual variants under discussion, what factors determine which types of option are, and which are not pursued?
>
> We are asking how scientists come to take certain kinds of new suggestions seriously in the first place—considering them to be worthy of investigation at all—rather than [what] standards they apply in deciding that those suggestions are in fact sound and acceptable.(11)

Toulmin recognizes that in many cases the justification for taking a particular kind of scientific hypothesis seriously has to be sought outside the intellectual content of the particular science. Like many historians of science, Toulmin recognizes that the selection criteria for hypotheses are so embedded in social and historical factors that it may be unrealistic to expect that they be extricated.

How do the traditional selection criteria for hypotheses stand up to the scrutiny of the historian or sociologist? Abner

Shimony delineates four criteria intended to keep hypothesis formulation value-free.(12) By providing conduct rules for hypothesis formulation that keep biasing factors in view, Shimony hopes to keep the process part of the internal norm of science. His list includes the following provisos:

1. That the hypothesis be clearly stated;
2. That the motivation for proposing it be explained;
3. That the explanation in some way acknowledge (but not necessarily accept) a recognized body of propositions regarding the subject; and
4. That it not be an arbitrary choice from a family of hypotheses which answer the same motivation.

Two of these factors—consciousness of motivating factors and freedom from arbitrariness—are by definition factors which cannot be objectively delineated, especially as they apply to complex phenomena, and are hence value constructs. Shimony's other tests for hypotheses are similarly limited, perhaps because Shimony may be more interested in demonstrating the internal consistency of science than in constructing ethical tests for the acceptability of its procedures.

Thus, rather than propose an external measure for hypothesis acceptability (such as social utility or consistency with established norms), Shimony would have the researcher assign priorities to hypotheses based on calculations of prior probabilities of likelihood of success in describing unexplained phenomena. His world of "tempered personalism" assigns each seriously proposed hypothesis a rank order in which no hypothesis is excluded from consideration. This idealized construct is one in which the researcher holds varying degrees of commitment to rival hypotheses, rather than allegiance to a central one. Such a system conflicts strongly with the expedient needs of scientific inquiry, which often mandate adherence to a single hypothesis until self-testing leads to refutation. But more important, it simply reinforces whatever modeling system worked in the past (for on what else will prior probabilities be derived?), and works within the traditional goal-model: that elucidation of truth for truth's sake is the rightful function of science.

V. Normative Questions in Hypothesis Selection

The conduct rules for the practices involved in empirical testing of hypotheses are well defined and do not appear to me to present novel categories of ethical inquiry. What constitutes "proper" conduct in the elaboration of hypotheses, however, is not well understood. What can be said? First, that it is impractical and wrongheaded to base an attack solely on freedom of inquiry or cultural biasing factors. Second, that it is evident that some discretionary latitude is necessary in different sciences to ensure an adequate complexity and richness in generation of scientific ideas. Third, that culturally influenced ideas and decisions are not in and of themselves objectionable; these may be the source of hypotheses which are particularly fruitful because they are based on experiential elements unique to a particular class of persons. (Fabre's observations and hypothesis-testing among the social insects are a classic example of a unique interplay between culture, ideology, and science.) But the assumption that hypothesis formulation is value-neutral when its objective is individuals (in the sense MacIntyre uses the word to embrace multilevel phenomena) is likely to be mistaken. As MacIntyre and Gorovitz observe: "The study of individuals cannot be nonevaluative in the way that properties is." Every "central question" of a science often embraces value constructs which force the language, thinking, and conceptualizations used to formulate them into new molds. This has proven especially true in genetics.

VI. Genetic Science as a Special Case

At face value, genetics appears to be a science which moves forward by proffering hypotheses which attempt to explain the causal network of molecular constructs which underlie all natural phenomena. A sociologist of science might ask first if there were value-related elements in this process which evoke certain classes of hypotheses for testing and not others. He might then ask if these elements were identifiable with specific cultural features of the class of persons who do the work. Finally, he might examine the implicit assumptions made by the

formulators as to the degree of confidence they attach to the presuppositions of genetic test systems.

In part, because the relationships which genetics seeks to establish are between "individuals" (expressed as phenotypes) and their genotypic and environmental substrates, there is a high probability that genetics will be used as a causal nexus for explaining a spectrum of human conditions, attributes, or behaviors which do *not* necessarily have internal causes; for example, social deviancy or mental disorders. Second, because genetics is in its infancy, competing hypotheses will proliferate and adherents will be marshalled in part according to their world views. This point was made clear by Richard Lewontin in his most recent work with regard to genetic variation.

> Indeed the whole history of the problem of genetic variation is a vivid illustration of the role that deeply embedded ideological assumptions play in determining scientific "truth" and the direction of scientific inquiry. . . . It is not the facts but a world-view that is at issue, a divergence between those who, on the one hand, see the dynamical processes in populations as essentially conservative, purifying and protecting an adapted and rational *status quo* from the nonadaptive, corrupting, and irrational forces of random mutation, and those, on the other, for whom nature is process, and every existing order is unstable in the long run, who see as did Denis Diderot that *Tout change, tout passe, il n'y a que le tout qui reste.*(13)

A third problem is that the categorization of human behaviors is in itself a value-based activity. The techniques chosen for measuring behavioral traits themselves delimit the scope of the attribute being tested, and in the process, rule out other traits which might warrant study. More important, as behavioral geneticists Fuller and Thompson point out, measuring devices may determine the nature of the traits which can be found.(14) In part, this means that the tests used to measure behaviors may come to define the phenomena they seek to measure (IQ test results come to be equated with intelligence). But the need to put behaviors into categories for explication violates the basic biological norm developed by Ernst Mayr which demands that characteristics which are continuously varying not be considered typologically. In Fuller and Thompson's words, the

behavior and biology of animals "do not readily fit into categories." Classical Mendelian genetics, of course, deals solely with categories.

A further complicating force is that even non-Mendelian genetic hypotheses must often attempt to explain a complex human trait in terms of simplifying assumptions which forcibly displace attention to the roots of causation from external factors to internal ones. This takes place, for example, whenever a complex (polygenic) condition like diabetes becomes ascribed to single genes with "reduced penetrance." The search for environmental correlates of the condition may then be suspended while intensive study is done on the putative genetic hypothesis. Geneticists often apply Occam's razor inappropriately to complex human conditions like diabetes, hypertension, or neural tube defects. Why is this so?

Admittedly, in order to "do" genetics in the laboratory, it is important to be able to exclude competing models or paradigms, and to suspend temporarily consideration of alternative hypotheses. For experimental systems, it is acceptable, even desirable, to isolate putative genetic factors from their environmental overlay; but in humans, this separation is difficult to attain in theory, if not impossible to achieve in practice. Moreover, isolation of environmental variables may violate ethical norms, as when testing to determine an intrinsic (i.e., genetic) basis for a malabsorption syndrome such as sprue, calls for institution of a diet known to cause intestinal injury. Since these and other limitations greatly restrict the ability of the environmentalist scientist to *dis*prove a genetic hypothesis, deciding to use a genetic model for explaining human ability or disability virtually assures a tenure of visibility of the hypothesis. Hence a major ethical issue in choosing any hypothesis for study which is not subject to refutation is the cost incurred in suppressing competing and potentially valid hypotheses.

For example, because heritability estimates of human IQ scores are restricted in their validity to measurements within groups sharing relatively common environments, between-group comparisons (for example, between whites and blacks) are likely to be unscientific and possibly invidious. The absence of

any reliable means of deriving and measuring heritability for nonmetric traits, and the dearth of any means of measuring white admixture among blacks further preclude a valid test of the proposition of the genetic basis of white/black IQ score differentials.

The decision to treat variations of human attributes like intelligence as primarily a problem in genetics, rather than a complex biological/cultural/economic/political problem, places the need to discern first causes above that of the persons they affect. The behavioral geneticist knows in advance that genetic differences for a given form of behavior cannot be discerned if the environment is sufficiently suppressive of that trait. In the face of analyses which question the validity of heritability estimates,(15) attempting to derive heritability data on IQ scores among general ghetto populations becomes not merely a questionable scientific enterprise, but a morally suspect one.

At least part of the problem is wrapped up in the understandable need of the scientist to lift out and isolate a portion of a larger problem which is fit for study (that is, quantitation) from its larger context. But treating a scientific problem in isolation when its object of study is a complex phenomenon courts omission of critical evaluative factors, for three reasons. First, as Whitehead has emphasized: "No science can be more secure than the unconscious metaphysics which tacitly it presupposes. The individual thing is necessarily a modification of its environment, and cannot be understood in disjunctión."(16) Second, the description of phenomena on the basis of idealized physical systems excludes interactional components and "bridging" rules which relate those systems to the behavior in question as it is evinced under real-world conditions.(17) Third, isolating the phenomenon may inadvertently exclude or downgrade one or more contributing factors, such as environmental factors in IQ scoring.

This threefold analysis suggests the kinds of value premises entailed in the exclusion of alternative hypotheses in favor of genetic ones. Genetic models may lead to an organization of the social world according to certain internal qualities unique to genetic systems, such as fixity, predetermination, and strong biological determinism. Such a view in its broadest sense may

diminish the attention given to powerful but subtle environmental influences or social factors which modify the expression of a trait. One such example is the intrauterine environment, or postnatal milieu, both of which potentially affect the prospect of normal biological and psychological development. Genetic hypotheses also embody a sense of determinism which conflicts with norms that the society may be deeply committed to, by virtue of its laws, mores, and general moral structure. By embodying the injunction that we are somehow obliged to restructure society along lines which recognize the primacy of fixed biological potentialities, attributes, and traits, genetic hypotheses work to deemphasize the moral, unfixed elements of humanness which have been integral to the emergence of culture and religion.

VII. Exclusion of Competing Hypotheses

A first-level test for the appropriateness of seriously putting forth a given hypothesis should include an estimation of the moral costs of not testing a competing one. Even where those competing hypotheses embody more difficult or complex refutation or other testing procedures, they should be evaluated on the basis of their *moral content* before being displaced. A second-level test has to do with the degree of human good which *acting out* the predictions of the hypothesis will likely engender. In the case of genetic hypotheses, their heuristic appeal and simplifying assumptions may make them better candidates for scientific inquiry than are environmental ones.(18) How are we to choose between "good" hypotheses which are good for scientific reasons and those which are good for moral ones? Which approach benefits society more?

In Table 1, I have outlined some of the more commonly used reasons for accepting hypotheses on the basis of scientific criteria. (I would emphasize that a hypothesis which is "good" in the scientific context usually embodies several of these features.)

Using criteria such as these generally ensures no more than that the hypothesis chosen can do what it claims to do—provide a set of testable predictions which embrace enough previously

TABLE 1
Examples of Scientific Criteria for Hypotheses

A. Falsifiability
B. Simplicity and parsimony
C. Heuristic appeal
D. Predictive power (scope and variety of predictions)
E. Exclusion of competing models
F. Mensurate qualities (availability of suitable instruments, equations, etc.)
G. Explanatory power (ability to account for more than one set of phenomena)

unexplained phenomena such that its solution will be scientifically meaningful. This simplified construction points to several weaknesses of hypothesis-formulation: first, that the scientific formulation assumes that it is unnecessary to evaluate the costs of what is left out by isolating a phenomena in terms of its physical systems; second, that it excludes the tests for appropriate mechanisms which lead to choosing a specific area and form of inquiry. These are part of the moral content of hypotheses. Examples of the nature of the input necessary to begin to analyze and weigh "moral content" are shown in Table 2.

Items listed in this second table would be used to gauge the moral content of the scientific criteria. For example, "heuristic appeal" would be scrutinized for its cultural loading factors (item A). The exclusion of competing hypotheses would be

TABLE 2
Identification of Value-Based Tests for Hypothesis Formulation and Testing

A. Identification and weighting of cultural biasing factors
B. Assessment of the costs of hypothesis selection
C. Assessment of the costs of performing the tests necessary for corroboration or refutation
D. Consideration of the moral factors attendant on verification
E. Projection of possible societal dislocations

subjected to analyses of its moral implications (item B). Evaluation of the possible ethical questions (experimental systems needed, etc.) raised by testing the predictions of the hypothesis would be made (item C). The possible costs as well as benefits of hypothesis verification would be weighed (items D and E).

This formulation immediately raises some vexing problems. Are we really saying that we should disallow some scientifically promising hypotheses or experiments because they are morally threatening? Whom do we expect to perform these analyses? How ought we balance the scientific criteria against the moral ones? How important a consideration should the moral content of any hypothesis be and how do we go about demonstrating it? A set of case studies may illuminate some of these apparent dilemmas.

It should be evident that the major class of hypotheses being considered involve predictions or assumptions that impinge more or less directly on human nature and social conditions. A set of examples from the interface between the "hard" biologic sciences (genetics) and the "soft" ones (sociology, psychiatry) will highlight the complexities of the thesis that moral considerations are an obligatory part of the construction of hypotheses.

VIII. A Classification Scheme for Assigning Moral Weights to Hypothesis Formulation

A. Class I: Hypotheses which are intrinsically dangerous. At face value, this is the simplest class of hypotheses to evaluate. Rules for abstaining from doing direct harm or injury are seemingly self-evident. As George Barnard Shaw noted in *The Doctor's Dilemma*, "No man is allowed to put his mother in the stove because he desires to know how long an adult woman will survive the temperature of 500 degrees Fahrenheit, no matter how important or interesting that particular addition to the store of human knowledge may be." However, in practice it may be difficult to project and weigh the class of harms which might ensue should an initial hypothesis be verified. For example, the need to construct a probe which could test the

construction of human genomes led to the development of DNA hybridization techniques which then became part of the technology needed to develop bacterial "plasmids" which could make multiple copies of mammalian gene sequences. This work immediately lent itself to the introduction of genes into a plasmid, which could confer oncogenicity (tumor-producing) or virulence (killing power) on a host cell. This potentiality, coupled with other unforeseen possibilities, led to the Berg letter in *Science* which called for a moratorium of genetic research on certain plasmid systems.(19) Thus, although testing the concept that virulence can be conferred to an intestinal bacterium may be "dangerous," the development of the technique itself could have been justified on the grounds of its fundamental worthwhileness for advancing molecular biology. Indeed, this is what was done.

B. Class II: Hypotheses which are mischievous. A "mischievous" hypothesis is one in which any logical sequence of testing generates equally unsatisfactory moral outcomes. A mischievous hypothesis is also one which is intrinsically untestable (that is, not subject to falsification). However, mischievousness might also involve a moral ascertainment, for example, that there has been an attempt to deceive, or that some morally weighted predictions of the hypothesis were formulated *prior* to the hypothetical construct itself.

Take, for instance, a hypothesis which proposes that heredity is the principal reason for success in business. If confirmed, the hypothesis would predict that businessmen achieved their status on the basis of inherited properties. But the presumed properties which lead to business success have never been systematically defined, nor the possibility of performing quantitative tests to determine their distribution in the population determined. Genetic markers for these nonexistent properties are unknown. By taking "business success" as a unitary phenomenon, one accepts this class of behaviors as scientifically defined. By agreeing to "test" such a hypothesis over time, there is every possibility that the scientist will have conferred a degree of respectability to a system he may never have intended to support.

C. Class III: Hypotheses which are socially invidious. An invidious hypothesis is one which posits properties or relationships among persons which imply the existence of morally questionable traits, characteristics, or behaviors. For example, the hypothesis that a specific ethnic group or population is inclined to deviant behavior for biologic or intrinsic reasons is invidious because it violates norms and assumptions about the autonomy of individuals who are members of groups or classes. A representative hypothesis here, for example, is one which posits that low IQ and race can be predicted on the basis of chromosome banding patterns.(20) Because both of the traits in question (race and IQ) are suspect classifications for what they purport to represent or measure, this hypothesis, like others in its class, will likely be disqualified for both scientific *and* moral reasons.

D. Class IV: Hypotheses which are holistically threatening. This class is characterized by hypotheses which posit a world view which violates social and moral norms. Here, it is critical to distinguish hypotheses which are holistically threatening by virtue of their *moral* content from those which ostensibly pose the same threat because of their revolutionary constructs. For example, Galileo's world view could be considered holistically threatening because of the perturbation it portended for man's theological view of himself, in contrast to the hypothesis of a growing number of health workers that genetic predisposition to disease (as, for example, determined by HL-A markers) is responsible for a large part of human disability,(21) is threatening because it abruptly shifts the burden of proof of being free from disease-producing conditions away from the society and to the individual. This latter shift in world view is thus holistically threatening in a different way from Galileo's.

By replacing a view of social causation of illness or disability with a genetic one, the genetic susceptibility hypothesis could threaten those segments of society which still have appreciable amounts of environmentally related disease. Individuals who were susceptible to disease by virtue of their social and economic conditions would thus be heavily penalized. Thus, whereas an emphasis on such epidemiologic hypotheses could

conceivably move society toward better standards of long-term medical prevention and ascertainment, the replacement of a world view which sees medicine as primarily serving individual needs in the present with one which sees medicine serving future needs obviously requires moral analysis.

That these two viewpoints represent assessments of hypotheses in the real world can be seen in an editorial in *The Lancet*(22) in which the mind-set of different health workers is described. The editorial writer makes the observation that there are "global-minded" and "research-minded" workers who compete for hypotheses on the grounds that the value of health services as a whole be given precedence (in the first instance) or that the value of individual patient-lives takes priority (the latter). Not only might one expect that different solutions to similar problems might be proposed by the two groups (the point of this editorial), but also that the weight given to recognizing the value of different approaches will differ depending upon the social conditions and acculturation that each group experiences. In this instance, as in most hypothesis formulation in the health sciences, the choice of a hypothesis may be not merely socially conditioned, but socially driving in terms of the attention given to solutions.

IX. Conclusion

From even this preliminary analysis, it should be evident that assigning a determinative or even contributory role to the moral content of hypotheses in selection of models for testing scientific propositions is fraught with difficulty. The balance point between what is morally threatening (compare categories in Table 2) and what is scientifically promising (see Table 1) may be impossible to determine with assurance. Not only are incommensurables being juxtaposed, but also the value system of the observer can shift the emphasis given to one set of priorities to the other, both within and between classes of criteria.

Whatever the ultimate value of a more refined system, it should be abundantly clear that the proliferation of scientific hypotheses under the rubric of freedom of inquiry can no longer proceed unexamined.

NOTES

1. Theodore Roszak, *Where the Wasteland Ends* (New York: Doubleday & Co., 1973) p. 142.
2. Karl Popper, *The Logic of Scientific Discovery* (New York: Basic Books, 1959).
3. George Wald, "Innovation in Biology," *Scientific American* 199 (September 1958), 100-13.
4. Conway Zirkle, *Marxian Biology and the Social Scene* (Philadelphia: University of Pennsylvania Press, 1959).
5. James Shapiro, L. Eron, and J. Beckwith, "Letter to the Editor," *Nature* (December 1969), p. 1337.
6. James Shapiro, quoted by James U. Glassman, "Harvard Researcher Quits Science for Politics," *Science* 167 (1970), 964-65.
7. Israel Sheffler, *Science and Subjectivity* (Indianapolis: Bobbs-Merrill Co., 1967), pp. v-vi. Cited in Stephen Brush, "Should the History of Science be Rated X?" *Science* 183 (1974), 1160-72.
8. Marc Lappé, "Accountability in Science" (Letter to the Editor), *Science* 187 (February 28, 1975), pp. 696-99.
9. Brush, "Should the History of Science be Rated X?"
10. Jerry Gaston, *Originality and Competition in Science: A Study of the British High Energy Physics Community* (Chicago: University of Chicago Press, 1974; Salvador Luria, "What Makes a Scientist Cheat," *Prism* (May 1975) pp. 15-18, 44; "The Sloan-Kettering Affair: Could It Have Happened Anywhere?" *JAMA* 229 (1974), 1391-1410.
11. Stephen Toulmin, "The Evolutionary Development of Natural Science," *American Scientist* 55 (1967), 456-71.
12. Abner Shimony, "Scientific Inference," in *The Nature and Function of Scientific Theories*, R. G. Colodny, ed. (Pittsburgh: University of Pittsburgh Press, 1970), pp. 79-172.
13. Richard Lewontin, *The Genetic Basis of Evolutionary Change* (New York: Columbia University Press, 1974), p. 157.
14. John Fuller and W. Robert Thompson, *Behavior Genetics* (New York: John Wiley & Sons, 1960).
15. David Layzer, "Heritability Analyses of IQ Scores: Science or Numerology?" *Science* 183 (1974), 1259-66. See also P. A. P. Moran, "A Note on Heritability and the Correlation Between Relatives," *Annals of Human Genetics* 37 (1973), 217, in which it is proven that a coefficient of heritability cannot be validly derived.
16. Alfred North Whitehead, *Adventures of Ideas* (Cambridge: Cambridge University Press, 1933), p. 154.

17. Frederick Suppe, "What's Wrong With the Received View on the Structure of Scientific Theories?" *Philosophy of Science* 39 (1972), 1-9.
18. Qutub Quazi and T. Reed, "A Possible Major Contribution to Mental Retardation in the General Population by Gene for Microcephaly," *Internal Journal of Clinical Genetics* 7 (1975), 85-90.
19. Paul Berg *et al.*, "Potential Biohazards of Recombinant DNA Molecules," *Science* 185 (1974), 303.
20. H. Lubs *et al.*, "Correlations Between Low IQ, Race and Variations in Q and C Banding," *American Journal of Human Genetics* 25 (1974), 47A.
21. Arne Svejgaard *et al.*, "HL-A and Disease Associations—A Survey," *Transplantation Reviews* 22 (1975), 3-43.
22. "Measuring Health and Disease," *Lancet* (June 9, 1973), pp. 1293-94.

Mr. THORNTON. Thank you very much, Dr. Lappé, for a very excellent presentation.

Unless there are any questions at this point, we will proceed to ask Dr. Clifford Grobstein, professor of biological science and public policy, the University of California, San Diego, to give us his presentation.

Dr. Grobstein.

[A biographical sketch of Dr. Grobstein follows:]

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Resume

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Professor of Biological Science and Public Policy

Academic Appointments:

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Dean, School of Medicine and Vice Chancellor, Health Sciences, UC San Diego. 1967-1973
Professor of Biology, UC San Diego. 1965-1977
Chairman, Dept. of Biology, UC San Diego. 1965-1967
Professor of Biology, Stanford Univ. 1956-1965
Executive Head, Dept. Biology, Stanford Univ. 1963-1965
Instructor in Zoology, Oregon State College. 1940-1943

Research Appointments:

Senior Research Fellow, National Cancer Institute. 1946-1947
Research Biologist, National Cancer Institute. 1947-1956

Military Service:

Aviation Physiologist, USAAF. 1943-1946

Professional recognition:

Member, National Academy of Sciences
Member, American Academy of Arts and Sciences
Past-President, American Society of Zoologists
Past-President, Society for the Study of Growth and Development
Brachet-laureate, Belgian Royal Academy of Sciences

Professional Service:

National Science Foundation consultant on developmental biology, science information, planning and institutional affairs, science for the citizen
National Institutes of Health consultant on cell biology, cancer research, child and maternal health, research center programs
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Macy Foundation consultant on medical education
Carnegie Commission consultant on medical education
Founding member, Coordinating Council on Medical education
Member, Editorial Board, Perspectives in Biology and Medicine; Science
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Publications on:

Research in developmental biology
Biological curricula
Theoretical biology
Science policy
Medical education
Strategy of Life, Freeman Co.

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STATEMENT OF DR. CLIFFORD GROBSTEIN, PROFESSOR OF BIOLOGICAL SCIENCE AND PUBLIC POLICY, UNIVERSITY OF CALIFORNIA

Dr. GROBSTEIN. Mr. Chairman and members of the committee, thank you very much for the opportunity to appear before you.

I will not fully cover the prepared statement that I submitted to you.

Mr. THORNTON. Without objection, the statement in full, including the attachments annexed to the statement, will be made a part of the record as fully as though it had been read, and we ask that you go ahead and summarize

Dr. GROBSTEIN. Thank you very much.

[The prepared statement of Dr. Clifford Grobstein, together with attachments, is as follows:]

STATEMENT BY CLIFFORD GROBSTEIN

Mr. Chairman and members of the Committee: My name is Clifford Grobstein. I am Professor of Biological Science and Public Policy at the University of California, San Diego. I should like to open with a brief statement as to the source of my interest and concern with recombinant DNA research. I am not a molecular geneticist. My quarter-century of activity as a laboratory scientist was in the neighboring field of embryology and developmental biology and terminated a little over ten years ago. I have since been in academic administration, as Dean of the Medical School at UC San Diego for six years, and then as Vice-Chancellor for University Relations. I left administrative duties for my present activity last July 1.

I followed the course of molecular genetics for many years because it was relevant to my own research interests. More recently I have regarded it as a bellwether issue for biomedical science and public policy, my present concern. My comments here today will reflect this more recent orientation.

I will concentrate in my prepared statement on two general points that I believe need emphasis at this juncture. The first has to do with the pitfalls of quick legislative "fixes" for complex scientifico-technical issues. I will illustrate these with two examples: (1) Changing risk assessment of recombinant DNA research; (2) The difficulty of forecasting the variety of future settings that may require surveillance and regulation.

The second point I will address is the need for comprehensive and deliberate assessment of the full implications of the matter before us. Included in such assessment must be the limits legitimately placed on either the advance of knowledge or the social intervention in that advance.

With respect to the first point, it is clear that Congressional interest in recombinant DNA research began with a presumption of considerable risk. This presumption was communicated by those involved in the research. They saw possible harm to health as a by-product of several conceivable lines of investigation. They were particularly concerned about creation of bacterial strains that might infect the investigators, their associates or even the general population. They envisioned the possibility that these strains, artifically endowed with appropriate recombinant DNA, might induce wide-spread disease or ecologic imbalance. The investigators pointed out that the evidence for this possibility was inconclusive but that considerable caution was indicated until the involved risk could be evaluated.

From this warning followed the Asilomar conference and the NIH guidelines. The basic principle adopted was logical and appropriate—matching of levels of containment to estimated risk. It was to generalize this concept to all sectors of activity that legislation later was called for by a federal inter-agenecy committee and Congressional consideration moved into high gear.

It is clearly important to take steps to reduce significant individual and social risks to acceptable levels, whether the activity be research or anything else. It is equally important, however, that the steps not overshoot beyond the requirements of the estimated risk. Overshoot can transform possible risk of the research itself into an equal or even greater risk of foregoing important new knowledge. Lively awareness of problems of over-regulation have developed in

other areas. Certainly we should not create a new problem of that kind, whether with respect to recombinant DNA research or innovation and imagination in general. Any required regulatory process must be suitably scaled to the problem.

As little as six months ago such words of caution did not seem relevant for recombinant DNA research. Public attention was riveted on possible massive biohazards, the media were busy getting the word out that dramatic new discoveries had been made and that dramatic new dangers had to be faced. The focus of attention was the the bacterium, E. coli, the favored object for study by molecular geneticists but also a general inhabitant of the human intestine. Certain strains of E. coli are known under appropriate conditions to behave as pathogens. It was easy and legitimate to doubt the safety of using this organism to propagate recombinant DNA. It was also natural to look to strong measures to contain the threat.

However, responsible circles are now suggesting that the risk envisioned by many molecular geneticists several years ago was overestimated—honestly and honorably. The recently developing expert consensus on risk of recombinant DNA research with E. coli (almost all the research currently being done) appears much lower. Has increased knowledge of only a year or two completely changed the risk estimate? That would be an overstatement. Passing time has contributed significant new information. But more importantly, additional expertise has come to bear. Molecular geneticists are not experts in microbiology, in infectious disease, ecology or evolution. Biomedical science is highly specialized and it takes considerable time and trouble to get various specialists into communication when a new problem arises that demands a multi-specialty approach.

The more comprehensive assessment, together with new developments specifically intended to reduce risk, have led, for example, Professor Roy Curtiss—among the most cautious of the molecular geneticists several years ago—to reverse his position (Attachment I). Having concentrated his own attention in the last several years on risk assessment and reduction he now concludes that recombinant DNA research with laboratory strains of E. coli "offers no danger whatsoever to any human being" who does not carelessly or deliberately swallow large amounts of particularly pathogenic organisms. Professor Haryln Halvorsen, President of the American Microbiology Society wrote to all members of Congress on 28 July, 1977 that "the dangers involved in this research are no greater than those encountered when dealing with natural pathogens." A special workshop held at Falmouth, Massachusetts on June 20–21, 1977 at which fifty experts in various aspects of E. coli biology and infectivity examined old and recent data, also found epidemic spread of recombinant E. coli extremely unlikely. (Attachment II)

The take-home lesson is not that all possible hazard has been eliminated in recombinant DNA research. Rather, it is that responsible expert estimates of potential immediate danger have dropped from potentially catastrophic and uncontrollable to potentially dangerous but controllable. From a public policy point of view, the earlier plans for stringent regulation were based on the best expert estimates at that time. Yet in only a year consideration must be given to whether the earlier plans are now appropriate to a new expert consensus based on some new data but more comprehensive analysis.

A further problem arises for a legislative "fix." Faced earlier with estimate of very large risk the important consideration was to get mitigating controls in place as rapidly as possible. If some overshoot occurred it would be on the side of safety and could be adjusted later. There was no time to think through the intricacies of each theatre in which regulation might operate. However, with the pressure of estimated risk reduced, it becomes clear that very different situations are being lumped together in one regulatory jacket. Academic research is currently largely covered by the NIH guidelines, how effectively no one has yet seriously examined. The academic setting is traditionally self-regulatory, it is gagging even under existing quasi-regulation and it is shuddering at talk of liability suits, fines, federal inspectors and secret proprietary knowledge. These suggestions stem, in part, from the recognized need to extend the NIH rationale to industrial research and development, clearly an entirely different setting. The public interest orientation of academic institutions is replaced in industrial research by corporate interest. There is a long and bitter history of federal-industrial regulatory interaction. Is that experience applicable to the academic area? How shall we translate the NIH guidelines, evolved primarily for academic recombinant DNA research, to mechanisms appropriate and necessary for an industrial setting?

Moreover, academic and industrial R&D settings are very different from those of manufacture and use. Every engineer knows the problems of scale-up and every specialist in communicable disease knows the difference between a successful laboratory vaccine and a public innoculation program. Is it reasonable to suppose that the same regulatory mechanism is going to deal simultaneously and effectively with academic laboratories, commercial development laboratories, factories and possibly agricultural operations? Granted that many and varied practical uses are still far down the road, is it not premature to try to visualize a regulatory authority capable of coping with such disparate situations under a common pattern?

This leads to my second point. One year has produced a changing risk assessment, possibly sufficient to alter both the pressure for and the scope of required legislation. We are dealing with the early stages of a major advance in knowledge. Is it too early to formulate a definitive public policy? Have all the perspectives necessary for sound policy been brought to bear? Is the logical next step a more comprehensive assessment rather than a hastily designed and simplistic regulatory mechanism?

After all, not only concerns about danger but opportunities to extend knowledge and its uses have recently been generated. These arise from the rapid advances of molecular genetics and also from the culturing of cell clones, by cell fusion and transformation, by tissue transplantation and other genetic and epigenetic procedures. Do we not need a comprehensive look at all of these matters—with an eye to potential risks and benefits but also to their interaction with our broader purposes and values?

Such an approach has been beneficial to the emotion-laden issues raised by experiments involving human subjects. The activities of the Commission on the Use of Human Subjects in Medical and Behavorial Research have cooled much of the heat and still added much light on these matters. Would a similar approach to the broader aspects of recombinant DNA research not be helpful? Such a comprehensive analysis might not only give a better perspective on risk and benefit of further advances, but on the risk of regulative procedures that might throw out the baby with the bath-water.

The latter is no less significant a risk than the former. We are in a very critical period in the relations between knowledge-generation and the body politic. The core of the recombinant DNA debate has been the threat of biohazard. Beneath the core, however, there lurks a greater issue—concern over the mixed promise and threat of advancing knowledge. Critics of recombinant DNA research see a sorcerer's apprentice, impelling us compulsively and almost mechanically toward unknown precipices. They ask whether knowledge is always "good" for us, whether we are "ready" for a given increment at a given time. Is the knowledge-process blind to our total human needs, should not human purpose and value direct knowledge-generation instead of the other way around?

These very old misgivings are recurring at the smashing culmination of a millennium that began in the Dark Ages but is terminating with a knowledge-platform for exploration and intervention both within ourselves and beyond the earth. A new millennium is almost upon us. Its advent will be marked by a concept of a natural order that is subject to deliberate and successful human intervention—from subatomic particles to the vastness of space. The potential power of human intervention will be the launch-point of the next millennium. This is reason enough to ponder where knowledge is taking us, whether we are called as masters or pawns of the cosmos now spread out before us.

There is evidence both ways—foot-steps on the moon and "smart," nuclear-tipped missiles in their silos. We are spread-eagled with one foot in a seeming earthly morass and the other on the way to Jupiter, Saturn and outer space. We are also deep into the intricacies of DNA, we are tinkering with its record of three billion years of evolution, we are intervening in our origins and perhaps on the verge of engineering our genetic future. Is there any wonder that uncertainty and fear of new unknowns are rising?

It is worth recalling, however, how we came to this state and how often fear of the unknown rose in the past. Fire, exploration beyond the horizon, dissection of human cadavers, flying—countless fears have waxed and waned in the history of human biocultural progression. Experience and its derivative knowledge have continued to grow and to provide the bridge between each new situation and appropriate reaction. Knowledge is our organized and cumlative experience. Like DNA in biological heredity, it is the continuing thread in cultural heredity. It has become so important in complex technological society that it has become a subsystem comparable to defense, transportation, communication or health-care. The knowledge-system or "knowledge-industry" has institutions, agencies, personnel,

sectors. They are interrelated and operate as a whole—sometimes almost unconsciously. They need to be viewed as a whole because inappropriate intervention can lead to malfunction of the system.

A fundamental question raised by the recombinant DNA debate is whether the knowledge-generating sector of the system should be controlled in terms of projected consequence and use of its products. When the consequence was seen as clear and present danger to public health the answer was prompt and affirmative. The search for knowledge requires informed consent of those whom it may threaten. New knowledge is not a higher value than the integrity of the human person nor the welfare of society. On the other hand, other possible consequences have other answers. Will recombinant DNA research lead to undesirable intervention in human heredity? That is a more difficult question and so far has had an incomplete response. What kind of intervention is or may be possible? What purposes will be served? What are the possible, probable, or certain consequences? And, most importantly, what other significance and contribution might the new knowledge make besides providing a tool for intervention in human heredity What are the consequences of foregoing knowledge that may have unfortunate effects? These questions need careful consideration. There is time for it, because intervention in human heredity other than for possible individual therapy is still far down the road.

What about such speculative scenarios as have been posed by Robert Sinsheimer who sees uncertain dangers in recombination between DNA of bacteria and higher organisms? My own view is that any claim to put limits on expanding knowledge requires more than speculation. There is risk in every new experience, there is at least equal risk in denying the need to have it. The propensity to explore, to learn and to understand is so deep in human behavior, and has played so consequential a role in the human cultural phenomenon, that it must be acknowledged as one of a set at the apex of human values. It is not absolute or inviolate, it must be weighed carefully, for example, against the protection of human dignity and individuality. It cannot, however, be surrendered casually to secondary values or floating anxiety.

Finally, we may ask by what mechanisms should social purpose operate on the pursuit of knowledge? This, too, will vary with case and circumstance but I would propose two general principles for discussion. First, the coupling between the knowledge-system and social purpose, as expressed in public policy, should be close and reciprocal. Second, the knowledge-system must develop a policy-oriented sector comparable to its technology and use-sector to focus on policy and decisional processes. Recombinant DNA research is now primarily directed at fundamental questions, it will shortly turn toward use and technology. Before the latter goes too far recombinant DNA should be the subject of full policy assessment. What is needed is an arena within which substantive experts, value perspectives, public perceptions and policy-makers can interact on a sustained basis. The objective should be to evaluate the current status, the projected course and the appropriate purposes and priorities.

This is a time too complex for town meetings. Even elected representatives with expanding staffs and intricate executive bureaucracies cannot keep up and cope with the proliferation of both knowledge and difficult issues. We clearly need a new form of policy discourse, a kind of policy theatre within which experts as actors, a near-expert chorus and a participant public audience of special and general interest advocates can play out scenarios. In such a theatre objective facts, ideologies and raw emotions might all interact, find their place and achieve resolution. The visible process might itself alleviate public anxiety. And it might yield comprehensive perspectives and options to thaw the frozen frustration of seemingly conflicting partial perspectives.

If some such process is initiated promptly we may avoid irrational and disorganizing regulation of the knowledge process. Molecular genetics is a two-edged implement. But it belongs in the tool kit of the next millennium, whether to solve terrestrial problems or to design new organisms for extraterrestrial niches. We will need allies in space as we have need of them on earth.

BIRMINGHAM, ALA., *April 12, 1977.*

DR. DONALD FREDRICKSON,
Director, National Institutes of Health,
Bethesda, Md.

DEAR DON, I have read with interest the interim report of the Federal Interagency Committee on Recombinant DNA Research: Suggested Elements for Legislation. I found the document informative and was partially reassured to find

that the suggested elements for legislation were more reasonable than some of the provisions contained in legislative bills previously introduced into the Senate and House. I am, however, extremely concerned that, based on fear, ignorance and misinformation, we are about to embark on over-regulation of an area of science and scientific activities. This letter is written to indicate my assessment of the risks associated with recombinant DNA activities and to suggest what I consder to be reasonable provisions in legislation which may be necessary to regulate research on and use of recombinant DNA. Although I have not included literature citations for the information contained in this letter, I will provide this on any point if that would be helpful.

Three years ago in August, 1974 after reading the Berg et al. letter in Science and Nature, I drafted an open letter to the authors which was also sent to over one thousand scientists here and abroad. In that letter I enumerated various factors that I thought had not been given sufficient attention by the Berg et al. committee and suggested a voluntary cessation of essentially all recombinant DNA research until "potential biohazards can be assessed and means to cope with them established". My beliefs then, later at the Asilomar Conference and as a member of the NIH Recombinant DNA Molecule Program Advisory Committee, have been conservative, which I believe to have been a responsible position until such time as more information was available about the likelihood for manifestation of potential biohazards. Since August, 1974 I have taken four actions, some of which have caused me to become far less apprehensive about recombinant DNA molecule research. First, since I had just initiated attempts to construct recombinant DNA, I decided to cease and have not yet resumed such research. Second, I conceived of possible means for manipulating Escherichia coli K–12 to make it safer for recombinant DNA research, an idea that was put forth in the report written and submitted by Novick, Clowes, Cohen, Falkow and myself at Asilomar, and then following Asilomar undertook, with the help of all of my laboratory colleagues, the design, construction and testing of safer, more useful strains of E. coli K–12 for recombinant DNA research. Third, I initiated an intense but intermittent education of myself with regard to all aspects of recombinant DNA research and all areas of knowledge necessary to assess the potential biohazards of such research. I did this by reading and by talking to colleagues expert in the areas of sanitary engineering, public health, infectious diseases, gastroenterology, oncology, virology, genetics, etc. Fourth, upon finding that certain information was not available, my colleagues and I have initiated experiments to obtain data that would allow a better assessment of the likelihood for manifestation of potential biohazards.

Much of the criticism and fear of recombinant DNA research has centered around the use of E. coli as a host for recombinant DNA. This species is comprised of thousands of different types, each with unique sets of attributes. Most strains of E. coli are relatively harmless commensals occupying the large intestines of warm-blooded animals. Some strains, however, have the capacity to occupy the small intestine and cause diarrheal disease, whereas others are often associated with infections of the urinary tract. A still smaller number of strains have the capacity, usually in individuals compromised by surgery, organ transplantation or diseases such as cancer, to invade healthy tissues and to multiply in the circulatory system. A still different group of E. coli strains includes those obtained from animal feces or sewage that have been maintained in the laboratory for many years. Many of these latter strains have become rather well adapted to the laboratory environment and have gradually lost the genetic attributes necessary to occupy the intestinal habitat and/or to cause disease. One such E. coli strain, designated K–12, was obtained from a human patient at Stanford University in 1922 and the NIH Guidelines stipulate that it is the only strain of E. coli into which foreign genetic information may be introduced. In considering the likelihood for the manifestation of a biohazardous condition during a recombinant DNA experiment, one must therefore consider the inherent potential of E. coli K–12 to exhibit pathogenicity (herein defined as causing disease or interfering with normal physiological activity) or to transmit recombinant DNA to some other microorganism encountered in nature that could exhibit pathogenicity. Pathogenicity requires that a microorganism colonize a given ecological niche within an "infected" individual and then manifest some virulence trait so as to overcome normal host defenses or interfere with normal physiological function. Sustained exhibition of pathogenicity of an epidemic nature also requires that a microorganism be communicable and survive long enough to be passed from one individual to another.

It has often been reported that E. coli K–12 is unable to colonize (persist for 7 or more days) in the large intestine when fed in large quantities to healthy, well-nourished mice, rats, chickens, pigs, calves and humans but that some E. coli K–12 cells can survive passage through the intestinal tract. Not much has been mentioned, however, as to why this is so, despite the fact that both published and unpublished information are available to provide a basic understanding of this observation. Normal strains of E. coli that inhabit the large bowel are "smooth" because they produce lipopolysaccharide (LPS) with carbohydrate side chains that are characteristic for any given strain and often have capsular surface antigens (composed of polysaccharides and/or proteins) which may further facilitate colonization. E. coli K–12 is defective in the production of LPS side chains because of defects in at least two genes that are located at widely separated regions of its chromosome; consequently it displays a "rough" phenotype. One of these defects in K–12's LPS genes appears to be a deletion (S. Falkow, personal communication) and therefore could not revert back to the wild-type state. Attempts to convert K–12 to a smooth phenotype by mating it under optimal laboratory conditions with smooth E. coli, Salmonella and Shigella donor strains have generally been unsuccessful. One exception is the ability to transfer genes to K–12 for the expression of the OS LPS side chain antigen.

These successful experiments, however, required the use of donors termed Hfr that efficiently transfer large segments of chromosome and are constructed in the laboratory; such donor types have never been isolated from nature. *E. coli* K–12 also does not make any capsular antigen, although under adverse conditions certain strains can produce the capsular polysaccharide colanic acid, which is not known to facilitate colonization by enteric bacterial strains that produce it. Colonization of the small intestine by enteropathogenic strains of *E. coli* is often facilitated by the presence of plasmids that specify protein surface antigens. Smith and Linggood have observed that the K88 plasmid present in most *E. coli* strains pathogenic for young pigs does not permit *E. coli* K–12 to colonize the pig intestine although the *E. coli* K–12 K88$^+$ strain tends to persist in the intestine somewhat longer than *E. coli* K–12 K88$^-$ strains. Similar findings have been made by Gyles, Falkow and their colleagues for K–12 strains possessing the K99 plasmid that specifies a protein surface antigen that allows enteropathogenic strains of *E. coli* to establish in the small intestine of calves. Shipley and Falkow have found that such K–12 derivatives produce large amounts of the K99 surface antigen, but the antigen does not readily adhere to the bacterial cell surface, presumably because of K–12's LPS defects, and is liberated into the culture medium. It thus seems highly unlikely (although not impossible) that one could introduce appropriate genetic information into an *E. coli* K–12 strain by a recombinant DNA experiment that would permit colonization of healthy, well-nourished individuals when the K–12 strains are already defective because of several mutational defects. For sake of completeness, it should be noted that *E. coli* K–12 can, of course, colonize gnotobiotic mice that lack a competing intestinal flora but is quickly eliminated when the mice are fed smooth *E. coli* strains of mouse origin. There is also a recent report that *E. coli* K–12 can colonize sheep that have been fasted for a day prior to ingesting the *E. coli* K–12 cells. In general, these studies imply that *E. coli* K–12 would colonize the intestinal tracts of individuals whose normal intestinal flora had been disturbed due to disease, fasting and/or recent prior antibiotic therapy. Although the NIH Guidelines stipulate that individuals in these categories not engage in recombinant DNA research, there is always the posibility of forgetfulness or an error in judgment that would expose such individuals to *E. coli* K–12 cells containing recombinant DNA. However, there is another safety feature in the use of EK1 hosts that has been overlooked during the recombinant DNA research debate. Most EK1 hosts currently in use are auxotrophs, having requirements for amino acids and frequently for thymine (or thymidine). Many of the strains are also recombination deficient. H.W. Smith and ourselves have both shown that thymine-requiring K–12 strains survive less well during passage through the intestinal tracts of humans and rats, respectively, than do strains that do not require thymine. We have also shown that recombination-deficient strains survive less well during passage through the rat intestinal tract. Indeed, *rec*$^-$ mutants are rather sick in that they are inordinately sensitive to sunlight and various chemicals and one out of every ten cells dies during each cell division even in the absence of exposure to these deleterious conditions. Amino acid requirements can also decrease maintenance of *E. coli* strains in the intestinal tract. We showed some years ago that mutant derivatives of smooth *E. coli* strains from mice that required amino acids, especially ones that were essential for the mouse, had a

decreased potential to successfully compete with wild-type prototrophic *E. coli* strains and thus soon disappeared from the intestinal flora. These are all important points since most of the feeding experiments with *E. coli* K–12 strains that are often cited have been done with strains that have few, if any, nutritional requirements. With EK2 hosts like χ1776 that are now required for those experiments deemed most likely to be potentially hazardous, the ability to colonize has been completely lost. χ1776 has six mutations each of which make colonization either unlikely or impossible and which collectively preclude survival during passage through the intestinal tract.

A second aspect of pathogenicity would be a mechanism to somehow overcome host defense mechanisms or interfere with normal physiological function. In this regard, people very often forget about the numerous efficient host defense mechanisms that include the presence of various bacteriocidal activities in tears, saliva, serum, etc. Indeed, in a study we have recently initiated which confirms earlier studies, most *E. coli* strains isolated from patients with bacteriemias, septicemias, wound infections, etc. are resistant to serum bacteriocidal activity. *E. coli* K–12 and specially EK2 hosts such as χ1776 are inordinately sensitive to serum bacteriocidal effects and do not seem to be able to mutate to resistance. Other studies have suggested that even compromised patients such as those receiving kidney transplants or those suffering from leukemia or lymphoma still exhibit serum bacteriocidal activity against various microorganisms. We are currently embarking on a study to verify whether this is so, particularly with regard to EK1 and EK2 *E. coli* hosts. Various species of Shigella and Salmonella possess the ability to invade tissues as part of the disease-causing process. It is known that mutations in LPS genes that result in a smooth to rough conversion cause these organisms to become avirulent. This change usually blocks cell penetration but when it does not, the rough cells fail to grow and multiply in the invaded cells. It is also known that the transfer of LPS genes from *E. coli* K–12 donor strains to *Shigella flexneri* 2a leads to partial or complete virulence of the latter strain. Formal, Gemski and LeBrec have introduced genes from virulent *Shigella flexneri* 2a into *E. coli* K–12 so that the *E. coli* K–12 hybrids express both the group-specific and type-specific surface antigens of *Sh.* flexneri 2a. These hybrids, which are antigenically identical to the *Sh. flexneri* 2a parental strain, were not able to cause disease in either animals or humans. It is also relevant to note that the transfer of *Sh. flexneri* 2a virulence genes into smooth *E. coli* cells expressing the 08 antigen also does not result in formation of virulent *E. coli* hybrids. This observation is important in that the genes for the 08 LPS antigen can be transferred to and expressed by *E. coli* K–12. In further experiments by these workers, a Shigella gene essential for Shigella's ability to penetrate mucosal cells was introduced into a K–12 strain without endowing the *E. coli* K–12 hybrid with invasiveness. The Shigella virulence gene was present in the K–12 cells as shown by the K–12 hybrid's ability to transfer the non-functional virulence gene into an appropriate avirulent Shigella mutant and re-endow it with the ability to invade mucosal cells. Furthermore, it is known from studies conducted by H. W. Smith, S. Falkow and colleagues that the introduction of plasmids specifying enterotoxins into strains of *E. coli* K–12 does not lead to the manifestation of disease even when the K–12 strains also possess another plasmid specifying synthesis of the K88 or K99 surface antigens that permit colonization of the small intestine by enteropathogenic *E. coli* strains. In view of the requirement for a normal smooth LPS to exhibit virulence, the failures to endow *E. coli* K–12 strains with virulence and the known and well-established mechanisms of host defense, it is difficult for me to believe that one could cause *E. coli* K–12 to display virulence or cause physiological harm by the introduction of foreign DNA sequences during a recombinant DNA experiment. This belief is augmented by the well-founded expectation that a display of virulence and/or physiological harm would most likely require that the *E. coli* K–12 cell be able to colonize some niche in or on humans. Since the ability to colonize is highly unlikely to be acquired in a recombinant DNA experiment in conjunction with introduction of a "virulence" trait, it is evident that even if a gene specifying a potent toxin were introduced into *E. coli* K–12 that the only individual possibly at risk would be a careless experimentalist that "inadvertently" ingested rather large quantities of the culture.

In terms of communicability of E. coli K–12, we know that enteric diseases caused by enteropathogenic E. coli and various strains of Shigella, Salmonella and Vibrio are transmitted by contaminated food and water and that manifestation of disease symptoms requires consumption of approximately one million bacteria. Such enteric diseases are seldom spread by aerosols. Indeed, it is well

known, for example, that cages of mice infected with Salmonella can be housed in the same room with uninfected mice which remain uninfected. The finding that E. coli cells can be recovered from the nasopharynx of approximately five percent of those humans tested might suggest that aerosol spread could occur. Such E. coli cells, however, are only intermittently present in the nasopharynx and are usually found at concentrations too low to initiate an infection even if they were representative of a pathogenic strain. They most likely get into the nasopharynx due to poor personal hygiene. After learning of these observations quite some years ago, I monitored my nostrils and skin for the presence of those E. coli K–12 strains I was working with. I was successful in detecting these strains about ten percent of the time when the monitoring was done at the end of the work day, but never obtained positive results when the monitoring was done the next morning. I should hasten to add that my research with E. coli K–12 at that time involved mouth pipetting and other aerosol-generating procedures on an open lab bench: procedures and conditions which are not permitted by the NIH Guidelines. These results, preliminary as they are, nevertheless suggest that E. coli K–12 does not colonize the nasopharynx. Based on these observations, the fact that E. coli's normal ecological niche is the colon and the fact that transmission of enteric diseases is by ingestion of contaminated water and food, I doubt that E. coli K–12 could be converted to an air-borne "infectious" agent by introduction of recombinant DNA. In terms of the more usual means for spread of enteric pathogens, it is evident that enteric diseases are very well controlled in the United States by sanitary engineering, even though there have been reports of poor water quality in some parts of the country and higher-than-desired levels of pollution of rivers, streams, etc. There is, however, a concerted effort to improve biological waste water treatment and thus lessen pollution and improve water quality. Even if there were a natural catastrophe such as caused by an earthquake, tornado, hurricane, etc., it is unlikely that E. coli K–12 containing recombinant DNA could initiate or sustain an epidemic in view of K–12's inability to colonize and overcome host defense mechanisms.

Since I believe that it is highly improbable that one could endow E. coli K–12 with pathogenicity and/or alter its means of communicability, it is then necessary to consider the potential of E. coli K–12 cells containing recombinant DNA to transmit that DNA to other microorganisms that might be encountered in nature. In terms of cloning onto the non-conjugative plasmid vectors pMB9 and pSC109, we have conducted a great diversity of experiments under laboratory conditions to measure as many parameters as possible that would affect conjugational transmission in nature. We have thus measured the frequencies of transfer of a diversity of conjugative plasmids to and from E. coli K–12 cells containing pMB9 or pSC101 and the frequency with which these conjugative plasmids mobilize the plasmid vector to another recipient cell. Measurements have also been made to determine the influences of temperature and cell densities on these frequencies. Using these experimentally determined values along with values from the literature on the frequencies of enteric bacteria with conjugative plasmids, the densities of suitable donor and recipient cells in natural environments and the occurrence of restriction as a barrier to inheritance of plasmid DNA, we estimate that the maximum probability for transmission of a non-conjugative plasmid vector from an EK1 host is 10^{-16} per surviving bacterium per day in the intestinal tract of warm-blooded animals. Since we have shown that conjugational transmission is most efficient at 37C and is essentially undetectable at 27C for most conjugative plasmids found in E. coli strains in nature, it is even more unlikely that conjugational transmission of a nonconjugative cloning vector containing recombinant DNA could occur at the ambient temperatures found in sewers, sewage treatment plants, streams and rivers, etc. In giving this less-than-10^{-16} probability per surviving cell per day, I have not taken into consideration the facts that conjugational ability (i) decreases with decreasing metabolic activity of donor and recipient bacteria (E. coli grow at generation times of 40 to 60 min under the optimal laboratory conditions used in our experiments and 5 to 12 hours in the intestinal tract), (ii) is inhibited by volatile fatty acids, bile and other constituents of the intestinal tract, (iii) occurs at suboptimal frequencies a pH 6.1 and at oxidation reduction potentials of −200 mV (the "usual" pH and Eh of the bowel contents) and (iv) can also be diminished by differences in the cell surface between donors and recipients. Although such conjugationally promoted transfer of non-conjugative plasmids has not, and indeed cannot, be measured in vivo, there have been a number of reports from the laboratories of Anderson, Richmond, Smith, Falkow and others which demonstrate that the transfer of a conjugative plasmid from one bacterium to another in vivo is seldom observed. Suc-

cessful detection of such transfer in these experiments requires use of numerous animals and/or repetitions and very often depends on the use of mutant plasmids that are transferred at frequencies 100- to 1000-times higher than those conjugative plasmids found in wild-type populations of enteric bacteria. Based on these data, it can be estimated that the frequency of conjugative plasmid transfer in the intestine is about 10^{-8} per donor cell per day. Since transfer of a non-conjugative plasmid requires two such conjugational events and since non-conjugative plasmid requires two such conjugational events and since non-conjugative plasmids are mobilized at frequencies of 10^{-3} to 10^{-4} compared to the frequency of transfer of the conjugative plasmid, the estimated overall probability for transmission of pSC101 or pMB9 from an EK1 host would be between 10^{-19} and 10^{-20} per surviving bacterium per day [10^{-8} x 10^{-8} x (10^{-3} or 10^{-4})]. These values, of course, take into account the contributions of the various environmental factors enumerated above. I should hasten to add, however, that the intestinal environment becomes much more conducive for conjugational plasmid transfer following antibiotic therapy since the pH, E_h and volatile fatty acid concentration change to more favorable values, there is a decrease in drug-sensitive normal flora that permits greater proliferation and titers of a newly introduced strain and a possible increase in drug-resistant flora that possess conjugative plasmids. These facts are, of course, one of the important reasons for stipulating in the NIH Guidelines that individuals not conduct recombinant DNA research during and for seven days after ceasing antibiotic therapy. In terms of the effects of inserting foreign DNA into non-conjugative plasmid vectors on the frequency of plasmid transfer, Crisona and Clark have found that insertion of certain sequences from conjugative plasmids can increase the frequency of pSC101 mobilization whereas Hamer has found either no effect or a decrease in pSC101 mobilization frequency by the insertion of different Drosophila DNA sequences.

In terms of transductional transmission of non-conjugative plasmid vectors containing recombinant DNA, we have only recently initiated our studies. We have found, however, that the frequency of plasmid transduction mediated by phage P1 decreases as the size of the plasmid vector decreases and is essentially undetectable for the plasmid cloning vectors PSC101 and pMB9. The transductional efficiency for these vectors is thus several orders of magnitude lower than for chromosomal markers, even though these plasmids are present in 5 and 40 copies per chromosomal DNA equivalent, respectively. In numerous experiments in which E. coli K–12 strains have been fed to rodents, we have seldom found phage that would infect the fed strain. In those animals with such phage, the titers were generally between 10^2 and 10^3 per gram of feces. Although these observations suggest that titers of potential transducing phages may be very low, we do not have sufficient quantitative data on their titers in various environments (i.e., intestinal contents, sewage, etc.) to make a very accurate estimate of the probability for transductional transmission of plasmid cloning vectors containing recombinant DNA. Based on our preliminary results, the typical concentrations of E. coli cells in the intestine and in sewage and the known properties of E. coli K–12 transducing phages, I believe it is probably as low or lower than the probability for conjugational transmission. It should also be noted that EK2 strains like x1776 are totally or partially resistant to all known transducing phages of E. coli K–12 and that many EK1 and all EK2 hosts require thymine or thymidine which is needed for productive temperate phage infection.

In terms of transformation, this is not known to naturally occur in enteric bacteria. One can induce to occur by treating E. coli with calcium chloride at 0C and then rapidly shifting to 42C for a one-minute heat shock; such conditions are unlikely to be encountered in nature. Nevertheless, the potential that recombinant DNA released from E. coli K–12 cells lysing in the intestine might be taken up by cells in the intestinal mucosa or even transform other enteric bacteria has led us to investigate the survival of DNA in rat intestine contents. We have found that a 1:6 dilution of the contents of the small intestine results in the total destruction (i.e., breakdown to acid-soluble material) of 90 percent of the DNA within the time it takes to add the DNA, mix it and remove a sample. Most likely, the nuclease(s) is introduced into the intestinal tract through the pancreatic duct, although it is also known that cells lining the intestine contain various deoxyribonucleases which might be secreted into the intestine. These results lead me to believe that experiments such as those to be conducted by Rowe and Martin to test whether mice fed E. coli containing polyoma DNA will become infected with polyoma will not give positive results.

In order to obtain additional information on the likelihood of transmission of recombinant DNA, we have also commenced to collect a diversity of E. coli strains obtained from patients with bacteriemias, wound infections and urinary tract infections, from healthy individuals and from sewage. We have been examining these strains for the presence of nonsense suppressor mutations that would allow for the replication and perpetuation of lambda or plasmid vectors that contain nonsense mutations and also for the ability of these strains to be infected by lambda DNA that is tagged by an antibiotic resistance marker. So far, in a test of some 100 strains, we have failed to detect any strain with a nonsense suppressor or that was infectable by lambda. R. Davis, P. Leder and their colleagues have also examined some 2000 E. coli strains for sensitivity to phage lambda and although they found a few strains that appeared partially sensitive to lambda, none would propagate the virus. We intend to test many more strains, but our preliminary results in conjunction with those obstained by Davis and Leder indicate that the use of lambda and plasmid vectors, especially if they possess amber suppressible mutations, provides a greater margin of safety than was previously verifiable by experimental data. In this regard, the three EK2 lambda vectors constructed by F. Blattner, P. Leder, P. Sharp and their colleagues each contain two amber suppressible mutations. Although none of the currently used non-conjugative plasmid vectors have such mutations, work is in progress to isolate these mutant plasmids.

Based on all of the foregoing, I consider that the transmission of recombinant DNA contained on various non-conjugative plasmid and lambda phage vectors to other microorganisms encountered in nature will be a most unlikely event. This conclusion is more certain with use of EK2 host-vectors than with EK1 host-vectors and could only be proven incorrect either by new data that would contradict the substantial body of data already accumulated or by the discovery of a mechanism of gene transfer as yet unkown that would facilitate the transmission of DNA at frequencies higher than those observable by conjugation, transduction and transformation.

The last point to consider in evaluating the likelihood of harm emanating from a recombinant DNA experiment is whether E. coli K–12 will obtain a selective advantage by the introduction of a DNA sequence that codes for some gene product that is foreign to the E. coli K-12 cell. Cameron and Davis have inserted random fragments representing at least 95 percent of the E. coli K-12 and yeast genomes into a lambda vector and then determined the rate with which specific clones gained ascendancy by examining the fragments still present in pooled lambda stocks after increasing numbers of cycles of propagation. They found that one to several unique hybrid phages gained prominence much faster when E. coli DNA was cloned than when yeast DNA was cloned. Thus yeast DNA had a more neutral effect than E. coli DNA which contains more sequences that are disadvantageous to the propagation of the vector. In other less complete studies in which there was no assurance that most of the genome had been cloned onto the lambda vector, these investigators found that DNA from Drosophila had a neutral effect like yeast DNA and that DNA from maize and Dictyostelium was detrimental with most sequences causing the hybrid to be at a distinct disadvantage. Although some highly selected hybrids with E. coli and yeast DNA gave yields of virus per infected cell equal to and in a few cases higher than yields after infection of cells with the original vector, in no case with any DNA insertion from any of the organisms studied was a hybrid found that gave higher yields than or could out compete wild-type lambda. In much more limited studies, S. Cohen and colleagues have found that insertion of foreign DNA onto the pSC101 plasmid vector placed the cells at a selective disadvantage relative to cells with only the pSC101 vector. Based on all these studies, I consider that the probability of a random DNA sequence either being completely netural or providing a selective advantage to a vector or an E. coli K-12 cell is probably less than 10^{-5}. Although it can be argued that these tests have not been performed in any of E. coli's various natural habitats, there are substantial arguments based on genetic and evolutionary considerations given by F. J. Ayala and B. Davis at the recent NAS Forum to believe that the results of Cameron and Davis and of Cohen would not vary appreciably irrespective of the environment of the test. In view of the already diminished survival potential of EK1 hosts that possess auxotrophic requirements and certainly of EK2 hosts, the ultimate survival and perpetuation of recombinant DNA requires that it be transferred to some other microorganism. Even if this remote possibility did occur, the same arguments would prevail and I would deem it highly unlikely that the foreign DNA would either be neutral or confer a selective advantage on that host.

In view of all the accumulating information discussed above, I have gradually come to the realization that the introduction of foreign DNA sequences into EK1 and EK2 host-vectors offers no danger whatsoever to any human being with the exception already mentioned that an extremely careless worker might under unique situations cause harm to him- or herself. The arrival at this conclusion has been somewhat painful and with reluctance since it is contrary to my past "feelings" about the biohazards of recombinant DNA research. As a means to challenge the above-stated conclusion, I have taken some worst-case scenarios thought up by myself, by my colleagues and by others and subjected them to critical analysis by obtaining information from those scientists most knowledgeable about the genetic control, biosynthesis, mode of action, production, etc. of the foreign gene product(s) in question. In no instance have I found evidence that the necessary genetic information could be cloned in one step, would permit E. coli K-12 to colonize the intestinal tract and lead to the production of the product(s) in the intestinal environment that would be harmful to the mammalian host. This is not to say, however, that an individual with considerable skill, knowledge (most of which is currently lacking) and luck could not construct in multiple steps a microorganism that would satisfy all these requirements.

In terms of the likelihood that an escaped E. coli K-12 containing recombinant DNA could cause harm to some non-human organism in the biosphere, there are, of course, less data upon which to base any definitive conclusion. However, the following points are relevant: (i) E. coli strains recovered from sewage, polluted rivers, farmlands, etc. are smooth rather than rough and are prototrophic rather than auxotrophic; (ii) it seems highly improbable that addition of foreign DNA could endow E. coli with the potential to colonize a new ecological niche such as soil or water and also confer ability to cause harm to some other organism; (iii) the probability for transmission of recombinant DNA to some other bacterial species that inhabits soil or water is known to be lower than the values given above for transmission to other strains of E. coli (indeed, plasmid cloning vectors are not likely to be stably maintained in many of these species); and (iv) there is a low probability that the foreign DNA will be either neutral or provide a selective advantage in any microbial host. Based on these considerations, I do not believe that cloning foreign DNA into E. coli K-12 host-vectors poses any threat to non-human organisms in the biosphere. Additional data to substantiate this assessment would, of course, be valuable.

During several recent meetings on recombinant DNA research, I have stated that adherence to the physical and biological containment requirements and practices for any given experiment as described in the NIH Guidelines would preclude manifestation of any potentially biohazardous conditions. I have noted, however, that human error might circumvent the safety afforded by physical and biological containment without really analyzing the degree to which this "feeling" might be true. If the foreign DNA is present in the appropriate EK1 or EK2 hostvector system, then an accident in which a large culture might be spilled would not seem likely to cause any harm if there were a second error in not implementing an accident to disinfect the spill. If there were either gross aerosolization or ingestion of large quantities of such organisms, harm could possibly occur to exposed individuals provided that the recombinant DNA contained in the bacterial host was either itself harmful or specified a harmful product that could be either released or produced in vivo and exhibit its harmful effects in that environment. Even though such an accident might occasionally occur, the likelihood of the other necessary conditions being met seems remote. If, in addition to the above accident, the worker had been receiving antibiotic therapy prior to the day in which the accident occurred the consequences for that worker might be more severe but still would not cause harm to anyone outside the work area. The error of working with recombinant DNA while taking antibiotics would also increase the likelihood of conjugational transmission of the recombinant DNA to some other intestinal microorganism. S. Falkow has found that antibiotic treatment increases the frequency of conjugative plasmid transfer 100-fold. Thus the probability for conjugational transmission of a non-conjugative cloning vector containing recombinant DNA would increase to a maximum value of 10^{-12} per surviving cell per day that reaches the colon, still a very improbable event.

Contamination of cultures during transformation with recombinant DNA has often been mentioned as a likely problem associated with poor technique. Most contaminants encountered in our own lab are Staphylococci shed from the skin (which cannot be transformed with E. coli vectors) and other airborne microorganisms that grow optimally at 20 to 30C and thus grow poorly or

not at all at 37C, the temperature customarily used for growth of E. coli. Even if such contaminants could be transformed with recombinant DNA and be recovered as colonies, an individual would have to not recognize the colony as a contaminant and grow up a substantial culture to achieve a sufficient "infective dose" and then have another accident prior to recognizing the initial error. One can also consider a potential worst case in which research with smooth E. coli and other enteric pathogens was being conducted in the same laboratory as recombinant DNA activities (a rather stupid and unlikely situation) such that a wrong culture was chosen as the recipient for transformation with recombinant DNA. First of all, it is known that smooth strains of enteric organisms are very poorly transformable with plasmid DNA and that mutants with defective LPS synthesis that cause a rough phenotype and thus avirulence are much more transformable. Secondly, one has a low probability that a cloned DNA fragment both specifies harmful information and would be neutral or confer a selective advantage for the survival of the host. In addition to these factors, there are a variety of other standard practices in recombinant DNA research that would further minimize the likelihood of either successful transformation of a contaminant or a "wrong" bacterial strain or of failing to recognize such a mishap. For example, the medium used to recover transformants of an EK2 host such as X1776 precludes growth of many types of contaminating microorganisms, has antibiotics added to it which prevent growth of still more contaminants and contains indicator dyes and a sugar that allows one to visually distinguish X1776 colonies from those of smooth as well as most rough enteric bacteria. Furthermore, the optimal method for transformation of X1776 gives 100- to 1000-fold fewer transformants when used for EKI hosts. In summary, after pondering these and other types of errors, I am convinced, because of the need for a sequence of errors and the improbabilities of constructing a microbe that both has a competitive advantage and displays a harmful trait, that construction and use of E. coli K–12 strains with recombinant DNA poses no threat whatsoever to humans (or other organisms) except for the remote chance that an individual constructing or using such strains as discussed above in the first examples of potential errors might experience some ill effects.

The recombinant DNA research debate has been necessary and valuable. I have become increasingly distressed, however, by the degeneration of the debate. Opinions have often been stated as a factual certainty, statements of "fact" have often been put forth that are in conflict wih published data and there has often been an unwillingness to adhere to the principles of scienific objectivity. I have also never heard or read any factual information during the debate that would contradict the conclusion about the safety of E. coli K–12 host-vector systems that I have just reached. It is thus my considered belief that we are about to embark on excessive regulation of an important area of biomedical research based almost solely on fear, ignorance and misinformation.

Although it is my current opinion that legislation to regulate research on and use of recombinant DNA may be unnecessary, there appears to be a consensus that some form of federal legislation is needed. Given that this is so, I would hope that the legislation enacted be kept as simple as possible. The provisions of such an act should, of course, require that the NIH Guidelines (or some slight modifications thereof) apply to all individuals using recombinant DNA molecules for whatever purpose. whether they be in the private or public sector. The legislation should require that proof of compliance be mandatory at the time any product or process utilizing recombinant DNA methodologies is submitted for approval. for testing or use to such agencies as the Food and Drug Administration, the Environmental Protection Agency and/or other agencies empowered with the responsibility for the certification of materials to be added to foods, used in treatment of disease, control of insects, etc. This latter provision is designed for the express purpose of ensuring compliance by those concerns which would not be disclosing their recombinant DNA activities to some governmental or funding agency until such time as they had applied for patent protection. The legislative act should contain sections on preemption of state and local laws, registration, imminent hazard, sanctions, employee rights and sunset.

I am not at all in favor of licensure of laboratories and/or scientists, nor am I in favor of inspections, except of P4 facilities. These provisions would be redundant of what is contained in the NIH Guidelines and would preempt and undermine the functions of local or institutional biohazards committees. The NIH Guidelines as now written require institutional biohazards committees to perform a number of very important functions on a regular basis. Members of

these committees are hard-working and conscientious. I doubt that they could continue to act in this manner if most of their functions were taken over by federal inspectors and examiners, who would only visit the institution intermittently and could not ever hope to provide the day-by-day advice that is needed by individuals embarking on recombinant DNA activities. It is thus my honest opinion that the establishment of a federal bureaucracy to license and inspect will be less effective than reliance on and trust in institutional biohazards committees. Certainly, a laboratory approved today can be malfunctioning tomorrow; therefore, peer pressure, availability of immediate expert advice and providing for the rights of employees who might object to a given procedure are more likely to lead to safe practices in the conduct of recombinant DNA activities than will dependence on federal licensing and inspections.

I am also opposed to provisions that might require that all P3 and P4 level experiments be conducted at regional national facilities. Such a decision would preclude certain types of experiments until such facilities were operational. This would very much impede basic biomedical research and any resultant improvements in health care delivery, etc., and could also result in some scientists leaving the country. The long-range effect would be for scientists to locate at these facilities and not at universities, thereby making them unavailable for training of graduate, medical and dental students. The worst possible provision would be a stipulation of specific liability. This would act as a de facto prohibition of recombinant DNA activities in this country, the consequences of which would be staggering.

There are in my opinion some subtle but not inconsequential ramifications of enacting and/or implementing excessive regulations for an area of research in which there are no known hazards and an accumulating body of evidence to indicate that there are none. First, it was the scientists most knowledgeable about recombinant DNA research who initially raised the possibility of potential biohazards. They have, of course, spent much time in debating the issues, in adopting stringent guidelines to preclude manifestation of potential biohazards and in gathering data to evaluate the likelihood of such potential biohazards. It therefore follows that if this area of scientific inquiry becomes encumbered with excessive constraints and is subsequently shown to be associated with no hazards, there may develop a degree of contempt for such regulations. Second, if our country embarks on excessive regulation of recombinant DNA activities, it may lead to regulation of other areas of biomedical research in which the biohazards are well known. In view of the commendable safety performance of individuals engaged in research with biohazardous materials and agents, such regulation of their activities is not likely to improve safety. After all, one cannot legislative against human error and I am sure that these individuals, who are well aware of the risks associated with their occupation, do not want to make errors that could result in harm to themselves. Third, it is evident that excessive and/or additional regulation of biomedical research will increase the cost and decrease the productivity of acquiring knowledge necessary to cure diseases and provide for the health care of our citizenry. Certainly, funds spent on enforcing and adhering to such regulations will diminish the funds available for such productive endeavors. Expenditure of funds for such regulation would only be justified if it were necessary to protect the public and therefore ensure the economic well-being of our country. Since recombinant DNA activities, at least with E. coli K–12 host-vectors, pose no known or expected threat, it is my opinion that legislative enactment of regulations, especially if excessive, are not easily justifiable. It would seem more reasonable to utilize available financial resources to train future scientists in the safe use of recombinant DNA technologies, to continue to evaluate potential biohazards under existing guidelines and to begin to reap the substantial benefits afforded by recombinant DNA research.

Sincerely yours,

ROY CURTISS III.

Dr. GROBSTEIN. In my prepared statement I made clear that the concerns that I shall address here today are twofold: First, that recombinant DNA and the research and use thereof is of profound, intrinsic importance as a field of scientific knowledge. Second, that the implications of this specific case for the general problem of interactions of new knowledge and public policy are equally unusual, in terms of their importance to the research itself.

In this less formal presentation I will concentrate on the second of these two points.

In the several years during which recombinant DNA has been receiving policy attention it has already passed through two phases and is at the moment under consideration for a third. It was for a period of time under a voluntary partial moratorium, based upon the decision of investigators in the field. It is now in a phase appropriately called quasi-regulation, under the guidelines of the National Institute of Health extended to all federally supported research. It is currently being examined by the Congress as a candidate for full legal regulation.

I would raise the question whether the events of the past several years, with the rapid changes that have been occurring in the manner in which the research is conducted, do not support that it is still too early for definitive public policymaking in this area. The question's whether the next logical step beyond quasi-regulation should not be more comprehensive assessment, to avoid a too hastily designed and simplistic new regulatory mechanism not up to the complexities of the issues that we face.

I believe that we have not yet pondered carefully enough the various relevent perspectives, whether these be scientific, ethical or social. Indeed, we have not found appropriate methods to synthesize considerations in these very different realms into appropriate public policy. We are dealing with the early stages of a major advance in knowledge, major in the long-term sense of history of science and culture. This including not only the specific step of artificial DNA recombination, but the entire complex of recent advances in knowledge of heredity in development, cloning, fusion and transformation of cells, tissue culture and transplantation, and other genetic and epigenetic procedures. These have generated conceivable dangers. They have also generated opportunities to extend knowledge and its uses.

Do we not need at this point, given the magnitude of what we are facing, a comprehensive look, not only with respect to risks and benefits, but also with respect to our broader purposes and values? In particular, do we not need to think carefully about the risk of overregulation that could throw the baby out with the bathwater?

We are in a very critical period in the relations between knowledge generation and the body politic. In the recombinant DNA debate there lurks beneath biohazard a greater issue—concern over the mixed promise and threat of penetrating the unknown. Critics see a sorcerer's apprentice, impelling us compulsively and almost mechanically toward unkonwn precipices. They ask whether knowledge is always "good" for us, whether we may be unprepared for it at a given time. They fear that the knowledge process is blind to total human needs. They ask whether human purpose and value should not direct what we seek to learn instead of the other way around.

These are historically familiar misgivings. They are recurring at the end of a millennium that began in the Dark Ages and is culminating with a knowledge platform for deep exploration, both within ourselves and beyond the Earth. We will enter the new millennium convinced that there is a natural order subject to deliberate and successful human intervention, from subatomic particles to the vastness of space. The launch point of the new millennium is the growing po-

tential for human intervention. There is, therefore, good reason to ponder—where knowledge is taking us, whether we are called to be masters or pawns in the cosmos now spread before us.

There is evidence both ways—footsteps on the Moon and "smart," nuclear-tipped missiles in their silos. We also are tinkering with the intricacies of DNA and its record of 3 billion years of evolution. There is ample justification for either exhiliration or anxiety.

It is worth recalling, however, how often fear of the unknown arose in the past. Fire, exploration beyond horizons, or outside of natural environments, dissection of human cadavers—countless fears have waxed and waned in our biocultural progression. What has sustained us, among other things, is organized, collective experience, knowledge, as a bridge between each new situation and its appropriate reaction. Knowledge is our organized, cumulative experience. Like DNA in biologicaly heredity, it is the continuing thread of cultural heredity. It has become so important in our complex technological society that we have developed a knowledge system comparable to transportation, communications, production, or defense. The knowledge system, or as it is sometimes called, the knowledge industry, has components: institutions, agencies, sectors, personnel. They operate and need to be viewed as a whole because inappropriate intervention at one point can lead to malfunction at another.

The fundamental question raised in the recombinant DNA debate is whether the knowledge-generating component of the system should operate in laissez-faire fashion or be controlled by anticipated social consequences as to its output. There is no general answer. There are, however, several kinds of cases. When the consequence is clear and present danger (individual or collective biohazard, for example) the answer has been affirmative in the recombinant DNA situation. There is need for consideration of consequence. The search for knowledge requires informed consent of those whom it may threaten. The search may not claim a higher value than the integrity of the human person or the welfare of society. However, when the consequence is longer term and less certain, careful evaluation of individual cases is required. Should recombinant DNA research be stopped because it may lead to undesirable intervention in human heredity? For the moment there is no clear answer. What kind of intervention is or may be possible? What purposes will be served? And, very importantly, what other benefits of the new knowledge can be expected, other than hereditary intervention? What do we lose if we discontinue research because of feared, but as yet unassessed, consequences?

In the third case, when the consequences are entirely speculative, I submit that the burden of proof is on the speculator.

Robert Sinsheimer's concern about recombination of DNA between bacteria and higher organizations deserves consideration, but limits on the expansion of knowledge require more than speculative hazard, of whatever kind. There is risk in every experience. There is at least equal risk in denying it. The propensity to explore, to learn and to understand is so deep in human behavior, and has been so productive in cultural advance, that it must be placed in the set at the apex of human values. It is not absolute or inviolate. It must be weighed carefully, for example, against the protection of human dignity and in-

dividuality. It cannot, however, be casually surrendered to secondary values or floating anxiety.

Finally, by what mechanisms should social purpose bear upon the pursuit of knowledge? This, too, will vary with case and circumstance. I propose two principles important to discuss that are not yet fulfilled: First, the knowledge system as whole should be closely and reciprocally coupled to public policy formation, as one way to assure that knowledge and social purpose are intimately related. We are moving in this direction, and the recombinant DNA debate is playing its part. We still have far to go. Second, to further the trend the knowledge system must develop a policy-oriented sector at least as effective as its technology and use sector. Our knowledge centers must somehow overcome their inertia and reluctance to undertake this. They must be helped by allocation of resources as deliberately as was done to encourage their involvement in technology and use. An immediate need is to create arenas in which substantive expertise, value perspectives, public perceptions and policymakers can interact on particular issues on a sustained basis.

We need a new form of policy discourse, a kind of policy theater within which experts are actors and near-experts make up a chorus, and a participating audience of special and general interest advocates can help play out scenarios. In such a theater objective facts, ideologies and even raw emotions might all interact, find their place and resolve a manageable number of policy options for decisionmakers to consider. The visible process might itself alleviate public anxiety about many issues. It might also yield more comprehensive options to thaw the frozen frustration of competing partial perspectives.

Prompt initiation of some such process for recombinant DNA may avoid a threatened slide toward disruptive and restrictive regulation of the knowledge process. Molecular genetics, like all new knowledge, is a two-edged implement. But it belongs in the toolkit of the next millennium, whether to help solve terrestrial problems or to design new organisms for extraterrestrial niches. We will need biological allies in space as we have need of them on earth.

In conclusion, my concern is not that recombinant DNA has become the subject of legislative scrutiny. It deserves and requires it, and I personally hope that clear public policy will emerge from the legislative consideration. I also hope, however, that adequate time will be taken to do the job right. What we need now is an interim step that will extend current principles to all recombinant DNA and uses, but simultaneously provide a mechanism for comprehensive and public examination of all relevant issues.

Expert opnion suggests now that we have time for this. It may assure that in seeking to contain one potential risk we do not generate new and greater ones by hobbling our knowledge-system when need for it may be greater than ever.

Thank you.

Mr. Thornton. Thank you very much, Dr. Grobstein, for a very fine presentation.

We will next hear from the distinguished associate professor of law at the Georgetown University Law Center, Ms. Patricia King. We're very pleased to have you as a witness, Ms. King, and please proceed.

[Biographical sketch of Ms. King follows:]

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Visiting Scholar, The Joseph and Rose Kennedy Institute for the Study of Human Reproduction and Bioethics - Fall Term, 1977

EMPLOYMENT (Cont'd.)

Summer 1976: Visiting Associate Professor of Law, University of Michigan, Ann Arbor, Michigan

October 1971 - July 1974: Deputy Director (for four months, Acting Director), Office for Civil Rights, HEW, Washington, D.C. (On leave 1973-1974 - Visiting Associate Professor of Law, Georgetown University)

August 1969 - October 1971: Special Assistant to the Chairman of the Equal Employment Opportunity Commission, Washington, D.C.

September 1968 - June 1969: Head of House, Wellesley College, Wellesley, Massachusetts

January 1967 - June 1968: Research Assistant for Professor Charles Nesson, Harvard Law School

January 1965 - September 1966: Budget Analyst, Department of State, Washington, D.C.

January 1964 - January 1965: Administrative Intern, Department of State, Washington, D.C.

Current Activities:

Member, National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1974 -

Member, Joint Commission On Prescription Drug Abuse, 1976 -

Member of a Policy and Data Safety Monitoring Board, National Heart, Lung and Blood Institute, National Institutes of Health, 1977 -

Fellow, Institute of Society, Ethics and the Life Sciences, 1977 -

Member, Washington Area Seminar On Science, Technology and Ethics, 1977 -

Member, Committee on Academic Freedom and Tenure, American Association of Law Schools, 1976 -

Member, Visiting Committee for Law, Harvard University Law School, 1975 -

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CURRENT ACTIVITIES (Cont'd)

Member, Board of the Institute for Public Interest Representation, Georgetown University, Washington, D.C., 1977 -

Member, United States Circuit Judge Nominating Commission, 1977 -

Director, Redevelopment Land Agency of the District of Columbia, Washington, D.C., 1976 -

PAST ACTIVITIES:

Member, Ad Hoc Committee on FDA Legislation and Policies Affecting Anti-Cancer Drugs, Institute of Medicine, National Academy of Sciences, 1977

Member, Department of Defense Task Force on the Administration of Justice in the Armed Forces, 1972

Member, Accreditation Committee, ABA Section on Legal Education and Admission to the Bar, 1975-1976

Member, ABA Council, Section on Legal Education and Admission to the Bar, 1976-1977

Governor, District of Columbia Bar Association (unified), 1973-1976

Member of the Board, Washington Council of Lawyers

Member, President's Advisory Committee, Wheaton College, 1972-1975

Member, Advisory Committee on Recruitment and Retention of Minority Correctional Employees, Howard University, Washington, D.C.

Commencement Speaker - Wheaton College, Norton, Massachusetts, June 4, 1972

Director, Channel 50 Inc., Washington, D.C.

Testified Before: HEW Secretary's Task Force On Immunization Policy, 1977

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Patricia A. King
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PAST
ACTIVITIES (Cont'd.)

Subcommittee of House Committee on Science and Technology; subject - Ethical Issues in Science Research, September 7, 1977

PROFESSIONAL
MEMBERSHIPS:

Member, American Assocation for the Advancement of Science

Member, American Bar Association

Member, District of Columbia Bar (unified)

AWARDS:

Distinguished Service Award
HEW, 1973

Secretary's Special Citation
(Elliot Richardson), 1972

STATEMENT OF PATRICIA KING, ASSOCIATE PROFESSOR OF LAW, GEORGETOWN UNIVERSITY LAW CENTER

Ms. KING. Thank you.

I should start by saying I, too, bring a unique background to this hearing. I am neither scientist nor ethicist, but, I hope, an informed layperson.

I will try not to repeat some of the points that have been made by other colleagues, and will take excerpts from my testimony.

Mr. THORNTON. Without objection, your testimony as prepared will be made a part of the record in full.

Ms. KING. No objection.

[The prepared statement of Ms. Patricia King is as follows:]

TESTIMONY OF PATRICIA A. KING BEFORE
HOUSE SUBCOMMITTEE ON SCIENCE,
RESEARCH AND TECHNOLOGY

September 7, 1977

My name is Patricia A. King. I am an Associate Professor of Law at Georgetown Law Center. I appreciate the opportunity to appear before you today and to share with you my thoughts on ethical issues in scientific research. I understand that your primary focus has been on science policy issues in recombinant DNA research. However, I am particularly interested in issues arising out of genetic research that has therapeutic potential for the treatment of genetic defects. Additionally, I'm interested in genetic research concerning future reproductive engineering, both to satisfy parental desires and to intentionally modify "natural" evolution. My observations are therefore, specifically pertinent to those areas of genetic research.

Human intervention in the genetic process for whatever reason raises significant questions. The first and most obvious question raised is whether such research is desirable irrespective of any possible therapeutic value. Should such research be prohibited, merely because it necessarily involves interfering with the "natural" processes of human development -- tampering with man himself?

I am not persuaded that all genetic research, because it tampers with man himself, is a priori immoral research. Nor am I convinced that such research is different in any relevant

way from any other research that is currently being conducted.[1/]

Some would argue that the potential intentional or unintentional misuse of the results of such research by a few is enough in and of itself to justify its prohibition. I disagree. It is, of course, conceivable that there will be some abuse, but that possibility exists with any new and powerful development. It certainly never stopped us in nuclear research. Prohibiting research that has potential for good because of possible misuse is like throwing out the baby with the bath water. Such over reaction is unwarranted. If we fear abuse the more logical approach would be to proceed cautiously and to devote time and energy to newer and more effective methods of control.

Others assert that to intentionally modify "natural" human processes is in effect to play God. To that assertion, one might ask equally simplistically whether the Wright brothers played God by giving man wings. Clearly we have already interfered with "natural" processes. Certainly, artifical organs, organ transplants, artifical insemination and prolongation of life (or dying) challenge traditional notions of what we mean by life, death and humanness. I have been unable to discern a relevant difference between these accepted treatments and procedures on the one hand and designed genetic change on the other. To be sure there are differences, but

1/ I am indebted here and in subsequent areas of my discussion to many writers, but particularly Cohen, Carl, "When May Research Be Stopped," The New England Journal of Medicine, Vol. 296, No. 21, pp. 1203-1210 (May 26, 1977).

only of degree.

Still others assert that we don't have the wisdom to handle implications of the knowledge once obtained. I believe that to be another variation of the "we cannot play God argument". However, the only way to acquire wisdom is not by delaying but by facing up to our awesome responsibilities. We do not have to start with a clean slate. There are past experiences with artificial insemination and compulsory sterilization of the mentally retarded which we can draw upon for guidance.

There are two other considerations which suggest that we ought not prohibit the research. First, although I do not take the position that advancement of knowledge is in and of itself always a good, the advancement of knowledge has always held a significant and prominent position in our society and a categorical prohibition would certainly seriously undercut that status. A categorical prohibition would not be difficult to enforce, particularly with respect to government-sponsored programs, but it would be or could be ignored by those who honestly believe that the results of their endeavors will have therapeutic potential. Clearly a categorical ban would set up a far more dangerous situation if it inspired activities out of the realm of informed scrutiny.

I do not mean to suggest by anything that I have written above that all genetic research on man must be permitted or encouraged. Within the broad category of research that involves reproductive engineering there could well be specific subsets

of such research that we wish to prohibit for compelling reasons. There may be others that we would severely constrain.

My position, succinctly stated, is that we proceed, but we proceed cautiously in the face of the unknown. Certainly strongly held fears and convictions about tampering with man's physical nature are not to be dismissed lightly, but at bottom such convictions are really tenets of faith that hold that results will not be beneficial. Such convictions have been advanced in the past against Galileo and Darwin for example, because they threatened prevailing views of man and his environment. I believe that they are deserving of no greater weight now than they were then.

What then should be done if there is agreement that such a ban is not in the best overall interest of mankind? There will obviously be important questions that we will have to answer. For example, (1) What are "good" and "bad" genes? (2) What are "good" and "bad" uses of the knowledge gained? (3) Is there a right to reproduce? What are the limits of the right? These and many other questions I suggest should be approached by using a cost/benefit analysis. When dealing with specific kinds of genetic research the question in every case must be asked: do the potential benefits from the knowledge to be gained outweight the risks of harm that might come about if we proceed?

A cost/benefit approach certainly has its difficulties, but I believe it is a plausible approach. Where there is doubt I would further suggest that as a matter of policy the

burden of proof should be on those who oppose the research. If the opponents meet the burden, then the research should be prohibited. Cost/benefit analyses moreover are not peculiarly appropriate for a scientist qua scientist to undertake. Such analyses would involve value judgments that the entire society is competent to address.

Should we proceed using a cost/benefit approach, we face two immediate procedural problems. How does society know when there is an issue to address and, how, by whom and with what standards are these determinations about potential benefits and risks of harm to be made?

Clearly, the only way the public becomes aware of scientific efforts is through disclosure by the scientist. This may occur at a pre-research stage if governmental funding is sought or post hoc through publication or publicity.

It must be a part of the scientist's ethics that he/she accept the responsibility of bringing to public attention issues raised by basic and applied research. Science is neutral in the sense that scientific facts may be objective, but the decision to ferret out facts, and decisions on how information is used involve value judgments to which scientists do not have exclusive claim. Fortunately, this is what occurred with recombinant DNA research when leading scientists called for a moratorium; thereby, alerting the public to implications of recombitant DNA research.

Sadly, of late there has been much mutual distrust between scientists and public bodies and decision-makers. Unfortunately, initial public reaction to what is perceived as threatening scientific research has been to restrict or prohibit. This was certainly the case with a congressionally mandated moratorium on research on the living human fetus. Such actions have made scientists resentful, defensive and mistrustful of the public's ability to respond rationally. On the other hand, the public, rightly in many cases, has felt that scientists have arrogantly made decisions they were ill-suited to make, often in isolation and without due regard to public concerns. Significantly, where issues have been studied and debated with more dispassion, and, where all views have been considered and discussed, there has been reasonable accommodation. This was true in the case of recombinant DNA research in Cambridge, Massachusetts, and with fetal research at the federal level. Certainly if moratoriums or prohibitions are imposed, they should only be imposed as the result of careful study and deliberation perferably not exclusively within the confines of legislative processes.

If there are to be future success stories it is essential that scientists and the public develop an appreciation of each other. It is almost impossible for the public to monitor effectively scientific research without the help of scientists. Likewise, it is almost impossible for science to continue advancements at recent rates without public support. It is therefore important that we encourage and maintain a healthy partnership.

Once an issue is put into the public arena, how do we go about resolving it? This problem is further complicated by the fact that the rapidity of scientific discovery and advancement has outstripped our ability to provide reasoned standards by which to judge proposed activities. For example, when the first kidney transplants were proposed with minor sibling or retarded sibling donors, judges were faced with very complicated issues and little legal or ethical precedent to guide them in attempting to reach decisions. They had no framework by which to measure risks of harm or potential benefits.

I believe there is no one way to proceed once an issue reaches the public. Obviously what is needed is some process that will result in the formulation of public policy. But the public policy will have to rest on justifications that reviewers can observe, criticize, approve, etc. There is no one answer because it's too early to tell what will be the most effective process. I am opposed at present therefore to the creation of a permanent public bureaucratic structure or any broad scale legislation aimed at resolution of issues in detail. I am opposed because these approaches are too permanent, and I fear will result in loss of flexibility. They also don't effectively utilize non-expert lay opinion. Greater flexibility and greater openness and broader participation is particularly desirable in the absence of standards by which judgments can be made. We need a prolonged period in which to experiment with a variety of approaches and processes. Legislation might appropriately be directed therefore at creating and supporting the experimental approaches and processes.

I am personally familiar with at least two experimental structures. I am a member of the National Commission for the Protection of Human Subjects and the Joint Commission on Prescription Drug Use. The latter commission, which is a private commission whose members were selected by public officials, I will not comment upon because it has been operating for only a few months.

The National Commission for the Protection of Human Subjects came into existence in December, 1974 and is scheduled to complete its work in March, 1978. It has a broad mandate which includes among other tasks the identification of ethical principles which should underlie research on human subjects. In carrying out our basic mandate we are to consider, (1) the boundaries between research and accepted and routine practice of medicine, (2) the role of risk-benefit criteria in determining appropriateness of research involving human subjects, (3) appropriate guidelines for subject selection, (4) the nature and definition of informed consent for research purposes, and (5) mechanisms for evaluating and monitoring performance of Institutional Review Boards. It has eleven members, no more than five of whom could be individuals who had engaged in research involving human subjects. All of the commission's proceedings must be conducted publicly. I believe it fair to say that the Commission has performed ably well beyond anyone's dreams. While we have not satisfied everyone, the evaluation of our work by most commentators has been favorable. We certainly have disabused the scientific community of the notion that we are anti-scientific without at the same time losing the confidence of the public.

While I believe we have been a success, I also believe that the structure needs careful evaluation. I fear that there has been too much emphasis on our strengths and not enough attention to actual or potential weaknesses. There are aspects that need re-examination and shoring up. First, the eleven commissioners have always worked together exceptionally well. [1/] Our success may be as much a result of unusual interpersonal chemistry as anything else. It may not be possible to replicate us. Second, there is a danger with us as with any commission or committee that the result will be majority rule for a number of different reasons not all overtly stated. To counteract such possibilities there must be institutional ways to encourage not only the creation of a policy, but also the articulation of the principled justifications that undergrid that policy. If different persons voted for different reasons, those reasons must be carefully stated so that the entire product can be analyzed, criticized, etc. We need to operate in a manner somewhat like the Supreme Court of the United States where the views of the Justices emerge in written opinions. Fortunately, unlike the Supreme Court of the United States if the Commission does not adequately clarify its positions, commentators have access to verbatum transcripts of deliberations from which they can draw conclusions.

One final observation! As I have previously stated I believe we need a long period in which to experiment with

1/ I regret to note the passing in August, 1977, of Professor David Louisell which reduced the Commission membership to ten members.

methods of resolving significant scientific issues. While the experiments are proceeding, the rest of society can't sit idly by. Academicians particularly should simultaneously be attempting principled formulations of alternative policy options. The two activities aren't mutually exclusive. On the contrary, they should be viewed as reinforcing. Those who think, debate, argue, and publish are not necessarily the best policy-makers. Alternatively, the best policy-makers may have difficulty articulating and exposing their rationale. Assuming there is a decision to proceed with some type of research, policy issues will continue to arise. Considering the significance of such issues, all sectors of society should be informed and encouraged to participate in their resolution.

Ms. KING. I understand that the primary focus, of the committee, has been on science policy issues in recombinant DNA research. However, I am particularly interested in issues arising out of genetic research that has therapeutic potential for the treatment of genetic defects. Additionally, I am interested in genetic research concerning future reproductive engineering, both to satisfy parental desires and to intentionally modify "natural" evolution. My observations are, therefore, specially pertinent to those areas of genetic research.

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I am not persuaded, or have not been persuaded, that all genetic research, because it tampers with man himself, is *a priori* immoral research. Nor am I convinced that such research is different in any relevant way from any other research that is currently being conducted.

Some would argue that the potential intentional or unintentional misuse of the results of such research by a few is enough in and of itself to justify its prohibition. I disagree. It is, of course, conceivable that there will be some abuse, but that possibility exists with any new and powerful development. It certainly never stopped us in nuclear research. Prohibiting research that has potential for good because of possible misuse is like throwing out the baby with the bath water. Such overreaction is unwarranted. If we fear abuse the more logical approach would be to proceed cautiously and to devote time and energy to newer and more effective methods of control.

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There are two other considerations which I suggest are pertinent when considering the question of whether we should prohibit this type of research. First, although I do not take the position that advancement of knowledge is in and of itself always a good, the advancement of knowledge has always held a significant and prominent position in our society, and a categorical prohibition would certainly seriously undercut that status. A categorical prohibition would not be difficult to enforce, particularly with respect to Government-sponsored programs, but it would be, or could be, ignored by those who honestly believe that the results of their endeavors will have therapeutic potential. Clearly a categorical ban would set up a far more dangerous situation if it inspired activities out of the realm of informed scrutiny.

I do not mean to suggest by anything that I have said that all genetic research on man must be permitted or encouraged. Within the broad category of research that involves reproductive engineering, for example, there could well be specific subsets of such research that

we wish to prohibit for compelling reasons. There may be others that we would seriously constrain.

What then should we do if there is agreement that such a ban is not in the best overall interest of mankind? There are obviously important questions that will have to be answered. These and other questions, I suggest, should be approached by using a cost/benefit analysis. When dealing with specific kinds of genetic research the question in every case must be asked, as it has been asked, I might add, in the area of human experimentation: Do the potential benefits from the knowledge to be gained outweigh the risks of harm that might come about if we proceed?

A cost/benefit approach certainly has its difficulties, but I believe it is a plausible approach, and where there is doubt I would further suggest that as a matter of policy the burden of proof should be on those who oppose the research. If the opponents meet the burden, then the research should be prohibited. Cost/benefit analyses moreover—I would stress this—are not peculiarly appropriate for a scientist qua scientist to undertake. Such analyses would involve value judgments that the entire society is competent to address.

Should we proceed using a cost/benefit approach, we face two immediate procedural problems: How does society know when there is an issue to address, and, how, by whom, and with what standards are these determinations about potential benefits and risks of harm to be made?

Clearly, the only way the public becomes aware of scientific efforts is through disclosure by the scientist. It must, therefore, be a part of the scientists ethics that he or she accept the responsibility of bringing to public attention issues raised by basic and applied research. Science is neutral in the sense that scientific facts may be objective, but the decision to ferret out facts and decisions on how information is used involve value judgments to which scientists do not have exclusive claim.

I further believe that there is not one way, or one single way, to proceed once an issue reaches the public. Obviously what we are in need of is some process that will result in the formulation of public policy. That public policy will have to rest on justifications that reviewers can observe, criticize, approve, et cetera. There is no one answer because it's too early to tell what will be the most effective process for a given issue. I am opposed, therefore, at present to the creation of a permanent public bureaucratic structure or any broad scale legislation aimed at resolution of issues in detail. I am opposed because these approaches are too permanent, and I fear will result in loss of flexibility. They also don't effectively utilize nonexpert lay opinion. Greater flexibility and greater openness and broader participation are particularly desirable in the absence of standards by which judgments can be made. We need a prolonged period in which to experiment with a variety of approaches and processes. Legislation might appropriately be directed towards the creation and support of the experimental approach or process.

I am personally familiar with at least two experimental structures. I am currently a member of the National Commission for the Protection of Human Subjects and the Joint Commission on Prescription Drug Use. The latter commission, which is a private commission whose

members were selected by public officials, I will not comment upon because it has been operating for only a few months.

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While I believe we have been a success, I also believe that the structure needs careful evaluation as a method of resolving some of the issues that we have been discussing. I fear that there has been too much emphasis on our strengths and not enough attention to actual or potential weaknesses. There are aspects that need reexamination and shoring up. For example, the 11 Commissioners have always worked together exceptionally well. Our success may be as much a result of unusual interpersonal chemistry as anything else. It may not be possible to replicate us.

Mr. THORNTON. Perhaps this might be an appropriate point to break in about cloning. [Laughter.]

Ms. KING. Second, there is a danger with us, as with any commission or committee, that the result will be majority rule for a number of different reasons, not all overtly stated. To counteract such possibilities there must be institutional ways to encourage not only the creation of a policy, but also the articulation of the principled justifications that undergird that policy. If different persons voted for different reasons, those reasons must be carefully stated so that the entire product can be analyzed, criticized, et cetera. We need to operate in a manner somewhat like the Supreme Court of the United States where the views of the Justices emerge in written opinions. Fortunately, unlike the Supreme Court of the United States, if the Commission does not adequately clarify its positions, commentators have access to verbatim transcripts of all deliberations from which they can draw conclusions.

One final observation: As I have previously stated, I believe we need a long period in which to experiment with the methods of resolving significant scientific issues. While these experiments—and I'm talking here now about structural experiments or processes—are proceeding, I don't expect the rest of us to sit idly by. Academicians particularly should simultaneously be attempting principled formulations of alternative policy options. Considering the significance of such issues, all sectors of society should be informed and encouraged to participate in their resolution.

Thank you.

Mr. THORNTON. Thank you very much, Ms. King, for a very excellent presentation.

Our concluding witness, before we embark upon our panel discussion, is Henry R. Luce Professor at the University of Chicago, Dr. Leon Kass.

Dr. Kass has prepared a very excellent presentation which, without objection, I would like to introduce and make a part of the record of this proceeding. Dr. Kass is also the author of an article published in the November 1971 issue of Science magazine, called The New Biology: What Price Relieving Man's Estate?, and I think that this should also be considered by members as we move forward in this discussion. I think it should be at least circulated to the members of the subcommittee and considered for possible inclusion in the record.

[The material referred to is as follows:]

[Reprinted from Science, November 19, 1971, Volume 174, pp. 779–788]

THE NEW BIOLOGY: WHAT PRICE RELIEVING MAN'S ESTATE?

EFFORTS TO ERADICATE HUMAN SUFFERING RAISE DIFFICULT AND PROFOUND QUESTIONS OF THEORY AND PRAISE

(Leon R. Kass)

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The author is executive secretary, Committee on the Life Sciences and Social Policy, National Research Council, National Academy of Sciences, Washington, D.C. 20418. This article is adapted from a working paper prepared by the author for the committee, as well as from lectures given at St. John's College in Annapolis, Maryland; at Oak Ridge National Laboratory, biology division, Oak Ridge, Tennessee; and at a meeting, in Washington, of the Council for the Advancement of Science Writing. The views expressed are those of the author.

Recent advances in biology and medicine suggest that we may be rapidly acquiring the power to modify and control the capacities and activities of men by direct intervention and manipulation of their bodies and minds. Certain means are already in use or at hand, others await the solution of relatively minor technical problems, while yet others, those offering perhaps the most precise kind of control, depend upon further basic research. Biologists who have considered these matters disagree on the question of how much how soon, but all agree that the power for "human engineering," to borrow from the jargon, is coming and that it will probably have profound social consequences.

These developments have been viewed both with enthusiasm and with alarm; they are only just beginning to receive serious attention. Several biologists have undertaken to inform the public about the technical possibilities, present and future. Practitioners of social science "futurology" are attempting to predict and describe the likely social consequences of and public responses to the new technologies. Lawyers and legislators are exploring institutional innovations for assessing new technologies. All of these activities are based upon the hope that we can harness the new technology of man for the betterment of mankind.

Yet this commendable aspiration points to another set of questions, which are, in my view, sorely neglected—questions that inquire into the meaning of phrases such as the "betterment of mankind." A *full* understanding of the new technology of man requires an exploration of ends, values, standards. What ends will or should the new techniques serve? What values should guide society's adjustments? By what standards should the assessment agencies assess? Behind these questions lie others: what is a good man, what is a good life for man, what is a good community? This article is an attempt to provoke discussion of these neglected and important questions.

While these questions about ends and ultimate ends are never unimportant or irrelevant, they have rarely been more important or more relevant. That this is so can be seen once we recognize that we are dealing here with a group of technologies that are in a decisive respect unique: the object upon which they operate

is man himself. The technologies of energy or food production, of communication, of manufacture, and of motion greatly alter the implements available to man and the conditions in which he uses them. In contrast, the biomedical technology works to change the user himself. To be sure, the printing press, the automobile, the television, and the jet airplane have greatly altered the conditions under which and the way in which men live; but men as biological beings have remained largely unchanged. They have been, and remain, able to accept or reject, to use and abuse these technologies; they choose, whether wisely or foolishly, the ends to which these technologies are means. Biomedical technology may make it possible to change the inherent capacity for choice itself. Indeed, both those who welcome and those who fear the advent of "human engineering" ground their hopes and fears in the same prospect: *that man can for the first time recreate himself.*

Engineering the engineer seems to differ in kind from engineering his engine. Some have argued, however, that biomedical engineering does not differ qualitatively from toilet training, education, and moral teachings—all of which are forms of so-called "social engineering," which has man as its object, and is used by one generation to mold the next. In reply, it must at least be said that the techniques which have hitherto been employed are feeble and inefficient when compared to those on the horizon.

This quantitative difference rests in part on a qualitative difference in the means of intervention. The traditional influences operate by speech or by symbolic deeds. They pay tribute to man as the animal who lives by speech and who understands the meanings of actions. Also, their effects are, in general, reversible, or at least subject to attempts at reversal. Each person has greater or lesser power to accept or reject or abandon them. In contrast, biomedical engineering circumvents the human context of speech and meaning, bypasses choice, and goes directly to work to modify the human material itself. Moreover, the changes wrought may be irreversible.

In addition, there is an important practical reason for considering the biomedical technology apart from other technologies. The advances we shall examine are fruits of a large, humane project dedicated to the conquest of disease and the relief of human suffering. The biologist and physician, regardless of their private motives, are seen, with justification, to be the well-wishers and benefactors of mankind. Thus, in a time in which technological advance is more carefully scrutinized and increasingly criticized, biomedical developments are still viewed by most people as benefits largely without qualification. The price we pay for these developments is thus more likely to go unrecognized. For this reason, I shall consider only the dangers and costs of biomedical advance. As the benefits are well known, there is no need to dwell upon them here. My discussion is deliberately partial.

I begin with a survey of the pertinent technologies. Next, I will consider some of the basic ethical and social problems in the use of these technologies. Then, I will briefly raise some fundamental questions to which these problems point. Finally, I shall offer some very general reflections on what is to be done.

THE BIOMEDICAL TECHNOLOGIES

The biomedical technologies can be usefully organized into three groups, according to their major purpose: (i) control of death and life, (ii) control of human potentialities, and (iii) control of human achievement. The corresponding technologies are (i) medicine, especially the arts of prolonging life, and controlling reproduction, (ii) genetic engineering, and (iii) neurological and psychological manipulation. I shall briefly summarize each group of techniques.

(1) *Control of death and life.* Previous medical triumphs have greatly increased average life expectancy. Yet other developments, such as organ transplantation or replacement and research into aging, hold forth the promise of increasing not just the average, but also the maximum life expectancy. Indeed, medicine seems to be sharpening its tools to do battle with death itself, as if death were just one more disease.

More immediately and concretely, available techniques of prolonging life—respirators, cardiac pacemakers, artificial kidneys—are already in the lists against death. Ironically, the success of these devices in forestalling death has introduced confusion in determining that death has, in fact, occurred. The traditional signs of life—heartbeat and respiration—can now be maintained entirely by machines. Some physicians are now busily trying to devise so-called "new definitions of death," while others maintain that the technical

advances show that death is not a concrete event at all, but rather a gradual process, like twilight, incapable of precise temporal localization.

The real challenge to death will come from research into aging and senescence, a field just entering puberty. Recent studies suggest that aging is a genetically controlled process, distinct from disease, but one that can be manipulated and altered by diet or drugs. Extrapolating from animal studies, some scientists have suggested that a decrease in the rate of aging might also be achieved simply by effecting a very small decrease in human body temperature. According to some estimates, by the year 2,000 it may be technically possible to add from 20 to 40 useful years to the period of middle life.

Medicine's success in extending life is already a major cause of excessive population growth: death control points to birth control. Although we are already technically competent, new techniques for lowering fertility and chemical agents for inducing abortion will greatly enhance our powers over conception and gestation. Problems of definition have been raised here as well. The need to determine when individuals acquire enforceable legal rights gives society an interest in the definition of human life and of the time when it begins. These matters are too familiar to need elaboration.

Technologies to conquer infertility proceed alongside those to promote it. The first successful laboratory fertilization of human egg by human sperm was reported in 1969 (*1*). In 1970, British scientists learned how to grow human embryos in the laboratory up to at least the blastocyst stage [that is, to the age of 1 week (*2*)]. We may soon hear about the next stage, the successful reimplantation of such an embryo into a woman previously infertile because of oviduct disease. The development of an artificial placenta, now under investigation, will make possible full laboratory control of fertilization and gestation. In addition, sophisticated biochemical and cytological techniques of monitoring the "quality" of the fetus have been and are being developed and used. These developments not only give us more power over the generation of human life, but make it possible to manipulate and to modify the quality of the human material.

(2) *Control of human potentialities.* Genetic engineering, when fully developed, will wield two powers not shared by ordinary medical practice. Medicine treats existing individuals and seeks to correct deviations from a norm of health. Genetic engineering, in contrast, will be able to make changes that can be transmitted to succeeding generations and will be able to create new capacities, and hence to establish new norms of health and fitness.

Nevertheless, one of the major interests in genetic manipulation is strictly medical: to develop treatments for individuals with inherited diseases. Genetic disease is prevalent and increasing, thanks partly to medical advances that enable those affected to survive and perpetuate their mutant genes. The hope is that normal copies of the appropriate gene, obtained biologically or synthesized chemically, can be introduced into defective individuals to correct their deficiencies. This *therapeutic* use of genetic technology appears to be far in the future. Moreover, there is some doubt that it will ever be practical, since the same end could be more easily achieved by transplanting cells or organs that could compensate for the missing or defective gene product.

Far less remote are technologies that could serve *eugenic* ends. Their development has been endorsed by those concerned about a general deterioration of the human gene pool and by others who believe that even an undeteriorated human gene pool needs upgrading. Artificial insemination with selected donors, the eugenic proposal of Herman Muller (*3*), has been possible for several years because of the perfection of methods for long-term storage of human spermatozoa.

The successful maturation of human oocytes in the laboratory and their subsequent fertilization now make it possible to select donors of ova as well. But a far more suitable technique for eugenic purposes will soon be upon us—namely, nuclear transplantation, or cloning. Bypassing the lottery of sexual recombination, nuclear transplantation permits the asexual reproduction or copying of an already developed individual. The nucleus of a mature but unfertilized egg is replaced by a nucleus obtained from a specialized cell of an adult organism or embryo (for example, a cell from the intestines or the skin). The egg with its transplanted nucleus develops as if it had been fertilized and, barring complications, will give rise to a normal adult organism. Since almost all the hereditary material (DNA) of a cell is contained within its nucleus, the renucleated egg and the individual into which it develops are genetically identical to the adult organism that was the source of the donor nucleus. Cloning could be used to produce sets of unlimited numbers of genetically identical individuals, each set derived

from a single parent. Cloning has been successful in amphibians and is now being tried in mice; its extension to man merely requires the solution of certain technical problems.

Production of man-animal chimeras by the introduction of selected nonhuman material into developing human embryos is also expected. Fusion of human and nonhuman cells in tissue culture has already been achieved.

Other, less direct means for influencing the gene pool are already available, thanks to our increasing ability to identify and diagnose genetic diseases.

Genetic counselors can now detect biochemically and cytologically a variety of severe genetic defects (for example, Mongolism, Tay-Sachs disease) while the fetus is still in utero. Since treatments are at present largely unavailable, diagnosis is often followed by abortion of the affected fetus. In the future, more sensitive tests will also permit the detection of heterozygote carriers, the unaffected individuals who carry but a single dose of a given deleterious gene. The eradication of a given genetic disease might then be attempted by aborting all such carriers. In fact, it was recently suggested that the fairly common disease cystic fibrosis could be completely eliminated over the next 40 years by screening all pregnancies and aborting the 17,000,000 unaffected fetuses that will carry a single gene for this disease. Such zealots ned to be reminded of the consequences should each geneticist be allowed an equal assault on his favorite genetic disorder, given that each human being is a carrier for some four to eight such recessive. lethal genetic diseases.

(3) *Control of human achievement.* Although human achievement depends at least in part upon genetic endowment, heredity determines only the material upon which experience and education impose the form. The limits of many capacities and powers of an individual are indeed genetically determined, but the nurturing and perfection of these capacities depend upon other influences. Neurological and psychological manipulation hold forth the promise of controlling the development of human capacities, particularly those long considered most distinctively human: speech, thought, choice, emotion, memory, and imagination.

These techniques are now in a rather primitive state because we understand so little about the brain and mind. Nevertheless, we have already seen the use of electrical stimulation of the human brain to produce sensations of intense pleasure and to control rage, the use of brain surgery (for example, frontal lobotomy) for the relief of severe anxiety, and the use of aversive conditioning with electric shock to treat sexual perversion. Operant-conditioning techniques are widely used, apparently with success, in schools and mental hospitals. The use of so-called consciousness-expanding and hallucinogenic drugs is widespread, to say nothing of tranquilizers and stimulants. We are promised drugs to modify memory, intelligence, libido, and aggressiveness.

The following passages from a recent book by Yale neurophysiologist José Delgado—a book instructively entitled *Physical Control of the Mind: Toward a Psychocivilized Society*—should serve to make this discussion more concrete. In the early 1950's. it was discovered that, with electrodes placed in certain discrete regions of their brains, animals would repeatedly and indefatigably press levers to stimulate their own brains, with obvious resultant enjoyment. Even starving animals preferred stimulating these so-called pleasure centers to eating. Delgado comments on the electrical stimulation of a similar center in a human subject (*4*, p. 185).

"[T]he patient reported a pleasant tingling sensation in the left side of her body 'from my face down to the bottom of my legs.' She started giggling and making funny comments, stating that she enjoyed the sensation 'very much.' Repetition of these stimulations made the patient more communicative and flirtatious, and she ended by openly expressing her desire to marry the therapist."

And one further quotation from Delgado (4, p. 88).

"Leaving wires inside of a thinking brain may appear unpleasant or dangerous, but actually the many patients who have undergone this experience have not been concerned about the fact of being wired, nor have they felt any discomfort due to the presence of conductors in their heads. Some women have shown their feminine adaptability to circumstances by wearing attractive hats or wigs to conceal their electrical headgear, and many people have been able to enjoy a normal life as outpatients. returning to the clinic periodically for examination and stimulation. In a few cases in which contacts were located in pleasurable areas, patients have had the opportunity to stimulate their own brains by pressing the button of a portable instrument, and this procedure is reported to have therapeutic benefits."

It bears repeating that the sciences of neurophysiology and psychopharmacology are in their infancy. The techniques that are now available are crude, imprecise, weak, and unpredictable, compared to those that may flow from a more mature neurobiology.

BASIC ETHICAL AND SOCIAL PROBLEMS IN THE USE OF BIOMEDICAL TECHNOLOGY

After this cursory review of the powers now and soon to be at our disposal, I turn to the questions concerning the use of these powers. First, we must recognize that questions of use of science and technology are always moral and political questions, never simply technical ones. All private or public decisions to develop or to use biomedical technology—and decisions *not* to do so—inevitably contain judgments about value. This is true even if the values guiding those decisions are not articulated or more clear, as indeed they often are not. Secondly, the value judgments cannot be derived from biomedical science. This is true even if scientists themselves make the decisions.

These important points are often overlooked for at least three reasons.

(1) They are obscured by those who like to speak of "the control of nature by science." It is men who control, not that abstraction "science." Science may provide the means, but men choose the ends; the choice of ends comes from beyond science.

(2) Introduction of new technologies often appears to be the result of no decisions whatsoever, or of the culmination of decisions too small or unconscious to be recognized as such. What can be done is done. However, someone is deciding on the basis of some notions of desirability, no matter how self-serving or altruistic.

(3) Desires to gain or keep money and power no doubt influence much of what happens, but these desires can also be formulated as reasons and then discussed and debated.

Insofar as our society has tried to deliberate about questions of use, how has it done so? Pragmatists that we are, we prefer a utilitarian calculus: we weigh "benefits" against "risks," and we weigh them for both the individual and "society." We often ignore the fact that the very definitions of "a benefit" and "a risk" are themselves based upon judgments about value. In the biomedical areas just reviewed, the benefits are considered to be self-evident: prolongation of life, control of fertility and of population size, treatment and prevention of genetic disease, the reduction of anxiety and aggressiveness, and the enhancement of memory, intelligence, and pleasure. The assessment of risk is, in general, simply pragmatic—will the technique work effectively and reliably, how much will it cost, will it do detectable bodily harm, and who will complain if we proceed with development? As these questions are familiar and congenial, there is no need to belabor them.

The very pragmatism that makes us sensitive to considerations of economic cost often blinds us to the larger social costs exacted by biomedical advances. For one thing, we seem to be unaware that we may not be able to maximize all the benefits, that several of the goals we are promoting conflict with each other. On the one hand, we seek to control population growth by lowering fertility; on the other hand, we develop techniques to enable every infertile woman to bear a child. On the one hand, we try to extend the lives of individuals with genetic disease; on the other, we wish to eliminate deleterious genes from the human population. I am not urging that we resolve these conflicts in favor of one side or the other, but simply that we recognize that such conflicts exist. Once we do, we are more likely to appreciate that most "progress" is heavily paid for in terms not generally included in the simple utilitarian calculus.

To become sensitive to the larger costs of biomedical progress, we must attend to several serious ethical and social questions. I will briefly discuss three of them: (i) questions of distributive justice, (ii) questions of the use and abuse of power, and (iii) questions of self-degradation and dehumanization.

DISTRIBUTIVE JUSTICE

The introduction of any biomedical technology presents a new instance of an old problem—how to distribute scarce resources justly. We should assume that demand will usually exceed supply. Which people should receive a kidney transplant or an artificial heart? Who should get the benefits of genetic therapy

or of brain stimulation? Is "first-come, first-served" the fairest principle? Or are certain people "more worthy," and if so, on what grounds?

It is unlikely that we will arrive at answers to these questions in the form of deliberate decisions. More likely, the problem of distribution will continue to be decided ad hoc and locally. If so, the consequence will probably be a sharp increase in the already far too great inequality of medical care. The extreme case will be longevity, which will probably be, at first, obtainable only at great expense. Who is likely to be able to buy it? Do conscience and prudence permit us to enlarge the gap between rich and poor, especially with respect to something as fundamental as life itself?

Questions of distributive justice also arise in the earlier decisions to acquire new knowledge and to develop new techniques. Personnel and facilities for medical research and treatment are scarce resources. Is the development of a new technology the best use of the limited resources, given current circumstances? How should we balance efforts aimed at prevention against those aimed at cure, or either of these against efforts to redesign the species? How should we balance the delivery of available levels of care against further basic research? More fundamentally, how should we balance efforts in biology and medicine against efforts to eliminate poverty, pollution, urban decay, discrimination, and poor education? This last question about distribution is perhaps the most profound. We should reflect upon the social consequences of seducing many of our brightest young people to spend their lives locating the biochemical defects in rare genetic diseases, while our more serious problems go begging. The current squeeze on money for research provides us with an opportunity to rethink and reorder our priorities.

Problems of distributive justice are frequently mentioned and discussed, but they are hard to resolve in a rational manner. We find them especially difficult because of the enormous range of conflicting values and interests that characterizes our pluralistic society. We cannot agree—unfortunately, we often do not even try to agree—on standards for just distribution. Rather, decisions tend to be made largely out of a clash of competing interests. Thus, regrettably, the question of how to distribute justly often gets reduced to who shall decide how to distribute. The question about justice has led us to the question about power.

USE AND ABUSE OF POWER

We have difficulty recognizing the problems of the exercise of power in the biomedical enterprise because of our delight with the wondrous fruits it has yielded. This is ironic because the notion of power is absolutely central to the modern conception of science. The ancients conceived of science as the *understanding* of nature, pursued for its own sake. We moderns view science as power, as *control* over nature; the conquest of nature "for the relief of man's estate" was the charge issued by Francis Bacon, one of the leading architects of the modern scientific project (5).

Another source of difficulty is our fondness for speaking of the abstraction "Man." I suspect that we prefer to speak figuratively about "Man's power over Nature" because it obscures an unpleasant reality about human affairs. It is in fact particular men who wield power, not Man. What we really mean by "Man's power over Nature" is a power exercised by some men over other men, with a knowledge of nature as their instrument.

While applicable to technology in general, these reflections are especially pertinent to the technologies of human engineering, with which men deliberately exercise power over future generations. An excellent discussion of this question is found in *The Abolition of Man*, by C. S. Lewis (6).

"It is, of course, a commonplace to complain that men have hitherto used badly, and against their fellows, the powers that science has given them. But that is not the point I am trying to make. I am not speaking of particular corruptions and abuses which an increase of moral virtue would cure: I am considering what the thing called "Man's power over Nature" must always and essentially be....

"In reality, of course, if any one age really attains, by eugenics and scientific education, the power to make its descendants what it pleases, all men who live after it are the patients of that power. They are weaker, not stronger: for though we may have put wonderful machines in their hands, we have pre-ordained how they are to use them. . . . The real picture is that of one dominant age . . . which resists all previous ages most successfully and dominates all subsequent ages most irresistibly, and thus is the real master of the human species. But even within this

master generation (itself an infinitesimal minority of the species) the power will be exercised by a minority smaller still. Man's conquest of Nature, if the dreams of some scientific planners are realized, means the rule of a few hundreds of men over billions upon billions of men. There neither is nor can be any simple increase of power on Man's side. Each new power won by man is a power *over* man as well. Each advance leaves him weaker as well as stronger. In every victory, besides being the general who triumphs, he is also the prisoner who follows the triumphal car."

Please note that I am not yet speaking about the problem of the misuse or abuse of power. The point is rather that the power which grows is unavoidably the power of only some men, and that the number of powerful men decreases as power increases.

Specific problems of abuse and misuse of specific powers must not, however, be overlooked. Some have voiced the fear that the technologies of genetic engineering and behavior control, through developed for good purposes, will be put to evil uses. These fears are perhaps somewhat exaggerated, if only because biomedical technologies would add very little to our highly developed arsenal for mischief, destruction, and stultification. Nevertheless, any proposal for large-scale human engineering should make us wary. Consider a program of positive eugenics based upon the widespread practice of a sexual reproduction. Who shall decide what constitutes a superior individual worthy of replication? Who shall decide which individuals may or must reproduce, and by which method? These are questions easily answered only for a tyrannical regime.

Concern about the use of power is equally necessary in the selection of means for desirable or agreed-upon ends. Consider the desired end of limiting population growth. An effective program of fertility control is likely to be coercive. Who should decide the choice of means? Will the program penalize "conscientious objectors"?

Serious problems arise simply from obtaining and disseminating information, as in the mass screening programs now being proposed for detection of genetic disease. For what kinds of disorders is compulsory screening justified? Who shall have access to the data obtained, and for what purposes? To whom does information about a person's genotype belong? In ordinary medical practice, the patient's privacy is protected by the doctor's adherence to the principle of confidentiality. What will protect his privacy under conditions of mass screening?

More than privacy is at stake if screening is undertaken to detect psychological or behavioral abnormalities. A recent proposal, tendered and supported high in government, called for the psychological testing of all 6-year-olds to detect future criminals and misfits. The proposal was rejected; current tests lack the requisite predictive powers. But will such a proposal be rejected if reliable tests become available? What if certain genetic disorders, diagnosable in childhood, can be shown to correlate with subsequent antisocial behavior? For what degree of correlation and for what kinds of behavior can mandatory screening be justified? What use should be made of the data? Might not the dissemination of the information itself undermine the individual's chance for a worthy life and contribute to his so-called antisocial tendencies?

Consider the seemingly harmless effort to redefine clinical death. If the need for organs for transplantation is the stimulus for redefining death, might not this concern influence the definition at the expense of the dying? One physician, in fact, refers in writing to the revised criteria for declaring a patient dead as a "new definition of heart donor eligibility" (7, p. 526).

Problems of abuse of power arise even in the acquisition of basic knowledge. The securing of a voluntary and informed consent is an abiding problem in the use of human subjects in experimentation. Gross coercion and deception are now rarely a problem; the pressures are generally subtle, often related to an intrinsic power imbalance in favor of the experimentalist.

A special problem arises in experiments on or manipulations of the unborn. Here it is impossible to obtain the consent of the human subject. If the purpose of the intervention is therapeutic—to correct a known genetic abnormality, for example—consent can reasonably be implied. But can anyone ethically consent to nontherapeutic interventions in which parents or scientists work their wills or their eugenic visions on the child-to-be? Would not such manipulation represent in itself an abuse of power, independent of consequences

There are many clinical situations which already permit, if not invite, the manipulative or arbitrary use of powers provided by biomedical technology: obtaining organs for transplantation, refusing to let a person die with dignity, giving

genetic counseling to a frightened couple, recommending eugenic sterilization for a mental retardate, ordering electric shock for a homosexual. In each situation, there is an opportunity to violate the will of the patient or subject. Such opportunities have generally existed in medical practice, but the dangers are becoming increasingly serious. With the growing complexity of the technologies, the technician gains in authority, since he alone can understand what he is doing. The patient's lack of knowledge makes him deferential and often inhibits him from speaking up when he feels threatened. Physicians *are* sometimes troubled by their increasing power, yet they feel they cannot avoid its exercise. "Reluctantly," one commented to me, "we shall have to play God." With what guidance and to what ends I shall consider later. For the moment, I merely ask: "By whose authority"

While these questions about power are pertinent and important, they are in one sense misleading. They imply an inherent conflict of purpose between physician and patient, between scientist and citizen. The discussion conjures up images of master and slave, of oppressor and oppressed. Yet it must be remembered that conflict of purpose is largely absent, especially with regard to general goals. To be sure, the purposes of medical scientists are not always the same as those of the subjects experimented on. Nevertheless, basic sponsors and partisans of biomedical technology are precisely those upon whom the technology will operate. The will of the scientist and physician is happily married to (rather, is the offspring of) the desire of all of us for better health, longer life, and peace of mind.

Most future biomedical technologies will probably be welcomed, as have those of the past. Their use will require little or no coercion. Some developments, such as pills to improve memory, control mood, or induce pleasure, are likely to need no promotion. Thus, even if we should escape from the dangers of coercive manipulation, we shall still face large problems posed by the voluntary use of biomedical technology, problems to which I now turn.

VOLUNTARY SELF-DEGRADATION AND DEHUMANIZATION

Modern opinion is sensitive to problems of restriction of freedom and abuse of power. Indeed, many hold that a man can be injured only by violating his will. But this view is much too narrow. It fails to recognize the great dangers we shall face in the use of biomedical technology, dangers that stem from an excess of freedom, from the uninhibited exercises of will. In my view, our greatest problem will increasingly be one of voluntary self-degradation, or willing dehumanization.

Certain desired and perfected medical technologies have already had some dehumanizing consequences. Improved methods of resuscitation have made possible heroic efforts to "save" the severely ill and injured. Yet these efforts are sometimes only partly successful; they may succeed in salvaging individuals with severe brain damage, capable of only a less-than-human, vegetating existence. Such patients, increasingly found in the intensive care units of university hospitals, have been denied a death with dignity. Families are forced to suffer seeing their loved ones so reduced, and are made to bear the burdens of a protracted death watch.

Even the ordinary methods of treating disease and prolonging life have impoverished the context in which men die. Fewer and fewer people die in the familiar surroundings of home or in the company of family and friends. At that time of life when there is perhaps the greatest need for human warmth and comfort, the dying patient is kept company by cardiac pacemakers and defibrillators, respirators, oxygenators, catheters, and his intravenous drip.

But the loneliness is not confined to the dying patient in the hospital bed. Consider the increasing number of old people who are still alive, thanks to medical progress. As a group, the elderly are the most alienated members of our society. Not yet ready for the world of the dead, not deemed fit for the world of the living, they are shunted aside. More and more of them spend the extra years medicine has given them in "homes for senior citizens," in chronic hospitals, in nursing homes—waiting for the end. We have learned how to increase their years, but we have not learned how to help them enjoy their days. And yet, we bravely and relentlessly push back the frontiers against death.

Paradoxically, even the young and vigorous may be suffering because of medicine's success in removing death from their personal experience. Those born since penicillin represent the first generation ever to grow up without the experience or fear of probable unexpected death at an early age. They look around and see that virtually all of their friends are alive. A thoughtful physician, Eric Cassell, has remarked on this in "Death and the physician" (8, p. 76):

"[W]hile the gift of time must surely be marked as a great blessing, the perception of time, as stretching out endlessly before us, is somewhat threatening. Many of us function best under deadlines, and tend to procrastinate when time limits are not set. . . . Thus, this unquestioned boon, the extension of life, and the removal of the threat of premature death, carries with it an unexpected anxiety; the anxiety of an unlimited future.

"In the young, the sense of limitless time has apparently imparted not a feeling of limitless opportunity, but increased stress and anxiety, in addition to the anxiety which results from other modern freedoms: personal mobility, a wide range of occupational choice, and independence from the limitations of class and familial patterns of work. . . . A certain aimlessness (often ringed around with great social consciousness) characterizes discussions about their own aspirations. The future is endless, and their inner demands seem minimal. Although it may appear uncharitable to say so, they seem to be acting in a way best described as "childish"—particularly in their lack of a time sense. They behave as though there were no tomorrow, or as though the time limits imposed by the biological facts of life had became so vague for them as to be nonexistent."

Consider next the coming power over reproduction and genotype. We endorse the project that will enable us to control numbers and to treat individuals with genetic disease. But our desires outrun these defensible goals. Many would welcome the chance to become parents without the inconvenience of pregnancy; others would wish to know in advance the characteristics of their offspring (sex, height, eye color, intelligence); still others would wish to design these characteristics to suit their tastes. Some scientists have called for the use of the new technologies to assure the "quality" of all new babies (9). As one obstetrician put it: "The business of obstetrics is to produce *optimum* babies." But the price to be paid for the "optimum baby" is the transfer of procreation from the home to the laboratory and its coincident transformation into manufacture. Increasing control over the product is purchased by the increasing depersonalization of the process.

The complete depersonalization of procreation (possible with the development of an artificial placenta) shall be, in itself, seriously dehumanizing, no matter how optimum the product. It should not be forgotten that human procreation not only issues new human beings, but is itself a human activity.

Procreation is not simply an activity of the rational will. It is a more complete human activity precisely because it engages us bodily and spiritually, as well as rationally. Is there perhaps some wisdom in that mystery of nature which joins the pleasure of sex, the communication of love, and the desire for children in the very activity by which we continue the chain of human existence? Is not biological parenthood a built-in "mechanism," selected because it fosters and supports in parents an adequate concern for and commitment to their children? Would not the laboratory production of human beings no longer be *human* procreation? Could it keep human parenthood human?

The dehumanizing consequences of programmed reproduction extend beyond the mere acts and processes of life-giving. Transfer of procreation to the laboratory will no doubt weaken what is presently for many people the best remaining justification and support for the existence of marriage and the family. Sex is now comfortably at home outside of marriage: child-rearing is progressively being given over to the state, the schools, the mass media, and the child-care centers. Some have argued that the family, long the nursey of humanity, has outlived its usefulness. To be sure, laboratory and governmental alternatives might be designed for procreation and child-rearing, but at what cost?

This is not the place to conduct a full evaluation of the biological family. Nevertheless, some of its important virtues are, nowadays, too often overlooked. The family is rapidly becoming the only institution in an increasingly impersonal world where each person is loved not for what he does or makes, but simply because he is. The family is also the institution where most of us, both as children and as parents, acquire a sense of continuity with the past and a sense of commitment to the future. Without the family, we would have little incentive to take an interest in anything after our own deaths. These observations suggest that the elimination of the family would weaken ties to past and future, and would throw us, even more than we are now, to the mercy of an impersonal, lonely present.

Neurobiology and psychobiology probe most directly into the distinctively human. The technological fruit of these sciences is likely to be both more tempting

than Eve's apple and more "catastrophic" in its result (*10*). One need only consider contemporary drug use to see what people are willing to risk or sacrifice for novel experiences, heightened perceptions, or just "kicks." The possibility of drug-induced, instant, and effortless gratification will be welcomed. Recall the possibilities of voluntary self-stimulation of the brain to reduce anxiety, to heighten pleasure, or to create visual and auditory sensations unavailable through the peripheral sense organs. Once these techniques are perfected and safe, is there much doubt that they will be desired, demanded, and used?

What ends will these techniques serve? Most likely, only the most elemental, those most tied to the bodily pleasures. What will happen to thought, to love, to friendship, to art, to judgment, to public-spiritedness in a society with a perfected technology of pleasure? What kinds of creatures will we become if we obtain our pleasure by drug or electrical stimulation without the usual kind of human efforts and frustrations? What kind of society will we have?

We need only consult Aldous Huxley's prophetic novel *Brave New World* for a likely answer to these questions. There we encounter a society dedicated to homogeneity and stability, administered by means of instant gratifications and peopled by creatures of human shape but of stunted humanity. They consume, fornicate, take "soma," and operate the machinery that makes it all possible. They do not read, write, think, love, or govern themselves. Creativity and curiosity, reason and passion, exist only in a rudimentary and multilated form. In short, they are not men at all.

True, our techniques, like theirs, may in fact enable us to treat schizophrenia, to alleviate anxiety, to curb aggressiveness. We, like they, may indeed be able to save mankind from itself, but probably only at the cost of its humanness. In the end, the price of relieving man's estate might well be the abolition of man (*11*).

There are, of course, many other routes leading to the abolition of man. There are many other and better known causes of dehumanization. Disease, starvation, mental retardation, slavery, and brutality—to name just a few—have long prevented many, if not most, people from living a fully human life. We should work to reduce and eventually to eliminate these evils. But the existence of these evils should not prevent us from appreciating that the use of the technology of man, uninformed by wisdom concerning proper human ends, and untempered by an appropriate humility and awe, can unwittingly render us all irreversibly less than human. For, unlike the man reduced by disease or slavery, the people dehumanized à la *Brave New World* are not miserable, do not know that they are dehumanized, and, what is worse, would not care if they knew. They are, indeed, happy slaves, with a slavish happiness.

SOME FUNDAMENTAL QUESTIONS

The practical problems of distributing scarce resources, of curbing the abuses of power, and of preventing voluntary dehumanization point beyond themselves to some large, enduring, and most difficult questions: the nature of justice and the good community, the nature of man and the good for man. My appreciation of the profundity of these questions and my own ignorance before them makes me hesitant to say any more about them. Nevertheless, previous failures to find a shortcut around them have led me to believe that these questions must be faced if we are to have any hope of understanding where biology is taking us. Therefore, I shall try to show in outline how I think some of the larger questions arise from any discussion of dehumanization and self-degradation.

My remarks on dehumanization can hardly fail to arouse argument. It might be said, correctly, that to speak about dehumanization presupposes a concept of "the distinctively human." It might also be said, correctly, that to speak about wisdom concerning proper human ends presupposes that such ends do in fact exist and that they may be more or less accessible to human understanding, or at least to rational inquiry. It is true that neither presupposition is at home in modern thought.

The notion of the "distinctively human" has been seriously challenged by modern scientists. Darwinists hold that man is, at least in origin, tied to the subhuman; his seeming distinctiveness is an illusion or, at most, not very important. Biochemists and molecular biologists extend the challenge by blurring the distinction between the living and the nonliving. The laws of physics and chemistry are found to be valid and are held to be sufficient for explaining biological systems. Man is a collection of molecules, an accident on the stage

of evolution, endowed by chance with the power to change himself, but only along determined lines.

Psychoanalysts have also debunked the "distinctly human." The essence of man is seen to be located in those drives he shares with other animals—pursuit of pleasure and avoidance of pain. The so-called "higher functions" are understood to be servants of the more elementary, the more base. Any distinctiveness or "dignity" that man has consists of his superior capacity for gratifying his animal needs.

The idea of "human good" fares no better. In the social sciences, historicists and existentialists have helped drive this question underground. The former hold all notions of human good to be culturally and historically bound, and hence mutable. The latter hold that values are subjective: each man makes his own, and ethics becomes simply the cataloging of personal tastes.

Such appear to be the prevailing opinions. Yet there is nothing novel about reductionism, hedonism, and relativism; these are doctrines with which Socrates contended. What is new is that these doctrines seem to be vindicated by scientific advance. Not only do the scientific notions of nature and of man flower into verifiable predictions, but they yield marvelous fruit. The technological triumphs are held to validate their scientific foundations. Here, perhaps, is the most pernicious result of technological progress—more dehumanizing than any actual manipulation or technique, present or future. We are witnessing the erosion, perhaps the final erosion, of the idea of man as something splendid or divine, and its replacement with a view that sees man, no less than nature, as simply more raw material for manipulation and homogenization. Hence, our peculiar moral crisis. We are in turbulent seas without a landmark precisely because we adhere more and more to a view of nature and of man which both gives us enormous power and, at the same time, denies all possibility of standards to guide its use. Though well-equipped, we know not who we are nor where we are going. We are left to the accidents of our hasty, biased, and ephemeral judgments.

Let us not fail to note a painful irony: our conquest of nature has made us the slaves of blind chance. We triumph over nature's unpredictabilities only to subject ourselves to the still greater unpredictability of our capricious wills and our fickle opinions. That we have a method is no proof against our madness. Thus, engineering the engineer as well as the engine, we race our train we know not where (*12*).

While the disastrous consequences of ethical nihilism are insufficient to refute it, they invite and make urgent a reinvestigation of the ancient and enduring questions of what is a proper life for a human being, what is a good community, and how are they achieved (*13*). We must not be deterred from these questions simply because the best minds in human history have failed to settle them. Should we not rather be encouraged by the fact that they considered them to be the most important questions?

As I have hinted before, our ethical dilemma is caused by the victory of modern natural science with its non-teleological view of man. We ought therefore to reexamine with great care the modern notions of nature and of man, which undermine those earlier notions that provide a basis for ethics. If we consult our common experience, we are likely to discover some grounds for believing that the questions about man and human good are far from closed. Our common experience suggests many difficulties for the modern "scientific view of man." For example, this view fails to account for the concern for justice and freedom that appears to be characteristic of all human societies (*14*). It also fails to account for or to explain the fact that men have speech and not merely voice, that men can choose and act and not merely move or react. It fails to explain why men engage in moral discourse, or, for that matter, why they speak at all. Finally, the "scientific view of man" cannot account for scientific inquiry itself, for why men seek to know. Might there not be something the matter with a knowledge of man that does not explain or take account of his most distinctive activities, aspirations, and concerns (*15*)?

Having gone this far, let me offer one suggestion as to where the difficulty might lie: in the modern understanding of knowledge. Since Bacon, as I have mentioned earlier, technology has increasingly come to be the basic justification for scientific inquiry. The end is power, not knowledge for its own sake. But power is not only the end. It is also an important *validation* of knowledge. One definitely knows that one knows only if one can make. Synthesis is held to be

the ultimate proof of understanding (*16*). A more radical formulation holds that one knows only what one makes: knowing *equals* making.

Yet therein lies a difficulty. If truth be the power to change or to make the object studied, then of what do we have knowledge? If there are no fixed realities, but only material upon which we may work our wills, ill not "science" be merely the "knowledge" of the transient and the manipulatable? We might indeed have knowledge of the laws by which things change and the rules for their manipulation, but no knowledge of the things themselves. Can such a view of "science" yield any knowledge about the nature of man, or indeed, about the nature of anything? Our questions appear to lead back to the most basic of questions: What does it mean to know? What is it that is knowable (*17*)?

We have seen that the practical problems point toward and make urgent certain enduring, fundamental questions. Yet while pursuing these questions, we cannot afford to neglect the practical problems as such. Let us not forget Delgado and the "psychocivilized society." The philosophical inquiry could be rendered moot by our blind, confident efforts to dissect and redesign ourselves. While awaiting a reconstruction of theory, we must act as best we can.

WHAT IS TO BE DONE?

First, we sorely need to recover some humility in the face of our awesome powers. The arguments I have presented should make apparent the folly of arrogance, of the presumption that we are wise enough to remake ourselves. Because we lack wisdom, caution is our urgent need. Or to put it another way, in the absence of that "ultimate wisdom," we can be wise enough to know that we are not wise enough. When we lack sufficient wisdom to do, wisdom consists in not doing. Caution, restraint, delay, abstention are what this second-best (and, perhaps, only) wisdom dictates with respect to the technology for human engineering.

If we can recognize that biomedical advances carry significant social costs, we may be willing to adopt a less permissive, more critical stance toward new developments. We need to reexamine our prejudice not only that all biomedical innovation is progress, but also that it is inevitable. Precedent certainly favors the view that what can be done will be done, but is this necessarily so? Ought we not to be suspicious when technologists speak of coming developments as automatic, not subject to human control? Is there not something contradictory in the notion that we have the power to control all the untoward consequences of a technology, but lack the power to determine whether it should be developed in the first place?

What will be the likely consequences of the perpetuation of our permissive and fatalistic attitude toward human engineering? How will the large decisions be made? Technocratically and self-servingly, if our experience with previous technologies is any guide. Under conditions of laissez-faire, most technologists will pursue techniques, and most private industries will pursue profits. We are fortunate that, apart from the drug manufacturers, there are at present in the biomedical area few large industries that influence public policy. Once these appear, the voice of "the public interest" will have to shout very loudly to be heard above their whisperings in the halls of Congress. These reflections point to the need for institutional controls.

Scientists understandably balk at the notion of the regulation of science and technology. Censorship is ugly and often based upon ignorant fear; bureaucratic regulation is often stupid and inefficient. Yet there is something disingenuous about a scientist who professes concern about the social consequences of science, but who responds to every suggestion of regulation with one or both of the following: "No restrictions on scientific research," and "Technological progress should not be curtailed." Surely, to suggest that certain technologies ought to be regulated or forestalled is not to call for the halt of all technological progress (and says nothing at all about basic research). Each development should be considered on its own merits. Although the dangers of regulation cannot be dismissed, who, for example, would still object to efforts to obtain an effective, complete, global prohibition on the development, testing, and use of biological and nuclear weapons?

The proponents of laissez-faire ignore two fundamental points. They ignore the fact that not to regulate is as much a policy decision as the opposite, and that it merely postpones the time of regulation. Controls will eventually be called for—as they are now being demanded to end environmental pollution.

If attempts are not made early to detect and diminish the social costs of biomedical advances by intelligent institutional regulation, the society is likely to react later with more sweeping, immoderate, and throttling controls.

The proponents of laissez-faire also ignore the fact that much of technology is already regulated. The federal government is already deep in research and development (for example, space, electronics, and weapons) and is the principal sponsor of biomedical research. One may well question the wisdom of the direction, given, but one would be wrong in arguing that technology cannot survive social control. Clearly, the question is not control versus no control, but rather what kind of control, when, by whom, and for what purpose.

Means for achieving international regulation and control need to be devised. Biomedical technology can be no nation's monopoly. The need for international agreements and supervision can readily be understood if we consider the likely American response to the successful asexual reproduction of 10,000 Mao Tse-tungs.

To repeat, the basic short-term need is caution. Practically, this means that we should shift the burden of proof to the *proponents* of a new biomedical technology. Concepts of "risk" and "cost" need to be broadened to include some of the social and ethical consequences discussed earlier. The probable or possible harmful effects of the widespread use of a new technique should be anticipated and introduced as "costs" to be weighed in deciding about the *first* use. The regulatory institutions should be encouraged to exercise restraint and to formulate the grounds for saying "no." We must all get used to the idea that biomedical technology makes possible many things we should never do.

But caution is not enough. Nor are clever institutional arrangements. Institutions can be little better than the people who make them work. However worthy our intentions, w e are deficient in understanding. In the *long* run, our hope can only lie in education: in a public educated about the meanings and limits of science and enlightened in its use of technology; in scientists better educated to understand the relationships between science and technology on the one hand, and ethics and politics on the other; in human beings who are as wise in the latter as they are clever in the former.

REFERENCES

1. R. G. Edwards, B. D. Bavister, P. C. Steptoe, *Nature* 221, 632 (1969).
2. R. G. Edwards, P. C. Steptoe, J. M. Purdy, *ibid.* 227, 1307 (1970).
3. H. J. Muller, *Science* 134, 643 (1961).
4. J. M. R. Delgado, *Physical Control of the Mind; Toward a Psychocivilized Society* (Harper & Row, New York, 1969).
5. F. Bacon, *The Advancement of Learning, Book I*, H. G. Dick, Ed. (Random House, New York, 1955), p. 193.
6. C. S. Lewis, *The Abolition of Man* (Macmillan, New York, 1965), pp. 69–71.
7. D. D. Rutstein, *Daedalus* (Spring 1969), p. 523.
8. E. J. Caswell, *Commentary* (June 1969), p. 73.
9. B. Glass, *Science* 171, 23 (1971).

10. It is, of course, a long-debated question as to whether the fall of Adam and Eve ought to be considered "catastrophic," or more precisely, whether the Hebrew tradition considered it so. I do not mean here to be taking sides in this quarrel by my use of the term "catastrophic," and, in fact, tend to line up on the negative side of the questions, as put above. Curiously, as Aldous Huxley's *Brave New World* [(Harper & Row, New York, 1969)] suggests, the implicit goal of the biomedical technology could well be said to be the reversal of the Fall and a return of man to the hedonic and immortal existence of the Garden of Eden. Yet I can point to at least two problems. First, the new Garden of Eden will probably have no gardens; the received, splendid world of nature will be buried beneath asphalt, concrete, and other human fabrications, a transformation that is already far along. (Recall that in *Brave New World* elaborate consumption-oriented, mechanical amusement parks featuring, for example, centrifugal bumble-puppy had supplanted wilderness and even ordinary gardens.) Second, the new inhabitant of the new "Garden" will have to be a creature for whom we have no precedent, a creature as difficult to imagine as to bring into existence. He will have to be simultaneously an innocent like Adam and a technological wizard who keeps the "Garden" running. (I am indebted to Dean Robert Goldwin, St. John's College, for this last insight.)

11. Some scientists naively believe that an engineered increase in human intelligence will steer us in the right direction. Surely we have learned by now

that intelligence, whatever it is and however measured, is not synonymous with wisdom and that, if harnessed to the wrong ends, it can cleverly perpetrate great folly and evil. Given the activities in which many, if not most, of our best minds are now engaged, we should not simply rejoice in the prospect of enhancing IQ. On what would this increased intelligence operate? At best, the programming of further increases in IQ. It would design and operate techniques for prolonging life, for engineering reproduction, for delivering gratifications. With no gain in wisdom, our gain in intelligence can only enhance the rate of our dehumanization.

12. The philosopher Hans Jonas has made the identical point: "Thus the slow-working accidents of nature, which by the very patience of their small increments, large numbers, and gradual decisions, may well cease to be 'accident' in outcome, are to be replaced by the fast-working accidents of man's hasty and biased decisions, not exposed to the long test of the ages. His uncertain ideas are to set the goals of generations, with a certainty borrowed from the presumptive certainty of the means. The latter presumption is doubtful enough, but this doubtfulness becomes secondary to the prime question that arises when man indeed undertakes to "make himself": in what image of his own devising shall he do so, even granted that he can be sure of the means? In fact, of course, he can be sure of neither, not of the end, nor of the means, once he enters the realm where he plays with the roots of life. Of one thing only can he be sure: of his power to move the foundations and to cause incalculable and irreversible consequences. Never was so much power coupled with so little guidance for its use." [*J. Cent. Conf. Amer. Rabbis* (January 1968), p. 27.] These remarks demonstrate that, contrary to popular belief, we are not even on the right road toward a rational understanding of and rational control over human nature and human life. It is indeed the height of irrationality triumphantly to pursue nationalized technique, while at the same time insisting that questions of ends, values, and purposes lie beyond rational discourse.

13. It is encouraging to note that these questions are seriously being raised in other quarters—for example, by persons concerned with the decay of cities or the pollution of nature. There is a growing dissatisfaction with ethical nihilism. In fact, its tenets are unwittingly abandoned by even its staunchest adherents, in any discussion of "what to do." For example, in the biomedical area, everyone, including the most unreconstructed and technocratic reductionist, finds himself speaking about the use of powers for "human betterment." He has wandered unawares onto ethical ground. One cannot speak of "human betterment" without considering what is meant by the human and by the related notion of the good for man. There questions can be avoided only by asserting that practical matters reduce to tastes and power, and by confessing that the use of the phrase "human betterment" is a deception to cloak one's own will to power. In other words, these questions can be avoided only by ceasing to discuss.

14. Consider, for example, the widespread acceptance, in the legal systems of very different societies and cultures, of the principle and the practice of third-party adjudication of disputes. And consider why, although many societies have practiced slavery, no slaveholder has preferred his own enslavement to his own freedom. It would seem that some notions of justice and freedom as well as right and truthfulness, are constitutive for any society, and that a concern for these values may be a fundamental characteristic of "human nature."

15. Scientists may, of course, continue to believe in righteousness or justice or truth, but these beliefs are not grounded in their "scientific knowledge" of man. They rest instead upon the receding wisdom of an earlier age.

16. This belief, silently shared by many contemporary biologists, has recently been given the following clear expression: "One of the acid tests of understanding an object is the ability to put it together from its component parts. Ultimately, molecular biologists will attempt to subject their understanding of all structure and function to this sort of test by trying to synthesize a cell. It is of some interest to see how close we are to this goal." [P Handler, Ed. *Biology and the Future of Man* (Oxford Univ. Press, New York 1970). p. 55.]

17. When an earlier version of this article was presented publicly, it was criticized by one questioner as being "antiscientific." He suggested that my remarks "were the kind that gave science a bad name." He went on to argue that, far from being the enemy of morality, the pursuit of truth was itself a highly moral activity, perhaps the highest. The relation of science and morals is a long and difficult question with an illustrious history, and deserves a more extensive discussion that space permits. However, because some readers may share the

questioner's response, I offer a brief reply. First, on the matter of reputation, we should recall that the pursuit of truth may be in tension with keeping a good name (witness Oedipus, Socrates, Galileo, Spinoza, Solzhenitsyn). For most human history, the pursuit of truth (including "science") was not a reputable activity among the many, and was, in fact, highly suspect.

Even today, it is doubtful whether more than a few appreciate knowledge as an end in itself. Science has acquired a "good name" in recent times largely because of its technological fruit: it is therefore to be expected that a disenchantment with technology will reflect badly upon science. Second, my own attack has not been directed against science, but against the use of some technologies and, even more, against the unexamined belief—indeed, I would say, superstition—that all biomedical technology is an unmixed blessing. I share the questioner's belief that the pursuit of truth is a highly moral activity. In fact, I am inviting him and others to join in a pursuit of the truth about whether all these new technologies are really good for us. This is a question that merits and is susceptible of serious intellectual inquiry. Finally, we must ask whether what we call "science" has a monopoly on the pursuit of truth. What is "truth"? What is knowable, and what does it mean to know? Surely, these are also questions that can be examined. Unless we do so, we shall remain ignorant about what "science" is and about what it discovers. Yet "science"—that is, modern natural science—cannot begin to answer them; they are philosophical questions, the very ones I am trying to raise at this point in the text.

Dr. Kass.

[A biographical sketch and prepared statement of Dr. Leon Kass follow:]

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ETHICAL ISSUES AND BIOMEDICAL SCIENCE AND TECHNOLOGY

(Leon R. Kass)

(Testimony prepared for delivery on September 7, 1977, before the Subcommittee on Science, Research, and Technology, Committee on Science and Technology, U.S. House of Representatives, for one of a series of hearings on the science policy implications of the DNA recombinant molecule research issue.)

I have found it very difficult to prepare this testimony. My task would have been simple if I had a clear and extreme position to defend, if, for example, I believed that science and technology were the handmaidens of an exploitative and oppressive society and must therefore be curtailed, or if, on the other hand, I believed that science and technology were always self-justifying activities, yielding benefits only, and that any attempt rationality to question the social worth of a given line of research or application is to commit the sin of Pope Urban against Galileo. I hold neither of these views. I very much respect the activity of scientific investigation and welcome many of the gifts of technological innovation. But I esteem other good things at least as highly—excellence of character, stable and fulfilling family and community life, public-spiritedness and other civic virtues, the beauties of nature, the wisdom of great thinkers—, recognize the heavy costs we have already paid for technological progress, and am concerned that the costs of some projected biomedical advances may far exceed the benefits.

Even thus divided, my task might yet have been simple were I able to discern a clear line between good and bad research and technology. But there exists no such clear line between things we should never let the scientists do and the things we should never prevent them from doing. There is not even an easy way of deciding what things, if any, deserve to be curtailed. All biomedical research worthy of the name, in addition to providing greater knowledge, holds forth the promise of *some* medical or agricultural or other benefit, for at least somebody—for the sick, for the hungry, for the depressed, for the mentally and physically handicapped. As I will try to indicate, some of the technological capacities I regard as most socially questionable are at the same time powers that promise great good to some of our fellows.

Lacking knowledge of clear boundaries, lacking any simple rules or prescriptions or exhortations, my message could be boiled down to two words: Be sensible—hardly a novel or exciting proposal, unexceptionable in speech, but hard to follow in deed.

For not only is there a need for moderation and prudence on the side of scientists and technologists in the powers for intervention they make possible and the hazards to which they might expose us. There is equal need for good sense on the part of the community and its representatives, of those who would attempt to regulate the development and use and consequences of biomedical research and technology. Attempts at regulation can be undertaken at the wrong time or in the wrong way or for the wrong reasons. Statutory prohibitions may be misdirected or unenforceable.

Despite these difficulties, I have prepared the following testimony hoping to promote greater thoughtfulness on these complicated and important matters.

DNA RECOMBINANT RESEARCH

DNA recombinant research has raised three distinct kinds of concerns: (1) about public health hazards, (2) concerns about human genetic manipulation, and (3) concerns about induced alterations in the variety and evolution of living organisms.

1. *Health and safety.*—The scientists doing the research asked if it was proper to proceed with research that might be hazardous to public health without prior assessment of risks and development of suitable safeguards. Their concern was appropriate and sensible. The moratorium they called on their own research initiated a series of events that have produced, to my mind, a good first-round assessment and adequate guidelines to permit the research to proceed, guidelines which include, by the way, self-imposed prohibitions of certain kinds of recombinations as too dangerous. The following observations may be in order.

(*a*) The ethical issue raised by the scientists is, in one respect, not very difficult. The identification of benefits as benefits and harms as harms was easy. For all the difficulty in quantifying the likelihood and severity of possible harm, everyone agrees that epidemics are bad. No one is in favor of causing plague or increasing the risks of cancer; safety of life and limb is a good to which everyone subscribes.

(*b*) The hazards of this research seem to me to be much exaggerated, at least in relation to other hazards to health from research and technology that we readily tolerate or even encourage without much concern, e.g., research with tumor viruses, bacterial pathogens, mutagens, radioactive isotopes, and organic solvents. Though it is clear why the DNA researchers would be concerned about the hazards of this new technique in their own field, I find it odd that these hazards should be singled out in the public discussions. This is not to say that the precedent of deliberate or inadvertent toleration of higher risks justifies a casual attitude toward any newer, more intentionally created potential hazards. Existing folly does not excuse its extension. Rather, it would be sensible to treat these new potential dangers in conjunction with existing dangers.

(*c*) I am quite satisfied with the care and conscientiousness of those responsible for the guidelines and am not unhappy about the procedures that have been followed that have given the scientists the lead role in the making of policy. Nevertheless, it should be clear that the issue of safety is not merely a technical issue.

To be sure, the identification of possible results, quantifying the probable incidence and extent of possible harms and benefits—these are largely technical matters. But the naming of a result as a harm or a good, the weighing of risks versus promises, the balancing of harms against goods, the evaluation of the de-

gree of goodness of the benefit and badness of the harm—these are not technical matters. How safe is safe *enough* is not a technical matter, especially as this judgment always depends on how much one desires the object. Those who have criticized the procedure of allowing the scientists to decide, without public participation, how safe is safe enough have a point. But it is not clear to me that alternative procedures would be better, at least in cases such as this where the risks seem to be similar to those of research on microorganisms generally, and where scientists, despite their self-interest in pursuing their research, are no less—and perhaps rather more—concerned about public health hazards than the rest of us. I repeat, no scientist is interested in causing or promoting epidemics.

2. *Human genetic engineering.*—Although the scientists who called the moratorium expressed concern only about biohazards, and ruled the issue of human genetic manipulation out of bounds at the Asilomar conference, I have little doubt that public fears about possible, eventual intervention into human heredity has fueled the controversy regarding this research. This explains, in part, why no comparable animus has been directed against those cancer scientists who work with probably more dangerous tumor virues. I even suspect that the acknowledged concern for ethical issues in the use of genetic knowledge on the part of some of the DNA recombinant researchers may have pricked their conscience to give the *safety* question of their research such unusual and prominent publicity.

Here, however, I believe there is little need for concern, at least at present. It is true that the technique of DNA recombination may be useful as one step on the long-road to human genetic manipulation. It is entirely appropriate to consider this research as contributing, eventually, to the acquisition of that power, and to begin thinking about the ethical and social issues that such power would raise. But human genetic engineering still seems to me to be a long way off. Many scientific and technical problems would need to be solved before gene therapy of inherited disease could be possible, including the identification and purification of specific human DNA, the discovery of the proper means for delivery of such therapeutic DNA to the proper organ for action, and so on.

Moreover, I suspect that both the promise and the dangers of human genetic manipulation by selective transfer of pieces of DNA are greatly exaggerated. On the one hand, other remedies for some genetic disease may more readily be found, e.g., via organ or tissue transplantation. On the other hand, even if effective and practical, gene therapy of existing individuals with genetic disease would raise no issues not already raised by sophisticated medical treatments [1]; subject to the usual concerns about safety and efficacy, and to the usual internal and external controls operating on the medical profession through whose hands any feasible gene therapy will pass. We may wish to consider, in allocating scarce funds for research and development, how vigorously we want to pursue a capacity for gene therapy, and other high technology routes to better health. We may want eventually to establish policy and guidelines for the use of gene therapy, or for the possible, even-more-futuristic eugenic use of DNA transfer. But we have years, even decades, to think about these matters, and there is absolutely no reason to block the current research, with its obvious scientific interest and likely productive application, because of these concerns.

3. *Altering the course of evolution.*—This is the most difficult concern to evaluate. DNA recombinant research will presumably permit the construction of new types of organisms. Public health hazards aside, I think it fair to say that we probably do not know what we are doing. This research thus highlights in a dramatic way the awesome powers we already hold for the manipulation and alteration of nature, powers we use with little knowledge about what we are really doing. Whether we like it or not, we have by our new powers acquired new responsibilities, not only for ourselves, but for our planet and for all things on it. We should proceed with humility and caution, aware of our great ignorance in the face of this awesome charge. This is not to argue that nature knows best and that we ought to keep hands off. Yet it should be clear from at least some of our manipulations of nature that we may not know any better, to say the very least. The requisite humility and search for wisdom are not easy to cultivate, and in any case, cannot be produced by regulatory commissions and statutes. Our hopes here must lie in education.

[1] I submit as an appendix to this testimony a letter I wrote in October, 1970, to Professor Paul Berg, in which I try to organize questions concerning the human application of DNA transfer research.

Why has the DNA recombinant research question generated such controversy and continued to hold public attention, far beyond the merits of the case in my opinion? I offer two related suggestions: First, a growing public concern over the acquisition of specific new powers to modify the bodies and minds of human beings, and about the moral and social questions raised by these prospects. Second, more generally, a growing public concern about the relation of science and the political community, and a desire on the part of at least some of our fellow-citizens to renegotiate explicitly the tacit contract beween science and society. Indeed, it is as an instance of what I believe will be an increasing number of occasions demanding a consideration of the place of science in our society that the current debate over DNA recombinant research holds the greatest interest and importance. I will devote the remainder of my testimony to these two matters.

Nearly seven years ago, in an article in Science ("The New Biology: What Price Relieving Man's Estate?") that I now submit as part of my testimony, I attempted to identify some of the ethical issues raised by advances in biomedical science and technology. Were I writing that article today, I would make some changes, but by and large, I still see the problem in the same way. I am equally impressed by the scientific discoveries, but less convinced of the medical usefulness of some of the promised developments—indeed, I am much more doubtful about the wisdom of pursuing improvements in health by continued expansion of highly sophisticated medical technologies. I am equally concerned about questions of distributive justice, about abuses and misuses of our existing and promised powers, and especially about the possibilities for willing-self-degradation and dehumanization. I am much less sanguine about the prospects for wise public regulation and am fearful that, however well-intentioned, public control of science and technology can cause as much mischief as the equally well-intentioned enterprises it seeks to manage. I am, at the same time, less worried about some of the likely developments, e.g., asexual reproduction via cloning and various possible uses of artificial fertilization of human eggs, which now seem to me both less imminent and of less social importance, though still, I would add, as repugnant.

I persist in thinking that the greatest dangers come not from the evil-doers or the mischievous but rather from the well-wishers and humanitarians amongst us, often in the very form of gifts that we would all too readily accept. I will illustrate this shortly in addressing some questions posed by your Committee: "From an ethical perspective, is there some limit or boundary beyond which science should not proceed? Is there ethical justification for slowing down some types of research?" But first, I need to address certain terminological and conceptual matters that, unless clarified, will confound my discussion.

1. *What is an ethical question?* I use the term "ethical" very broadly. It is not restricted to matters touching particular religious or other moral commandments, prohibitions, or injunctions, to certain alleged rights or duties, or to certain virtues and vices of character. Rather I mean by an ethical question any question of action, of what-to-do, because any such question considers, however tacitly, what is *good* to do, and not merely what is *possible* to do or what are the likely results of doing or not-doing. What is possible and what is likely are, of course, germane, even crucial to deciding what to do, but that decision is guided by the pursuit of a desired goal, sought by particular means, and justified by certain reasons.

Ethical questions arise about the desirability of the ends or means and about the adequacy of the reasons. None of this is academic or prissy; neither is it the special province of ethicists or moral philosophers. It is the daily stuff of politics and private choice, of all human action. A familiar concrete example may illustrate the point: One can be for or against the goal of limiting population growth, one may or may not regard abortion as an unacceptable means, and one may quarrel with reasons given in justification of choices both of the end or the means.

2. *The relation between science and technology, between theory and practice.* This is a complicated matter, yet a crucial one for considering policy for the control of technology and science. On first glance, and speaking crudely, there would appear to be a clear and unmistakable difference between scientific inquiry, which seeks to discover the truth about nature, and technological application, which uses discovered truths to command nature in action, for the sake of some human purpose. Science is theoretical in its intent, technology

is practical. Yet the distinction is in fact not so sharp. First of all, there is a difference between inquiry and research. Formulating a question is not the same as doing the experiments that seek to answer it, even if, in some fields of science, it is only the experimentally testable questions that are deemed worthy of being asked.

The point is that, unlike mathematics and astronomy, unlike theoretical physics and taxonomic biology, nearly all of modern biomedical science is *experimental* science. Biomedical inquiry is more than asking questions and thinking about them; inquiry becomes research, and research involves experimentation, and experimentation *is action*. As such, it necessarily comes under ethical and legal scrutiny, as does all action, even when such scrutiny decides that such action should be immune from interference (e.g., public speech or the publication of newspapers). Regulations governing the use of radioactive isotopes in research, guidelines for experimentation in human subjects, liability of companies for the hazards of industrial research or of hospitals for those of clinical research, safeguards governing research with pathogenic bacteria and viruses—all these testify to the recognition of the distinction between inquiry and research and to the acceptability of some controls over experimentation—not, to be sure, over the questions to be asked, but over the procedures used to gain the answers. The guidelines proposed for the safety of DNA recombinant research have ample precedent.

What does not have ample precedent, at least not in liberal democratic regimes, is the acceptability of any control over questions to be investigated. The freedom to inquire is a hard-won yet ever-precarious freedom, a good in itself, and a means to the discovery of many important matters. Even those, such as myself, who favor the social regulation of many technologies, are extremely wary of any attempts to limit research, except as already indicated. But there might be reasons for reconsidering this matter if the distinction between theory and practice, between science and technology breaks down in yet other ways. And I fear that it does.

Much of biomedical research has more than a theoretical intent; indeed, it has a dual intent and justification, a practical one as well. It aims to provide the power to intervene in the biological processes that it attempts to understand. in fact, by that very understanding. This conjunction of theory and practice, the identity of knowledge and power—and I mean this literally and not pejoratively—is the hallmark of modern experimental science, first trumpeted by its founders in the early 17th century. Indeed, the test of the validity of our knowledge of phenomena is often held to be the power to modify and control them. That insulin was the long-sought agent responsible for preventing the disorders of diabetes could finally be proved only by injecting diabetics with the hormone and altering the diabetic picture. That DNA, and not protein, was the genetic material was proved by experiments which transformed one strain of bacteria into another by means of the transfer of DNA.

Now many scientists are not especially interested in the applications of their research. They are rather more devoted to unraveling nature's secrets for the satisfaction of knowing how things work. This purely intellectual aspiration remains for many scientists, including perhaps the best ones, their guiding passion, no matter how much they would welcome practical benefits to society flowing from their research and no matter how much they advertise such practical benefits when seeking government funds for research, which research is in fact supported by society precisely for these benefits.

This relative indifference to practical application leads many scientists to discount the intimate connection between knowing how and know-how, between knowledge of and power to. They may or may not be right in thinking that what other people do with their findings is not their responsibility, but they are mistaken, at least in *some* kinds of research, in ignoring that the power and the knowledge came together, that application flows directly and sometimes immediately from discovery, or rather, from its publication. Thus, for example, the published report of the hallucinogenic properties of LSD announced the power to alter consciousness, a power that was soon exploited and escaped from responsible professional control.

It is true that in many cases the line connecting basic research and practical application is indirect. In my own example, the hallucinogenic properties of LSD were quite unexpected. Basic research leads to unexpected findings, and so-called targeted research often turns up empty handed—a compelling argument for supporting seemingly impractical but fundamental research. Yet there certainly

are other areas in which certain technological powers can be predicted as flowing from prerequisite basic studies—even in the case at hand, how else could scientists predict the beneficial uses of DNA recombinant research unless there were some connection between basic research and application.

To sum up this rather long and general discussion, my point is simply this: because of the close tie between knowledge and power, we may in the future have to consider placing restraints on the kinds of knowledge to be sought, if the powers such knowledge would inevitably bring were too dangerous for us to handle.

Where the application of knowledge requires complicted or expensive apparatus or highly trained personnel, it may be possible in practice to continue the usually salutary practice of permitting research and attempting to regulate the development and use of technology. This practice may need to be modified where dangerous powers are immediately, indiscriminately, and cheaply available in the scientific discovery. Biologically active chemicals, i.e., drugs, present the best class of examples, especially as their manufacture is often easy, their visibility low, and the difficulty of regulating their use very high. Among the examples of worrisome research (to which I now turn), those likely to give chemical applications deserve more careful scrutiny than those, like the artificial heart or artificial placenta, that are costly, complicated, and impossible to use without someone noticing.

WORRISOME RESEARCH

I am much less concerned about biohazards such as those incident to DNA recombinant research than I am about certain powers, not yet available but foreseeable as outgrowths of current research, that would alter decisively fundamental features of human life: powers to provide new modes of conception and birth (including extracorporeal fertilization and gestation, predetermination of gender, and asexual reproduction), powers to alter the human life cycle (most especially by increasing the maximum human life span), and powers to alter behavior, desires, emotions, and states of consciousness. These are the prospects for something fundamentally new and different, and therefore deserving our serious attention. Let me briefly consider three cases that have already received some attention in the bioethics literature (see, e.g., *Assessing Biomedical Technologies: An Inquiry into the Nature of the Process*, prepared for the National Science Foundation by the Committee on the Life Sciences and Social Policy, National Research Council) : 1) predetermining sex of children, 2) retarding of aging, 3) a powerful pleasure pill. (In each case, let us assume that the power is made available by means of a drug.)

1. *Predetermining the sex of children.*—Parents would choose in advance the gender of their children, but the boys and girls generated would be as they are now. Few moral objections have been raised against exercising such a choice (though many may wonder why anyone would want to exercise such power), but there would be reasonable concern for possible untoward social consequences of possible imbalances in the overall sex-ratio, should the practice of gender choice become widespread.

With a drug or other cheap, home-administered, and reliable method for predetermining sex, it would be difficult to prevent the use of the technique, and we might therefore wonder whether we ought to permit such a pill to be developed at all. However, with proper preparation in our demographic studies, it would be very easy to monitor the choices people were in fact making, and comparatively easy to provide incentives for correcting any imbalance in the sex-ratio perceived to be dangerous. Provided we are alert, I doubt that this power is really so dangerous and the research leading to it so worrisome—precisely because the primary effects of use are immediately obvious and the worrisome consequences derivative and delayed.

2. *Retardation of aging.*—We would all welcome relief from the gradual processes of decay and decline and from the chronic ailments these produce in our advancing years. Many would also want to live longer than our current maximum of fourscore. Fundamental research into the biological processes of aging holds out the promise of powers not only to retard the rate of senescence and decay but also to extend the maximum life expectancy. When Congress established the

National Institute of Aging in 1974, the responsible House Committee's statement on the "Purpose of Legislation" stated that the new Institute would "provide a natural focus for the research necessary to achieve the great goal of keeping our people as young as possible as long as possible."

Is this really a desirable goal? Would it be a good idea to add 20 years to the human life span? Fifty years? More? These are long questions, and I am not sure that I could persuade you, in the absence of long conversation, that such attempts to roll back mortality are the height of folly. But the power to do so is clearly one goal of basic research on aging, and a possible consequence. And Congress has endorsed that goal and launched the public support of the enabling research without, I believe, adequately thinking through the consequences of success. Unlike the case of a pill for gender choice, the scale of use of an anti-aging pill might be hard to measure quickly, the range of consequences would be more massive, and incentives to cease and desist much harder to supply.

3. *The pleasure drug.*—What is the neurophysiology or the chemistry that mediates the subjective experience of pleasure? This is an interesting scientific question, now under investigation. The development of a drug that produced powerful and intense feelings of euphoria might be one fruit of current psychopharmacological studies of the brain. Such a drug would be useful in the treatment of severe depression and as a "positive reinforcer" par excellence in all kinds of behavior modification programs. But should we have such a drug? Precisely its desired euphoriant effects and its exquisite usefulness in behavior modification make it something much to be feared, especially as, like other drugs, it would likely prove difficult if not impossible to keep under strict control for only therapeutic uses.

I have here cited three examples of current research that could directly yield powers to make basic changes in human affairs, powers that would probably have wide popular appeal but whose consequences might very well, on balance, be highly undesirable. If this initial appraisal is even moderately correct—and the subject clearly needs much more thought and exploration—then a case might need to be made for the establishment of some limits for basic research into these areas.

I make this suggestion with much misgiving. There are so many uncertainties. Yet in these limited matters of such immense consequences as the length of human life and the divorce of the experience of pleasure from all activity producing pleasure, I do not think that we can adopt the attitude of letting the genie out of the bottle and only later finding out whether he has brought more harm than good. Human beings can no doubt get used to anything—this is, at the same time, our virtue and our vice. But as people so awesomely responsible for the shape of the future, we cannot justify our bringing forth the Brave New World (toward which I fear we are already far along) on the grounds that our descendants would not mind living in it.

How sensible guidance is to be given to research is a complicated matter. Restriction of any lines of investigation is repugnant to most scientists and flies in the face of tradition. It might also mean foregoing or forestalling the possibility of certain benefits. Yet here again we face on a massive moral and social scale the usual problem of what to do, with prospective benefits and harms of unknown proportions and weighted differently by different assessors. To go forward or not to go forward, to fuel these areas of research with public monies or not, these decisions are now being made and they ought not to be made lightly or thoughtlessly.

I should emphasize that I would open the question of limitations on research for a very few areas indeed. In many other cases of worrisome technologies, I believe that we can trust our capacities to regulate their use and to manage their undesirable consequences. I am aware that other people may have other areas of research that worry them even more. I am aware that what I am saying will be perceived as a threat to all of scientific inquiry, and it may well be. Yet the penalties for libel have hardly weakened our freedom of speech, and I am far from convinced that the freedom of scientific inquiry as a whole would suffer if certain highly sensitive areas are carefully controlled or even curtailed. The good to be done by organized science can only be completed by the harm it humbly and responsibly refuses to do.

APPENDIX

REGARDING ETHICAL ISSUES PERTINENT TO POSSIBLE FUTURE HUMAN APPLICATION OF DNA RECOMBINANT RESEARCH

NATIONAL RESEARCH COUNCIL,
October 30, 1970.

Prof. PAUL BERG,
Department of Biochemistry,
Stanford University School of Medicine,
Palo Alto, Calif.

DEAR PAUL: It was a great pleasure to meet and talk with you. Your sensitivity to the possible ethical and social implications of your own work gave me much encouragement for proceeding with mine.

Here is a sketchy outline and fragmentary discussion of some of the questions which occur to me and which I think merit serious consideration, sooner rather than later.

1. Ethical questions related to safety-and-efficacy. These are merely sophisticated versions of general problems related to clinical trials of a new therapy or experiments to discern whether a new agent is potentially therapeutic.

(*a*) Is the procedure efficacious? Or more modestly, have we ruled out obvious reasons why it might be useless?

Here appropriate trials in tissue culture and animals should precede first trial in human. Special attention needs to be given to the problem of delivery of the viral vector to the appropriate target organ or tissue.

(*b*) Is the procedure safe? How safe? Have cellular and animal studies been performed to detect possible deleterious effects of introducing the carrier viral DNA? Has a prospective study been designed to accompany the administration of the viral therapy to the first human patients?

(*c*) Difficult judgments concerning:

1. Comparative value of other available therapy—e.g., organ or tissue transplantation.

2. Weighing likely chance of success, natural history of the untreated condition, likely and suspected harmful "toxic" effects.

2. Medical-ethical questions dependent upon the stage of "life" treated.

(*a*) In the case of a child or adult known to have a particular genetic defect, or even in the case of an embryo or fetus on whom a definite diagnosis is made, the difficult judgments (1c, above) are ethically no different than for any other form of therapy. To be sure, unforeseen tragic consequences may ensue, but the physician would have acted rightly because he was seeking to treat a known serious disease in an existent human being or existent fetus.

(*b*) Far greater certainty with respect to safety and efficacy would be required to perform the same manipulations on the germ cells prior to fertilization. Here, by no stretch of argument can it be said that one is engaged in therapy of existing persons with known disease. To manipulate germ cells is a form of experimentation, albeit well-meaning, on a not-yet-existent and not-yet-afflicted human being. *Ignorance* of untoward consequences that might result is here no excuse; considerable *knowledge* that *no* such consequences will follow gene manipulation would be a prerequisite for going ahead. Childlessness or adoption are to be preferred to subjection of the unconceived to potentially hazardous manipulation.

(3) Therapeutic and other purposes. The ethical questions about genetic manipulation will be dependent in part upon the purpose served. Obviously, once a technique is introduced for one purpose, it can then be used for any purpose. Therapeutic use is one thing; eugenic, scientific, frivolous, or even military are quite another. Thus there are two questions to be considered:

(*a*) What would be the range of ethically legitimate purposes?

(*b*) How could one limit use to those purposes?

I have my own views on the first for which I would argue ("therapeutic use only"), but more importantly, I would insist that we need to foster public deliberation about this question, since I don't think this is a matter to be left to private tastes or to scientists alone. I defer the question of control until later.

4. Possible undesirable consequences of ethical use for ethical purposes.

In the previous paragraph, I considered the problem of so-called "good" *vs* "bad" ends. We have also to consider "bad" consequences of a technique used only for "good" purposes. This is a far more difficult problem, and unfortunately, I think, a more pervasive one in the whole biomedical area. The inevitable social costs of desired progress are probably higher than the costs of progress willfully perverted by bad men. We must consider and weigh the following kinds of questions in deciding about the *first* use of a new technique:

(*a*) What are the biological consequences in future generations of widespread use of gene therapy on afflicted individuals? Anything but treatment of gonads, gametes, and zygotes will work to increase the frequency of the given gene in the population.

1. Are we wise enough to be tampering with the balance of the gene pool? That we do so inadvertently already is no argument for our wisdom to do so deliberately.

2. What are our obligations to future generations? Do we want to commit them to the necessity of more and more genetic screening and genetic therapy to detect and correct the increasing numbers of defects which our efforts will have bequeathed to them?

(*b*) Do we ourselves wish to embark upon a massive program of screening and intervention? With federal support? Under compulsion of law?

(*c*) Are we not moving toward more and more laboratory control over procreation? What are the *human* costs of this development, especially for marriage and the family?

5. How can these developments be monitored and kept under control?

The more I think about this question, and the more I contemplate the possible widespread consequences of genetic manipulation, the more I believe that all decisions to employ new technologies and even to develop them for employment in human beings should be public decisions. How to do this is not obvious, although the question is now being actively explored by various groups. Regardless of who should decide and who should control, the problem of whether control is possible remains. Here, much depends upon the demand for the new technology, its expense, the scale in which it will be used, and the know-how needed to use it. The smaller the demand and scale or the greater the cost or know-how, the better the possibility for control.

6. What are the obligations of the basic scientist whose research brings closer a new biomedical technology? What would be the ingredients of an ethical warrant for him to go ahead? Let me suggest the following.

(*a*) Consideration of the kinds of questions outlined above (they are meant to be suggestive and exemplary, not definitive) by himself, with his co-workers, and with appropriate colleagues, scientific and non-scientific.

(*b*) To be responsible for helping to set forth in advance standards and procedures for testing safety and efficacy.

(*c*) Calling the attention of responsible publics to the technological possibilities his research (and that of the field generally) makes more imminent. This would best be done, it seems to me, merely by writing articles in a responsible journal (e.g. *Science*, outlining the technological possibilities and some possible social and ethical problems they present, and then inviting sober and responsible public deliberation concerning implementation and control of the technology.

(*d*) To be willing and prepared to abide by a public judgment which may undermine his own research (especially true in applied research or in those areas of basic research where there may be little or no gap between knowledge and use—as in psychopharmacology).

You will, I think, be interested to read Paul Ramsey's book, *Fabricated Man: The Ethics of Genetic Control* (Yale University Press, "Fastback" series, 1970, $1.95). It is the only book I know of devoted solely to the ethical problems of genetic engineering. Also, I am enclosing a copy of a paper of mine on cloning.

Lastly, I would be interested, both scientifically and otherwise, in the progress of your work. Please keep me posted. I would be delighted to continue our dialogue by mail or when next we meet.

With very best regards,

Sincerely,

LEON R. KASS,
Executive Secretary.

STATEMENT OF DR. LEON R. KASS, HENRY R. LUCE PROFESSOR, UNIVERSITY OF CHICAGO

Dr. KASS. Thank you very much, Mr. Chairman.

I, too, will be only reading portions of the testimony, and, if I may, in passing take the liberty of trying to sharpen up places where my outlook might differ from some analysis of the testimony.

Mr. THORNTON. I think that would be very helpful at this time.

Dr. KASS. I will do it very briefly though.

I have found it very difficult to prepare this testimony. My task would have been simple if I had a clear and extreme position to defend, if, for example, I believed that science and technology were the handmaidens of an exploitative and oppressive society and must therefore be curtailed, or if, on the other hand, I believed that science and technology were always self-justifying activities, yielding benefits only, and that any attempt rationally to question the social worth of a given line of research is to commit the sin of Pope Urban against Galileo. I hold neither of these views. I very much respect the activity of scientific investigation and welcome many of the gifts of technology. But I esteem other good things at least as highly, and am well aware of the heavy costs we have already paid for technological progress, and am concerned that the costs of some projected biomedical advances may far exceed the benefits.

Even thus divided, my task might yet have been simple were I able to discern a clear line between good and bad research and technology. But there exists no such clear line between things we should never let the scientists do and the things we should never prevent them from doing. There is not even an easy way of deciding what things, if any, deserve to be curtailed. All biomedical research worthy of the name, in addition to providing greater knowledge, holds forth the promise of some medical or agricultural or other benefit, for at least somebody—for the sick, for the hungry, for the depressed, for the mentally and physically handicapped. As I will try to indicate, some of the technological capacities I regard as most socially questionable are at the same time powers that promise great good to some of our fellows.

Lacking knowledge of clear boundaries, lacking any simple rules or prescriptions or exhortations, my message could be boiled down to two words: Be sensible, hardly a novel or exciting proposal, unexceptionable in speech, but hard to follow in deed.

For not only is there a need for moderation and prudence on the side of scientists and technologists in the powers for intervention they make possible and the hazards to which they might expose us; there is equal need for good sense on the part of the community and its representatives, of those who would attempt to regulate the development and use and consequences of biomedical research and technology. Attempts at regulation can be undertaken at the wrong time, or in the wrong way, or for the wrong reasons. Statutory prohibitions may be misdirected or unenforceable. Our scientific excellence is a precious national resource that needs to be safeguarded.

Despite these difficulties, I have prepared the following testimony, hoping to promote greater thoughtfulness on these complicated and important matters.

Part 1, on DNA recombinant research: DNA recombinant research has raised three distinct kinds of concerns: (1) concerns about public health hazards, (2) concerns about human genetic manipulation, and (3) concerns about induced alterations in the variety and evolution of human organisms.

HEALTH AND SAFETY

The scientists doing the research asked if it was proper to proceed with research that might be hazardous to public health without prior assessment of risks and development of suitable safeguards. Their concern was appropriate and sensible and has, to my mind, issued a good first-round assessment and adequate guidelines to permit the research to proceed, guidelines which include, by the way, self-imposed prohibitions of certain kinds of recombinations as being too dangerous. Still, the following observations may be in order:

(*a*) The ethical issue raised by the scientists is, in one respect, not very difficult. The identification of benefits as benefits and harms as harms was easy. For all the difficulty in quantifying the likelihood and severity of possible harm, everyone agrees that epidemics are bad. No one is in favor of causing plague or increasing the risks of cancer; safety of life and limb is a good to which everyone subscribes.

(*b*) The hazards of this research seem to me much exaggerated, at least in relation to other hazards to health from research and technology that we readily tolerate or even encourage without much concern, for example, research with tumor viruses, bacterial pathogens, mutagens, radioactive isotopes, and organic solvents. Though it is clear why the DNA researchers would be concerned about the hazards of this new technique in their own field, I find it odd that hazards of this research should be singled out in public discussions. This is not to say that the precedent of deliberate or inadvertant toleration of higher risks justifies a casual attitude toward any newer, more intentionally created potential hazards. Existing folly does not excuse its extension. Rather, it would be sensible to treat these new potential hazards in conjunction with existing dangers, perhaps not making it the subject of specific legislation.

(*c*) I am quite satisfied with the care and conscientiousness of those responsible for the guidelines, and am not unhappy about the procedures that have been followed to date that have given the scientists the lead role in the making of policy. Nevertheless, it should be clear that the issue of safety is not merely a technical issue. The naming of a result as a harm or a good, the weighing of risks versus promises, the balancing of harms against goods, the evaluation of the degree of goodness of the benefit and badness of the harm, these are not technical matters. How safe is safe enough is not a technical matter, especially as this judgment always depends upon how much one desires the object whose pursuit is hazardous. Those who have criticized the procedure of allowing the scientists to decide, without public participation, how safe is safe enough have a point. But it is not clear to me that alternative procedures would be better, at least in cases such as this where the risks seem to be similar to those of research on microorganisms generally, and where scientists, despite their self-interest in pursuing their research, are no less, and perhaps rather more, concerned about public health hazards than the rest of us.

2. MATTERS RELATED TO HUMAN GENETIC ENGINEERING

Although the scientists who called the moratorium expressed concern only about biohazards, and ruled the issue of human genetic manipulation out of bounds at the Asilomar conference, I have little doubt that public fears about possible, eventual intervention into human heredity has fueled the controversy regarding this research. I even suspect that the acknowledged concern for ethical issues in the use of genetic knowledge on the part of some of the DNA recombinant researchers may have pricked their own conscience to give the safety question of their research such unusual and prominent publicity.

Here, however, I belive there is little need for concern, at least at present. It is true that the technique of DNA recombination may be useful as one step on the long road to human genetic manipulation. But human genetic enginering still seems to me to be a long way off. Many scientific and technical problems would need to be solved before gene therapy of inherited disease could become a possibility. Moreover, I suspect that both the promise and the dangers of human genetic manipulation by selective transfer of pieces of DNA are greatly exaggerated. On the one hand, other remedies for some genetic disease may be more readily found, for example, via organ transplantation. On the other hand, even if effective and practical, gene therapy of existing individuals with genetic disease would raise no issues not already raised by sophisticated medical treatments, and subject to the usual internal and external controls operating on the medical profession through whose hands any feasible gene therapy must pass. We may wish to consider, in allocating scarce funds for research and development, how vigorously we want to pursue a capacity for gene therapy and other high technology routes to better health. We may want eventually to establish policy and guidelines for the use of gene therapy, or for the possible, even more futuristic eugenic use of DNA transfer. But we have years, even decades, to think about these matters, and there is absolutely no reason to block the current research, with its obvious scientific interest and likely productive application, because of these concerns.

3. ALTERING THE COURSE OF EVOLUTION

This is the most difficult concern to evaluate for reasons Dr. Grobstein has already alluded to. DNA recombinant research will presumably permit the construction of new types of organisms. Public health hazards aside, I think it fair to say we probably do not know the implications of what we are doing. This research thus highlights in a dramatic way the awesome powers we already hold for the manipulation and alteration of Nature, powers we use with little knowledge about what, in fact, we are really doing.

And here I would like to suggest, perhaps for discussion with Dr. Grobstein or others, that our circumstances may in this regard be radically new, that precisely not because of this power or that, but because of the powers in the aggregate and the need not only for knowledge but for a certain kind of unprecedented wisdom, that our circumstances may not be simply continuous with certain circumstances in the past.

Whether we like it or not, we have, by our new powers, acquired new responsibilities, not only for ourselves, but for our planet and for all things on it. We should proceed with humility and caution, aware of our great ignorance in the face of this awesome charge. The requisite humility and search for wisdom are not easy to cultivate and, in any case, cannot be produced by regulatory commissions and statutes. Our hopes here must lie in education.

The second part of the testimony deals with ethical issues in biomedical research more generally.

Why has the DNA recombinant research question generated such controversy and continued to hold public attention, far beyond the merits of the case, in my opinion? I offer two related suggestions: First, a growing public concern over the acquisition of specific new powers to modify the bodies and minds of human beings, and about the moral and social questions raised by these prospects. Second, more generally, a growing public concern about the relation of science and the political community, and a desire on the part of at least some of our fellow citizens to renegotiate explicitly the tacit contract between science and society. Indeed, it is an instance of what I believe will be an increasing number of occasions demanding a consideration of the place of science in our society that the current debate over DNA recombinant research holds the greatest interest and importance. The remainder of my testimony is devoted to these matters.

Nearly 7 years ago, in the article in Science to which you referred I attempted to identify some of the ethical issues raised by advances in biomedical science and technology. Were I writing that article today, I would make some changes, but by and large, I still see the problem in the same way. I am equally impressed by the scientific discoveries, but I am much more doubtful about the wisdom of pursuing improvements in health by continued expansion of highly sophisticated medical technologies.

I am equally concerned about questions of distributive justice, about abuses and misuses of our existing and promised powers, and especially about the possibilities for willing self-degradation and dehumanization, and here it's not so much the things that are unknown that frighten me, but the things that are perhaps altogether too well-known, too likely, and again, not the powers of the misuse and abuse of some technology but, indeed, about the likely social consequences of the very thing we want, and I'll try to give some instances here again. I am much less sanguine than I once was about the prospects of wise public regulation and am fearful that, however well-intentioned, public control of science and technology can cause as much mischief as the equally well-intentioned enterprise it seeks to manage. I persist in thinking that the greatest dangers come not from the evil-doers or the mischievous but rather from the well-wishers and humanitarians amongst us, often in the very form of gifts that we would all too readily accept. I will illustrate this, as I say, shortly. I want to consider particularly the question posed by your committee: "From an ethical perspective, is there some limit or boundary beyond which science should not proceed?" First, I need to address briefly certain terminological and conceptual matters that, unless clarified, will confound my discussion.

1. WHAT IS AN ETHICAL QUESTION?

I here use, and suggest the value of using, the term "ethical" very broadly, not restricted to matters touching particular religious or other moral commandments, prohibitions, or injunctions, not to certain alleged rights or duties, or to certain virtues and vices of character. Rather, I mean by an ethical question any question of action, of what-to-do, because any such question considers, however tacitly, what is good to do, and not merely what is possible to do or what are the likely results of doing or not doing?

What is possible and what is likely are, of course, germane, even crucial to deciding what to do, but that decision is guided by the pursuit of a desired goal, sought by particular means, and justified by certain reasons. Ethical considerations arise about the desirability of the ends or means and about the adequacy of the reasons. None of this is academic or prissy; neither is it the special province of ethicists, or moral philosophers. It is the daily stuff of politics, of private choice, of all human action.

2. THE RELATION BETWEEN SCIENCE AND TECHNOLOGY, BETWEEN THEORY AND PRACTICE

This is a most complicated matter, yet a crucial one for considering policy for the control of science and technology. On first glance, and speaking crudely, there would appear to be a clear and unmistakable difference between scientific inquiry, which seeks to discover the truth about nature, and technological application, which uses discovered truths to command nature in action, for the sake of some human purpose. Science is theoretical in its intent; technology is practical. Yet this distinction is in fact not so sharp. First of all, there is a difference between inquiry and research. Asking a question is not the same thing as doing the experiments that seek to answer it, even if, in some fields of science, it is only the experimentally testable questions that are deemed worthy of being asked.

The point is that, unlike mathematics and astronomy, nearly all modern biomedical science is experimental science. Biomedical inquiry is more than asking questions and thinking about them; inquiry becomes research, and research involves experimentation, and experimentation is action. As such, it necessarily comes under ethical and legal scrutiny, as does all action, even when such scrutiny decides that such action should be immune from interference. Regulations governing the use of radioactive isotopes in research, guidelines for experimentation in human subjects, liability of companies for the hazards of industrial research, and so on, all these testify to the recognition of the distinction between inquiry and research and to the acceptability of some controls over experimentation, not, to be sure, over the questions to be asked, but over the procedures used to gain the answers. The guidelines proposed for the safety of DNA recombinant research have ample precedent.

What does not have ample precedent, at least not in liberal democratic regimes, is the acceptability of any control over questions to be investigated. Even those, such as myself, who favor the social regulation of many technologies, are extremely wary of any attempts

to limit research, except as already indicated. But there might be reasons for reconsidering this matter if the distinction between theory and practice, between science and taught technology, breaks down in yet other ways. And I fear that it does.

Much of biomedical research has more than a theoretical intent; it has a practical one as well. It aims to provide the power to intervene in the very biological processes that it attempts to understand, in fact, by that very understanding. This conjunction of theory and practice, the identity of knowledge and power—and I mean this literally and not pejoratively—is the hallmark of modern experimental science. Indeed, the test of the the validity of our knowledge of phenomena is often held to be the power to modify and control them.

Now many scientists are not especially interested in the applications of their research. They are rather more devoted to unravelling nature's secrets for the satisfaction of knowing how things work. This intellectual aspiration remains for many scientists their guiding passion, no matter how much they would welcome practical benefits to society and no matter how much they advertise such practical benefits when seeking government funds for research, which research is in fact supported by society precisely because it wants these benefits. This relative indifference to practical application leads many scientists to discount the intimate connection between knowing how and know-how, between knowledge and power to. They may or may not be right in thinking that what other people do with their findings is not their responsibility, but they are mistaken, at least in some kinds of research, in ignoring that the power and the knowledge come together, that application flows directly and sometimes immediately from discovery, or rather, from its publication. To cite one example, the published report of the hallucinogenic properties of LSD announced simultaneously the power to alter consciousness, a power that, as you know, was soon exploited and escaped from responsible professional control.

It is true that in many cases the line connecting basic research and practical application is indirect. Basic research leads to unexpected findings, and so-called targeted research often turns up emptyhanded. Yet there are other areas in which certain technological powers can reliably be predicted as flowing from prerequisite basic studies—even in the case at hand. How else could scientists predict the beneficial uses of DNA recombinant research unless there were some connection between basic research and application.

My point is simply this: Because of the close tie between knowledge and power, we may in the future have to consider placing restraints on the kinds of knowledge to be sought, if the powers such knowledge would inevitably bring will be too dangerous for us to handle.

Where the application of knowledge requires complicated or expensive apparatus or highly trained personnel, it may be possible in practice to continue the usually salutary procedures of permitting research and attempting to regulate development and use of technology. This practice may need, however, to be modified where dangerous powers are immediately, indiscriminately, and cheaply available directly in the scientific discovery. Biologically active chemicals, that is, drugs, present the best class of examples, especially as their manu-

facture is often easy, their visibility low, and the difficulty of regulating their use very high. Among the examples of worrisome research—to which I now turn, in conclusion—those likely to give chemical applications deserve more careful scrutiny than those, like the artificial heart or artificial placenta, that are costly, complicated, and impossible to use without somebody noticing.

Worrisome Research, the final part:

I am much less concerned about biohazards such as those incident to DNA recombinant research than I am about certain powers, not yet available but foreseeable as outgrowths of current research, that would alter decisively fundamental features of human life: Powers to provide new modes of conception and birth, powers to alter the human life cycle, most especially by increasing the maximum human lifespan, and powers to alter behavior, desires, emotions, and states of consciousness. These are the prospects for something fundamentally new and different, and therefore deserving our serious attention. Let me briefly consider three cases that have already received some attention in the bioethics literature:

Predetermining the sex of children; retarding of aging; and the powerful technology of pleasure. In each case, let us assume the power is made available by means of a drug.

1. PREDETERMINING THE SEX OF CHILDREN

Parents would choose in advance the gender of their children, but the boys and girls generated would be as they are now. Few moral objections have been raised against exercising such a choice, but there would be reasonable concern for possible untoward social consequences of possible imbalance in the overall sex ratio, should the practice of gender choice become widespread. With a drug or other cheap, home-administered, and reliable method for predetermining sex, it would be difficult to prevent the use of the technique, and one might therefore wonder whether we ought to permit such a pill to be developed at all.

However, with proper preparation in our demographic studies it would be very easy to monitor the choices people were in fact making, and comparatively easy to provide incentives for correcting any imbalance in the sex ratio perceived to be dangerous. Provided we are alert, I doubt that this power is really so dangerous and the research leading to it so worrisome—precisely because the primary effects of use are immediately obvious and the worrisome consequences derivative and delayed.

2. RETARDATION OF AGING

Fundamental research into the biological processes of aging holds out the promise of powers not only to regard the rate of senescence and decay but also to extend the maximum human life expectancy. When Congress established the National Institute of Aging in 1974, the responsible House Committee's statement on the "Purpose of Legislation" stated that the new Institute would "provide a natural focus for the research necessary to achieve the great goal of keeping our people as young as possible as long as possible." Is this really a desirable goal? Would it be a good idea to add 20 years to the human life span? Fifty years? More? These are long questions, and I'm not sure

that I could persuade you, in the absence of long conversation, or even then, that such attempts to roll back mortality are the height of folly. But the power to do so is clearly one goal of basic research on aging, and a possible consequence. And Congress has endorsed that goal and launched the public support of the enabling research without, I believe, adequately thinking through the consequences of success.

3. THE TECHNOLOGY OF PLEASURE

What is the neurophysiology or the chemistry that mediates the subjective experience of pleasure? This is an interesting scientific question, now under investigaiton. The development of a drug that produced powerful and intense feelings of euphoria might be one fruit of current psychopharmacological studies of the brain. Such a drug would be useful in the treatment of severe depression and as a "positive reinforcer" par excellence in all kinds of behavior modification programs. Should we have such a drug? Precisely its desired euphoriant effects and its exquisite usefulness in behavior modification make it something much to be feared—and these are not unknown fears—especially as, like other drugs, it would likely prove difficult if not impossible to keep under strict control for only therapeutic uses.

I have here cited three examples of current research that could directly yield powers to make basic changes in human affairs, powers that would probably have wide popular appeal, but whose consequences in the aggregate might very well, on balance, be highly undesirable. If this initial appraisal is even moderately correct—and the subject clearly needs much more thought and exploration—then a case might need to be made for the establishment of some limits for basic research into these areas.

I make this suggestion with much misgiving. There are so many uncertainties. Yet in these limited matters—and I stress these limited matters—of such immense consequence I do not think that we can adopt the attitude of letting the genie out of the bottle and only later finding out whether he has brought more harm than good. Human beings can no doubt get used to anything. This is, at the same time, our virture and our vice. But as people so awesomely responsible for the shape of the future, we cannot justify our bringing forth the brave New World on the grounds that our descendants would not mind living in it.

How sensible guidance is to be given to research is a complicated matter. Restriction of any lines of investigation is repugnant to most scientists and flies in the face of tradition. It might mean foregoing or forestalling the possibility of certain benefits. To go forward or not to go forward, to fuel these areas of research with public monies or not, these decisions are now being made and they ought not be made lightly or thoughtlessly.

I should emphasize again that I would open the question of limitations on research for a very few areas indeed. In many other cases of worrisome technologies, I believe that we can trust our capacities to regulate their use and to manage their undesirable consequences. I am aware that what I am saying will be perceived as a threat to all scientific inquiry, and it may well be, and here, it seems to me, and it's

differing from Ms. King, I think we can do better than saying that in all cases the burden of proof lies on the opponents. I think there's probably room for discriminating amongst those technologies that are worrisome for particular reasons, and perhaps in those cases place the burden of proof on intent. The penalties for libel, however, hardly weaken our freedom of speech. I am far from convinced that the freedom of scientific inquiry as a whole would suffer if certain highly sensitive areas are carefully controlled or even curtailed. The good to be done by organized science can only be completed by the harm it humbly and responsibly refuses to do.

Thank you. I apologize for the length of my statement.

Mr. THORNTON. Thank you very much, Dr. Kass.

I want to compliment each of the panelists for your initial presentations.

The subject is most complex and difficult to get a grasp on, but I wonder if I might have any comment as to whether our situation might be considered parallel to discovering, as passengers on a ship that's traveling through time and space, or an ocean, or whatever, toward a goal or objectives which we hope to be good, we as humans become aware that there's a rudder on that ship, and we began to make judgments whether we should manipulate that rudder and change the direction in which we're traveling and, having done so, only then begin to wonder what course we should pursue. Is that what we are concerned about? Is the problem one that we find it hard to define? What are those objectives that we want to seek? You listed them in your prepared testimony and omitted some of them in your verbal testimony: Excellence of character, stable and fulfilling family and community life, public-spiritedness and other civic virtues, the beauties of nature, the wisdom, et cetera. In a sense are we not already with our hand on the rudder? Are we able to make that judgment now, and answer that question now, whether we should take steps to affect the course of man's role on the Earth?

Is my question too hazy, Dr. Kass, to answer, or do you want to take a stab at it?

Dr. KASS. I think I understand the question.

It does seem to me that our hand has been on the rudder for some time, and I think the goals toward which we were proceeding might rightly have been assumed to be good, and many of them, it seems to me, remain good. No one is opposed to improving health and peace of mind, obviously the kind of medical and mental problems that biomedical research can help us with.

It does seem to me though that the acquisition of greater powers does require a greater wisdom in steering that rudder. It has made, therefore, much more explicit on how much, or what kinds of assumptions we've made in the past, and maybe it's even called some of those assumptions into question.

I think the basic problem is, it's not just a problem of the abuse of power. If it's really the case that to have some good things means sacrificing willy-nilly others, and that seems to be our lot, not only here but wherever, then we may only have improved health by so rearranging our institutions on better health and better safety, by so rearranging our institutions as to interfere with certain family values, intruding upon sex and reproduction.

The question is, though, the cost that we pay in civic life, in community life, and devotion to a few of these things that I did mention, as some kind of direct consequence of our concern for greater materialness and prosperity. Asking this kind of question, I think we have become more aware of where we are headed now that science and technology are not perceived as simply something that's good, as they had been before.

Mr. THORNTON. Ms. King, you say that the test should be whether the potential benefits from the knowledge to be gained outweigh the risks of harm that might come about if we proceed, and I think properly defined that certainly is a very good equation and a very brief synopsis of the kind of decisionmaking that we have to do.

But don't you then immediately get drawn into a question as to weighing the values? If the potential benefits are quite large in general, prosperity, say, for the population as a whole, and the harm is destruction or material disruption of the lives of a few people, how do we weigh and balance that kind of a decision?

Ms. KING. I should like to stress that one of the points that apparently didn't come through very well in my testimony is that in making value judgments, that first we could look at a formal system of ethics, and we could do what our commission has been attempting to do, which is to identify formal ethical principles.

It seems to me the more important question is how does one apply those formal ethical principles to specific circumstances and instances, and it seems until we get to the second stage, and here we're talking about values and people offering justifications, individuals offering different justifications for doing or not doing something we are faced with the proverbial problem, and that is, how do we resolve the conflicts, and I'm trying to suggest that the only way, it seems to me, to resolve the conflicts is to work out processes by which those who are affected—I hate this term, "informed consent of the public"—those who will be affected in society, not all of whom can participate, but will be able to participate in some representative fashion.

My second point is, that representative fashion is not necessarily the legislature, I might add, that I was talking about processes, or perhaps working on processes that we have not experimented with before because we have been somewhat satisfied with the legslative process.

I think that these issues require, with all due respect, a lot more time and attention than legislators can really adequately give to them, and by using just legislators, we are using a fairly small and select number of people in the process. Unlike Professor Grobstein's attempt to talk about the evolutionary process in stages, or in tiers, I am focusing on one process at a time.

Mr. THORNTON. As a matter of fact, I wanted to reemphasize in this discussion: I personally have been gradually coming toward the view that something parallel to the Commission on Experimentation on Humans and Protection of Human Subjects might be the kind of institution that would be appropriate in this area of DNA research. I'm very happy that you are a witness here because I have wondered if this structure might be appropriate for the area in which the Congress is now involved.

I'm also interested in your suggestion that you don't necessarily use the same model, or the same institution, for resolution of all different kinds of ethical and science problems.

Ms. KING. One comment on the Commission. I think as a structure that a commission might be an appropriate structure. I haven't thought a great deal about it being an appropriate structure for the recombinant DNA question. It seems to me, though, that a structure like it has certain advantages, which I did not bother to identify because I keep hearing people talk about them all the time. One, it has advantages in terms of its composition. It has, I think, restored confidence, at least in the public eye, in the public and scientific community, which I thought was very important. We had the first moratorium on scientific research to deal with—fetal research. I thought that by deliberating in public—and the commission worked very hard to increase public participation, or to at least show one of our modes of educating the public—that that was in the strength of the commission.

Mr. THORNTON. Let me ask very quickly: I do recall the moratorium on funding of fetal research. Was that not directly a Federal moratorium on funding?

Ms. KING. Which stopped our fetal research even though it was limited to Federal funding. The research stopped as far as we were concerned. It was able to restrict research, all research, on living human fetus, at least until the moratorium was lifted.

Mr. THORNTON. Even that which informed medical opinion might consider to be beneficial to the fetus, is that correct?

Ms. KING. As far as we were able to learn in that period, it stopped it all. There was fear of treading into an area where lines were not necessarily clear between what was good and what was bad research, and for fear of treading into what was prohibited, in effect, no more research was done, at least until the moratorium was lifted.

Mr. THORNTON. Did this have to do with the question of consent? You mentioned that once earlier, that you wouldn't permit research without consent, although it's most difficult where you have a minor child with a kidney transplant. I believe that was contained in your paper. I don't recall it in your verbal presentation.

Ms. KING. It wasn't contained in the context of consent. My interest in the human experimentation end of the research area is not focused so much on the technicalities of obtaining consent because I have long since been convinced that normal, competent adults don't necessarily understand, or are motivated necessarily in their activities by their knowledge. They may even be more motivated by faith in their physician. So I'm not that impressed with discussion about informed consent.

Mr. THORNTON. I have some concern about whether you should operate upon a child 6, or 8, or 10 years old without that child being in a position to have his interest expressed in the operation.

Ms. KING. I would agree with you.

Mr. THORNTON. You would?

Ms. KING. But I would not call that informed consent. I would call that, would denominate that as a process by which we seek to give recognition to as much autonomy or capacity as an individual has, and I would include within that group children and the mentally retarded and the mentally incompetent, merely because they are chil-

dren and incompetent does not mean they shouldn't be consulted. That is not the way the commission has talked about informed consent, which has taken on a very definite and narrow meaning, most of it coming from the law, I might add.

Mr. THORNTON. Consider please the inoculation program, or something like that, where you may have resistances which are not, to society's views, reasonable. What do you do about situations like that?

Ms. KING. It would appear to me that we as a society have never, at least up until this point, hesitated when it was necessary to impose restrictions or limitations on us all, if we had a clear enough view of what was the common good, and it seems to me that there also are analogies—I wouldn't take them too far—to public health, some public health concerns about recombinant DNA research. However, I think those analogies could be cut both ways. You could argue that the danger to the public health might justify a societal prohibition. Also, it seems to me, you could argue that one of the potential public goods would justify permitting the research to go forward or help permit the research to go forward, even at the cost of something happening to some individual. Certainly we know that some people will react, for example, to inoculation, and may react unfavorably, but we don't stop giving inoculations.

I'm not answering your questions. I'm probably raising more.

Mr. THORNTON. No. And I think that's excellent.

I think it would be very important to emphasize though for everyone in attendance that the nature of the Commission on Human Experimentation on which you serve is a commission to study our problems and to advise and make recommendations, but that commission has no power to regulate or to impose standards, or to issue rules and regulations which are binding upon the general public.

When I said that I had been coming to the view that such an advisory group might be useful, I wanted to make it clear that I was speaking of this kind of commission on which you serve.

Ms. KING. I agree with that.

Mr. THORNTON. Dr. Grobstein, do you have any comment with regard to the conversation, or shall I fire a question at you concerning your presentation? Would you like to comment?

Dr. GROBSTEIN. There are something of the order of six items that came up in the exchange that just took place that I would dearly love to comment on. Each one of them will take 5 to 10 minutes, but I won't try to do that.

Mr. THORNTON. Pick two or three.

Dr. GROBSTEIN. Let me first comment on the remarks that you made, Mr. Chairman, and also Ms. King's discussion of the activities of the commission on which she serves.

I personally am very strongly of the view that the area that we're talking about, whether we limit it to recombinant DNA or talk more generally of molecular genetics or genetics as a whole enough has been going on and enough is hanging in the air so that establishment of a commission to clarify some of the issues would be one of the most important things that the Congress could do at this present time.

I was especially interested in Ms. King's comments on some of the disadvantages or possible improvements that she sees in the way

the "Human Use" Commission is structured because certainly it is my experience, in talking with people, that over the last several years a very apprehensive view of the Commission has changed into a generally approving one. To a very considerable degree that can be laid at the door of the members of the Commission. I think, however, that it can also be attributed to the good sense of the decision to establish the Commission and to establish it in exactly the way that you, Mr. Thornton, have emphasized. It should function as a study commission, free of any requirements to make immediate decisions or to respond to immediate emergencies. It is important at this time to have a study commission which is free of regulatory responsibility to look into the matter of recombinant DNA and all that surrounds that subject.

Now if I may make just a second comment? It goes back to your initial question to us, which I assume that you intended to be considered by all of the panelists.

Mr. THORNTON. That is correct.

Dr. GROBSTEIN. I think that you posed a useful analogy for the issue that we are discussing. You put us in a ship with a rudder. You didn't tell us where either the ship or the rudder came from. In human experience, however, we are not presented with a ship and a rudder and then start to steer it. The ship and the rudder themselves came out of human experience. Something else follows. In producing devices like ships and rudders there is some formed human purpose in mind, or objective, or goal, or what-have-you.

You put us in what presumably was a rather primitive ship with a primitive rudder and you left us with the choice of whether to use it or not, as though we didn't even know for sure what it was for.

My suggestion is that over time our rudder has been getting better and better. We are able to steer ourselves much more effectively. I use the term "better and better" here not necessarily to mean that we have gotten greater satisfaction or greater good out of it, but that we are able to steer much better than we were before.

Mr. THORNTON. The degree of accuracy of control.

Dr. GROBSTEIN. The degree of accuracy of control is improved in many areas but, obviously, not totally. But at the same time another interesting thing has happened. You put us in the ship with the rudder; you didn't tell us how big the body of water was that we were in. One of the things that has happened, of course, particularly in the last half century, is that the body of water that we're in has expanded enormously and, therefore, our options have increased enormously.

Mr. THORNTON. Or our perceptions of our options.

Dr. GROBSTEIN. And perceptions of our options. That at the moment is giving us trouble. We are not sure, given this widening world that we're presented with, that we intended to ge there initially. Nonetheless, we are launched and in some fashion we have to both steer and figure out where we want to go. The latter problem is really the pressing one, rather than how to steer.

Mr. THORNTON. I am always reluctant to use a metaphor because it does always require a further definition.

I do want to say that I appreciate the additional definition you've given this metaphor. It does bring out some of the other areas of concern.

I want to recognize our distinguished senior minority member of the subcommittee, Mr. Hollenbeck, now for such questions as he may have.

I do want to also acknowledge that I have been advised—and this shows an instance where the rudder control is not exactly precise—that one of our witnesses may have to catch an airplane at 4:30, and that being so, I would understand it if that witness were to stand up, wave goodbye, and leave at an appropriate time in order to make the flight. That is you, is it not, Dr. Lappé?

Mr. HOLLENBECK. If he's taking the Metro, he shouldn't wait, or he'll be late. The Metro is waiting right now. I understand it's a 45-minute ride. [Laughter.]

I have a couple of questions. I'll start with one, with the time remaining. It's a two-part question.

The argument has been advanced that this is not the time for comprehensive control legislation concerning DNA research, and I want to know, first of all, which of you agree with that and which disagree. The second part is: Assuming that it is too early, that an experimental period is in order, what role do you perceive this Congress, the national legislative body, playing with regard to DNA research during that period?

Ms. King, do you want to lead off on that? I think you advanced that theory.

Ms. KING. I also stated, I don't guess publicly, that I don't honestly consider myself knowledgeable, about recombinant DNA, especially the bills on certain recombinant technology.

I would say this: that from what I have seen, it might now be the time to extend such controls as exist to industry as well as to Government funded regulation.

It seems to me however, that there's a danger in doing that unless we at the same time provided some flexible mechanism. The guidelines in research are just that; they are guidelines, and my fear of legislation is it's always easy to pass it the first time and always gets to be a terrible chore to go back and amend it or change it.

That's my only comment about the current legislation, about which I don't know a great deal.

I stated in my testimony what I think the role of Congress should be at this point, and that is, that I hope that it legislates into creation those groups that will give it advice.

I might also state, something that I also didn't mention, our commission has been a very expensive proposition, and you don't do this—and it seems to me another important role of Congress is to really appreciate that—

It seems to me that we also have to recognize that what we are proposing to do costs money, lots of it in many instances, and, too, it seems to me that your role, at least for the time being, should not be regulator, and I wouldn't set up a regulatory agency. I would set up—I think it's now time to generate a great deal of discussion.

Dr. LAPPÉ. Before I leave—and I have great faith in the fact that the plane will be late as well as the Metro. [Laughter.]

I have been a very strong proponent in this area of research of the need for special considerations, regulations, and controls because I do think the recombinant DNA issue is unique, and I'll say one thing about that, and then specify the areas that I think deserve regulation.

I think that, unlike virtually any other agent, chemical, or device that has been created by technology, recombinant DNA is dealing with the only molecule we know of which has come into existence for virtually the sole purpose of projecting itself into the future, and if there's a truism to be devolved from our knowledge of evolution it's that, unlike human intent, the purposes of nature cannot at this point really be divined. As far as we know, there is no other reason for the existence of DNA except to perpetuate itself.

An accident with a DNA molecule is potentially—and I emphasize potentially—an irrevocable one, of an order that we haven't anticipated before. It may be the fact that DNA molecules at some point, like radioactive isotopes, have some kind of half-life, that they diminish their impact over time. But as far as we know to date—and I think Professor Grobstein could probably comment more knowledgeably than me—my understanding of this particular molecule is that its nature is very much like that of a sorcerer's apprentice. It produces one broom, which makes two, which makes four, which makes eight, and so on, and although the purposes which we believe we perceive in the natural process, be they ships, or rudders, or what-have-you, appear to offer us guidance of how to proceed, I'm not at all convinced that we can proceed with wisdom in the area of constructing molecules that have the opportunity for self-replication.

Now to basics: What kind of limits, if any, should be placed on research, and when?

Professor Grobstein has emphasized that it's only at the advent of a clear and present danger that restrictions of any broad sort should be imposed.

I think we would all agree with Leon, that sensible persons would agree that any knowledge which can be developed which has clearly very injurious consequences immediately perceivable, should be under very strict regulation. There is less agreement that when it's only a probabilistic, if not conjectural, estimate it should be controlled. There would probably be universal agreement that when knowledge aims at development of agencies for killing or injuring human beings it should be constrained.

But there is the third area of research, in which the knowledge to be developed has a very high probability of being used in a manner which potentially causes social or societal dislocations, which, there is some kind of agreement, constitutes harm, that I think should be considered, and I think it would be a dereliction of my duty to raise my hand and wave goodbye without specifying at least two or three examples of that.

First of all, I think scientists would agree that there are such things as, besides worrisome research, mischievous research. Hypotheses which are presented and put into the public arena, which cannot be disproven, acquire a currency of their own. Ideas themselves can be dangerous, first.

Second, there are particular ideas in science, and particularly those that involve genetics because genetic carries such a sense of permanence and immutability, although this is not in fact the case, where a socially invidious idea that there is, for example, criminal behavior concentrated in a particular ethnic group, or associated with a chomo-

somal abnormality, is sufficiently hazardous in itself that some constraints on the promulgation of that idea might be considered.

Finally, I think that society does have to consider—and this is where I definitely tread in the same steps as Pope Urban and Cardinal Bellarmine—when you have to consider whether or not an idea or a new innovation is holistically threatening to those fundamental goods that society itself has held up as good.

Let me give you a for instance that involved genetic engineering, which is the closest metaphor, or closest analogy, I can have to recombinant DNA, to ground this in reality:

Nobody thought that anything but the most-bountiful consequences would come from genetic engineering plants, particularly the creation of new hybrids, that would have higher yields for protein or productivity per hectare in the area of rice and wheat. Nevertheless, because the genes programed an incredible dependency on those plants, on high energy use, on fertilizers, and on irrigation, that is, they were energy-intensive crops, rather than labor-intensive crops, there were extraordinarily societal dislocations that were produced in the Philippines, Mexico, and elsewhere by the introduction, that disrupted political progress toward land reform, and that generated dislocations that could have been anticipated, mind you, but were done because the genetics, if you will, of the crops themselves dictated, and in a very imperialistic kind of way, the conditions of life for people without their participation in choosing those conditions.

So I would say that wisdom, more wisdom than we certainly have now, is needed before massively introducing these new genetic technologies, and then, therefore, a commission that would be set up to study and make recommendations of this plethora and whole range of implications of new research would, indeed, be justified.

Mr. HOLLENBECK. Thank you.

Dr. Grobstein?

Dr. GROBSTEIN. I would comment on several of the things that Dr. Lappé said. I expect him to walk out on me while I'm doing it. [Laughter.]

First of all, I would point out, with respect to DNA and its replication, that DNA does not replicate by itself. DNA is not self-replicative in that sense. DNA only replicates in the presence of a number of other materials. It only replicates as part of a living or synthetically controlled environment. Therefore, to assume that if a wicked DNA combination were to appear that it would necessarily automatically proliferate and take over the Earth is a distortion of the way in which DNA operates.

We doubt, as a matter of fact, at the moment, although we don't know, that the earliest self-replicating organisms did so by means of DNA. DNA was very likely a later stage in the process of biological replication. So DNA isn't that independent. As a matter of fact, one of the things that we are learning about DNA with respect to its possible transfer of infective qualities to micro-organisms is that in most instances the characteristics of the organism are a very complex product of the particular DNA and are not easily achieved by inserting a short segment of a particular DNA.

I say this not to suggest that Dr. Lappé's statement that there is a quality in this which is somewhat different, say, from an ordinary

toxic substance, is not true. There is a different quality. But on the other hand, we can exaggerate that quality by thinking of DNA as an independent material that is capable of proliferating indefinitely. DNA is very sensitive to its surroundings, its environment, and it is very much controlled, when functioning within an organism, by other activities and other processes within that organism.

I am concerned also about some of the other things that Dr. Lappé said.

When he, for example, refers to the danger of ideas and suggests that perhaps we should be considering the control of promulgation of ideas, we are clearly well beyond the area of science. We are talking of political concepts, for which people have shed blood over many centuries. I think I would want to see a very powerful commission, indeed, at work on that question before accepting Dr. Lappé's suggestion, before we took the step of deciding to control the promulgation of ideas.

This, however, comes close, although I don't suggest it's identical with something that Dr. Kass said and said he would like to discuss, and I certainly would be very interested in hearing his comment.

Dr. Kass said that knowledge is power, and, of course, ideas are part of knowledge, and so perhaps he might be agreeing with Dr. Lappé that ideas in and of themselves can be dangerous, because he does seem to me to be saying that in some instances—and he certainly was careful to point out that he did not mean in all instances—that in some instances he felt that scientific knowledge is equivalent to power and, therefore, must be treated as action, which is the way he characterized his basic definition of, or basic requirement for ethics.

Is it your judgment that knowledge is of itself power, or is it that certain kinds of knowledge is so obviously convertible to power that you doubt that it would fail to be converted?

I personally maintain a distinction between the knowledge itself and what one does with it, and certainly it is the case that knowledge today is an extremely powerful part of our whole social operation. But whether I would say that knowledge is power, and in the same sense that Dr. Lappé says, "Ideas can be dangerous, and, therefore, should be contained in their promulgation," that would give me trouble. So I would be interested in your comments.

Dr. KASS. I think ideas of all sorts are influential, and in that sense have power. There are probably few ideas as powerful as those in the Declaration of Independence, for the effect that they had on subsequent events in the world.

But I have no thought at all about attempting to regulate ideas or speech, and I would agree with you entirely, although I don't think we should simply treat knowledge, as thought of, as good. It's a very powerful thing, indeed, a most powerful thing, indeed.

I think that precisely because scientific knowledge is a knowledge of how things work that it provides very often the knowledge of how to make things work differently, and in that sense there is a very close connection between the knowledge, what I call the knowledge of how and know-how, and maybe one can stand in the narrows and say, "This theory is theoretical," and "This is practical." But so often the tests of that knowledge are intervennig in nature, even in the laboratory, that I think we have to, at least in some cases, examine the validity

of the distinction, and in those cases where for practical reasons it would be hard to hold the gap, that one might want to worry about the particular line of research.

Again, I have some misgivings about raising this, and I don't follow Dr. Lappé anywhere down that road the he has taken, much as I would want to affirm the great power of ideas.

Mr. HOLLENBECK. I have nothing further right now, Mr. Chairman.

Mr. THORNTON. Thank you very much, Mr. Hollenbeck.

Mr. HOLLENBECK. Mr. Chairman, I have some constituents I'm scheduled to meet in my office. If you don't mind, I'd like to be excused.

I do have a question that I would like permission to submit in writing. It involves Dr. Lappé.

Mr. THORNTON. Unfortunately, we did not obtain his consent.

Mr. HOLLENBECK. I believe his office has given consent.

Mr. THORNTON. Very fine.

I'd like to ask each of our other witnesses if they would be willing to respond to such questions in writing as might be indicated after we've had a chance to review the testimony.

[Chorus of "Yes" from the panelists.]

Mr. THORNTON. Excellent.

I think I probably would have a couple of questions I would like to submit.

Thank you very much, Mr. Hollenbeck.

Mr. HOLLENBECK. Thank you, Mr. Chairman.

Mr. THORNTON. I think each of the witnesses today has emphasized the need for education. Trying to help people to become more informed is certainly a desirable goal.

How do you propose to go about this education? Are you talking about educating the public generally in formalized educational methods, or are you talking about educating just those people who are decisionmakers, or whom? Can you be more specific? How would you go about educating people so that they can make a better choice? I believe you said "coupling between the knowledge-system and social purpose," Professor Grobstein; and Dr. Kass said "vocalizing education"; and I note that the thrust of your testimony, Ms. King, accentuated education.

Do you have any clarification as to how we could proceed?

Dr. GROBSTEIN. Well, in the comment that I made, I was not referring to general education of the public. I was talking about discourse between policymakers, decisionmakers, expertise, and such other elements as may be necessary. For the policymaker I wouldn't want to use the term, "educated." I would rather use the term, "well informed," since all policymakers are presumed to be very well educated before they become policymakers.

We should be assured that the policymakers have access to all available information with respect to any particular question that they have before them and need to make a decision about.

With respect to the matter of education in general, as an educator for many years I am, of course, entirely in favor of education of the public, whether it be through formal education, or through other means of public education. Certainly, it is important at this time for more people to be familiar with the kinds of issues that we have been dis-

cussing with respect to recombinant DNA or biomedical research in general, or research even more broadly than that.

I am inclined to doubt that in the society in which we live today or in the one toward which we're progressing, whatever it may be, that it will be possible on each issue that comes up to expect the general public to be fully enough informed, particularly when there are scientific and technical contents involved, so as to participate actively in the decisions. This is one of the reasons why I feel that devices such as study commissions or other new devices are needed. It's going to be increasingly difficult for the general population to have enough information to deal with a particular issue.

On the other hand, it seems to me that the way in which we're moving makes it more and more important to see to it that as large a portion of the population as we can possibly arrange is at least scientifically and technically literate.

Very early in our educational history in the United States we came to understand that there were certain basic kinds of things that a citizen required in order to function within the society. In the old days it was reading, writing, and arithmetic. Those things are still important, although there's some suggestion, from recent results with SAT scores, and so on, that we are losing ground.

But the kind of literacy necessary to function within society today includes a degree of scientific and technical literacy. The more the population has that kind of literacy the more it will be able to participate in discussions of this kind of technical decision and the less likely it will be to be anxious afterward about the decisions that are made for fear that something is happening that they don't understand.

Mr. THORNTON. Thank you, Professor Grobstein.

Dr. Kass?

Dr. KASS. It seems to me that in the area of education several things might be possible. Some of them, I think, are already going on as a result of the large reexaminations of the place of science and technology in our human affairs. I think the generation now entering science, as excited as it may be about the prospects of discovery, are also much more aware than I was in beginning my work in science, of the mixed blessings that some of the fruits of science to a degree might be. I think it's only since the atomic bomb and various other such things that widespread questioning of the goodness of technological progress really came into being, and that means there a proliferation of courses of studies and conversations, including lists and materials that are prepared, through this committee, by the Congress, find their way into the hands of people who teach, that are discussed quietly among the young scientists, and I think have become increasingly responsive.

I think since—and I agree with Dr. Grobstein—that the technical nature of many of the issues means that scientists and technologists necessarily will have to play an important role, at least in indicating the limits of the possible and the likely consequences. I don't think they're uniquely qualified to make the judgment of what's desirable to do, but that means that the more they can synthesize the implications of their work and be thoughtful about those things the better off we'll be.

With respect to the education of policymakers, I haven't had a chance yet to join with my colleagues in endorsing the use of some kind of research gathering and discussion-promoting apparatus through the Congress.

I'm not sure that the national commission would be the thing I would first think of, although I'm very impressed with its work. It's far exceeded my expectations for it. But I think, more because of the things that I'm more worried about, that something like the Office of Technology Assessment, and, again, not when there are perceived clear present dangers—that happens to be one of the problems of legislation—but something that would couple more closely with the funding of basic research for which Congress already has the responsibility.

One might, for example, have an office which requested from the National Institute of Health or the sponsors of biomedical research periodic statements of those scientific developments likely to lead to certain scientific powers that the society ought to be thinking of. We need more advanced warning. We need some time to be thinking about the implications. Otherwise, Congress is going to be caught with public outcry, having to pass legislation to appease certain kinds of interests. That's not the way to address policy. So that anything that would give us some lead time would be very helpful.

Mr. THORNTON. I think it's a very excellent suggestion.

Ms. King, without preempting your right to add such comments as you might want to make with regard to education, I do want to aim at you the question of whether you think it might be appropriate, considering that lawyers are licensed to practice law and subject to disbarment procedures if they do not adhere to certain standards of professional conduct; and doctors are required to take the Hippocratic oath and are also subject to peer discipline; and engineers have professional associations; whether some useful purpose might be served by establishing a professional association of research scientists—I suppose this would have to originate from within the research scientists themselves—to recognize them as a group which not only engages in the search for scientific truths, but also for adherence to certain standards. What do you think about such an idea? Of course, I'm ending it, as a lawyer.

As a lawyer some of our code of ethics has been recently struck down by the courts. We had a provision that made it seem wrong to solicit or advertise for business, and now we're told we can do that.

But go ahead.

Ms. KING. I think lurking in this is a very difficult question, and if you will take the answer in the same spirit, I'm giving my first impressions, and hope not binding myself permanently to what I'm about to say?

Mr. THORNTON. Yes.

Ms. KING. I'm not so sure I like that as an idea. My short exposure to scientists, to researchers, has been—and maybe I've been too enamored, I don't know, but I like their peer review system a lot better than I like our own. It seems to me without the formal mechanism of a code of ethics and disciplinary procedures that all too often have not worked dramatically in recent years, that what is loosely referred to as peer review in the scientific community may have been far more effec-

tive, which is a sharp, tough criticism from one's colleagues, because your ideas or what you were doing were more often exposed, at least within that community, than what we lawyers do within the larger community of lawyers.

I would like to think about that. But in initially tackling the question I have not discovered, at least within the legal community, except with those lawyers who are also public officials, that within the legal community there is the immense feedback, or any feedback for that matter, that talks about how effective or how good a lawyer is in a situation.

As you probably know, the Federal judges are concerned about this now, and are working on a system to accomplish or to design some mechanism, because in everybody's opinion it's a good idea, to tell us whether a lawyer is performing not only ethically but adequately, because we have not had that kind of feedback from our peers.

So I would like to explore the idea a little bit more. It seems to me that the law office might look a little bit more to a client's response in attempting to weed out its incompetent or unethical participants.

Mr. THORNTON. Thank you very much.

Dr. Grobstein, do you have any suggestions with regard to this question, as to whether a formalized peer review system might be appropriate?

Dr. GROBSTEIN. I think, as Dr. King has said, there is a very effective peer review system in the scientific community. I don't wish to suggest that it is perfect by any means, and I certainly do not wish to appear to be casting any stones at neighboring professionals. But the fact is that the entire scientifico-social system of science puts very heavy emphasis on approval of an individual by his peers. As a matter of fact, it's the only way a scientist has to gain recognition, by approval of peers. It's a powerful mechanism.

On the other hand, as we know, there are breeches of it and, as a matter of fact, within the scientific community itself the very question that you raise has been discussed on a number of occasions—whether there should be something comparable to the Hippocratic oath of the medical profession, and, indeed, whether there should be something comparable to licensure. The fact that it doesn't exist makes clear that it hasn't struck much enthusiasm within the scientific community. The equivalent is found on this more informal basis.

The medical profession certainly now is moving in the direction of peer review, and finding it difficult to do because the nature of medical practice is rather different from the nature of scientific practice, and, I suspect, very different from the legal practice as well.

So to use per review clearly requires the right characteristics, not in the ethical sense, but in the matching sense, in the profession itself. I'm not sure that it's generally applicable to all professional activities.

I would say that at this time some kind of external system of certification does not seem very helpful in dealing with the kinds of problems we are discussing. These problems stem not so much from the behavior of individual scientists as from the collective directions that scientists take within a given field. What we have been discussing today are the directions taken by science as a community rather than by individual scientists.

Mr. THORNTON. Perhaps it is because of the nature of the profession, that of all the groups, the lawyers have adopted the most legalistic approach, namely, there's a codified code of ethics, adherence to which presumably makes you ethical, and nonadherence to which makes you unethical.

I wonder if we could agree upon a broad outline of code of ethics with regard to scientific research? What kind of challenge might that bring?

Ms. KING. Could I add one thing? I thought you were talking about recombinant DNA, and I didn't want to talk about the legal profession.

But may I perhaps, being a lawyer, offer some perspective?

Two things about codes of ethics and licensure, and that is that they have often, most often, served not to increase ethics or increase competence in a profession, but to keep people out of a profession, and to make it impossible, even within those canons of ethics, for certain types of legal activities not to go on, not because they were so bad or because society didn't approve of them, but they served to, in my opinion, make it more profitable for other types of lawyers in carrying out their legal business. I have in mind, for example, there are several ways of looking at ambulance chasing, which has always been prohibited, and one way is to say that's bad conduct for a lawyer because you catch people when they're most vulnerable. On the other hand, if you don't have a good legal system that gets to the most vulnerable people easily it becomes a public debate.

So I find it very difficult, even among the canons of ethics I've seen, to make sure that the canons accomplish what they're designed to do and don't inadvertently accomplish something else.

One last point about the scientific community, which I complimented, and I'd like to say that that same peer review system which I complimented, I also feel has worked, in some instances, to keep people out because of the way the system operates with its informal mechanisms, although there are certainly some good points about the system.

Mr. THORNTON. Dr. Kass, do you have any comment?

Dr. KASS. Yes.

I don't see much role for a system of licensure or a code of ethics for scientists.

I agree with Dr. Grobstein about what the nature of the problem is. If scientists have any deficiencies as a class it would be more sort of exaggerating perhaps the importance of science to the public good. If that's right, with any kind of defects of moral virtue, bad behavior, and so on, it's up to the political process to, hopefully, make an informed judgment about the relation between science and society, between science and the public.

I think the reason the peer review system works so well in science is because it addresses matters about which there is a fairly clear and accurate judgment as to what is good science, and I would much prefer to discuss that than the things that we've been talking about.

I would be curious to know as to what it is in your suggestion you would think of licensing scientists for.

Mr. THORNTON. Please don't regard my question as being a suggestion as to something that I would advocate.

I do admit that, having now established for all of us in Congress a code of ethics of our own, this does give us some advantage in suggest-

ing promulgation of codes for others. But I think, by the same token, it may also highlight that perhaps the greatest incentive toward ethical behavior is the presence of a disclosure and reporting apparatus, which brings to the attention of the people on whose judgment our jobs depend, any aberrations in our behavior.

What I was really suggesting, was more than whether a formalized apparatus might be appropriate, because I rather anticipated the kind of response that came forward would be the response that would be received. Assume that I'm a scientist in a laboratory, and that I'm concerned with the development of a new scientific research project in which I am totally wrapped up. The project looks like good research to me; not only is it good, it might be published, and it might be published first by me. I wonder if I am well-equipped to make the judgment as to whether this is the kind of good research objective that as you outlined in your case, should be sought.

Dr. KASS. It does seem to me that we have several opportunities currently available that could be enlarged upon without something so formal as codes or licensures. There's been discussion amongst editors of professional journals about considering ethical implications of research as part of the criteria for accepting publication. That's something one could think about. One could ask, as one now does on the grant applications to NIH, where it now asks for the social significance of this research. One might invite investigators to ask, not knowing the medical benefits, but ask: Are there any possibly socially problematic or troublesome things that might grow out of your research, either immediately or down the road?

Now these things get treated rather perfunctorily by many scientists, I think. They know that most research is approved by their peers on scientific merit and not on practical benefits.

But it might be salutary to ask scientists in this informal way to begin thinking about it and to be obligated perhaps to report to others, and to make public most of the implications, or possible implications, of their research.

It seems to me that if a scientist is doing something potentially dangerous and publishes it you can pretty much count on their being some members of the club who will raise those questions with him, as, I think, in this case, the recombinant DNA issue, will be dealt with, and I'm sure it would. So that publication really brings these things to public notice, and if the scientists don't do it the press and other people will and we'll get a chance to be thinking about these matters.

But let me reemphasize, I think one of the most useful things, if one wants to institutionalize something, is to think about ways in which the scientific community can begin to think ahead of the likely, the possibly problematical consequences of their work, and perhaps be more obliged to bring those to public notice. It seems to me to be in the best interest of science to be cooperative in that way. Otherwise, if we're stubborn we're going to have the kind of furor that you see around this issue.

Mr. THORNTON. Do you have any comments, Professor Grobstein?

Dr. GROBSTEIN. Yes, sir.

We do have problems with our limitations in projecting consequences. Dr. Lappé made the point that in connection with the green

revolution many unanticipated and less fortunate consequences occurred than had been anticipated.

I would worry some—although I think that the point that you're making is certainly worth consideration—about individuals leaning over backward making judgments, afraid that if they moved on something that their peers would feel that that was not evidence of sufficient social responsibility, that they might do something when, in fact, it might be perfectly OK down the road.

So we're in the area of how well we can predict. You mentioned, for example, that the Office of Technology Assessment might be a more appropriate approach to some of these problems than the commission. There are some people who are concerned about whether or not we may not be overestimating our own ability to assess.

Dr. KASS. Fair enough.

Mr. THORNTON. I wondered as you were both talking if what you were describing might not be a suggestion that scientists should engage, though, in some kind of minitechnology assessment or research assessment as they go into a field, making some effort to foresee, as well as they could, the consequences of their work. The problem is again here a lack of information on which to base that kind of assessment, because the individual who's called upon to do that may be the most able person in the world in his research field and not have the knowledge to foresee the consequences of that research in a broad societal sense.

Dr. KASS. I think that's right, and I don't think they get perfect assessments, and there are these dangers Dr. Grobstein mentioned.

On the other hand, that we begin thinking, that we try to improve our ability to see what's ahead, I think, is certainly very desirable. In some areas it does seem to be more easy to see what might be coming. In other areas it's pretty happenstance.

Mr. THORNTON. I'm going to invite any of you who feel that a comment at this stage would summarize or clear up any particular point that you feel needs to be cleared up to do so. I'll accept voluntary final statements if any are offered.

Otherwise, I want to thank you for you excellent presentations, for your exchange of views, and I declare that the hearings are now adjourned.

Thank you.

[Whereupon, at 4:30 p.m., the subcommittee adjourned.]

SCIENCE POLICY IMPLICATIONS OF DNA RECOMBINANT MOLECULE RESEARCH

SEPTEMBER 8, 1977

HOUSE OF REPRESENTATIVES,
COMMITTEE ON SCIENCE AND TECHNOLOGY,
SUBCOMMITTEE ON SCIENCE, RESEARCH AND TECHNOLOGY,
Washington, D.C.

The subcommittee convened at 8:07 a.m., in room 2325, Rayburn House Office Building, Hon. Ray Thornton (chairman of the subcommittee) presiding.

Mr. THORNTON. The hearing will come to order.

This morning we are continuing our hearings on Science Policy Implications of the DNA Recombinant Molecule Research Issue, discussing in somewhat broader sense the relationship between ethical standards and science research and we are pleased to have four distinguished witnesses scheduled for appearance this morning.

I appreciate your adjusting your schedules to meet at this 8 o'clock schedule which has been necessitated because of the House going into session at 10 with a bill which emerges from this subcommittee being one of the first bills on the floor of the House, which will require that I be there to handle that legislation when the House goes into session.

I don't think that it is starting too early. In fact, I imagine you gentlemen start this early or earlier frequently. But I did want to express my appreciaion to you for rescheduling to an earlier hour.

This morning I would like to follow the same procedures that we have in past hearings of asking each of the witnesses to make a statement, and following the statement by each of the witnesses, to go forward with a panel discussion in which we have some interreaction between the views which are presented.

Dr. Sorenson, it is a real privilege to have you with us today.

Dr. James Sorenson is an associate professor of sociomedical science and community medicine, the Boston University Medical School.

We are pleased to have you with us and would like to ask you to proceed at this time.

[A biographical sketch of Dr. Sorenson follows:]

Biographic Sketch

SORENSON, James Roger, Professor, medical sociologist, social psychologist; born Yakima, Washington, February 9, 1943; Paul Olaf and Helen (Anderson): B.A., Phi Beta Kappa, magna cum laude, University of Washington, 1965, M.A., University of Washington, 1966, Ph.D., Cornell University, 1970; married Nancy O'Neal, May 24, 1968; Assist. Professor of Sociology, Princeton University, 1969-1974; Assoc. Professor of Socio-Medical Sciences, Boston University School of Medicine, 1974-; member American Sociological Association, Eastern Sociological Society, Institute for Society, Ethics, and Life Sciences (Fellow); American Men and Women of Science: 1974; Whos Who in the East 16th edition, 1977-1978; Author articles sociology, applied human genetics, and sociometry; The Social Aspects of Applied Human Genetics, 1971; Home: 86 Forest Street, Wellesley Hills, Massachusetts 02181.

July 197

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Vital Statistics

Birth Date: February 9, 1943
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Academic Degrees

B.A. Sociology, University of Washington, Seattle, Washington, 1965 (Magna cum laude, Phi Beta Kappa)
M.A. Sociology, University of Washington, Seattle, Washington, 1966
Ph.D. Social Psychology, Cornell University, Ithaca, New York, 1970

Employment

Associate Professor of Socio-Medical Sciences, Boston University School of Medicine, 1974-
Assistant Professor of Sociology, Princeton University, 1969-1974
Research Fellow, Social Psychology Laboratory, Cornell University, Ithaca, New York, 1968-1969
Research Co-Director, Project Achievement, for DuPont-Fort Lewis School District, DuPont, Washington, March 1966-August 1966
Research Fellow, Institute for Sociological Research, University of Washington, Seattle, Washington, 1966

Research Grants

National Fund for Medical Education Research Grant, Principal Investigator, "Evaluation of The Boston University Six Year Liberal Arts-Medical Education Program," July 1975-June, 1977

National Foundation-March of Dimes, Co-Principal Investigator (with N. Scotch and J. Swazey), "An Evaluation of Genetic Counseling Services," April 1975-March 1978

Research Grants (continued)

Russell Sage Foundation Research Grant, Principal Investigator, "Genetic Counselors: Professionals in Applied Human Genetics," February 1972-March 1975

Russell Sage Foundation Research Grant, Principal Investigator, "Genetic Counseling Planning Study," July 1970-August 1972

Fields of Specialization

Medical Sociology, Research and Theory
Social Psychology, Decision Making Processes
Organizational Analysis and Theories of Formal Organizations

Courses Taught

Undergraduate:

Medical Sociology
Introductory Social Psychology
Advanced Social Psychology
Introductory Social Biology
Research Design and Methodology

Graduate:

Seminar in Contemporary Theories and Research on Formal Organizations
Seminar in Theory and Research in Social Psychology
Medical Sociology

Publications

Published:

Social Aspects of Applied Human Genetics, New York, Russell Sage Foundation, December, 1971a

"Task Demands, Group Interaction, and Group Performance," Sociometry, December, 1971b, 34, 4, 483-495

Social Aspects of Applied Human Genetics: A Bibliography, U. S. Government Printing Office, Fogarty International Center, National Institutes of Health, 1973a

"Sociological and Psychological Factors in Applied Human Genetics," in Proceedings of Conference on Ethical Issues in Genetic Counseling and the Use of Genetic Knowledge, New York, Plenum Press, 1973b

Publications (continued)

"Social Aspects of Applied Human Genetics," in Thomas R. Mertens and Sandra K. Robinson's Human Genetics and Social Problems, New York, MSS Information Corporation, 1973c

"Counselors: A Self Portrait," Genetic Counseling, Vol. 1, No. 5, October, 1973d

"Group Member Traits, Group Process, and Group Performance," Human Relations, Vol. 26, No. 5, pp. 639-655, 1974a

"Some Social and Psychological Issues in Genetic Screening," National Foundation - March of Dimes Original Articles Series, 1974b

"Genetic Counseling: Some Psychological Considerations," Our Children's Genes: New Genetic Options for Man and Society, New York: Plenum Press, 1974c

"Biomedical Innovation, Uncertainty, and Doctor-Patient Interaction," Journal of Health and Social Behavior, December, 15:(4) 366-374, 1974d

"From Social Movement to Clinical Medicine: The Role of Law and the Medical Profession in Regulating Applied Human Genetics," in Genetics and Law, New York, Plenum Press, 1976a

"Applying the New Genetics," New York Education Quarterly, Summer, 1976b

Griffin, M., C. Kavanagh, and J. Sorenson, "Genetic Information, Client Perspectives and Genetic Counseling," Social Work in Health Care, Vol. 2, (2) Winter, 1977, pp. 171-180.

In Press

"Genetic Counselors and Counseling Orientations: Unexamined Topics in Evaluation," Genetic Counseling, U.S. Department of Health, Education, and Welfare, Public Health Service, Washington, D.C., Government Printing Office 1977a

Scotch, N. A. and J. R. Sorenson, "Public Education and Genetic Counseling in Tay Sachs Screening Programs," in Tay Sachs Disease: Screening and Prevention, M. Kaback, & D. Bergsma, (eds.) Alan R. Liss, Publishing, N.Y. 1977b

Sorenson, J. and A. Culbert, "Counseling Orientations," in Genetic Counseling: Facts, Values, and Norms, (edited by Lappe, Capron, Murray and Twiss). National Foundation - March of Dimes, 1977c

Unpublished

"The Client and the Professional in Genetic Counseling and Genetic Screening," Princeton University, 1971

"Group Interaction, Process and Task Demands," Princeton University, 1971

"Factors Shaping Decision Making in Applied Human Genetics: Professional and Client Perspectives," paper read at ASA Session on Critical Decisions in Medical Practice, New Orleans, August, 1972.

"The Science of Genetics in the Domain of Medicine," read in Seminar in the Sociology of Applied Knowledge, ASA Annual Meeting, New York City, 1973

Eastern Sociological Society Meeting - 1976 "Genetics and Bioethics: A Sociological View."

"Special Study Scholarly Adjunct" Report to the National Commission for the Protection of Human Subjects, December, 1976

"Ethical Issues in Genetic Screening and Counseling for Huntington's Disease " in Report of Working Group on Medico-Legal-Ethical Issues in Huntington's Disease, 1977.

Manuscripts in Preparation

Genetic Counselors: Experts in Applied Human Genetics, for the Russell Sage Foundation

Professional Memberships

American Sociological Association
Eastern Sociological Society
Institute for Society, Ethics and Life Sciences (Fellow)
American Association for the Advancement of Science

Professional Activities and Honors

Member, Eastern Sociological Society Papers Committee, 1970-71; 1972-73
Member, Genetic Counseling Core Group, Institute for Society, Ethics, and Life Sciences, 1971-
Consultant, Educational Decision Making Project, Rutgers, The State University, Newark, New Jersey, September 1970-74. Dr. William M. Phillips, Jr.
Changing Role of Women Committee, NIMH, 1971.
National Institute of Child Health and Human Development (issues on genetic counseling and applied genetics)
Consultant, various research projects assessing impact of genetic counseling/screening
Member, National Foundation-March of Dimes Clinical Research (Human) Advisory Committee, 1974-1975
Scientific Associate, Boston City Hospital, 1975-

Eastern Sociological Society, 45th Anniversary Falk Lecturer in Medical Sociology, 1975-1976
Associate - Gerontology Center, Boston University 1976 - (Member, Research Committee)
Member - Scholarly Adjunct, National Commission for the Protection of Human Subjects in Biomedical & Behavioral Research in 1976-1977.
American Men and Women in Science, 1975.
Member - Working Group on Medico-Legal-Ethical Issues in Huntington's Disease, 1977.

STATEMENT OF DR. JAMES SORENSON, ASSOCIATE PROFESSOR OF SOCIOMEDICAL SCIENCE AND COMMUNITY MEDICINE, BOSTON UNIVERSITY MEDICAL SCHOOL

Dr. SORENSON. Thank you very much, Mr. Thornton.

I would like to thank the Subcommittee on Science, Research and Technology for inviting me to appear today. It is indeed a pleasure to share my thoughts with the committee regarding recombinant DNA research and to explore the issues that have surfaced in discussions about work in this area of contemporary molecular biology.

Since the report out of the 1973 Gordon Research Conference drawing attention to recombinant DNA research we have witnessed a rather remarkable series of events in the history of basic science research in this country. Beginning with the concerns of some basic scientists about the safety of certain types of recombinant DNA research, interest in this field has broadened in the past 4 years to encompass not only the researchers working in this field, but the larger scientific community, a variety of governmental agencies at the local, State, and national level and the public at large.

Just as the number of parties interested in this dialog has grown, so, too, have the issues. While the original concerns of scientists were couched primarily in terms of immediate research biohazards, such issues as the right of the public to participate in the regulation of research and questions about the possible limits to scientific investigation have appeared also.

The distance from the discussions at the Gordon Research Conference to the debates at the Cambridge City Council appears great from a number of perspectives. So, too, does the distance from a discussion of immediate biohazards, attendant on some specific research, to debate on the possible limits of scientific inquiry itself. Such distances, however, as we have and are learning, at least in the case of recombinant DNA research, may, in fact, not be so great after all, or they may be traveled very rapidly. This is perhaps particularly true in a society which on the one hand supports the scientific enterprise and its attendant inquisitiveness and on the other hand, increasingly articulates the desires for accountability of this enterprise.

Also this may be particularly true in a society which, again on the one hand recognizes real differences in technical sophistication between scientists and laymen, and on the other hand, adheres to an ideology of public participation and democratic decisionmaking.

In approaching the many issues that have been raised over the past 4 years one is tempted to select for discussion discreet issues, limited in scope, issues which one can grasp and about which one can appear to come to some rational conclusion. To do so, however, would be to miss, in my view, the real significance of what has happened and is happening between science and society as exemplified by the recombinant DNA issue.

In the limited time available today I have chosen to focus on only a couple of what I feel to be basic science society tensions the recombinant DNA issue has surfaced. These tensions are in a sense generic problems confronting science in a democratic society. They are not really new tensions nor are they likely to disappear, even if we are to solve all the specifics of the recombinant DNA issue. These ten-

sions highlight the fact, I believe, that science and society are beginning to alter their existing contract, a contract in the past based on numerous assumptions about the value of science, the rights of the citizenry, and the social responsibilities of both the individual scientist and science as a social institution. In examining these assumptions, we are entering into a dialogue that is at once technical and political, a dialogue requiring us to make clear our values and priorities.

The two topics I would like to raise for discussion are first of all, consideration of the adequacy of existing mechanisms of self-regulation by the scientific community to, first of all, assure society of the preservation of those things society values, and (2) to assure society of protection from harm or injury in the case of dangerous research.

Second, I want to briefly outline a rationale as to why some additional regulation or monitoring of some kinds of basic research activity may be both pragmatically useful and ethically justified. Of course, I can only raise these issues here but their direct relevance to much of the discussion on the recombinant DNA issue mandates that we begin to analyze them more carefully.

Certainly one of the most basic issues surfaced by the recombinant DNA discussion is whether the basic science community can adequately regulate itself so as to assure preservation of those things society deems of value, as well as in pursuing research, assure society that such research can be done safely. The major concerns that have been voiced by both sides to this issue seem to have been two types.

First, for those who argue scientists can regulate themselves, a position is taken that any externally imposed formal regulation over the conduct of research is an abridgement of a right of freedom of inquiry, a right, it is argued that is a necessary condition for the health of the scientific enterprise.

For those who take the position that external control is needed, the argument is often made that it is unsound practically to ask any group to monitor and regulate itself, including scientists. Were a clash to occur between a societal value and a scientific one, it is likely that the latter would predominate, because of the natural self-interest of the scientific community.

Additional arguments can be added to each side of this issue, such as claims that nonscientists lack technical sophistication to regulate scientific inquiry and claims that the public has a right to have a say in this largely publicly-supported undertaking.

It is important to note that the idea that science has and now operates with total freedom of inquiry is simply (of course) not true. There are powerful forms of control internal to science such as the peer review system and external, such as the largely political shaped funding priorities of the various Federal and State research funding agencies, that dramatically shape the direction and the contour of scientific inquiry.

In approaching the issue of the freedom of science, I would like to emphasize that we are really talking about two different freedoms. First, there is the freedom of science to pursue any line of inquiry on any issue, within certain constraints, such as respect for the individual and his rights. Such open inquiry may at times promise or suggest developments that pose a threat to societally valued activities, such as the development of a capacity to genetically engineer humans, as op-

posed to the reproductive method we now consider normal and appropriate.

The second freedom has to do with the freedom of science to assess the known and potential risks and benefits of some research and to exercise sole discretion in deciding to forgo or undertaken the risk. With respect to the first freedom, the freedom to research any issue without question, but within certain ethical constraints, our society has operated, and largely continues to operate, on the assumption that knowledge is superior to ignorance on almost every issue. Based on this premise we have supported the scientific enterprise as an investment, an investment that while it sometimes pays, huge profits, sometimes returns nothing at all.

To attempt to regulate science at this level; that is, permitting or restraining basic research because of possible applications, is probably largely futile and also needless. It is futile because it is nearly impossible to be able to make a positive link between any given avenue of basic inquiry and the specific purposes, good or bad, to which such research may be put. It is a truism that any given piece of scientific work may be used for either good or bad purposes. But the goodness or the badness does not reside in the basic science per se, but in how we use it.

It seems much more practical to me to maintain a distinction between inquiry and application, between science and technology, and an attempt to regulate the uses of science when in fact we see where a given discovery is leading. As a society we have already begun to explore new vehicles for better understanding and controlling technology. The establishment of the Office of Technology Assessment is one such experiment. An analogous Office of Basic Science Assessment, I think, would be both futile and perhaps in the long run very costly, in terms of curtailing potentially useful research, because of our inability to predict accurately from basic research to practical application.

With respect to the second type of scientific freedom, while I endorse an effort to maintain ethically responsible scientific freedom of inquiry, I do think it is necessary to carefully reconsider the current rights generally granted to science to assess the risks and benefits of dangerous research, and to permit science to be the sole judge of whether risky research should proceed to be terminated.

It seems to me that it is both logically sound and ethically imperative that in the conduct of basic research, we adhere to the same principles that underlay the establishment of procedures to protect individual human subjects in biomedical and behavioral research. Namely, it is ethically requisite that human subjects of biomedical and behavioral research be informed of the risk known and reasonably expected prior to their making a voluntary decision to participate. As a corollary, I suggest that at the societal level, it is ethically requisite that society knows of the risk to its health or well-being of basic research when such risks are significant, and that society have a voice in the decisions to let the research proceed or not. This principle should be adhered to, whether humans are the immediate object of research or not.

The rationale for this position rests essentially upon the observation that while the identification and the specification of the magnitude of a risk in research are largely technical issues, the decision as to what magnitude of risk to accept is essentially a question of values and

priorities. As such, the decision to take a risk is not really a scientific decision or question and as such cannot be left solely to the scientific establishment. If society, a community or a small group of people are to be exposed to real risk because of scientific research, then they should be so informed and have a say in the continuance or discontinuance of that basic research.

Such a principle, of course, puts an enormous weight and responsibility on our ability to be aware of and to assess the immediate risk surrounding any specific basic research. I do not believe this is an easy task, but it is certainly an ethically responsible one. As such it would seem that considerablly more effort needs to be given to assessing the highly probable and not so probable risk, health and otherwise, of basic research. Research scientists with their highly refined technical expertise are essential ingredients in identifying such risks, but they cannot be the sole participants. This is so both because of their vested interest in the continuance of research and also because of a tendency by scientists to attempt to define risk largely in terms of technical criteria, ignoring the fundamental questions of alternative values and priorities that also exist.

Adherence to the principle outlined above will, of course, have some costs. For one, it may slow down some research. But this is in itself not necessarily bad and public awareness of adherence to such a principle could be beneficial in helping to sustain public confidence in the scientific enterprise.

Adherence to the principle outlined above necessitates of course specification of some mechanism by which it may operate. It is the case that external controls have been imposed on research in the past, particularly clinical or research employing human subjects. In this regard I think it is worth mentioning that in the case of recombinant DNA research, it was a group of the basic researchers themselves who raised for discussion the possible safety issues. By contrast, if one examines the history of other areas of research where regulation exists, such as clinical research, it is rare to find a case of a researcher speaking out before some accident or injury. More often, as has been noted, regulations have been imposed after a catastrophe or an accident, sometimes several. In the light of this, it is commendable that basic researchers in recombinant DNA did step forward. But as a matter of social policy I did not think it wise to count on such courage and conviction as the sole means of bringing risky research to public attention.

Mechanisms already exist in science, of course, to provide assessment of risk. This assessment is reflected in regulations covering research involving infectious agents for example. However, as a principle such self-regulation must be viewed as somewhat suspect, again because of the self-interest of the research community.

It is important to point out that the measures and the reward structure of science are such that it is costly for an individual scientist to voice concern about the safety of research. In fact, some of the individual scientists who initially voiced concern about the safety of recombinant DNA work have suffered public rebuke from members of the scientific community.

What those considerations suggest is that it may be necessary to establish a mechanism independent of science to identify risk in research and to provide more explicit means for public discussion and

debate of such risk. Certainly one of the most involved ideas to appear to date is that of a certified public scientist, a person with appropriate qualifications and resources to identify problem areas, but a person isolated from or immune to the pressures and the reward structure of the practicing scientist. The function of this person would be to identify areas of concern and provide appropriate notification.

I also suspect it is a case that the mechanism for resolving issues brought to the attention by such a position already in fact exists. Increasingly public debate on scientific research issues have taken place in governmental agencies, in Congressional hearings and in some organizations such as the AAAS and the National Academy of Scientists. It seems to me that there is sufficient merit in the idea of a certified public scientist to warrant continued discussion.

By way of summary, the rapid and intense polarization of sides in the debates considering recombinant DNA research, both within the scientific community, but especially between scientists and non-scientists is reflective of several things, but it must be interpreted cautiously. Public opinion polls indicate that while the public has much concern over technology and its control, it is still supportive of science and has faith in its ultimate significance. In addition, while the public feels disenfranchised from the scientific enterprise, it is neither disinterested nor disenchanted with science.

The dramatic polarization of public officials and scientific spokesmen at the Cambridge City council may be reflective as much if not more of unfamiliarity with each other than with basic distrust or disenchantment. But this polarization and the corollary designation of rights and duties of each side is but the first step, as alluded to above, of a longer process of compromising, bargaining and negotiating a new compact between science and society. Science is an investment, a valuable one. But as a society it is not our only one, perhaps not even our most valuable investment. We as a society are committed ideologically to the democratic process as a way of researching differences and disputes. In addition we are committed to certain principles regarding the rights of individuals in our society to control our fate and to have a voice in our destiny. The new contract between science and society must reflect these values.

Thank you.

Mr. THORNTON. Thank you very much, Dr. Sorenson.

Again I want to thank you for being here at this time which is earlier than planned and for a very excellent statement which you have presented to us.

At any time that anyone has any questions in clarification, we may proceed to those. However, what I would like to do as far as formal questioning is concerned is to go ahead with the presentation by each of the witnesses and then get an interplay between the members and the panelists.

If you have a question at any point, I would be pleased to recognize you for that purpose, Mr. Ottinger.

Mr. OTTINGER. Thank you very much. Unfortunately, my time here this morning is going to be limited and I cannot come back.

Mr. THORNTON. If, before you leave, you want to ask any questions, just signal me and I will recognize you for that purpose.

Mr. OTTINGER. I appreciate your courtesy.

Mr. THORNTON. Our next witness is Dr. H. Bentley Glass, distinguished professor of biology, emeritus, State University of New York, Stony Brook; and chairman American Association for the Advancement of Science Committee on Scientific Freedom and Responsibility.

Dr. Glass, I am very pleased that you are here today. I noted a coincidence in your name which I called to my staff's attention. In the hearings which this subcommittee held a couple of years ago for the preparation of a new bill for agricultural research in education, which has now been passed by both the House and the Senate as a part of the farm bill, we not only had testimony by Dr. Orville Bentley as an agricultural witness, but also by Dr. Glass, who is an entomologist from Cornell.

So today we have a combination, we have Dr. Bentley Glass and we are very pleased to have you with us, sir.

[A biographical sketch of Dr. Glass follows:]

DR. BENTLEY GLASS

Born in Laichowfu, Shantung, China, of American missionary parents, on January 17, 1906. He graduated from Baylor University, A.B., 1926 and taught for two years in the high school of Timpson, Texas. His graduate study was continued at Baylor University, M.A. 1929, and at the University of Texas, Ph. D. 1932, where he worked in genetics under H. J. Muller. He received a National Research Council postdoctoral fellowship, and spent one year in Norway and Germany (Berlin) and a second at the University of Missouri. He subsequently taught at Stephens College (4 years), Goucher College (9 years), and the Johns Hopkins University (18 years) before going to the State University of New York at Stoney Brook as its Academic Vice President and Distinguished Professor of Biology in 1965. He retired from administration in 1971, and from professional duties in 1976. He has received 8 honorary Doctor of Science degrees and 2 LL.D.'s. He was elected to the National Academy of Sciences in 1959, to the American Philosophical Society in 1963, and is a foreign member of the Czechoslovak Academy of Sciences.

He has edited the Quarterly Review of Biology since 1945, as chief editor since 1958. He edited the 9-volume McCollum-Pratt Symposia on the biochemistry of minor elements, the biological basis of heredity and of development, and of light and life. For 25 years he served as an advisory editor for biology for the Houghton Mifflin Company. He was the first chairman of the Conference of Biological Editors, 1957–59. He was the original chairman of the Biological Sciences Curriculum Study, 1959–65, which prepared, under grants from the National Science Foundation, the high school textbooks, auxiliary books and materials, and films that revolutionized the teaching of biology in American schools in the 1960's.

He was a member of the National Academy of Sciences Committee on the Genetic Effects of Atomic Radiation, 1955–64, and became widely known as a speaker on the consequences of radioactive fallout. He served on the Advisory Committee of Biology and Medicine of the Atomic Energy Commission from 1955–63, and was its chairman in 1962–63. He also served on the Governor's Advisory Committee on Nuclear Energy in the State of Maryland, 1959–65. He was a member of the U.S.-Japan Committee on Scientific Cooperation, Panel on Science Education, 1963–66. He was chairman of the Committee to Assess the Biological Programs of NASA, under the Space Science Board of the National Academy of Sciences, 1969–70.

He has had many offices in scientific organizations and professional organizations in education. He was president of the American Association for the Advancement of Science, 1968–69, and chairman of the Board of Directors in 1970. He is currently chairman of the standing committee on Scientific Freedom and Responsibiilty of that organization. He was president of the American Association of University Professors in 1958–60; of the American Institute of Biological Sciences, 1954–56; of the American Society of Naturalists, 1965; of Biological Abstracts, 1958–60; of the American Society of Human Genetics,

1967; of Phi Beta Kappa, 1967–70; and of the National Association of Biology Teachers, 1971. He was chairman of the Board of Trustees of the Cold Spring Harbor Laboratory, 1967–73.

He has served as a national lecturer for Sigma Xi and Phi Beta Kappa. In addition to the many books he has edited or to which he contributed, he has written "Genes and the Man," 1943; "Science and Liberal Education," 1960; "Science and Ethical Values," 1965; and "The Timely and the Timeless," 1970. His bibliography contains more than 300 scientific, professional, and general articles.

He served on the Board of School Commissioners of Baltimore City, 1954–58, and took a profound interest in the integration of the Baltimore schools. He has worked in the cause of the civil liberties. For many years he was one of the leaders in the organization of the Pugwash Conferences on Science and World Affairs.

STATEMENT OF DR. H. BENTLEY GLASS, DISTINGUISHED PROFESSOR OF BIOLOGY, EMERITUS, STATE UNIVERSITY OF NEW YORK, STONY BROOK, AND CHAIRMAN, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE COMMITTEE ON SCIENTIFIC FREEDOM AND RESPONSIBILITY

Dr. GLASS. Thank you.

Mr. Chairman and members of the committee, I am pleased that the purview of this discussion is not to be limited to the ethical implications of recombinant DNA research, but will extend more broadly to encompass basic ethical issues in science.

I intend to begin, therefore, with the broader aspects and will return to recombinant DNA research only in my concluding remarks. That is not because the immediate problem is not of great importance but rather, because I believe it should be seen in a larger context.

The noted British geneticist and developmental biologist C. H. Waddington described man as "the ethical animal" or "the ethicizing animal." It is certainly one mark of human uniqueness among living beings that humans do concern themselves with ethical values. Both Waddington and I trace this common human tendency back into our evolutionary origins. Our ethical roots lie deep among the characteristics that over millions of years promoted survival and the transmission of genetic characteristics to the descendants. That, of course, is no new idea. Darwin developed it very well in discoursing on the moral qualities of man in his book "The Descent of Man," and attributed it to the action of natural selection. The most profound human characteristics, he wrote, are reason—that is, intelligence—and sympathy—that is, a basis for cooperativeness and altruism. Modern ecologists and students of animal behavior recognize that altruism, even to the point of self-sacrifice, promotes the selection of genes of family likeness in the relatives who are preserved by the death of the one.

Yet it would be a grave mistake to suppose that, because our ethical values have a biological basis and biological roots, they are biological and nothing more. Human culture transcends biological nature, and the rate of its evolution is vastly more rapid than the slow rate of biological evolution which depends on random mutations that must slowly pass through the screen of natural selection, becoming more abundant in a population until eventually possessed by all.

We must, therefore, look at the ethical values of mankind as being both biological in origin and cultural in evolution. If natural science has become the chief human instrument of discovery and power over the forces and the resources of the environment, including all other living thing on the Earth, then we must look at the value of human science not alone in terms of the power it confers upon man, but also in the light of the consequences it evokes in the environment in which humans live.

Psychologists and students of animal behavior have shown beyond cavil that a young developing animal or a human baby cannot mature properly in an environment that is devoid of the normal stimuli of the senses, as well as the company of a parent and fellow companions of its own age. Those things are just as necessary to its normal growth and development as the food, water and air it consumes. In other words, we do not end with our skins. The environment about us is actually a vital part of us, this earth, this air, these waters, these green and growing things and all that moves and has life about us. It follows that with growing power to modify our environment, we inevitably change ourselves, too. The greatest "manipulation" of human nature is not that to be envisaged by replacing in a person's body, one or two genes that are defective with genes that may work better. It is the pervasive, wholesale alteration of the environment to which we were once biologically well adapted.

Until about 10,000 years ago, all of mankind lived by hunting and gathering. Communities of people were sparsely distributed over the Earth which seemed to them illimitably vast and inexhaustible in its resources. The human being was but one of many forms of life that were clearly interknit in dependence upon one another. The ethnic that prevailed in those far-off times was perhaps best exemplified by the religion of the American Indians before the white man came, for the Indians lived still in the ways of Stone Age man. The Earth was the great mother; the birds and beasts, even though one had to kill to eat, were one's brothers; and man felt himself an intimate, integral part of his environment.

With the advent of agriculture and later of metal tools and weapons, humans in the Old World devised a new ethic. It is perhaps best exemplified by the Judeo-Christian attitude toward nature. The world and all within it were given to man by God—or the gods—to use and to exploit to the best of his ability. That was done. Especially in the past 300 years, and most remarkably in this present century, man has developed the methods of natural science for exploring the nature of things, and from that knowledge he has welded a power, through technology, to build our present civilizations. But Earth itself still seemed an inexhaustible mine of resources, and little heed was paid to the side effects and the aftereffects of exploitation. Immediate gain was all that counted in the cost-benefit analysis with which we grew up.

Not until the middle of this century did it become fearfully apparent that the ethnic of exploitation would not serve us any longer. It was not simply that there were now billions of people everywhere in the world, that many were starving and others poor beyond the

imagination of such primitive humans as the prehistoric American Indians. It was revealed to us that the Earth is finite and that we are pushing its limits as a healthy environment for all life. The revelation began not with Hiroshima and Nagasaki—I was in Hiroshima just last month—but with the weapons testing of megaton hydrogen bombs in the 1950's. It soon became clear that the radioactive fallout from those explosions was worldwide in distribution, and endangered the genes of both people and other organisms everywhere. The ban on atmospheric weapons testing was achieved, not so much because we wished détente with our chief competitor as a superpower, as because we did not dare continue, ourselves, to poison the Earth with our radioactivity. I speak of what I know, since for 10 years I worked intensively on these matters, and my last testimony before a congressional committee was on this matter. Also in the fifties, there came the strong impact of "Silent Spring," the book by Rachel Carson which showed that by means of our industrial processes, all laudably aimed at controlling disease, fertilizing the soil, controlling insect pests, and making new products for our technological society, we were sowing pollutants of a lasting nature in the environment, until our birds were dying, and insidious stuffs had reached even the Antarctic and the remotest deserts of the Earth.

What has been the role of the scientist in all this? Until midcentury, a strong belief in scientific freedom as an absolute value prevailed almost entirely. You will see that I agree completely with Mr. Sorenson in these matters.

Only now do we see, in this age of nuclear and industrial pollution, that what is done with our new-found knowledge is an inescapable responsibility of science—of the scientists themselves. As I wrote in 1965:

> Science is no longer—can never be again—the ivory tower of the recluse, the refuge of the social man. Science has found its social basis, and has eagerly grasped for social support, and it has therefore acquired social responsibilities and a realization of its own fundamental ethical principles. The scientist is a man, through his science doing good or evil to other men, and receiving from them blame and praise, recrimination and money. Science is not only to know, it is to do and in the doing it has found its soul.

The American Association for the Advancement of Science, recognizing these new relationships between scientists and society and science and the environment, recently established a standing committee to deal with such matters, and I am currently serving as its chairman. The name of the committee is most significant. It is the Committee on Scientfic Freedom and Responsibility. Henceforth, forever, these two concepts must be coupled indissolubly.

That is why, to my mind, the present widespread public interest in recombinant DNA research is of such great importance. It is the first time when the collective conscience of an entire scientific corps has publicly announced the possible hazards of their type of research and have proposed a moratorium on certain kinds of experiments until the risks can be contained. This is a historic moment in human history, for that reason alone. As for an assay of the seriousness of the risks, I hold that some of them are immediate and real, but that there are good prospects for preventing the release into the environment of an E. coli which has been converted into a ravaging pathogen

instead of remaining a peaceful human symbiont. Other risks, of human gene manipulation, for example, I regard as technically so remote that we need not be concerned much about them just now. We have time to look ahead and prepare for such eventualities. In terms of real, immediate risk to the human environment and to human nature, the problems of atomic wastes and of industrial pollutants are infinitely closer and more deadly, but all of these risks, these unanticipated side effects and long-term effects of our science and our technology must be given enormously greater attention in the future by scientists and governments alike. Our people, too, must be educated to realize that the era of terrestrial exploitation is over. Henceforth we are managers of a finite environment that we are pushing to the limit. And not simply managers for our own interests or those of other people in the world. We have entered the era of acknowledged trusteeship for Earth's environment in the interest of all of the generations yet to come, who must live in what might else be the stinking remains of a once fair planet. We acknowledge our interdependence with the green plants that provide us with oxygen as well as food and with the beasts of the Earth, the fowl of the air and the fish of the seas whose welfare, we now see, is our own. Thus, the watchery of the first half of the 20th century, "enlightened self-interest," is transformed into the ethic of trusteeship, in which all men of every tribe and nation must share with each other. To preserve ourselves we must protect them all.

Mr. THORNTON. Thank you very much for an excellent statement.

Without objection the article which you have written for Bioscience and published in the April 1977 issue will be considered by the staff for inclusion as an appendix to the record of these hearings. It is an excellent article and complements the presentation which you have made.

Dr. GLASS. Thank you.

[The material referred to follows:]

THE SCIENTIST: TRUSTEE FOR HUMANITY

(By Bentley Glass)

As both C. H. Waddington (Waddington 1960) and I (Glass 1965) have attempted to show, the roots of human ethics are traceable to our evolutionary past, to the forces of natural selection molding mankind to the environments of those past ages in which intelligence and culture developed. For Darwin, writing in "The Descent of Man" (Darwin 1871), morality and mutual aid spring from selection exerted upon those hereditary factors that contribute to "reason" and "sympathy" (see Glass 1972). Muller, a century later, identified the same primary elements in the evolution of humanity, although he termed them "intelligence" and "cooperativeness" (Muller 1967).

The sympathy that Darwin recognized as important he conceived to be primarily within the close group of the family or tribe (Darwin 1871, pp. 129–30, 143). Muller's cooperativeness, based upon human empathy by one person for fellow human beings in the same circumstances, or at least in conceivably similar circumstances, was likewise limited to relations between members of the species.

Today, as the papers contributed to this special issue bear witness, sympathy and cooperativeness require a broader definition if man is to survive at all in the world that he rules by dominating force, that he modifies at will by his activities. Every exhaustion of natural resources, every irremediable pollution of the terrestrial environment, leads us closer to the evil day when a man may find the earth no longer a pleasant abode but a stinkhole of diminishing fitness

for life. In this fate not only mankind, but every living plant and animal, every microbe and virus, is bound up together. Human survival may ultimately depend upon the ability of other species of life to replenish our atmosphere, purify our oceans and fresh waters, and recycle our resources of minerals.

For an ethics suitable for this novel concept of a universal symbiosis, we have no precedent, unless it be fore-shadowed in the sympathy expressed by Saint Francis of Assisi for all creatures of God's creation, large and small. The views of the participants in this special issue unite is a call for a new, far broader conception of human ethics than any of the older religions or philosophies have comprehended.

The Greeks combined the myths of Prometheus and Pandora. Prometheus, who pitied the sad estate of mortals, defied the will of Zeus by stealing fire from the sun in order to bring to man a gift of power from which there blossomed the early technologies of man as toolmaker, traveler, and foodgrower. For this act Prometheus was condemned to eternal torture, and the Gods on Olympus schemed to prevent mankind from fully possessing the fruits of their growing power, lest in time man might displace them altogether. Accordingly they created Pandora, in the fullness of Aphrodite's beauty. Hermes bestowed upon her the gift of persuasion, and Apollo gave her music to entice the heart of man. Besides these attributes, she was endowed with burning curiosity, and hence inevitably pried into the box, which was said to contain her dowry but which she had been sternly forbidden to open. Thence escaped a thousand plagues to discourage hapless humankind, and only hope was left behind.

Somehow the Greeks had grasped a great truth. Prometheus and Pandora are part of the same myth. For every gift of new knowledge that expands human power and enters the fabric of our civilization, there are offsetting plagues and worries. These are generated by the very gifts of Prometheus, who has come to symbolize in modern life our science and technology. We would do well to adopt Pandora as an equally fitting symbol of the fruits of knowledge through science. Every new scientific discovery, every new advance in technology creates long-term effects and side effects, which subtract substantially from whatever immediate benefits accrue.

Until we can establish appropriate social institutions for technology assessment, to examine with great care and by scientific means what adverse consequences are likely to flow from particular technological innovations and how those consequences may be circumvented, we will continue to be the children of Pandora. The real tragedy of Prometheus was not his defiance of the gods, nor yet his kindness toward suffering men, but rather his fatal blindness to foresee the full spread of consequences.

The immediate gains from the development of nuclear energy for power must, for example, be balanced against the steady input to the environment of tons of high-level radioactive wastes with physical half-lives of tens of thousands of years. And they must be balanced against the probability that any recourse to fast-breeder reactors that generate more fuel than they consume will simply enhance the risks of both exposure to incredibly toxic plutonium and hijacking by political extremists who, with one atomic bomb in their possession, could threaten the world order. The immediate gains in the United Arab Republic from building the Aswan Dam and irrigating thousands of arid hectares must be balanced against the spread through the irrigation canals of the snails that carry the dread agents of schistosomiasis, the collapse of the Mediterranean fisheries because of the loss of the fertilizing effect of the Nile on the sea, the need for more (and more expensive) artificial fertilizers for the lands deprived of the fertilizing floods of the great river, and the increase of population that has rapidly neutralized all gains in production of food. Many more examples could be cited; these are sufficient to make the point.

Many long-term or side effects can be avoided by a combination of foresight and restraint. The foresight can be supplied by further development of science and its application to the technological problems. The restraint must be governmental, since otherwise the selfish interests of those who benefit immediately from any technological innovation will rule. But governmental restraints are not likely to arise unless there is a new spirit among the people, a spirit which demands such deliberate control and will not be satisfied until it is forthcoming.

In all such matters, then, a great educational effort must be expended to enlighten the people about ultimate consequences. The issues of distributive justice, within nations and between the peoples of different countries, and the understanding that ultimately a steady-state economy rather than one of con-

tinued exponential growth must prevail—these especially must be thoroughly debated and expounded.

The educational effort alone will be insufficient. I believe that only a religious ethic will serve to protect us, an ethic that regards man as the trustee of nature for the welfare of all people, now and into the remote future. This is because, again, the Prometean tragedy is neither defiance nor pride; it is in essence the blindness and greed that make men grasp for immediate rewards.

The trusteeship of man must not be limited to a concern only for human beings or for those organisms now living. If our children and our children's children to unnumbered generations are to live in pleasantness upon this earth, so tiny a planet, so limited in resources, we who now live must develop a deep and abiding concern for the human environment of the future. Human life now depends, and will continue to depend, upon the coexistence of all other species of animals, and especially of the green plants which photosynthesize and the microbes that decompose and recycle the dead. Even the inanimate environment must be preserved, much as it is, if human life is to persist on earth. Changes that may not be fatal to existence may nevertheless provoke a profound, perhaps catastrophic, alternation in our psychological adjustment to life.

With knowledge comes power. With power comes responsibility. Our scientific knowledge in this century has increased by approximately six doublings and is now some 64 times as great as in 1900. By the end of the century, it may well be 250 times as great. With the accrued based on this knowledge, we are transforming the face of nature. All other species must adjust to our decisions or die. Many of them, indeed, have already perished because they could not adjust to our depredations, which destroyed the habitats to which their own evolution had adapted them. Has our sense of responsibility, during this century, multiplied to keep pace with our power? Has it even doubled once?

As human beings concerned with values, we must quickly recognize that the scales and mutations of values far transcend our own immediate subjective desires. These are limited by our position at one level in the hierarchical scale of biological organization; this we wilfully subordinate all values at levels below our personal individuality to the values of the individual, gladly sacrificing our cells or organs to the welfare of the body as a whole. We, furthermore, close our eyes to the values that apply to higher levels of organization, such as the community and the biosphere. (For a more detailed consideration of the hierarchy of human values, see Glass 1965, pp. 13–34.) There is indeed grave peril that ere long—maybe in the 21st century the human species will have destroyed its entire delicate biosphere, if not by nuclear war, then by callous treatment of the environment, treatment destroying the balance of nature. We must learn very soon to endure the thought that human survival itself, not merely our pleasure or comfort, depends on the preservation of our relations with the rest of life on earth and on the maintenance of the great cycles of nature that restore the life-giving properties of our environment.

As I have written elsewhere (Glass 1965, p. 34):

"We cannot turn the clock back. We cannot regain the Garden of Eden or recapture our lost innocence. From now on we are responsible for the welfare of all living things, and what we do will mold or shatter our own heart's desire."

Evolutionary processes adapt a species to its own existing, current environment. What the future human environment is to be, however, we can hardly imagine at this date. Do we, then, wish to adapt the human populations of the earth more fittingly to the present environment, with all its ackowledged imperfections? Surely not. Then do we wish to adapt our species more fittingly to the nature of the future environment, which we cannot foresee or define? The choice before us would seem to lie rather in the direction of modifying our present environment in desirable directions, with due deliberation, assessment of all impact upon it of technological innovations, and refusal to take any step that is irreversible. That may be difficult, but at least it is the more hopeful way. We do at least have some knowledge about certain undesirable aspects of our environment, for the most part those introduced in the past by ourselves. And at least we have a certain vision of a suitable environment in which each child can develop to its fullest physical and mental capacities and live in harmony with man and nature.

If all this is so, then we can dismiss as visionary and quite unnecessary those genetic procedures aimed to alter man's nature, but which cannot in actuality achieve such adaptation. In other words, genetic engineering in the sense of improving the basic aspects of human genotypes affecting intelligence, cooperative-

ness, or other fundamental characteristics of humanity should be set firmly aside until we have attained a more perfect environment.

What is needed by mankind in the present juncture is not a retreat from scientific ways of thinking, but an expansion into the consciousness of every man of the ways in which science and technology may be directed toward the prevention of Pandora's evils. The trustee is the one held accountable.

REFERENCES CITED

Darwin, C. 1871. *The Descent of Man*, rev. ed. (1896). D. Appleton & Co., New York.

Glass, B. 1965. *Science and Ethical Values*. University of North Carolina Press, Chapel Hill.

———. 1972. Eugenic implications of the new reproductive technologies. *Soc. Biol.* 19: 326–336.

Muller, H. J. 1967. What genetic course will man steer? Pages 521–543 in *Proc. III Intern. Congr. Human Genet.* Johns Hopkins Press, Baltimore, Md. [Reprinted in C. J. Bajema, ed. *Natural Selection in Human Populations*. John Wiley & Sons, New York, 1971.]

Waddington, C. H. 1960. *The Ethical Animal*. George Allen & Unwin, London. [University of Chicago Press, Chicago, 1967.]

Mr. THORNTON. Our next witness is Dr. Lewis Thomas, who is president of the Memorial Sloan-Kettering Cancer Center, and professor of medicine and pathology, Cornell University Medical College.

Dr. Thomas, we are very pleased to have you with us this morning. And we would like to ask you to go ahead with your presentation at this time.

[A biographical sketch of Dr. Thomas follows:]

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Present Positions:

President and Chief Executive Officer, Memorial Sloan-Kettering Cancer Center.
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Honorary Degrees: Yale, M.A., 1969.
Rochester, Sc.D., 1974.
Princeton, Sc.D., 1976.
Johns Hopkins, L.L.D., 1976.
Duke, L.H.D., 1976.
Medical College of Ohio, Sc.D., 1976.
Reed College, L.H.D., 1977.

Previous Academic Appointments:

..Research Fellow and Assistant in Medicine, Thorndike Memorial Laboratory, Boston City Hospital and Harvard Medical School, 1941-42 (Tilney Memorial Fellow).
..Visiting Investigator, Rockefeller Institute for Medical Research. Assigned to Naval Medical Research Unit, under direction of T.M. Rivers, M.D., 1942-44.
..U.S. Naval Medical Research Unit Number 2, Guam and Okinawa, 1944-45.
..Asst. Professor of Pediatrics, Johns Hopkins University Medical School, 1946-48.
..Assoc. Professor of Medicine, Tulane University School of Medicine, New Orleans, La., 1948-49.
..Professor of Medicine, Tulane University School of Medicine, 1949-50.

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Previous Academic Appointments: (Cont'd)

..Professor of Pediatrics and Internal Medicine, American Legion Heart Research Professor, Univ. of Minnesota Medical School, Minneapolis, Minn., 1950-54.
..Professor and Chairman, Dept. of Pathology, New York University-Bellevue Medical Center, 1954-58.
..Professor and Chairman, Dept. of Medicine, New York University-Bellevue Medical Center, 1958-66.
..Dean, New York University School of Medicine, 1966-69.
..Professor and Chairman, Dept. of Pathology, Yale-New Haven Medical Center, 1969-73.
..Dean, Yale University School of Medicine, 1972-July 1973.

Previous Hospital Appointments:

..Intern, Boston City Hospital, IV Medical (Harvard) Service, 1937-39.
..Resident, Neurology, Neurological Institute of New York. 1939-41.
..Pediatrician, Harriet Lane Home for Invalid Children, Johns Hopkins Hospital, 1946-48.
..Director of Bacteriology Laboratory, Harriet Lane Home, Johns Hopkins Hospital, 1946-48.
..Director, Division of Infectious Disease, Tulane University School of Medicine, New Orleans, La., 1948-50.
..Director, III & IV Medical Divisions, Bellevue Hospital, 1958-66.
..President, Medical Board of Bellevue Hospital, 1963-65.
..Director of Medicine, University Hospital, 1959-66.
..Consultant, Manhattan Veterans Administration Hospital, 1954-69.
..Chief of Pathology, Yale-New Haven Hospital, 1969-73.

Government Activities:

..Consultant, Surgeon General, U.S. Army, 1952-66.
..Member, Pathology Study Section USPHS, 1955-59.
..Member, Commission on Streptococcal and Staphylococcal Diseases, Dept. of Defense, Armed Forces Epidemiological Board, 1950-62.
..Member, National Advisory Health Council, N.I.H., 1960-64.
..Member, National Advisory Child Health and Human Development Council, N.I.H., 1964-68.
..Narcotics Advisory Committee, New York City Health Research Council (Chairman), 1961-63.

3.

Government Activities (Cont'd):

..Consultant, Committee on Research, President's Committee on Heart Disease, Cancer and Stroke, 1964-65.
..Member, Board of Directors, Public Health Research Institute of City of New York, 1960-69.
..Member, Board of Health of the City of New York, 1955-69.
..Member, President's Science Advisory Committee, 1967-70.
..Chairman, Committee to Review National Cancer Plan, National Academy of Sciences, 1972.
..Member, Health Research Council of the City of New York, 1974-75.
..Chairman, Overview Cluster, President's Biomedical Research Panel, 1975-76.

Editorial Boards:

American Journal of Pathology
Cellular Immunology
Journal of Medicine and Philosophy
Inflammation
Perspectives in Biology and Medicine
Human Nature
Journal of Developmental and Comparative Immunology
Daedalus

Military Service:

Lt. Commander, MC, USNR, 1941-46.

Scientific and Professional Societies:

National Academy of Sciences
Institute of Medicine (Council 1973--)
American Academy of Arts and Sciences
Association of American Physicians
American Pediatric Society
American Society for Clinical Investigation
International Academy of Pathology
American Association of Immunologists
American Academy of Neurology
Society for Experimental Biology and Medicine
Society for Pediatric Research
Harvey Society
New York Academy of Science - Fellow
American Rheumatism Association
Interurban Clinical Club
Century Association
Practitioners Society
American Academy of Microbiology - Charter Member
Peripatetic Clinical Society

4.

Miscellaneous Activities:

..Medical Advisory Committee, Unitarian Service Committee, 1955-60.
..Trustee, NYC Rand Institute, 1967-71.
..Committee on Education, Brown University (Div. of Biology and Medical Science), 1974--.
..Board of Directors, Squibb Corporation, 1969--.
..Medical Advisory Committee of the Center for Biomedical Education, CUNY, 1972--.
..Scientific Advisory Board, Scripps Clinic & Research Foundation, LaJolla, California, 1973--.
..Scientific Advisory Committee, Massachusetts General Hospital, 1969-72.
..Committee on Scientific Advisors, Vincent T. Lombardi Cancer Research Center, 1974--.
..Trustee, Cold Spring Harbor Laboratory, 1974--.
..Trustee, Draper Laboratory Corp., 1974--.
..Committee on the Health Professions of the Board of Trustees, Univ. of Pittsburgh School of Medicine, 1974--.
..Scientific Advisory Committee, The Institute for Cancer Research (Fox Chase), 1974--.
..Director-at-Large, Board of Directors, American Cancer Society, 1974--.
..Medical Advisory Committee, Irvington House Institute, NYC, 1974--.
..Board of Trustees, Rockefeller University, 1975--.
..Committee on Medical and Scientiric Programs, American Cancer Society, 1975--.
..Committee on Legislative and Government Programs, American Cancer Society, 1975--.
..Distinguished Service Member, Association of American Medical Colleges, 1975--.
..Board of Overseers, Harvard University, 1976--.
..Trustee, Guggenheim Foundation, 1975--.
..National Advisory Council of Hospice, 1975--.
..Executive Committee, Friends of the Earth Foundation, 1975--.
..Board of Directors, Josiah Macy Jr. Foundation, 1975--.
..Visiting Committee, Medical School and School of Dental Medicine, Harvard University, 1976--.
..Council of Visitors, Bank Street College of Education, 1975--.
..Scientific Board, C.V. Whitney Laboratory for Experimental Marine Biology & Medicine, 1976--.
..Chairman, Museum of Comparative Zoology Visiting Committee, (Harvard University), 1976--.
..Board of Directors, The East Side Assn., Inc., 1976--.
..Advisory Council, Institute for Advanced Research in Asian Science and Medicine, 1976--.
..Bd.Trustees, Educational Broadcasting Corp., 1977-1980.

5.

Miscellaneous Activities (Cont'd):

..Scientific Board, Whitney Laboratory for Experimental Marine Biology and Medicine, 1976--.
..Chairman, Visiting Committee, Museum of Comparative Zoology, Harvard University, 1976--.
..Board of Trustees, Hellenic Anticancer Institute, Greece, 1977--.
..Consultant, St. Savas Hospital, Athens, 1977--.

Special Awards:

..National Book Award in Arts and Letters for "The Lives of a Cell", Viking Press, 1974.
..Modern Medicine's 1975 Award for Distinguished Achievement.
..Awarded Membership to Phi Beta Kappa by Alpha of Connecticut at Yale University, 3/1/76.
..Awarded Membership to Phi Beta Kappa Assn. of New York, 1976--.

STATEMENT OF LEWIS THOMAS, M.D., PRESIDENT, MEMORIAL SLOAN-KETTERING CANCER CENTER, PROFESSOR OF MEDICINE AND PATHOLOGY, CORNELL UNIVERSITY MEDICAL COLLEGE

Dr. LEWIS. Thank you.

I am grateful to the committee for this opportunity to present my views on a subject which is of the utmost importance for the future of science in this country.

I wish to acknowledge, at the outset, that there is every justification in the world for the passage of laws and the setting of regulations concerning the introduction of new technologies based on science. The assessment of public hazard from particular types of technology, and the protection of the public welfare by laws wherever needed, are matters of obvious public responsibility.

This is a totally different matter from the regulation of science itself. Although it is true that virtually all of the new technologies introduced in this century were made possible because of new information provided in the first place by basic research, it is not true that any of these advances could have been forecast with any accuracy at the time when the basic research was being done. Indeed, it is a characteristic feature of basic research—one which in fact identifies the activity—that there can be no certainty at all about where the work will lead, or what its ultimate applicability, if any, may be. The sort of question which governs the setting up of experiments in this kind of science is the "what if?" inquiry. The work is aimed at getting explanations for things, at discovering how mechanisms work; in short, at gaining an understanding of nature.

Applied science, by contrast, is necessarily based on a very high degree of certainty. The assumption has to be made that all of the necessary facts are already at hand, and the type of question is a "how to?" question. The work is aimed at making use of information in order to accomplish something, to manufacture penicillin or set foot on the Moon, or to explode a bomb.

The uncertainty and unpredictability of basic science are extremely difficult matters to explain in a practical world. If not clearly understood, they tend to give the public the impression of a dreamy, ivory-tower, irresponsible kind of activity, in which wholly impractical people are bumping into new information by accident. Nothing could be farther from the truth.

Basic science is a very sharp, intense, direct inquiry into the unknown. Its methods, when it is done well, are based on the most hard-headed acknowledgement of the existence of the unknown. It relies on predictions for the design of experiments, but these predictions are necessarily hypothesis rather than solid forecasts. For the really hard problems, where matters of profound significance may be at stake, the odds against any prediction being correct are at their highest. A good basic scientist is an optimist—he almost has to be in such a trade—but he knows in his heart that most of his ideas, and therefore most of his experiments, are going to turn out to be mistaken. If he is highly skilled, and also lucky, he may hit a jackpot in one of a hundred tries, but he must live with the possibility that it might be one in a million, or never. He also knows that someone else in another laboratory, maybe in another country and another

decade, may pick up an observation he had made and recorded, and make use of it for an illuminating discovery he could never have thought of alone.

This is the way that work goes, and it has been going like this for about three centuries. On balance, if one looks back over the whole record, it has gone extremely well. We have built a civilization on it, and at the same time we have come a certain distance—not far, perhaps, but nonetheless a certain distance toward understanding how nature works.

We should go very carefully before making fundamental changes in the way basic science is carried out, or we will run the risk of causing fundamental damage to an enterprise on which the whole world—not just the Western, industrialized World—has come to depend on for its long-term future. It is, for all its great scale and complexity, a delicate and vulnerable system, as certain totalitarian societies have already learned to their regret from their experiments in the control of scientific thought. I can think of no human endeavor, not even poetry, in which freedom of the mind plays a more crucial role than it does in science.

Once we begin the attempt to regulate the sorts of questions that science is to be permitted to ask about nature, on grounds that this or that field of basic inquiry might lead to this or that dangerous sort of technology, there will be no end to the regulation.

Human imagination being what it is, risks can be discovered in every field of science that I can think of, and there will be constituencies mobilized in opposition to each of them. If today's imaginative rhetoric about the dangers of recombinant DNA research had been in fashion 50 years ago, voices would have been raised against the use of staphylococci or poliomyelitis virus in laboratories, and we might have lost the information which led, ultimately and quite unpredictably, to penicillin and the polio vaccine.

I can easily imagine some committee, charged with the legal responsibility to make an apprehensive scrutiny of medical science, deciding that organisms like rabies virus, or meningococci, or typhoid bacilli, or typhus rickettsia, were simply too dangerous to be worked on. Today, one of the most useful techniques in cell biology is called cell fusion; you can take a human cell in tissue culture and fuse it with a cell from any other species—a mosquito cell, say, or even a plant cell—and you end up with a single cell with a single nucleus containing all of the pooled chromosomes. Somewhere, surely, there is a committee that would conclude that that technique is a violation of nature and ought to be forbidden. We would end up with a list of acceptable, conventional, predictable and fashionable fields of science, all of them obviously safe from everyone's point of view, and science itself would come to a grinding stop.

What we really need at this stage of the debate is a very sharp and rigid definition of our terms. The regulation of new technologies is a feasible undertaking for the law, but it is very important that whatever regulations are written be closely focused on precisely the matter at hand, ad hoc to the particular technology in question—like the NIH guidelines for the recombinant DNA technology. If the law becomes even slightly loose and generalized in its language, we will quickly find ourselves with restraints on scientific thinking and imagining,

and we could lose the exploratory aspects of research, which would of course, mean the loss of science itself.

Mr. THORNTON. Thank you very much, Dr. Thomas.

I want also to compliment you on an excellent article that appeared in the New England Journal of Medicine, February 10, 1977. It was, as a matter of fact, one of the first things that I read as I got into this issue of recombinant DNA research. I want to suggest that this article be annexed to the record of these hearings. And I would like to share with the other panelists one paragraph from that article, which I think is really an excellent statement.

Dr. Thomas says: "It is hard to predict how science is going to turn out, and if it is really good science it is impossible to predict. This is the nature of the enterprise. The things to be found are actually new. They are by definition unknown in advance. And there's no way of foretelling in advance where a really new line of inquiry will lead. You cannot make choices in this matter, selecting things you think you are going to like and shutting off the lines that make for discomfort. You either have science or you don't."

[The full article referred to, and Dr. Thomas' prepared statement follow:]

NOTES OF A BIOLOGY-WATCHER—THE HAZARDS OF SCIENCE

(By Lewis Thomas, M.D.)

The codeword for criticism of science and scientists these days is *hubris*. Once you've said that word, you've said it all; it sums up, in a word, all of today's apprehensions and misgivings in the public mind—not just about what is perceived as the insufferable attitude of the scientists themselves but, enclosed in the same word, what science and technology are perceived to be doing to make this century, this near to its ending, turn out so wrong.

Hubris is a powerful word, containing layers of powerful meaning, which is a peculiar thing when you consider its seemingly trivial history in etymology. It turned up first in popular English usage as a light piece of university slang at oxford in the late 19th century, with the meaning of intellectual arrogance and insolence, applicable in a highly specialized sense to certain literary figures within a narrow academic community. But it was derived from a very old word, and as sometimes happens with ancient words it took on a new life of its own, growing way beyond the limits of its original meaning. Today, it is strong enough to carry the full weight of disapproval for the cast of mind that thought up atomic fusion and fission as ways of first blowing up and later heating cities, as well as the attitudes that led to strip-mining, off-shore oil wells, Kepone, food additives, SST's, and the tiny spherical particles of plastic recently discovered clogging the waters of the Sargasso Sea.

The biomedical sciences are now caught up with physical science and technology in the same kind of critical judgment, with the same pejorative word. Hubris is responsible, it is said, for the whole biologic revolution. It is hubris that has given us the prospects of behavior control, psychosurgery, fetal research, heart transplants, the cloning of prominent politicians from bits of their own eminent tissue, iatrogenic disease, overproduction and recombinant DNA. This last, the new technology that permits the stitching of one creature's genes into the DNA of another, to make hybrids, is currently cited as the ultimate example of hubris. It is hubris for man to manufacture a hybrid, on his own.

This is interesting, for the word hybrid is a direct descendant of the ancient Greek word hubris. Hubris originally meant outrage; it was in fact a hybrid word from two Indoeuropean roots: *ud*, meaning out, and *gwer*, meaning rage. The word became *hybrida* in Latin, and was first used to describe the outrageous offspring from the mating of a wild boar with a domestic sow; these presumably unpleasant animals were, in fact, the first hybrids.

Since then the word hybrid has assumed more respectable meanings in biology, and also in literary and political usage. There have been hybrid plants and hybrid vigor, hybrid words and hybrid bills in parliament for several centuries. But always there has been a hidden meaning of danger, of presumption and arrogance, of risk. Hybrids are things fundamentally to be disapproved of.

And now we are back to the first word again, from hybrid to hubris, and the hidden meaning of two beings joined unnaturally together by man is somehow retained. Today's joining is straight out of Greek mythology: it is the combining of man's capacity with the special prerogative of the gods, and it is really in this sense of outrage that the word hubris is being used today. This is what the word has grown into, a warning, a code-word, a short hand signal from the language itself: if man starts doing things reserved for the gods, deifying himself, the outcome will be something worse for him, symbolically, than the litters of wild boars and domestic sows were for the ancient Romans.

To be charged with hubris is therefore an extremely serious matter, and not to be dealt with by murmuring things about antiscience and anti-intellectualism, which is what many of us engaged in science tend to do these days. The doubts about our enterprise have their origin in the most profound kind of human anxiety. If we are right, and the critics are wrong, then it has to be that the word hubris is being mistakenly employed, that this is not what we are up to, that there is, for the time being anyway, a fundamental misunderstanding of science.

I suppose there is one central question to be dealt with, and I am not at all sure how to deal with it although I am certain about my own answer to it. It is this: are there some kinds of information leading to some sorts of knowledge, that human beings are really better off not having? Is there a limit to scientific inquiry not set by what is knowable but by what we ought to be knowing? Should we stop short of learning about some things, for fear of what we, or someone, will do with the knowledge? My own answer is a flat no, but I must confess that this is an intuitive response and I am neither inclined nor trained to reason my way through it.

There has been some effort, in and out of scientific quarters, to make recombinant DNA into the issue on which to settle this argument. Proponents of this line of research are accused of pure hubris, of assuming the rights of gods, of arrogance and outrage; what is more, they confess themselves to be in the business of making live hybrids, with their own hands. The mayor of Cambridge, Massachusetts, and the Attorney General of New York have both been advised to put a stop to it, forthwith.

It is not quite the same sort of argument, however, as the one about limiting knowledge, although this is surely part of it. The knowledge is already here, and the rage of the argument is about its application in technology. Should DNA for making certain useful or interesting proteins be incorporated into *Escherichia coli* plasmids, or not? Is there a risk of inserting the wrong sort of toxins, or hazardous viruses, and then having the new hybrid organisms spread beyond the laboratory? Is this a technology for creating new varieties of pathogens, and should it be stopped because of this?

If the argument is held to this level, I can see no reason why it cannot be settled, by reasonable people. We have learned a great deal about the handling of dangerous microbes in the last century, although I must say that the opponents of recombinant-DNA research tend to downgrade this huge body of information. At one time or another, agents as hazardous as those of rabies, psittacosis, plague and typhus have been dealt with by investigators in secure laboratories, with only rare cases of self-infection of the investigators themselves, and none at all of epidemics. It takes some high imagining to postulate the creation of brand-new pathogens so wild and voracious as to spread from equally secure laboratories to endanger human life at large, as some of the arguers are now maintaining.

But this is precisely the trouble with the recombinant-DNA problem: it has become an emotional issue, with too many irretrievably lost tempers on both sides. It has lost the sound of a discussion of technologic safety, and begins now to sound like something else, almost like a religious controversy, and here it is moving toward the central issue: are there some things in science we should not be learning about?

There is an inevitably long list of hard questions to follow this one, beginning with the one that asks whether the mayor of Cambridge should be the one to decide, first off.

Maybe we'd be wiser, all of us, to back off before the recombinant-DNA issue becomes too large to cope with. If we're going to have a fight about it, let it be confined to the immediate issue of safety and security of the recombinants now under consideration, and let us by all means have regulations and guidelines to assure the public safety wherever these are indicated, or even suggested. But if it is possible let us stay off that question about limiting human knowledge. It is too loaded, and we'll simply not be able to cope with it.

By this time it will have become clear that I have already taken sides in this matter, and my point of view is entirely prejudiced. This is true, but with a qualification. I am not so much in favor of recombinant-DNA research as I am opposed to the opposition to this line of inquiry. As a long-time student of infectious-disease agents I do not take kindly the declarations that we do not know how to keep from catching things in laboratories, much less how to keep them from spreading beyond the laboratory walls. I believe we learned a lot about this sort of thing, long ago. Moreover, I regard it as a form of hubris-in-reverse to claim that man can make deadly pathogenic micro-organisms so easily. In my view, it takes a long time and a great deal of interliving before a microbe can become a successful pathogen. Pathogenicity is, in a sense, a highly skilled trade, and only a tiny minority of all the numberless tons of microbes on the earth has ever involved itself in it; most bacteria are busy with their own business, browsing and recycling the rest of life. Indeed, pathogenicity often seems to me a sort of biologic accident in which signals are misdirected by the microbe or misinterpreted by the host, as in the case of endotoxin, or in which the intimacy between host and microbe is of such long standing that a form of molecular mimicry becomes possible, as in the case of diphteria toxin. I do not believe that by simply putting together new combinations of genes one can create creatures as highly skilled and adapted for dependence as a pathogen must be, any more than I have ever believed that microbial life from the moon or Mars could possibly make a living on this planet.

But, as I said, I'm not at all sure this is what the argument is really about. Behind it is that other discussion, which I wish we would not have to become enmeshed in. And I will tell you why.

I cannot speak for the physical sciences, which have moved an immense distance in this century by any standard, but it does seem to me that in the biologic and medical sciences we are still far too ignorant to begin making judgments about what sort of things we should be learning or not learning. To the contrary, we ought to be grateful for whatever snatches we can get hold of, and we ought to be out there on a much larger scale than today's, looking for more.

We should be very careful with that word hubris, and make sure it is not used when not warranted. There is a great danger in applying it to the search for knowledge. The application of knowledge is another matter, and there is hubris in plenty in our technology, but I do not believe that looking for new information about nature, at whatever level, can possibly be called unnatural. Indeed, if there is any single attribute of human beings, apart from language, that distinguishes them from all other creatures on earth, it is their insatiable, uncontrollable drive to learn things and then to exchange the information with others of the species. Learning is what we do, when you think about it. I cannot think of a human impulse more difficult to govern.

But I can imagine lots of reasons for trying to govern it. New information about nature is very likely, at the outset, to be upsetting to someone or other. The recombinant-DNA line of research is already upsetting, not because of the dangers now being argued about but because it is disturbing, in a fundamental way, to face the fact that the genetic machinery in control of the planet's life can be fooled around with so easily. We do not like the idea that anything so fixed and stable as a species line can be changed. The notion that genes can be taken out of one genome and inserted in another is unnerving. Classical mythology is peopled with mixed beings—part man, part animal or plant—and most of them are associated with tragic stories. Recombinant-DNA is a reminder of bad dreams.

The easiest decision for society to make in matters of this kind is to appoint an agency, or a commission, or a subcommittee within an agency, to look into the problem and provide advice. And the easiest course for a committee to take, when confronted by any process that appears to be disturbing people or making them uncomfortable, is to recommend that it be stopped, at least for the time being.

I can easily imagine such a committee, composed of unimpeachable public figures, arriving at the decision that the time is not quite ripe for further exploration of the transplantation of genes, that we should put this off for a while, maybe until next century, and get on with other affairs that make us less uncomfortable. Why not do science on something more popular?

The trouble is, it would be very hard to stop once this line was begun. There are, after all, all sorts of scientific inquiry that are not much liked by one constituency or another, and we might soon find ourselves with crowded rosters, panels, standing committees, set up in Washington for the appraisal, and then the regulation, of research. Not on grounds of the possible value and usefulness of the new

knowledge, mind you, but for guarding society against scientific hubris, against the kinds of knowledge we're better off without.

It would be absolutely irresistible as a way of spending time, and people would form long queues for membership. Almost anything would be fair game, certainly anything to do with genetics, anything relating to population control, or, on the other side, research on aging. Very few fields would get by.

The research areas in the greatest trouble would be those already containing a sense of bewilderment and surprise, with discernible prospects of upheaving present dogmas. I can think of several of these, two current ones in which I've been especially interested, and one from the remote past of 40 years ago.

First, the older one. Suppose this were the mid-1930's, and there were a Commission on Scientific Hubris sitting in Washington, going over a staff report on the progress of work in the laboratory of O.T. Avery in New York. Suppose, as well, that there were people on the Commission who understood what Avery was up to and believed his work. This takes an excess of imagining, since there were vanishingly few such people around in the 1930's, and also Avery didn't publish a single word until he had the entire thing settled and wrapped up 10 years later. But anyway, suppose it. Surely, someone would have pointed out that Avery's discovery of a bacterial extract that could change pneumococci from one gentic type to another, with the transformed organisms now doomed to breed true as the changed type, was nothing less than the discovery of a gene; moreover, Avery's early conviction that the stuff was DNA might turn out to be correct, and what then? To this day, the members of such a committee might well have been felicitating each other on having nipped something so dangerous in the very bud.

But it wouldn't have worked in any case, unless they had been equally prescient about bacteriophage research and had managed to flag down phage genetics before it got going a few years later. Science can be blocked, I have no doubt of that, or at least slowed down, but it takes very fast footwork.

Here is an example from today's research on the brain, which would do very well on the agenda of a Hubris Commission. It is the work now going on in several laboratories here and abroad dealing with the endorphins, a class of small polypeptides also referred to as the endogenous opiates. It is rather a surprise that someone hasn't already objected to this research, since the implications of what has already been found are considerably more explosive, and far more unsettling, than anything in the recombinant-DNA line of work. There are cells in the brain, chiefly in the limbic system, which possess at their surfaces specific receptors for morphine and heroin, but this is just a biologic accident; the real drugs, with the same properties as morphine, are the pentapeptide hormones produced by the brain itself. Perhaps they are switched on as analgesics at times of trauma or illness; perhaps they even serve for the organization and modulation of the physiologic process of dying when the time for dying comes. These things are not yet known, but such questions can now be asked. It is not even known whether an injection of such pentapeptides into a human being will produce a heroin-like reaction, but that kind of question will also be up for asking, and probably quite soon since the same peptides can be synthesized with relative ease. What should be done about this line of research—or rather, what should have been done about it two or three years ago when it was just being launched? Is this the sort of thing we are better off not knowing? I know some people who might think so. But if something prudent and sagacious had been done, turning off such investigations at an early stage, we would not have glimpsed the possible clue to the mechanism of catatonic schizophrenia, which was published just this month from two of the laboratories working on endorphins.

It is hard to predict how science is going to turn out, and if it is really good science it is impossible to predict. This is in the nature of the enterprise. If the things to be found are actually new, they are by definition unknown in advance, and there is no way of foretelling in advance where a really new line of inquiry will lead. You cannot make choices in this matter, selecting things you think you're going to like and shutting off the lines that make for discomfort. You either have science, or you don't, and if you have it you are obliged to accept the surprising and disturbing pieces of information, even the overwhelming and upheaving ones, along with the neat and promptly useful bits. It is like that.

And even if it were possible to call most of the shots in advance, so that we could make broad selections of the general categories of new knowledge that we like, leaving out the ones we don't have a taste for, there would always be slips, leaks, small items of shattering information somehow making their way through.

I have an example of this sort of thing in mind, a small item largely overlooked in its significance, a piece of news to match in importance, for what it tells us about ourselves and our relation to the rest of nature, anything else learned in biology during the past century. This is the astonishing tale—astonishing to my ears anyway—of the true nature of mitochondria and chloroplasts.

Between them, these organelles can fairly be said to run the place. They are, from every fair point of view, in charge. The chloroplasts tap the energy of the sun, and the mitochondria make use of it. Without them we might still have a world of microbes, but we could not have eukaryotic forms of life, nor metazoans, nor any of ourselves. Now, as it turns out, both of these can be viewed as living entities, organisms rather than organelles. The mitochondria live in our cells, and the chloroplasts in the cells of plants, as symbiotic lodgers. They replicate on their own, independently of nuclear division, with their own DNA and RNA, their own ribosomes, their own membranes, and these parts are essentially similar to the corresponding parts of bacteria and blue-green algae from which they are now believed to have descended. They are, in fairness, the oldest living inhabitants of the earth, and the least changed by evolution.

Well, this is the sort of knowledge I would call overwhelming, even overturning, in its implications. It has not yet sunk in, really, but when it does it is bound to affect our view of ourselves as special entities, as selves, in charge of our own being, in command of the earth. Another way to put it is that what we might be, in real life, is a huge collection of massive colonies of the most primitive kind of bacteria, which have adapted themselves for motile life in air by constructing around themselves, like a sort of carapace, all the embellishments and adornments of the modern human form. When you settle down to think a thought, you may think it is all your own idea, but perhaps it is not so. You are sharing the notion around, with more creatures than you could count in a lifetime, and they are the ones that turned the thought on in the first place. Moreover, there is more than a family resemblance, maybe even something like identity, between the mitochondria running your cells and those in control of the working parts of any cloud of midges overhanging a summer garden, or of seagulls, or the mouse in the basement, or all the fishes in the sea. It is a startling relationship, of such strange intimacy that none of use could have counted on before the facts began coming in. Would you prefer not to know about this? It is too late for that. Or would you prefer to stop it here and learn no more, leaving matters where they stand, stuck forever with one of the great ambiguities in nature, never to know for sure how it came out?

The only solid piece of scientific truth about which I feel totally confident is that we are profoundly ignorant about nature. Indeed, I regard this as the major discovery of the past 100 years of biology. It is, in its way, an illuminating piece of news. It would have amazed the brightest minds of the 18th-century enlightenment to be told by any of us how little we know, and how bewildering seems the way ahead. It is this sudden confrontation with the depth and scope of ignorance that represents the most noteworthy contribution of 20th-century science to the human intellect.

We are, at last, facing up to it. In earlier times, we either pretended to understand how things worked or ignored the problem, or simply made up stories to fill the gaps. Now that we have begun exploring in earnest, doing serious science, we are getting glimpses of how huge the questions are, and how far from being answered. Because of this, these are hard times for the human mind, and it is no wonder that we are depressed. It is not so bad being ignorant if you are totally ignorant; the hard thing is knowing in some detail the reality of ignorance, the worst spots and here and there the not-so-bad spots, but no true light at the end of any tunnel nor even any tunnels that can yet be trusted. Hard times, indeed.

But we are making a beginning, and there ought to be some satisfaction, even exhilaration, in that. The method works. There are probably no questions we can think up that can't be answered, sooner or later, including even the matter of consciousness. To be sure, there may well be questions we can't think up, ever, and therefore limits to the reach of human intellect that we will never know about, but that is another matter. Within our limits, we should be able to work our way through to all our answers, if we keep at it long enough, and pay attention.

I am putting it this way, with all the presumption and confidence that I can summon, to raise another, last question. Is this hubris? Is there something fundamentally unnatural, or intrinsically wrong, or hazardous for the species, in the ambition that drives us all to reach a comprehensive understanding of nature, including ourselves? I cannot believe it. It would seem to me a more unnatural thing, and more of an offense against nature, for us to come on the same scene endowed as we are with curiosity, filled to overbrimming as we are with questions, and naturally talented as we are for the asking of clear questions, and then for us to do nothing about it, or worse, to try to suppress the questions. This is the greater danger for our species, to try to pretend that we are another kind of animal, that we do not need to satisfy our curiosity, that we can get along somehow without inquiry and exploration, and experimentation, and that the human mind can rise above its ignorance by simply asserting that there are things it has no need to know. This, to my way of thinking, is the real hubris, and it carries danger for us all.

A Statement presented to the
House of Representatives
Subcommittee on Science, Research and Technology
September 8, 1977

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President, Memorial Sloan-Kettering Cancer Center
Professor of Medicine and Pathology, Cornell
University Medical College
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I am grateful to the Committee for this opportunity to present my views on a subject which is of the utmost importance for the future of science in this country.

I wish to acknowledge, at the outset, that there is every justification in the world for the passage of laws and the setting of regulations concerning the introduction of new technologies based on science. The assessment of public hazard from particular types of technology, and the protection of the public welfare by laws wherever needed, are matters of obvious public responsibility.

This is a totally different matter from the regulation of science itself. Although it is true that virtually all of the new technologies introduced in this century were made possible because of new information provided in the first place by basic research, it is not true that any of these advances could have been forecast with any accuracy at the time when the basic research was being done. Indeed, it is a characteristic feature of basic research -- one which in fact identifies the activity -- that there can be no certainty at all about where the work will lead, or what its ultimate applicability, if any, may be. The sort of question which governs the setting up of experiments in this kind of science is the "what if?" inquiry. The work is aimed at getting explanations for things, at discovering how mechanisms work, in short at gaining an understanding of nature.

Applied science, by contrast, is necessarily based on a very high degree of certainty. The assumption has to be made that all of the necessary facts are already at hand, and the type of question is a "how to?" question. The work is aimed at making use of information in order to accomplish something, to manufacture penicillin or set foot on the moon, or to explode a bomb.

The uncertainty and unpredictability of basic science are extremely difficult matters to explain in a practical world. If not clearly understood, they tend to give the public the impression of a dreamy, ivory-tower, irresponsible kind of activity, in which wholly impractical people are bumping into new information by accident. Nothing could be farther from the truth. Basic science is a very sharp, intense, direct inquiry into the unknown. Its methods, when it is done well, are based on the most hard-headed acknowledgement of the existence of the unknown. It relies on predictions for the design of experiments, but these predictions are necessarily hypotheses rather than solid forecasts. For the really hard problems, where matters of profound significance may be at stake, the odds against any prediction being correct are at their highest. A good basic scientist is an optimist -- he almost has to be in such a trade -- but he knows in his heart that most of his ideas, and therefore most of his experiments, are going to turn out to be mistaken. If he is highly skilled, and also lucky, he may hit a jackpot in one of a hundred tries, but he must live with the possibility that it might be one in a million,

or never. He also knows that someone else in another laboratory, maybe in another country and another decade, may pick up an observation he has made and recorded, and make use of it for an illuminating discovery he could never have thought of alone.

This is the way the work goes, and it has been going like this for about 3 centuries. On balance, if one looks back over the whole record, it has gone extremely well. We have built a civilization on it, and at the same time we have come a certain distance -- not far, perhaps, but nonetheless a certain distance toward understanding how nature works.

We should go very carefully before making fundamental changes in the way basic science is carried out, or we will run the risk of causing fundamental damage to an enterprise on which the whole world -- not just the western, industrialized world -- has come to depend on for its long-term future. It is, for all its great scale and complexity, a delicate and vulnerable system, as certain totalitarian societies have already learned to their regret from their experiments in the control of scientific thought. I can think of no human endeavor, not even poetry, in which freedom of the mind plays a more crucial role than it does in science.

Once we begin the attempt to regulate the sorts of questions that science is to be permitted to ask about nature, on grounds that this or

that field of basic inquiry might lead to this or that dangerous sort of technology, there will be no end to the regulation. Human imagination being what it is, risks can be discovered in every field of science that I can think of, and there will be constituencies mobilized in opposition to each of them. If today's imaginative rhetoric about the dangers of recombinant DNA research had been in fashion 50 years ago, voices would have been raised against the use of staphylococci or poliomyelitis virus in laboratories, and we might have lost the information which led, ultimately and quite unpredictably, to penicillin and the polio vaccine. I can easily imagine some committee, charged with the legal responsibility to make an apprehensive scrutiny of medical science, deciding that organisms like rabies virus, or meningococci, or typhoid bacilli, or typhus rickettsia, were simply too dangerous to be worked on. Today, one of the most useful techniques in cell biology is called cell fusion; you can take a human cell in tissue culture and fuse it with a cell from any other species -- a mosquito cell, say, or even a plant cell -- and you end up with a single cell with a single nucleus containing all of the pooled chromosomes. Somewhere, surely, there is a committee that would conclude that that technique is a violation of nature and ought to be forbidden. We would end up with a list of acceptable, conventional, predictable and fashionable fields of science, all of them obviously safe from everyone's point of view, and science itself would come to a grinding stop.

What we really need at this stage of the debate is a very sharp and rigid definition of our terms. The regulation of new technologies is a feasible undertaking for the law, but it is very important that whatever regulations are written be closely focussed on precisely the matter at hand, ad hoc to the particular technology in question -- like the NIH guidelines for the recombinant DNA technology. If the law becomes even slightly loose and generalized in its language, we will quickly find ourselves with restraints on scientific thinking and imagining, and we could lose the exploratory aspect of research, which would of course mean the loss of science itself.

Dr. Ryan, I am very pleased to be able to introduce you as our wrap-up witness this morning. I appreciate your rescheduling—the earlier hour was necessitated because of Congress going into session at 10 o'clock. And we apologize for having to reschedule. But I am delighted you are here.

Dr. Kenneth Ryan is chief of staff of the Boston Hospital for Women and is chairman of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.

You are welcome, Dr. Ryan, and we would like to ask you to proceed.

[A biographical sketch of Dr. Ryan follows:]

C U R R I C U L U M V I T A E

KENNETH JOHN RYAN

Born:	August 26, 1926, New York, New York
1948	Northwestern University
1952	M.D. Harvard Medical School - magna cum laude
1943-46	United States Naval Reserve
1952-53	Intern in Medicine, Massachusetts General Hospital
1953-54	Resident in Medicine, Massachusetts General Hospital
1954-55	Research Fellow in Biochemistry, Harvard Medical School
1955-56	Research Fellow in Medicine, Harvard Medical School
1956-57	Resident in Medicine, Columbia Presbyterian Hospital
1957-60	Resident in Obstetrics and Gynecology, Boston Lying-in Hospital and Free Hospital for Women
1960-61	Instructor in Obstetrics and Gynecology, Harvard Medical School
1960-61	Director, Fearing Research Laboratory, Free Hospital for Women
1961-70	Arthur H. Bill Professor of Obstetrics and Gynecology, Case Western Reserve University School of Medicine
1961-70	Chairman, Department of Obstetrics and Gynecology, Case Western Reserve University School of Medicine
1961-70	Director, Department of Obstetrics and Gynecology, University Hospitals of Cleveland
1968-70	Chairman, Department of Reproductive Biology, Case Western Reserve University School of Medicine
1969-70	Coordinator, Biological Sciences, Case Western Reserve University School of Medicine
1970-72	Chairman, Department of Obstetrics and Gynecology, University of California, San Diego, School of Medicine
1970-72	Professor of Reproductive Biology, University of California, San Diego, School of Medicine
1973-	Chairman, Department of Obstetrics and Gynecology, Harvard Medical School
1973-	Kate Macy Ladd Professor of Obstetrics and Gynecology, Harvard Medical School
1973-	Chief of Staff, Boston Hospital for Women
1974-	Director, Laboratory of Human Reproduction and Reproductive Biology, Harvard Medical School
1974-	Chairman, National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
1975-	William Lambert Richardson Professor of Obstetrics, Harvard Medical School

Certification:

1964	American Board of Obstetrics and Gynecology

Memberships:

1975	American Academy of Arts and Sciences (Fellow)
	American Fertility Society
	American Gynecological Society
1969-71	American Society of Clinical Investigation (Council)
	Board of Scientific Counsellors, NICHD
1972-75	Division of Reproductive Endocrinology, American Board of Obstetrics and Gynecology (Director)
1969-71	Endocrine Society (Council)
	Massachusetts Medical Society
	National Academy of Sciences, Institute of Medicine
	National Advisory Council - USPHS
1968-77	President's Committee on Mental Retardation
	The American College of Obstetricians and Gynecologists (Fellow)

Honors:

1951	Schering Award
1952	Soma Weis Award (Harvard)
1952	Borden Award (Harvard)
1964	Ernst Oppenheimer Award of Endocrine Society
1971	Weinstein Award of United Cerebral Palsy
1972	Squibb Prize Paper, American Fertility Society
1975	Sidney Farber Memorial Research Award

PUBLICATIONS

1. Engel, L.L. and Ryan, K.J.: The in vitro metabolism of the natural estrogens by normal and neoplastic tissue. Second International Congress of Biochemistry, Resumes, p. 462, 1952.

2. Ryan, K.J. and Engel, L.L.: The interconversion of estrone and estradiol-17β by rat liver slices. Endocrinology, 52:277-286, 1953.

3. Ryan, K.J. and Engel, L.L.: The interconversion of estrone and estradiol by human tissue slices. Endocrinology, 52:287-291, 1953.

4. Ryan, K.J. and Engel, L.L.: Steroid 21-hydroxylation by adrenal microsomes and reduced triphosphopyridine nucleotide. J. Am. Chem. Soc., 78:2654-2655, 1956.

5. Ryan, K.J. and Engel, L.L.: Estrogen metabolites in human serum. Endocrinology, 59:499-501, 1956.

6. Ryan, K.J. and Engel, L.L.: Steroid 21-hydroxylation. J. Biol. Chem., 225:103-114, 1957.

7. Ryan, K.J.: Conversion of androstenedione to estrone by placental microsomes. Biochim. Biophys. Acta, 27:658-659, 1958.

8. Ryan, K.J.: The conversion of Δ5-androstene-3β, 16α, 17β-triol to estriol by human placenta. Endocrinology, 63:392-394, 1958.

9. Ryan, K.J.: Biological aromatization of steroids. J. Biol. Chem., 234:268-272, 1959.

10. Ryan, K.J.: Metabolism of C-16-oxygenated steroids by human placenta: The formation of estriol. J. Biol. Chem., 234:2006-2008, 1959.

11. Ryan, K.J.: Estrogen formation by the human placenta: Studies on the mechanism of steroid aromatization by mammalian tissue. Acta Endocrinol. (Suppl. 51), 35:697-698, 1960.

12. Ofner, P., Sasse, J., Munson, P.L. and Ryan, K.J.: Some biological characteristics of Δ1-3-ketosteroids of the androstane series. Acta Endocrinol. (Suppl. 51), 35:849-850, 1960.

13. Ryan, K.J., Benirschke, K. and Smith, O.W.: Conversion of androstenedione-4-C^{14} to estrone by the marmoset placenta. Endocrinology, 69(3):613-618, 1961.

14. Ryan, K.J. and Smith, O.W.: Biogenesis of estrogens by the human ovary. I. Conversion of acetate-1-C^{14} to estrone and estradiol. J. Biol. Chem., 236:705-709, 1961.

15. Ryan, K.J. and Smith, O.W.: Biogenesis of estrogens by the human ovary. II. Conversion of progesterone-4-C^{14} to estrone and estradiol. J. Biol. Chem., 236:710-714, 1961.

16. Ryan, K.J. and Smith, O.W.: Biogenesis of estrogens by the human ovary. III. Conversion of cholesterol-4-C^{14} to estrone. J. Biol. Chem., 236:2204-2206, 1961.

17. Ryan, K.J. and Smith, O.W.: Biogenesis of estrogens by the human ovary. IV. Formation of neutral steroid intermediates. J. Biol. Chem., 236(8):2207-2212, 1961.

18. Smith, O.W. and Ryan, K.J.: Biogenesis of estrogens by the human ovary. The conversion of androstenedione-4-C^{14} to estrone and estradiol in high yield. Endocrinology, 69:869-872, 1961.

19. Smith, O.W. and Ryan, K.J.: Biogenesis of estrogens by the human ovary. Formation of neutral steroid intermediates from progesterone-4-C^{14}, androstenedione-4-C^{14} and cholesterol-4-C^{14}. Endocrinology, 69:970-983, 1961.

20. Ofner, P., Harvey, H.H., Sasse, J., Munson, P.L. and Ryan, K.J.: A comparison of some biological characteristics of Δ^1 and Δ4-3-ketosteroids of the androstane series. Endocrinology, 70:149-158, 1962.

21. Smith, O.W. and Ryan, K.J.: Estrogen in the human ovary. Am. J. Obstet. Gynecol., 84:141-153, 1962.

22. Ryan, K.J.: Hormones of the placenta. Symposium on the placenta. Am. J. Obstet. Gynecol., 84:1695-1713, 1962.

23. Ofner, P., Ryan, K.J., Smith, O.W., Fried, J. and Munson, P.L.: Androstane derivatives of interest in therapy of breast cancer: Classification of androgens according to convertibility to estrogens in vitro. Second Conference Experimental Clinical Cancer Chemotherapy, Washington, D. C., November 2-3, 1961. Cancer Chemother. Rep., 16:285-292, 1962.

24. Ryan, K.J.: Biogenesis of estrogens. In Proceedings of the Fifth International Congress of Biochemistry, Vol. VII, Biosynthesis of Lipids. Ed.: G. Popjak. New York, MacMillan Co., pp. 381-394, 1963.

25. Ryan, K.J.: Synthesis of hormones in the ovary. In The Ovary. Ed.: H. Grady. Baltimore, Williams and Wilkins, pp. 69-83, 1963.

26. Ryan, K.J.: The conversion of pregnenolone-7-H^3 and progesterone-4-C^{14} to estradiol by a corpus luteum of pregnancy. Acta Endocrinol., 44:81-89, 1963.

27. Ryan, K.J., Meigs, R.A., Petro, Z. and Morrison, G.: Estrogen-induced 16-hydroxysteroid dehydrogenase activity in rat kidney. Science, 142(3589):243-244, 1963.

28. Ryan, K.J.: Fetal anoxia. In Current Therapy. Ed.: H. F. Conn. Philadelphia, W. B. Saunders Company, pp. 594-595, 1964.

29. Klausner, D.A. and Ryan, K.J.: Estriol secretion by the human term placenta. J. Clin. Endocrinol. Metab., 24(1): 101-104, 1964.

30. Magendantz, H.G. and Ryan, K.J.: Isolation of an estriol precursor, 16α-hydroxy-dehydroepiandrosterone from human umbilical sera. J. Clin. Endocrinol. Metab., 24:1155-1162, 1964.

31. Ryan, K.J.: Oestrogens: Blood and placental levels and the factors which control them. Excerpta Medica International Congress Series #83, Proceedings of the Second International Congress of Endocrinology, London, pp. 727-731, August 1964.

32. Ryan, K.J. and Short, R.V.: Formation of estradiol by granulosa and theca cells of the equine ovarian follicle. Endocrinology, 76:108-114, 1965.

33. Ryan, K.J. and Smith, O.W.: Biogenesis of steroid hormones in the human ovary. Recent Prog. Horm. Res., 21:367-409, 1965.

34. Ryan, K.J.: Steroid hormone formation in the human ovary. Physiology for Physicians, 3(4):1-5, 1965.

35. Morrison, G., Meigs, R.A. and Ryan, K.J.: Biosynthesis of progesterone by the human placenta. Steroids, Suppl. II, pp. 177-188, 1965.

36. Ryan, K.J.: Humane abortion laws and the health needs of society. Western Reserve Law Rev., 17:424-434, 1965.

37. Ryan, K.J. and Petro, Z.: Steroid biosynthesis by human ovarian granulosa and thecal cells. J. Clin. Endocrinol. Metab., 26:46-52, 1966.

38. Ryan, K.J. and Short, R.V.: Cholesterol formation by granulosa and thecal cells of the equine follicle. Endocrinology, 78:214-216, 1966.

39. Ainsworth, K. and Ryan, K.J.: Steroid hormone transformation by endocrine organs from pregnant mammals. I. Estrogen biosynthesis by mammalian placental preparations in vitro. Endocrinology, 79:875-883, 1966.

40. Meigs, R.A. and Ryan, K.J.: 16α-hydroxysteroid dehydrogenase of rat kidney. J. Biol. Chem., 241:4011-4015, 1966.

41. Ryan, K.J., Meigs, R. and Petro, Z.: The formation of progesterone by the human placenta. Am. J. Obstet. Gynecol., 96:676-682, 1966.

42. Ryan, K.J., Meigs, R.A. and Petro, Z.: Biosynthesis of progesterone in the human placenta. Excerpta Medica International Congress Series No. 132, Proceedings of the Second International Congress on Hormonal Steroids, Milan, May 1966. New York, Excerpta Medica Foundation, pp. 663-666, 1967.

43. Ryan, K.J.: Steroid metabolism in the human ovary. In Advances in Obstetrics and Gynecology, Vol. I. Eds.: S. L. Marcus and C. C. Marcus. Baltimore, Williams and Wilkins Co., pp. 340-353, 1967.

44. Ryan, K.J. and Ainsworth, L.: Comparative aspects of steroid hormones in reproduction. In Comparative Aspects of Reproductive Failure. Ed.: K. Benirschke. New York, Springer-Verlag, pp. 154-166, 1967.

45. Arceo, R. and Ryan, K.J.: Conversion of androstenedione-4^{14}C to estrogens by subcellular fractions of human corpus luteum. Acta Endocrinol., 56:225-230, 1967.

46. Ainsworth, L. and Ryan, K.J.: Steroid hormone transformation by endocrine organs from pregnant mammals. II. Formation and metabolism of progesterone by bovine and sheep placental preparations in vitro. Endocrinology, 81: 1349-1356, 1967.

47. Ryan, K.J., Petro, Z. and Kaiser, J.: Steroid formation by isolated and recombined ovarian granulosa and thecal cells. J. Clin. Endocrinol. Metab., 28:355-358, 1968.

48. Ryan, K.J.: Biosynthesis and metabolism of ovarian steroids. In Progress in Infertility. Ed.: S. J. Behrman and R. W. Kistner. Boston, Little, Brown and Company, pp. 275-298, 1968.

49. Magendantz, H.G., Klausner, D., Ryan, K.J. and Yen, S.S.C.: Estriol determinations in the management of high-risk pregnancies. Obstet. Gynecol., 32:610-619, 1968.

50. Meigs, R.A. and Ryan, K.J.: Cytochrome P-450 and steroid biosynthesis in the human placenta. Biochim. Biophys. Acta, 165:476-482, 1968.

51. Ainsworth, L. and Ryan, K.J.: Steroid hormone transformation by endocrine organs from pregnant mammals. III. Biosynthesis and metabolism of progesterone by the mare placenta in vitro. Endocrinology, 84:91-97, 1969.

52. Ainsworth, L., Daenen, M. and Ryan, K.J.: Steroid hormone transformations by endocrine organs from pregnant mammals. IV. Biosynthesis and metabolism of estrogens and progesterone by primate placental preparations in vitro. Endocrinology, 84(6):1421-1429, 1969.

53. Preumont, P., Ryan, K.J., Younglai, E.V. and Solomon, S.: Specificity of aromatization and 16-hydroxylation in the human ovary. J. Clin. Endocrinol. Metab., 29:1394-1403, 1969.

54. Preumont, P., Cooke, I. and Ryan, K.J.: Oestrogen biosynthesis and steroid metabolism in the porcine ovary. Acta Endocrinol., 62:449-460, 1969.

55. Ainsworth, L. and Ryan, K.J.: Steroid hormone transformation by endocrine organs from pregnant mammals. V. The biosynthesis and metabolism of progesterone and estrogens by orangutan placental tissue in vitro. Steroids, 14(3):201-314, 1969.

56. Ryan, K.J.: Theoretical basis for endocrine control of gestation - A comparative approach. In The Foeto-Placental Unit. Ed.: A. Pecile and C. Finzi. Amsterdam, Excerpta Medica Foundation, pp. 120-131, 1969.

57. Ainsworth, L. and Ryan, K.J.: Biosynthesis and metabolism of steroid hormones by the mammalian placenta in vitro. In Progress in Endocrinology. Ed.: C. Gual. Amsterdam, Excerpta Medica Foundation, pp. 755-762, 1969.

58. Meigs, R.A. and Ryan, K.J.: 16α-hydroxylated dehydrogenase from rat kidney in steroids and terpenoids. In Methods in Enzymology, Vol. XV. Ed.: R. B. Clayton. New York, Academic Press, pp. 753-757, 1969.

59. Townsend, L. and Ryan, K.J.: The in vitro metabolism of pregnenolone-7α-^{3}H, progesterone-4-^{14}C and androstenedione-4-^{14}C by rat placental tissue. Endocrinology, 87(1):151-155, 1970.

60. Ryan, K.J.: Ovarian function and gynecologic endocrinopathies. Int. J. Gynaecol. Obstet., 8(4):608-612, 1970.

61. Davies, I.J., Ryan, K.J. and Petro, Z.: Estrogen synthesis by adrenal-placental tissues of the sheep and the iris monkey in vitro. Endocrinology, 86(6):1457-1459, 1970.

62. Ainsworth, L. and Ryan, K.J.: Steroid hormone transformations by endocrine organs from pregnant mammals. VI. The conversion of Δ^4-androstene-3, 17-dione to estrogens by goat placental preparations in vitro. Steroids, 16(5):553-559, 1970.

63. Yen, S.S.C., Vela, P. and Ryan, K.J.: Effect of clomiphene citrate in polycystic ovary syndrome: Relationship between serum gonadotrophin and corpus luteum function. J. Clin. Endocrinol. Metab., 31:7-13, 1970.

64. Meigs, R.A. and Ryan, K.J.: Enzymatic aromatization of steroids. I. Effects of oxygen and carbon monoxide on the intermediate steps of estrogen biosynthesis. J. Biol. Chem., 246(1):83-87, 1971.

65. Ryan, K.J.: Endocrine control of gestational length. Am. J. Obstet. Gynecol., 109(2):299-306, 1971.

66. Satoh, K. and Ryan, K.J.: Adenyl cyclase in the human placenta. Biochim. Biophys. Acta, 244:618-624, 1971.

67. Naftolin, F., Ryan, K.J. and Petro, Z.: Aromatization of androstenedione by the diencephalon. J. Clin. Endocrinol. Metab., 33:368-370, 1971.

68. Naftolin, F., Ryan, K.J. and Petro, Z.: Aromatization of androstenedione by limbic system tissue from human foetuses. J. Endocrinol., 51:795-796, 1971.

69. Ryan, K.J.: Cyclic ovarian function and its neuroendocrine control. In Textbook of Obstetrics and Gynecology. Ed.: D. Danforth. New York, Harper and Row, pp. 123-137, 1971.

70. Ryan, K.J. and Gibson, D.C.: Menopause and Aging. Bethesda, U. S. Department of Health, Education and Welfare, Publication No. (NIH) 73-319. (Summary report and selected papers from a research conference on Menopause and Aging, May 23-26, 1971, Hot Springs, Arkansas.)

71. Reid, D.E., Ryan, K.J. and Benirschke, K.: Principles and Management of Human Reproduction. Philadelphia, W. B. Saunders Co., 1972.

72. Naftolin, F., Ryan, K.J. and Petro, Z.: Aromatization of androstenedione by the anterior hypothalamus of adult male and female rats. Endocrinology, 90:295-298, 1972.

73. Davies, I.J. and Ryan, K.J.: The uptake of progresterone by the uterus of the pregnant rat in vivo and its relationship to cytoplasmic progesterone-binding protein. Endocrinology, 90(2):507-515, 1972.

74. Davies, I.J. and Ryan, K.J.: Comparative endocrinology of gestation. Vitam. Horm., 30:223-279, 1972.

75. Satoh, K. and Ryan, K.J.: Prostaglandins and their effect on human placental adenyl cyclase. J. Clin. Invest., 51(2):456-458, 1972.

76. Ryan, K.J.: Estrogen and the menopause. Medical World News Review Series, Obstetrics and Gynecology, pp. 73-75, 1972.

77. Yen, S.S.C., Rebar, R., VandenBerg, G., Naftolin, F., Ehara, Y., Engblom, S., Ryan, K.J., Benirschke, K., Rivier, J., Amoss, M. and Guillemin, R.: Synthetic luteinizing hormone-releasing factor: A potent stimulator of gonadotropin release in man. J. Clin. Endocrinol. Metab., 34(6):1108-1111, 1972.

78. Ryan, K.J., Naftolin, F., Reddy, V., Flores, F. and Petro, Z.: Estrogen formation in the brain. Am. J. Obstet. Gynecol., 114(4):454-460, 1972.

79. Ehara, Y., Ryan, K.J. and Yen, S.S.C.: Insensitivity of synthetic LRF in LH-release of rhesus monkey. Contraception, 6(6):465-478, 1972.

80. Kirshen, E., Naftolin, F. and Ryan, K.J.: Intravenous prostaglandin $F_{2\alpha}$ for the therapeutic abortion. Am. J. Obstet. Gynecol., 113:340-344, 1972.

81. Naftolin, F., Kirshen, E.J. and Ryan, K.J.: Therapeutic abortion utilizing local application of prostaglandin $F_{2\alpha}$. In The Prostaglandins, Clinical Applications in Human Reproduction. Ed.: E. M. Southern. Mt. Kisco, New York, Futura, pp. 423-431, 1972.

82. Naftolin, F., Kirshen, E.J. and Ryan, K.J.: Therapeutic abortion utilizing local application of prostaglandin $F_{2\alpha}$. J. Reprod. Med., 9:437-441, 1972.

83. Rebar, R., Yen, S.S.C., VandenBerg, G., Naftolin, F., Ehara, Y., Engblom, S., Ryan, K.J., Rivier, J., Amoss, M. and Guillemin, R.: Gonadotropin responses to synthetic LRF: Dose-response relationship in men. J. Clin. Endocrinol. Metab., 36(1):10-16, 1973.

84. Ryan, K.J.: Endocrine subspecialization. J. Reprod. Med., 10(1):21-23, 1973.

85. Flores, F., Naftolin, F. and Ryan, K.J.: Aromatization of androstenedione and testosterone by rhesus monkey hypothalamus and limbic system. Neuroendocrinology, 11:177-182, 1973.

86. Shinada, T. and Ryan, K.J.: The in vitro biosynthesis and metabolism of progesterone and estrogens by chimpanzee placental tissue. Steroids, 21(2):233-244, 1973.

87. Davies, I.J. and Ryan, K.J.: The modulation of progesterone concentration in the myometrium of the pregnant rat by changes in cytoplasmic "receptor" protein activity. Endocrinology, 92(2):392-401, 1973.

88. Reddy, V.V.R., Naftolin, F. and Ryan, K.J.: Aromatization in the central nervous system of rabbits: Effects of castration and hormone treatment. Endocrinology, 92(2):589-594, 1973.

89. Flores, F., Naftolin, F., Ryan, K.J. and White, R.J.: Estrogen formation by the isolated perfused rhesus monkey brain. Science, 180:1074-1075, 1973.

90. Ryan, K.J.: Steroid hormones in mammalian pregnancy. In Handbook of Physiology. Ed.: E. Astwood and R. Greep. Bethesda, American Physiological Society, pp. 285-293, 1973.

91. Challis, J.R.G., Davies, I.J. and Ryan, K.J.: The concentration of progesterone, estrone and estradiol-17β in the plasma of pregnant rabbits. Endocrinology, 93:971-976, 1973.

92. Challis, J.R.G., Davies, I.J. and Ryan, K.J.: The relationship between progesterone and prostaglandin F concentrations in the plasma of pregnant rabbits. Prostaglandins, 4:509-516, 1973.

93. Davies, I.J. and Ryan, K.J.: Glucocorticoid synthesis from pregnenolone by sheep fetal adrenals in vitro. J. Endocrinol., 58:485-491, 1973.

94. Ryan, K.J. (Ed.): Obstetrical endocrinology. Clin. Obstet. Gynecol., 16:23-165, 1973.

95. Yen, S.S.C., Rebar, R., VandenBerg, G., Naftolin, F., Ehara, Y., Ryan, K.J. and Guillemin, R.: Clinical studies with synthetic LRF (sLRF). In Hypothalamic Hypophysiotrophic Hormones. Ed.: C. Gual and E. Rosemberg. Amsterdam, Excerpta Medica, pp. 217-229, 1973.

96. Ryan, K.J. and Hopper, B.: Comparative biosynthesis and metabolism of steroid hormones in primates. In Advances in Primatology, Vol. 2. Ed.: W. P. Luckett, C. Noback and W. Montagna. New York, Appleton-Century-Crofts, pp. 285-293, 1973.

97. Stubblefield, P.G., Naftolin, F., Frigoletto, F.D. and Ryan, K.J.: Pre-treatment with laminaria tents before mid-trimester abortion with intra-amniotic prostaglandin $F_{2\alpha}$. Am. J. Obstet. Gynecol., 118:284-285, 1974.

98. Reddy, V.V.R., Naftolin, F. and Ryan, K.J.: Conversion of androstenedione to estrone by neural tissues from fetal and neonatal rats. Endocrinology, 94:117-121, 1974.

99. Feder, H.H., Naftolin, F. and Ryan, K.J.: Male and female sexual responses in male rats given estradiol benzoate and 5α-androstan-17β-01-3-one propionate. Endocrinology, 94:136-141, 1974.

100. Challis, J.R.G., Osathanondh, R., Ryan, K.J. and Tulchinsky, D.: Maternal and fetal plasma prostaglandin levels at vaginal delivery and cesarean section. Prostaglandins, 6:281-288, 1974.

101. Ryan, K.J. and Hopper, B.R.: Placental biosynthesis and metabolism of steroid hormones in primates. Contrib. Primat., 3:258-283, 1974.

102. Challis, J.R.G., Davies, I.J., Hendrickx, A.G. and Ryan, K.J.: Prostaglandin F in the peripheral plasma of the rhesus monkey in normal pregnancy and after the administration of dexamethasone and $PGF_{2\alpha}$. Prostaglandins, 6:389-396, 1974.

103. Challis, J.R.F., Davies, I.J. and Ryan, K.J.: The concentrations of progesterone, estrone and 17β-estradiol in the myometrium of the pregnant rabbit, and their relationship to the peripheral plasma steroid concentrations. Endocrinology, 95:160-164, 1974.

104. Davies, I.J., Challis, J.R.G. and Ryan, K.J.: Progesterone receptors in the myometrium of pregnant rabbits. Endocrinology, 95:165-173, 1974.

105. Reddy, V.V., Naftolin, F. and Ryan, K.J.: Steroid 17β oxidoreductase activity in the rabbit central nervous system and adenohypophysis. J. Endocrinol., 62:401-402, 1974.

106. Challis, J.R.G., Davies, I.J., Benirschke, K., Hendrickx, A.G. and Ryan, K.J.: The concentrations of progesterone, estrone, estradiol-17β in the peripheral plasma of the rhesus monkey during the final third of gestation and after the induction of abortion with $PGF_2\alpha$. Endocrinology, 95:457-553, 1974.

107. Challis, J.R.G., Porter, D.G. and Ryan, K.J.: The effects of prostaglandin $F_2\alpha$ and ovariectomy on the peripheral plasma steroid concentrations and the evolution of uterine activity in the pregnant rabbit. Endocrinology, 95:783-792, 1974.

108. Challis, J.R.G., Erickson, G.F. and Ryan, K.J.: Prostaglandin F production in vitro by granulosa cells from rabbit preovulatory follicles. Prostaglandins, 7:182-193, 1974.

109. Challis, J.R.G., Davies, I.J., Benirschke, K., Hendrickx, A.G. and Ryan, K.J.: The effects of dexamethasone on plasma steroid levels and fetal adrenal histology in the pregnant rhesus monkey. Endocrinology, 95:1300-1305, 1974.

110. Erickson, G.F., Challis, J.R.G. and Ryan, K.J.: A developmental study on the capacity of rabbit granulosa cells to respond to trophic hormones and secrete progesterone in vitro. Develop. Biol., 40:208-224, 1974.

111. Davies, I.J., Siu, J., Naftolin, F. and Ryan, K.J.: Cytoplasmic binding of steroids in brain tissues and pituitary. In Advances in the Biosciences, Vol. 15. Ed.: G. Raspe. Oxford, Pergamon Press/Viewig, pp. 89-103, 1975.

112. Naftolin, F., Ryan, K.J., Davies, I.J., Petro, Z. and Kuhn, M.: The formation and metabolism of estrogens in brain tissues. In Advances in the Biosciences, Vol. 15. Ed.: G. Raspe. Oxford, Pergamon Press/Viewig, pp. 105-121, 1975.

113. Challis, J.R.G., Davies, I.J. and Ryan, K.J.: The effects of dexamethasone and indomethacin on the outcome of pregnancy in the rabbit. J. Endocrinol., 64:363-370, 1975.

114. Challis, J.R.G., Davies, I.J., Benirschke, K., Hendrickx, A.G. and Ryan, K.J.: The effects of dexamethasone on the peripheral plasma concentrations of androstenedione, testosterone, and cortisol in the pregnant rhesus monkey. Endocrinology, 96:185-192, 1975.

115. Makris, A. and Ryan, K.J.: Progesterone, androstenedione, testosterone, estrone, estradiol synthesis in hamster ovarian follicle cells. Endocrinology, 96:694-701, 1975.

116. Canick, J.A. and Ryan, K.J.: The inhibition of 16α-hydroxy-testosterone aromatization by carbon monoxide. Biochem. Biophys. Res. Commun., 63:496-501, 1975.

117. Nimrod, A. and Ryan, K.J.: Aromatization of androgens by human abdominal and breast fat tissue. J. Clin. Endocrinol. Metab., 40:367-372, 1975.

118. Davies, I.J., Naftolin, F., Ryan, K.J. and Siu, J.: A specific high-affinity, limited-capacity estrogen binding component in the cytosol of human fetal pituitary and brain tissues. J. Clin. Endocrinol. Metab., 40:909-912, 1975.

119. Davies, I.J., Naftolin, F., Ryan, K.J. and Siu, J.: Estradiol receptors in the pituitary and anterior hypothalamus of the rat: Measurement by agar gel electrophoresis. Steroids, 25:591-609, 1975.

120. Davies, I.J., Naftolin, F., Ryan, K.J., Fishman, J. and Siu, J.: The affinity of catechol estrogens for estrogen receptors in the pituitary and anterior hypothalamus of the rat. Endocrinology, 97:554-557, 1975.

121. Erickson, G.F. and Ryan, K.J.: The effects of LH/FSH, dibutyryl cyclic AMP and prostaglandin on the production of estrogens by rabbit granulosa cells in vitro. Endocrinology, 97:108-113, 1975.

122. Morishita, H., Naftolin, F., Todd, R.B., Wilen, R., Davies, I.J. and Ryan, K.J.: Lack of effect of dihydrotestosterone on serum luteinizing hormone in neonatal female rats. J. Endocrinol., 67:139-140, 1975.

123. Naftolin, F., Morishita, H., Davies, I.J., Todd, R., Ryan, K.J. and Fishman, F.: 2-hydroxyestrone induced rise in serum luteinizing hormone in the immature male rat. Biochem. Biophys. Res. Commun., 84:905-910, 1975.

124. Naftolin, F., Ryan, K.J., Davies, I.J., Reddy, V.V., Flores, F., Petro, Z., White, R.J., Takaoka, Y. and Wolin, L.: The formation of estrogens by central neuroendocrine tissues. Recent Prog. Horm. Res., 31:295-319, 1975.

125. Stubblefield, P.G., Naftolin, F., Frigoletto, F. and Ryan, K.J.: Laminaria augmentation of intraamniotic prostaglandin $F_{2\alpha}$ for midtrimester pregnancy termination. Prostaglandins, 10:413-422, 1975.

126. Naftolin, F. and Ryan, K.J.: The metabolism of androgens in central neuroendocrine tissues. In Hormonal Steroids, Proceedings of the IVth International Congress on Hormonal Steroids. J. Steroid Biochem., 6:993-997, 1975.

127. Ryan, K.J.: The legitimacy of a diverse society. J.A.M.A., 233:781, 1975.

128. Tulchinsky, D., Frigoletto, F., Ryan, K.J. and Fishman, J.: Plasma estetrol as an index of fetal well-being. J. Clin. Endocrinol. Metab., 40(4):560-567, 1975.

129. Ryan, K.J.: Biosynthesis and metabolism of ovarian steroids. In Progress in Infertility. Second Edition. Eds.: S. J. Behrman and R. W. Kistner. Boston, Little, Brown and Co., pp. 281-297, 1975.

130. Nimrod, A., Erickson, G.F. and Ryan, K.J.: A specific FSH receptor in rat granulosa cells: Properties of binding in vitro. Endocrinology, 98:56-64, 1976.

131. Stubblefield, P.G., Naftolin, F., Lee, E.Y., Frigoletto, F.D. and Ryan, K.J.: Combination therapy for midtrimester abortion: Laminaria and analogues of prostaglandins. Contraception, 13(6):723-720, 1976.

132. Fishman, J., Naftolin, F., Davies, I.J., Ryan, K.J. and Petro, Z.: Catechol estrogen formation by the human fetal brain and pituitary. J. Clin. Endocrinol. Metab., 42:177-180, 1976.

133. Naftolin, F., Ryan, K.J. and Davies, I.J. (Eds.): Subcellular Mechanisms in Reproductive Neuroendocrinology. Amsterdam, Elsevier, 1976.

134. Davies, I.J., Naftolin, F., Ryan, K.J. and Siu, J.: Specific binding of steroids by neuroendocrine tissues. In Subcellular Mechanisms in Reproductive Neuroendocrinology. Eds.: F. Naftolin, K. J. Ryan and I. J. Davies. Amsterdam, Elsevier, pp. 263-275, 1976.

135. Davies, I.J., Yoshinaga, K. and Ryan, K.J.: The effects of combined dexamethasone and indomethacin treatment on the outcome of pregnancy in the rabbit. Biol. Reprod., 15:551-554, 1976.

136. Osathanondh, R., Canick, J., Ryan, K.J. and Tulchinsky, D.: Placental sulfatase deficiency: A case study. J. Clin. Endocrinol. Metab., 43:208-214, 1976.

137. Canick, J.A. and Ryan, K.J.: Cytochrome P-450 and the aromatization of 16α-hydroxytestosterone and androstenedione by human placental microsomes. Mol. Cell. Endocrinol., 6:105-115, 1976.

138. Ryan, K.J.: Estrogens and atherosclerosis. Clin. Obstet. Gynecol., 19:805-815, 1976.

139. Erickson, G.F. and Ryan, K.J.: Spontaneous maturation of oocytes isolated from ovaries of immature hypophysectomized rats. J. Exp. Zool., 195:153-158, 1976.

140. Erickson, G.F. and Ryan, K.J.: Stimulation of testosterone production in isolated rabbit thecal cells by LH/FSH, dibutyryl cyclic AMP, $PGF_{2\alpha}$ and PGE_2. Endocrinology, 99:452-458, 1976.

141. Challis, J.R.G., Naftolin, F., Davies, I.J., Ryan, K.J. and Lanman, T.: Endogenous steroids in neuroendocrine tissues. In Subcellular Mechanisms in Reproductive Neuroendocrinology. Eds.: F. Naftolin, K. J. Ryan and I. J. Davies. Amsterdam, Elsevier, pp. 247-261, 1976.

142. Naftolin, F., Ryan, K.J. and Davies, I.J.: Androgen aromatization by neuroendocrine tissues. In Subcellular Mechanisms in Reproductive Neuroendocrinology. Eds.: F. Naftolin, K. J. Ryan and I. J. Davies. Amsterdam, Elsevier, pp. 347-355, 1976.

143. Schiff, I., Wilson, E., Newton, R., Shane, J., Kates, R., Ryan, K.J. and Naftolin, F.: Serum luteinizing hormone, follicle-stimulating hormone, and testosterone responses to gonadotropin-releasing factor in males with varicoceles. Fertil. Steril., 27(9):1059-1061, 1976.

144. Canick, J.A., Vaccaro, D.E., Ryan, K.J. and Leeman, S.E.: The aromatization of androgens by primary monolayer cultures of fetal rat hypothalamus. Endocrinology, 100:250-253, 1977.

145. Callard, G.V., Petro, Z. and Ryan, K.J.: Identification of aromatase in the reptilian brain. Endocrinology, 100:1214-1218, 1977.

146. Makris, A. and Ryan, K.J.: Aromatase activity of isolated and recombined hamster granulosa cells and theca. Steroids, 29:65-72, 1977.

147. Erickson, G.F., Challis, J.R.G. and Ryan, K.J.: Production of prostaglandin F by rabbit granulosa cells and thecal tissues. J. Reprod. Fertil., 49:133-134, 1977.

148. Ryan, K.J.: New concepts in hormonal control of parturition. Biol. Reprod., 16:88-94, 1977.

149. Ryan, K.J.: The reproductive system. Chapter 18 in The Horizons of Health. Eds.: H. Wechsler, J. Gurin and G. F. Cahill, Jr. Cambridge and London, Harvard University Press, pp. 268-277, 1977.

150. Callard, G.V. and Ryan, K.J.: Gonadotropin action and androgen synthesis in enzyme dispersed testicular cells of the turtle (Chrysemys picta). Gen. Comp. Endocrinol., (In press).

151. Barbieri, R.L., Canick, J.A., Makris, A., Todd, R.B., Davies, I.J. and Ryan, K.J.: Danazol inhibits steroidogenesis. Fertil. Steril. (In press).

A B S T R A C T S

A1. Ryan, K.J.: Steroid 21-hydroxylation by adrenal cell fractions. Fed. Proc., 15:344, 1956.

A2. Ryan, K.J.: Steroid ring A aromatization by human placental microsomes. Fortieth Annual Meeting, Endocrine Society, June 1958.

A3. Ryan, K.J.: Conversion of androgens to estrogens by human placental microsomes. Fed. Proc., 17:138, 1958.

A4. Ryan, K.J.: Metabolism of 16-ketosterone by human placenta. Endocrinology, 66:491-494, 1960.

A5. Magendantz, H.G. and Ryan, K.J.: Isolation of a new estriol precursor. Fed. Proc., 23:275, 1964.

A6. Meigs, R.A. and Ryan, K.J.: 16α-hydroxysteroid dehydrogenase of rat kidney. Fed. Proc., 24(2):414, 1965.

A7. Ryan, K.J.: Metabolism of steroids by the isolated granulose and theca of the human ovarian follicle. Excerpta Medica International Congress Series No. 99, VIth Pan American Congress on Endocrinology, Abstract 370, Mexico, D.F., October, 1965.

A8. Naftolin, F., Ryan, K.J., Flores, F., Petro, Z. and Reddy, V.: Aromatization of androgens by neuroendocrine tissues in humans and other species. Fourth International Congress of Endocrinology, Washington, D.C., 1972.

A9. Reddy, V.V., Ryan, K.J. and Naftolin, F.: Aromatization in the central nervous system of rabbits. Fed. Proc., 31(2): 429 Abs. (Abstract #1190), 1972.

A10. Challis, J.R.G., Davies, I.J., Benirschke, K., Hendrickx, A.G. and Ryan, K.J.: Plasma concentrations of progesterone, oestrogens and PGF preceding parturition in the rhesus monkey and the effects of administered $PGF_{2\alpha}$ and dexamethasone. Endocrine Society, Atlanta, Abstract #181, June, 1974.

A11. Canick, J.A. and Ryan, K.J.: Cytochrome P-450 and the aromatization of 16α-hydroxytestosterone and androstenedione. Endocrine Society, 57th Annual Meeting, June, 1975.

A12. Challis, J.R.G., Davies, I.J., Benirschke, K., Hendrickx, A.G. and Ryan, K.J.: Effects of dexamethasone on plasma steroid concentrations and foetal adrenal histology in the pregnant rhesus monkey. J. Endocrinol., 65:40-41, 1975.

A13. Erickson, G.F., Challis, J.R.G. and Ryan, K.J.: The differentiation of rabbit granulosa cells. Mexico, Excerpta Medica Foundation (In press).

STATEMENT OF KENNETH J. RYAN, M.D., CHAIRMAN, NATIONAL COMMISSION FOR THE PROTECTION OF HUMAN SUBJECTS OF BIOMEDICAL AND BEHAVIORAL RESEARCH, PROFESSOR OF OBSTETRICS AND GYNECOLOGY, HARVARD MEDICAL SCHOOL, BOSTON HOSPITAL FOR WOMEN

Dr. RYAN. Thank you very much.

I apologize for being late. And I am sorry I did not hear my colleagues speak. I will try to be brief, and hope I don't go over previously plowed ground.

I would like to start by saying that the National Commission for the Protection of Human subjects of Biomedical and Behavioral Research was formed under Public Law 93–348 and part of its mandate is to determine "the ethical principles underlying the conduct of research on human subjects". The Commission's complete report has not as yet been prepared and any testimony presented today on ethical issues is the responsibility solely of the speaker and not of the Commission.

I am not speaking for the Commission. I want to acknowledge, however, that I have had available resource material prepared by the staff and by outside contractors for the Commission.

Mr. THORNTON. Dr. Ryan, if I may, let me suggest that we make this paper part of the record at this point in its entirety and then you may summarize it or highlight it as you choose.

Dr. RYAN. Thank you. I will do that.

[The prepared statement of Dr. Ryan follows:]

Testimony Before Subcommittee on Science, Research

and Technology of the

Committee on Science and Technology

U.S. House of Representatives

September 8, 1977

by

Kenneth J. Ryan, M.D., Chairman
National Commission for the Protection
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Ethical Issues in Scientific Research

INTRODUCTION:

The National Commission for the Protection of Human subjects of Biomedical and Behavioral Research was formed under Public Law 93-348 and part of its mandate is to determine "the ethical principles underlying the conduct of research on human subjects". The Commission's complete report has not as yet been prepared and any testimony presented today on ethical issues is the responsibility solely of the speaker and not of the Commission. I do wish to acknowledge the availability of resource material prepared by staff and outside contractors for the Commission, all of which are public documents.

Ethical Bases for Political Decision-Making:

Ethics is a system of moral principles or values usually distinctive for a given group or culture. In our own pluralistic society composed of diverse groups and subcultures, there is in fact no single system of ethics. This was highlighted for the National Commission when nine ethicists each wrote papers on Fetal Research that presented a wide spectrum of what in their minds was "ethically" permissable. Fortunately, the Commission ultimately found a middle ground.

This limitation of ethics in solving problems was stated clearly by Alsadair MacIntyre in an essay for the Commission: "disagreements among moral philosophers parallel and reflect the disagreements among moral agents themselves (common man); moral philosophers turn out to be merely the

more articulate and systematic examples of moral agents; philosophy cannot as of now resolve these rivalries in any logically compelling way.

Although ethicists even argue about what constitutes an ethical principle, it includes such characteristics as being: prescriptive, universal, over-riding, of material or social content and supportable by a certain method of reasoning.

The Commission is currently working with three such principles: respect for persons, justice, and beneficence that are applicable to not only research on human subjects but research in general. MacIntyre, however, emphasizes what should be apparent to us all: "that the accepted maxims of morality (ethical principles) by themselves will yield no answer (just as for a judge, the crucial precedent-setting cases of judgement are those in which the accepted laws give no answer)".

While the ethicist may help with the enunciation of principles or a logical approach to problem-solving, he (or she) is not necessarily morally superior in the application of "rules" to conduct.

It is fitting that in this political setting, one should ask ethical questions about what is good or what is right, but it would be foolhardy to expect more than guidance from ethics in the process.

Public Issues in Recombinant DNA Research:

Recombinant DNA technology is a major step toward furthering knowledge in cellular regulation and function, allowing as it does the insertion of foreign genetic material into test organisms.

The new genetic combinations might be fashioned to do predictable (and perhaps unpredictable) feats such as the manufacture of scarce hormones, enzymes, immune substances, and other proteins of use to man. It provides a basis for understanding the genetic derangement of cancer, for possible creation of novel nitrogen-fixing or photosynthetic processes or scavanger organisms to clear up oil spills. At the very least, the technology offers hope for a better understanding of the basic life processes, a point on which most observers agree.

The benefit to be derived from the research aside from its intrinsic value in furthering knowledge is, however, one major factor in the debate when questions of potential hazards arise. The judgements range from euphoria about the possibilities for application to human needs to a general cynicism about the value of such scientific endeavors when there are more immediate social, environmental, and health problems.

On balance, one would have to conclude that the research is new, powerful and could result in beneficial applications.

Such a conclusion would clearly have to be based upon reasonable expectations and "value" judgements.

The second major issue in DNA-recombinant research is its potential for immediate hazards. This includes the possible creation of dangerous hybrid organisms with capacity to infect man or animals, to induce cancers or to disrupt the natural environment. Fears of this prompted the original self-imposed moratorium by scientists, the many conferences, and the belated public outcry about safety, not only to laboratory workers, but to people at large. The "Andromeda Strain", recently a popular novel and movie, became a metaphorical reality. Scientists responded to these concerns with guidelines for physical containment research facilities following the known models of contagious disease research and the decontamination procedures following space travel. In addition, biological containment was introduced by the attempt to create test organisms that were not capable of propagation outside the laboratory. The weight of years of experience in Communicable Disease and germ warfare laboratories has been mobilized for reassurance. In addition, recent experience and current experiments have converted some doubters.

Many opponents of DNA research are still not satisfied with the record, with the guidelines or current solutions for dealing with possible risks. They are not happy with either physical containment and very dubious about biological

containment. They quote accidents in industry, and in nuclear and infectious disease facilites as a basis for mistrust of the systems proposed. There are renowned scientists on both sides of the argument.

On balance, there is a potential risk admitted by both advocates and opponents of DNA research. The argument is in the probability and extent of harm and whether the anticipated benefits can justify any risk-taking.

A final major issue with metaphysical dimensions is the question of whether the knowledge gained by DNA research or the application to which it could be put is so disruptive of evolution and of man's perception of himself and the world that the seeking of such knowledge should cease or proceed with extreme caution. Sinsheimer has been the most prominent proponent of this philosophy. This is echoed by the statement of the National Conference of Catholic Bishops, "that we are not obliged to accomplish everything through science whatever risk or at the price of assaulting time-honored values. Ethical constraints might slow down or even preclude some scientific advances".

Central to all three issues is the question of who shall decide how to proceed and in what forum. Congressional hearings and local jurisdictions have now placed the problem in the main stream of our political process.

Current Status of Recombinant DNA Research:

The Director of NIH has issued Guidelines Involving Recombinant DNA to establish controlled conditions for the conduct of experiments and has prepared a draft environmental impact statement. The University of Michigan, after much debate, and the city of Cambridge, after issuing a moratorium, have allowed DNA research to proceed. Several state legislatures are preparing bills to regulate research and several bills are pending before the Congress. Industry has been divided on the question of voluntary compliance with NIH Guidelines, and the need for some ordering of the regulatory processes seems apparent. Much debate has centered around the late and insufficient inclusion of the general public in these matters, a situation now certain be be rectified.

Ethical Considerations in Recombinant DNA Research:

Recombinant DNA research has received much publicity, but is only one symptom of a general public cynicism and mistrust in the "good" of scientific technology and the priority-setting of the government and large institutions that control our daily lives. Similar arguments have been advanced against nuclear technology, space exploration, and the pervasive computer and information systems that invade one's privacy.

There has been a growing desire to head off application of technology by thwarting its development. "Brave New World" seems too close for comfort.

The ethical dimension to any consideration of public

policy in this area should be a rational review of facts and issues at hand, attention to the over-riding applicable principles that are basic to our society and the selection of reasonable options for a just policy decision.

This would be preferable to the rancor of the public debates that have typified the DNA problem thus far. The issues for recombinant DNA research are:

1.) potential for benefit
2.) hazards in conduct of the research
3.) deleterious consequences of interfering with natural processes and opportunities for misuse and social repression.

A central ethical principle which we as a people have institutionalized is repect for the individual. This includes freedom of thought and freedom of inquiry. Its limits should properly be only infringements upon the rights and freedoms of others, including risks to others. Respect for individuals would tend to support academic enterprise, and we have customarily placed the burden of proof on any attempt at restriction of individual freedom. Knowledge can also be sought to do good and is consonant with a utilitarian or beneficence principle as well.

We should make no mistake that restriction of personal freedom and free inquiry typically occurs in societies such as Russia or China where personal values are subservient to some collective "good". The deleterious effects on science,

academic life and personal freedom are too well known to bear repeating here.

The principle of justice would require that the apportionment of resources and the application of knowledge be fair and equitable. Our society has yet to achieve this in many spheres including health and medicine, and this is a source of distrust in the research enterprise.

The inclusion of the general public in priority and decision making would serve both respect for individuals and justice, and the mechanisms for this in a free society are generally available and desirable. The Freedom of Information Act, popular elections, public hearings, and the use of private citizens on advisory boards can and do serve these ends.

Respect for persons and beneficence require that harms be minimized and thus the same principles that foster inquiry temper its free expression. To this extent, a risk-benefit calculus is part of much policy decision making. Valid value judgements can be made only when sufficient factual information is available. The bitter debates and public posturing in the DNA controversy have confused the issue over what is known and what is conjecture. The likely outcome will be to proceed with caution.

The call for a moratorium on seeking new knowledge is probably the most troubling of the issues in DNA research, and the substance which makes for profound ethical arguments.

The problem is compounded by the fact that the seeking of new knowledge via recombinant techniques already involves an application which some fear will let the genie out of the bottle, analagous to the splitting of the atom. On balance, these concerns cannot be simply dismissed, but there probably is an ethical prescription for their solution. Study of the history of human endeavor thus far might or might not encourage people to go on probing the unknown. There have always been thosewho would turn back to a more innocent, trouble-free world, but if there is any evidence for an ethical or natural imperative for man, it must be to open closed doors, to ask questions. To do otherwise would be to change the nature of man.

I personally believe the NIH guidelines provide a sound basis for proceeding with DNA research. Legislation to cover non-NIH funded activities seems appropriate. An ethical commission could provide a forum for further rational discourse and guidance.

Dr. RYAN. I would like to speak about something that may not have been covered thus far. And that is the ethical basis for political decisionmaking.

Ethics is a system of moral principles or values usually distinctive for a given group or culture. In our own pluralistic society composed of diverse groups and subcultures, there is in fact no single system of ethics. This was highlighted for the National Commission when nine ethicists each wrote papers on fetal research that presented a wide spectrum of what in their minds was ethically permissible. Fortunately, the Commission ultimately found a middle ground.

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> Disagreements among moral philosophers parallel and reflect the disagreements among moral agents themselves (common man); moral philosophers turn out to be merely the more articulate and systematic examples of moral agents; philosophy cannot as of now resolve these rivalries in any logically compelling way.

Although ethicists even argue about what constitutes an ethical principle, it includes such characteristics as being: prescriptive (that is, telling you what to do, although not always how), universal, overriding, of material or social content and supportable by a certain method of reasoning. The latter may be contentious.

The Commission is currently working with three such principles: respect for persons, justice, and beneficence that are applicable to not only research on human subjects but research in general. MacIntyre, however, emphasizes what should be apparent to us all:

> The accepted maxims of morality (ethical principles) by themselves will yield no answer (just as for a judge, the crucial precedent-setting cases of judgment are those in which the accepted laws give no answer).

While the ethicist may help with the enunciation of principles or logical approach to problem solving, he (or she) is not necessarily morally superior in the application of "rules" to conduct.

It is fitting that in this political setting, one should ask ethical questions about what is good or what is right, but it would be foolhardy to expect more than guidance from ethics in the process.

The public issues in recombinant DNA research revolve around benefits and hazards. I am sure the committee has heard a good deal about all of the good things that genetic recombinant DNA work can do. And I will not repeat them here. I think at the very least the technology offers hope for a better understanding of basic life processes: and I think everyone will agree on that. It is perhaps the most conservative thing I could say about it.

The benefit to be derived from it, however, is part of the debate when a question of potential hazards arise. The judgments range from euphoria about the possibilities for application to human needs to a general cynicism about the value of such scientific endeavors when there are more immediate social, environmental, and health problems. And on balance, I would have to conclude that the research is new, powerful, and could result in beneficial applications. But that is, in fact, a value judgment, based on reasonable expectations.

The hazards have been mentioned in the past: They include the possible creation of hybrid organisms with the capacity to do such things as create cancer and disrupt the natural environment. And it

was information of this that prompted the scientists themselves to start the moratoriums and the conferences and the public outcry about safety. And you will note that an "Andromeda Strain" now has become a metaphorical reality.

The response to this has been physical containment procedures, and also, biological containment. The weight of years of experience of communicable disease and germ warfare laboratories has been mobilized for reassurance. There are still people who are dubious and not satisfied. And distinguished scientists on both sides of the argument quote the same source material, for instance, to suggest that it is either safe or dangerous. They quote accidents in industry, nuclear, and infectious disease facilities, and so on.

On balance, there is potential risk admitted by both advocates and opponents of DNA research. The argument is in the probability and extent of harm and whether the anticipated benefits can justify any risktaking.

And the final major issue, which I think is sort of a metaphysical one—in fact Dr. Thomas referred to it—is the question of whether the knowledge gained by DNA research or the application to which it could be put is so disruptive of evolution and of man's perception of himself and the world that the seeking of such knowledge should cease or proceed with extreme caution. Sinsheimer has been the most prominent proponent of this philosophy. This is echoed by the statement of the National Conference of Catholic Bishops, "that we are not obliged to accomplish everything through science whatever risk or at the price of assaulting time-honored values. Ethical constraints might slow down or even preclude some scientific advances." I am quoting that out of context, they have a lot of very well balanced statements to make about the subject but even there this question is raised.

Central to all three issues is the question of who shall decide how to proceed and in what forum. Congressional hearings and local jurisdictions have now placed the problem in the mainstream of our political process.

You all know the current status of recombinant DNA research—but I just think it ought to be highlighted that there are guidelines in place created by the Director of NIH and a draft statement on environmental impact has been prepared.

The University of Michigan, after much debate, and the city of Cambridge, after issuing a moratorium, have allowed DNA research to proceed. Several State legislatures are preparing bills to regulate research and several bills are pending before the Congress. Industry has been divided on the question of voluntary compliance with NIH guidelines, and the need for some ordering of the regulatory processes seems apparent. Much debate has centered around the late and insufficient inclusion of the general public—and this situation, I think, will certainly be rectified now.

You have asked some questions about the ethical considerations in recombinant DNA research. And I will try and outline them briefly.

Recombinant DNA research has received much publicity, but is only one symptom of a general public cynicism and mistrust in the "good" of scientific technology and the priority-setting of the Government and large institutions that control our daily lives. Similar arguments have been advanced against nuclear technology, space exploration, and the

pervasive computer and information systems that invade one's privacy.

There has been a growing desire to head off application of technology by thwarting its development. "Brave New World" seems too close for comfort.

The ethical dimension to any consideration of public policy in this area should be a rational review of facts and issues at hand, attention to the overriding applicable principles that are basic to our society and the selection of reasonable options for a just policy decision.

This would be preferable to the rancor of the public debates that have typified the DNA problem thus far. The issues for recombinant DNA research are:

1. Potential for benefit.
2. Hazards in conduct of the research.
3. Deleterious consequences of interfering with natural processes and opportunities for misuse and social repression.

A central ethical principle which we as a people have institutionalized is respect for the individual. This includes freedom of thought and freedom of inquiry. Its limits should properly be only infringements upon the rights and freedoms of others, including risks to others. Respect for individuals would tend to support academic enterprise, and we have customarily placed the burden of proof on any attempt at restriction of individual freedom. So one asks, where does the burden of proof lie? In our society it has been on those who would restrict individual freedom. Knowledge can also be sought to do good and is consonant with a utilitarian or beneficience principle as well.

We should make no mistake that restriction of personal freedom and free inquiry typically occurs in societies such as Russia or China where personal values are subservient to some collective "good." The deleterious effects on science, academic life, and personal freedom are too well known to bear repeating here.

The principle of justice would require that the apportionment of resources and the application of knowledge be fair and equitable. Our society has yet to achieve this in many spheres including health and medicine, and this is a source of distrust in the research enterprise.

The inclusion of the general public in priority and decisionmaking would serve both respect for individuals and justice, and the mechanisms for this in a free society are generally available and desirable. The Freedom of Information Act, popular elections, public hearings, and the use of private citizens on advisory boards can and do serve these ends.

Respect for persons and beneficence require that harms be minimized and thus the same principles that foster inquiry temper its free expression. To this extent, a risk-benefit calculus is part of much policy decisionmaking. Valid value judgments can be made only when sufficient factual information is available. The bitter debates and public posturing in the DNA controversy have confused the issue over what is known and what is conjecture. The likely outcome will be to proceed with caution.

The call for a moratorium on seeking new knowledge is probably the most troubling of the issues in DNA research, and the substance which makes for profound ethical arguments.

The problem is compounded by the fact that the seeking of new knowledge via recombinant techniques already involves an applica-

tion which some fear will let the genie out of the bottle, analogous to the splitting of the atom. On balance, these concerns cannot be simply dismissed, but there probably is an ethical prescription for their solution. Study of the history of human endeavor thus far might or might not encourage people to go on probing the unknown. There have always been those who would turn back to a more innocent, trouble-free world, but if there is any evidence for an ethical or natural imperative for man, it must be to open closed doors, to ask questions. To do otherwise would be to change the nature of man.

I personally believe the NIH guidelines provide a sound basis for proceeding with DNA research. Legislation to cover non-NIH funded activities seems appropriate. An ethical commission could provide a form for further rational discourse and guidance. Thank you.

Mr. THORNTON. Thank you very much, Dr. Ryan.

Your last statement parallels the concluding statement in the article to which I previously referred about the greater danger being not to ask questions or change the basic nature of man in that way.

Of course, what we are really concerned with here is maybe a balancing of scientific exploration with a sense of practicality and ethical judgments. It has been echoed frequently yesterday and today that when you approached the unknown that you should do so with caution. That. it seems to me, is almost axiomatic. With the nature of man being what it is, we should not ask that we turn aside and refuse to at least examine the boundaries of the area that we are concerned about. Nor should we plunge into it, as though to dive into a pool of water without first ascertaining how deep it is.

We are facing in this area of research many unknowns—and prudence, it would seem to me, dictates that we exercise great caution. This is not only true with regard to the scientific community exploring what it shall do with this new dimension of science which explores the very essence of life, but it might also be applicable to those of us in Congress who are dealing with the question of when Congress should regulate, and to what degree it should regulate, the activities of scientists in exploring the world. Perhaps the same cautionary guidelines that should be applied to scientific inquiry should also be applied to congressional regulation.

I wonder if I could get any comment on that observation.

Dr. RYAN. I think the things that we have been talking about with respect to ethics applies to all of human conduct, and sometimes more importantly in areas other than science.

Dr. GLASS. Mr. Chairman, I have a comment, which is raised in particular by Dr. Ryan's remark in the next to the last paragraph of what he presented to us. That some persons fear that the recombinant DNA techniques will let the genie out of the bottle is analogous to splitting the atom—I would like to draw an analogy and say that in my own view the genie is already out of the bottle. We know enough in this area in basic science for the technological applications to proceed.

In other words, I think we are the precise stage of development in the exploration of these aspects of the nature of life as the nuclear scientists were when all of the original experiments on the splitting of the atom had been done and the United States and other great nations were at war with Hitler Germany—and when they wrote that famous

letter from Einstein and others to President Roosevelt suggesting that the United States could and ought to go ahead with the development of a nuclear bomb.

What remains to be done in this area of recombinant DNA research falls to a very considerable extent not into the area of basic science about which Dr. Thomas talked so eloquently; but into the area of applied science. And here the regulatory responsibility of the Congress is very clear. Regulation can be achieved simply by the appropriation of large funds for the development of the technology, or the refusal to appropriate large sums for the development of the technology.

Mr. THORNTON. Dr. Glass, I have no great difficulty with the idea that it is entirely appropriate for Congress to decide what scientific research it will fund and what research it will not fund. I have a little more difficulty with the question of whether Congress should set out to determine for other institutions, individuals, and universities, and other organizations of people, what research they should or should not engage in. I think there is a difference between that and Congress' self-assessment of what it will fund.

Go ahead.

Dr. GLASS. I think I have made my point. I would add just this, that I don't agree at all with the statement that is sometimes made, that because we have acquired the power to do something it will necessarily follow that we will go ahead and do it. In this question of the manipulation of human nature by genetic means, which is the basis of the great fear that many people express about the development of recombinant DNA research, I want to point out that for the best part of this century, and perhaps going back much further, we have had the power through more conventional genetic means of modifying the nature of man, just as we modify the nature of our domestic animals and our cultivated plants, by controlled breeding. But we have not chosen to do that. And I cannot conceive even of a tyrant on Earth who would really undertake to do that. Hitler's efforts in that direction were really very mild and ineffective compared to what he might have done had he really intended to produce a profound change in human characteristics within his people.

And so I think it is a false fear, a bogey fear that says that because we might learn so much that we could change human nature in this way, we will necessarily undertake to do so. At the present time we know so little about the human genetics of the characteristics that we are really fearful of having manipulated—personality characteristics, and intelligence—that it would be very difficult indeed to proceed technologically on the basis of a gene by gene kind of alteration rather than a wholesale kind of manipulation, such as could be done by controlled breeding.

I think that a good deal of the hysteria in the discussion of the recombinant DNA research is consequently misplaced.

Mr. THORNTON. I thank you for that fine response.

It seems to me that there is, however, a proper role for society, acting through the Government or through other institutions short of government, to engage in self-regulation, and to determine what are unacceptable risks. I offer this as a counterpoint to what I just said about the danger of government regulating private research, and particularly in a field such as research on human subjects. We

have a clear cut example of certain types of research being unacceptable, presumably, to society. I think it is useful to see exactly how we have explored this question.

Dr. Sorenson suggests that an organization similar to the OTA would not be appropriate for resolving this kind of issue, in part because we don't really know how to make a technology assessment of research. It is difficult enough to make a technology assessment of some applied product of research, much less the unknown results of basic research.

Still to balance the ethical standards of society with the code of behavior of scientists is a problem that deserves attention. I wonder what the thought of the panel is as to whether a commission similar to the Commission on Research on Human Subjects might be an appropriate way to pull together information on something as vital as DNA recombinant research.

Dr. Thomas, I believe you have stated that you didn't much like that idea. But go ahead.

Dr. THOMAS. I really don't, because I don't regard it as a very practical undertaking. I don't know where a commission or committee charged with this large matter would end. It seems to me that it would be confronted by allegations of risk for almost every experiment that I have ever engaged in myself or that I know about going on in science today.

One of my apprehensions about the public debate over the recombinant DNA matter is that I am fearful that the public has gotten the impression that all of our medical science is somehow dangerous, that we have become enormously powerful, that we know almost everything and we are now in a kind of end game. We just need to put some things together. And not enough has been said about the profundity of our ignorance about the nature of humanity, about human consciousness—a great number of totally imponderable, absolutely mystifying problems lie ahead for solution.

And I think most of the work that has been going on in this country and the laboratories that we know about in Western Europe is good, sound science, and it is not going to do anybody any harm at all.

I am afraid, though, that with the atmosphere that has been created in the last several years, false apprehensions about danger and minor degrees of danger, are now being greatly exaggerated.

I would like to add, Mr. Thornton, that I think that system is highly monitored in this country at the present time. There is nothing like the closeness of scrutiny that all applications in research funded by Federal, State, and State-local bodies receive by peer review bodies. I am afraid I do not agree with Dr. Sorenson that scientists are incapable of checking ongoing research for risk.

It has been my experience that scientists are, if anything, more sensitive to genuine risk, and more likely to try to criticize proposed research on the grounds of danger, than anyone else in society. I don't think that their self interest, as Dr. Sorenson seemed to be suggesting, would prevent them from behaving ethically in this regard.

Mr. THORNTON. Dr. Sorenson.

Dr. SORENSON. Yes, if I could respond to two or three points there.

First of all, I don't believe I stated that they were incapable of assessing the risk—in fact, I think I pointed out that it was quite

laudatory that public awareness of the risk in recombinant DNA was first raised by the basic researchers in this field themselves.

And it is not a matter of being incapable, but it is rather an appeal to an ethical principle that when there are risks involved, those people who are put at risk ought to be informed of the nature of the risk, and have some say in whether or not they should be exposed to that risk.

In many respects I see this principle is not dissimilar to, I think, some of the principles underlying the regulations on research involving human subjects. So it is not a matter of scientists being incapable. It is an appeal to an ethical principle and, I think, that if the public became aware of it, there would be less suspicion of scientists and perhaps more willingness to support a variety of scientific undertakings.

It is also the case, I think, with respect to your concern about growing public uneasiness of science, that that may reside in part in public ignorance about what the scientific enterprise is about. I don't think as scientists we have done an adequate job of informing the public about the nature of the science or the uncertainties that we face and the regulatory mechanisms that exist. It is very interesting, if one looks at public attitudinal studies about different institutional sectors in society, that one institutional sector that society expresses its greatest uncertainty and lack of knowledge about is science.

So perhaps we need more education in this realm.

And finally, I too have some mixed reservations, mixed concerns about the establishment of an ethical commission, let's say, in this area. I do think however it would be worth exploring the idea that under conditions of risk, where one is aware of risk in research, somehow the public ought to be informed of this and have some say in it. I think this needs further exploration.

Mr. THORNTON. I think the public, if it perceives that its well-being is at issue, will become involved in research or any other question. It would seem to me to be vital that we find means of providing for education, which was mentioned frequently yesterday, of the public and of policymakers as to what are the risks involved in a particular area.

You mentioned the creation of what would be called certified public scientists.

Yesterday I asked our panelists if they thought it might be useful for scientists to be grouped together in professional associations like lawyers subject to a licensing and disbarment and subject to the canons of ethics, like doctors with the Hypocratic oath, and engineers with their society. Is this what you are referring to?

Dr. SORENSON. No, this idea certainly is not original with me. It has been around now for a period of 2 years. And I believe it appeared first at a New York Academy of Science-Hastings Center conference on recombinant DNA research in 1975.

No, I am not making reference to that type of licensing procedure.

Mr. THORNTON. Are you referring to the licensing of people to do a particular kind of research?

Dr. SORENSON. I am talking about the establishment of a position that would be filled by a person who is a qualified scientist, who has gone through requisite training and who has all other qualifications to look into the issues. When it becomes a question of threat to the

public safety and health, this person can recommend what we do. Again, I think as a matter of policy it is not adequate to rely upon the scientists themselves to do this.

As I think I indicated in the paper, it is very costly for an individual scientist to speak up when he perceives a problem of safety. It is costly in terms of diverting time from doing research, and it is also costly because it is likely that if he is not a well established scientist, he will suffer some censure from so doing.

This is not to say that scientists are not concerned with doing research safely. I am saying that the nature of the reward structure of science is that if it is not profitable for an individual scientist to concern himself with these issues. And I perceive the role of the certified public scientist as one idea in this area, or it had been suggested as one possible mechanism in this area, of disassociating a person from the nature of the scientific enterprise such that he perhaps can more carefully analyze the possible risk and take more time to do it. It should certainly not be his decision to say research should go ahead or not—I think we have public forums, such as hearings like this, and hearings that AAAS has, and so forth, in which these issues are brought to the public attention adequately. But it would be the function of such a person to give sustained thought to and dig in carefully to possible risks, and where there seems to be a reasonable risk or a significant risk, to bring this to public attention. But it would not involve, and I don't think it has been suggested that it would involve, licensing of practitioners.

Mr. THORNTON. You are talking about the structure of a review. Are you suggesting one individual to do this, like a science advisor?

Dr. SORENSON. At this point it is a concept, to actually work it out would take considerably more thought. But it would probably require several people, I would suspect.

Mr. THORNTON. You mentioned the AAAS. I would like to inquire whether there is a role there for the Committee on Scientific Freedom and Responsibility, which is known to interact with Congress, legislators, and other people by advising them on scientific issues. Is there a role for that committee to help the scientific community understand and deal with ethical issues?

Dr. GLASS. I can speak to that.

Certainly the committee is not composed at the present time entirely of scientists. We have some distinguished representatives of the law, and persons who are interested in the interaction of science and society on the community. We hope very much that as time passes the interaction with Congress will be closer and greater. I think the participation of Congress in holding this hearing is a very significant step in that direction.

I fear, however, that such a committee as that of the AAAS can never play the broader role that you are speaking of, simply because it does represent the scientific community as such, and is speaking largely to scientists in their professional role. The American Association for the Advancement of Science has as one of its main objectives greater public understanding of science. But it has been very difficult over the years to know how to pursue that goal effectively on the part of a scientific organization.

Perhaps certain journals and journalists do it better than the official scientific community. So I think there is a need for some sort of body, whether established by Government or not, to speak on these matters in conjunction with scientists about hazards and about safety and about the possible future directions of science, and of applied science in particular.

Mr. THORNTON. Let me go to the brief outline which Dr. Sorenson gave at the start of his presentation, in which he grouped the concerns into three broad areas.

One, the question of bio-hazards.

Second, the right of the public to participate in decisions relating to regulating science or research.

And third, the debate as to whether there were indeed limits which would be imposed on scientific research itself.

It seems to me that this is a very reasonable articulation of the dimensions of the problem. In analyzing it in that way I would assume that there would be no great dispute that as to regulation of bio-hazards, that this is an appropriate matter for governmental intervention. This would hold not only with regard to such things as dangerous or potentially dangerous recombinant DNA molecule research, but also as to the use of certain pesticides, fertilizers, and chemicals; the application here rather than the research of different materials which might be deleterious to our environment being the important factor.

Is that agreed, Dr. Ryan

Dr. RYAN. I agree with that aspect of the regulation. But I wanted to go on into this question of the right of the public to participate.

Mr. THORNTON. Let me first assure myself, that all of you agree that as far as bio-hazards are concerned that this is an appropriate area for governmental intervention as the need is demonstrated. And then let's go on.

Dr. RYAN. It is an obligation of Government to provide protection against such hazards.

Mr. THORNTON. It is an obligation. OK.

Dr. Ryan. I think the right of the public to participate has been one of the major issues. The question is, who is the public? You have many public advocacy groups and consumer advocates, many of whom have questionable constituencies. I want to tell you what a commission can do, because I am sensitive to the rights of the public to participate.

We sponsored a minority conference, run by the National Urban League, under the auspices of our commission, to find out what people had in mind about research involving human subjects. And it was a huge conference held near Washington. In spite of good intentions, at the end of the conference there was a minority caucus saying that our Pacific islanders and Indians were not adequately represented. No matter how hard you try to represent all the public, it is extremely difficult to do so and satisfy everyone.

We have elected representatives in the Congress. That should satisfy the need for representation except that people feel that the Congress is under pressure from large industry and from the scientific establishment, and the individual doesn't have an opportunity to have his voice heard—even coming down here to testify is extremely difficult.

Mr. THORNTON. If you think the scientific community is affected by public cynicism and distrust you should look at some of the other institutions.

Dr. RYAN. So that every time you talk about an ethics committee within a scientific organization, the public looks at it and says, it is self-serving. There is an opportunity for conflict of interest. It is true for medicine and it is true for basic science.

Let me just tell you about the commission for 1 minute—it is composed mainly of nonscientists. Even so, people have complained about the composition, that there aren't enough poor people on it, for instance. But it could be composed of whomever you wished it to be composed of. One would hope that they would be people who would work and be morally responsible. By holding public hearings and by discussing the issue over a long enough time—without having to look at the clock so often—one has an opportunity to discuss the details and invite people for public testimony. This has been done with the Civil Rights Commission and others. The mechanism includes holding hearings under the Freedom of Information Act, in which everything is public, in which anyone who wants to come to testify can come to testify. All of the material can be put together plus the opportunity exists to let out contracts, to ask the questions about what the hazards really are or determine the best evidence, rather than having someone giving a speech about it, and then someone else disagreeing, and the two never talking together. It might be better to get the two of them in one room, not posturing for the public, not posturing for the press, but really trying to address the issues.

When you talk about ethics, there is more than just principle involved. It is a responsibility to look at information and facts, and not the strawmen that are raised.

Now, Dr. Thomas said that there is really no harm in basic science, that people are going to get overly concerned about recombinant DNA. For the most part I agree with him. But what people are concerned about is not necessarily the immediate hazards. People are concerned that you are finding things that are going to change their world.

With every new technology you have a new ethical problem for people. You don't have techniques like renal dialysis without creating problems. And people are worried about these ethical problems. They want to be able to plan for them, especially when they get into the question of health and health technology.

Now, we have the the Cat scan—it is a tremendous diagnostic device. The question people are asking is: How many do you need? Do you really need them? How many lives do they save? Are they economically feasible, and so forth.

This goes back to the question of the right of the public to know, and what is the best forum for that. I don't know whether you want commissions or something else, but there has to be some way that the public can have its input, and then interface with the Government. Our Commission's interface is largely with the Secretary of HEW, but we do send reports to the Congress as well. And the Secretary is responsible for responding within 180 days, he has to do something or explain why he is not going to do it.

Now, that is the kind of interaction between public and Government which can, in fact, get something done.

Thus far our Commission has sent in four reports. You may like them or you may not, but the process is still going on. With respect to fetal research, or research in prisons—to which the Secretary has not yet responded—or with psychosurgery, or research in children, and matters of this nature, there are facts available which the public can look at.

The trouble is that in this same kind of public debate people are asking questions or criticizing the reports when they haven't even read them. Ethical considerations mean not only thinking about ethical principles, but it is also a responsibility to have a rational method for proceeding, for getting the facts straight.

Mr. THORNTON. I think I should interrupt at this stage to point out that the present structuring of the Commission is to do exactly this, to gather information, to assimilate it, to arrive at recommendations, formulate conclusions, and to report. But you do not have authority presently to issue rules and regulations.

Dr. RYAN. And I would not want them.

Mr. THORNTON. You would not want that kind of authority?

Dr. RYAN. I would not want regulatory powers. I am not thinking of that for our present Commission, because we have plenty to do. There have been other commissions, and I do think the structure works in a democratic fashion.

Mr. THORNTON. Yesterday there was some confusion, I think, between the present functioning of the Commission, which is as we have just outlined, and a suggestion that a commission should be given the authority to promulgate rules and regulations.

Dr. RYAN. I am not interested in regulatory powers. There may have been some confusion about that. I don't care whether it is a Presidential commission or an independent commission, it should be outside of the political arena and not susceptible to political pressures in the usual sense, if it is going to serve the public. I wouldn't care if it is an advisory committee to the Secretary of HEW, or Dr. Frederickson's NIH committee if it served the same purpose. I think it is the process that is important, not what you call it. The public does want input. It is very easy for Hans Jonas to write those very beautiful articles about the responsibility of science, and that everything you do now should be open to public scrutiny and control. The point is, I think any rational person has to agree, that this is another straw man. Scientist seek public funds. And to that extent they are obligated to account for the use of those funds publicly. I don't think there is any question about that.

In addition to that, we operate in public institutions. I am in a large hospital within a medical school. We are in a fish bowl. I am not sure that it is all bad. The commission was one of the first advisory commissions to operate under the Freedom of Information Act. Everyone said you won't be able to discuss profound ethical issues. You won't be able to be open and free. And in point of fact. after we got to know one another and sat down, we could talk freely. And I am happy that we operated that way, that everything is a matter of public record. My statement about the value of commissions was not necessarily our commission, but the process.

Mr. THORNTON. Thank you very much, Dr. Ryan.

Let me very briefly outline again the picture that is emerging from my thinking as a result of this presentation. I will try to articulate

this without stating it as a conclusion but as an observation of what has been said. That is that there is this tripartite division of biohazards which should be regulated, where there is an obligation or duty to regulate biohazards; and second, the right of the public to participate in decisions relating to regulating science research; and then finally, at the other extreme, a debate on the limits of scientific research itself.

It seems to me that we have come to a conclusion that biohazards should be regulated, but basic science research should not be, and that the tension that exists between science and society is on the determination of just exactly what this middle area is. Should the public be participating in decisions relating to the application of science research—altering the contract, which until recently has said that anything that has the label of science on it is good, and it is going to lead to good results; but now reviewing that contract, and trying to find ways to determine what falls into the biohazard field, and what is pure science research?

I think the answer is, the public must be a participant. We are trying to find ways of approaching that.

Dr. RYAN. I am reminded of the Cambridge situation which illustrates a way for the public to participate. "Recombinant DNA is just too complex for common man to understand," is often quoted.

In point of fact they got a group of mostly lay people in Cambridge who sat down and heard all the scientists, heard all the public advocacy groups and decided where the middle road should be and proceeded, I think, in a rather responsible way for the city of Cambrige. That was a public commission composed largely of lay people who could clearly cut through the extreme posturings that take place in the arenas in which they are held, either in a congressional hearing or in the chambers of the city of Cambridge.

But the public can understand, and I think it is an obligation of the scientists to present things in a way that they can cope with.

Mr. THORNTON. The problem that we are really trying to review, then, is what kind of structure might be useful in resolving these tensions, whether, as has been suggested, we might take the good work that has been done thus far as federally funded research, the NIH guidelines, and expand them and make them statutorily obligatory upon the whole arena of scientific research; or whether this kind of determination should be resolved into statutory form at this time.

Is this something where, as the circumstances change, we may want to have the ability to adjust the rules in accordance with changing knowledge?

Dr. Thomas?

Dr. THOMAS. I would suggest that if this were to be done, it would really have to be done ad hoc to clearly identifiable risk, acknowledged to be risky technologies, one by one. And I think that if an official body were set up with its portfolio being the whole area of possible hazard in basic science, I don't see how it could get its work done with any effectiveness.

I am afraid that it would continually bog down with problems that are probably non problems.

I may be overstating the case, but I really don't believe that there are any questions confronting science that humanity would be better

off having unanswered. There are techniques of science that we had better not employ, that we had better go very carefully with human experimentation, for example. But as far as posing questions and trying to get them answered, I can't imagine any sort of question that I would regard as potentially damaging to society, to mankind. But there are a lot of people who don't agree with this.

There are people who feel, for instance, that now that it has been discovered that there are pentapeptide molecules in the normal brain, with many of the properties of opiates, mimicing the effects in some cases of heroin, and perhaps governing human behavior in a sort of internal endocrine system, this kind of work is taking things too far, and you had better not go on with questions of that order. I simply don't agree with that. But I can imagine an official body, having been set up, being compelled by the nature of its charge to get into things like this. And once in, I don't know how they would ever get out again.

Mr. THORNTON. I take your statement to be that while knowledge may in some instances be dangerous, that ignorance is more dangerous.

Dr. THOMAS. Much more.

Dr. RYAN. I couldn't agree more with Dr. Thomas—but I thought you were addressing a specific question, and that is recombinant DNA. You have the NIH DNA guidelines. Some scientists think they are too strict. And others think they are too lenient. And I think that they are a reasonable response to the question of biohazards. The only thing that is unanswered is that your major hazard will not be in the university or in the NIH funded laboratories, but in industry. The question is, now—and this is where the question of public trust comes in—what will Congress do if industry says we do not want to abide by these guidelines, that is where you need some action.

The two questions for private industry are patent infringement, which sometimes seems more important than people, and the question of batch size. If you think it is important that the biohazards have to be met by the NIH guidelines, in institutions funded by NIH, and that it is a Federal Government obligation to protect the public in that manner, then you must evenhandedly apply that to all such work going on in this country. And that includes industrial application, where the risk, because of batch size, and because of privacy—industrial secrecy—poses problems for adequate regulation.

I think that the question of public mistrust comes out in the pesticide stories, where people were severely damaged in industrial accidents. The NIH guidelines seem reasonable; responsible people put them together and they have been looked at for about 2 years. Research is proceeding under these guidelines which include strong biohazards committees in each institution. You could take those guidelines and make them apply to industry. I think this would answer one of the immediate problems.

Mr. THORNTON. Dr. Glass.

Dr. GLASS. I would like to reinforce that statement as strongly as I can. I was going to raise exactly the same point. It seems to me that the issue now is how we get the specific guidelines extended to all groups that might wish to participate in recombinant DNA research. And that primarily means industry.

Mr. THORNTON. Of course, I have to say that I have some misgivings about the statutory enactment of the NIH guidelines, or freezing

or crystalizing those rules and regulations into a form that would require legislative action to undo, or provide restraints. I think there is a great deal to be said for having the flexibility to adjust the determination of biohazards as the circumstances change. Do you agree with that?

Dr. RYAN. Doesn't the FDA and the Secretary of HEW have the responsibility for ongoing rulemaking, which could have the force of law in a regulatory sense. I think if one has the ability to change and to regulate as problems arise, that you would meet the kind of concern that you have.

Mr. THORNTON. And not to attempt to develop sanctions which are peculiar to one particular line of scientific research as a generic classification.

Dr. RYAN. Correct. I think that the NIH and the Public Health Service are going to have this as a continuing problem, every time a new research area opens up.

Mr. THORNTON. This interchange has been very useful.

I would like to ask Mr. Hollenbeck if he has any questions?

Mr. HOLLENBECK. No, I do not, Mr. Chairman.

Mr. THORNTON. Mr. Brown, do you have any questions?

Mr. BROWN. No, Mr. Chairman.

Mr. THORNTON. Thank you very much for your attendance.

I would like to ask if you would be willing to respond in writing to such questions as might be submitted to you at a later time?

Dr. RYAN. Yes.

Mr. THORNTON. Thank you, each of you, for your excellent testimony.

We will recess until 2 o'clock this afternoon, at which time we will continue this series of hearings.

You are excused.

We are now adjourned.

[Whereupon, the hearing was recessed for lunch at 9:50 a.m., to reconvene at 2 p.m.]

AFTERNOON SESSION

Mr. THORNTON. The hearing will come to order.

This hearing this afternoon marks the end of a series of hearings on the science policy implications of DNA recombinant molecule research.

In the first of these hearings, which was conducted on March 29 of this year, I tried to emphasize that this series of hearings was not intended to focus upon any specific legislative proposal which might then be before the Congress, but rather on the broad questions of science policy that this issue raises. And I expressed our subcommittee's wish—and I would like to quote from my statement at that time—"To provide a forum in which we all may learn and discuss and even disagree, and be able to do this in an atmosphere which we hope is relatively free of prejudice and devoid of hostility."

I think we have accomplished that objective in this series of hearings with the help of our many distinguished witnesses. We have heard from some 50 outstanding individuals. And we have presented thoughts during 12 hearings on such subjects as diverse as the basic biology of DNA recombinant molecule research, the attendant risk

and benefits of this research, public participation in scientific decision-making, and issues of law and of ethics in science.

This afternoon we will hear from three equally distinguished and outstanding witnesses who will conclude this series with some general views and perspectives on the implications of the recombinant DNA issues and all of the questions which it raises, for both the health and the conduct of basic research in this country.

Our first witness this afternoon will be the Honorable Howard T. Markey, who is the chief judge of the U.S. Court of Customs and Patent Appeals.

Chief Judge Markey is the 1977 recipient of the Jefferson medal, an award which is made by the New Jersey Patent Association to that individual who has, in its opinion, made the most outstanding contribution to the field of intellectual property law and patents.

Chief Judge Markey, we are delighted to have you with us today. And we ask you to proceed with your statement.

Chief Judge Markey, may I first invite our distinguished colleague, Mr. Hyde, if he would like to do so to join us up here.

Mr. HYDE. Thank you, Mr. Chairman, I would like to.

Whenever Judge Markey has something to say I always want to hear it.

Mr. THORNTON. Excellent.

Would you like to add any remarks at this time, Mr. Hyde?

Mr. HYDE. None other than that I had the pleasure of studying in law school with Judge Markey, and everything good I ever learned I learned from him, and everything bad.

[A biographical sketch of Chief Judge Markey follows:]

HOWARD T. MARKEY

1. Engineering test pilot of America's first jet planes in World War II.
2. Served 5 years in World War II and 21 months in the Korean War.
3. Awarded: Distinguished Service Medal, Legion of Merit, Distinguished Flying Cross, Soldier's Medal, Purple Heart, Air Medal, Bronze Star, Military Merit Ulchi (Government of Korea) and Nine Service Medals.
4. Retired Major General, Air Force Reserve.
5. Awarded: George Washington Honor Medal, Freedoms Foundation, Valley Forge, 1964; Jefferson Medal, New Jersey Pat. Law Assoc., 1977.
6. JD, cum laude, Loyola University; Master of Patent Law, John Marshall Law School; Doctor of Laws, Honoris Causa, New York Law School.
7. Engaged in the practice of law, 1949–50, 1952–72.
8. Lecturer: Loyola University School of Law, 1970–1971.
9. Chief Judge, United States Court of Customs and Patent Appeals, Washington, D.C.—June 1972 to present.
10. Member: Judicial Conference of the United States; Board of Certification for Circuit Executives; Subcommittee on Judicial Improvements of the Judicial Conference of the U.S.; World Conference of Judges; American Judicature Society; American Bar Association; National Conference of Lawyers and Scientists; Chairman: Science Liaison Task Force, Federal Judicial Center; Committee on Professional Ethics, Federal Bar Assoc.; Coordinator: Federal Judiciary Celebration of the Bicentennial of the Declaration and the Constitution.
11. Author: "Thomas More—Circa 1975," 21 Loyola L. Rev. (New Orleans) 807; "Special problems in Patent Cases," 57 JPOS 675–95 (Nov. 1975), 66 FRD 529–47 (July, 1975); "Old Wine in New Bottles," 122 Cong. Rec. H–5107 (Daily Ed. June 1, 1976); "Trademarks on Appeal—A View from the Bench," 66 TM Rep't. 279–84 (July–Aug., 1976); "The Status of the American Patent System—Can Myth, Sans Fiction," 59 JPOS 164 (March 1977); "A Forum For Technocracy?" 6 Judicature 365 (March, 1977); "Science and Law—Toward a Happier Marriage," JPOS 343 (June, 1977).

Mr. THORNTON. Judge Markey.

STATEMENT OF CHIEF JUDGE HOWARD T. MARKEY, U.S. COURT OF CUSTOMS AND PATENT APPEALS

Judge MARKEY. Mr. Chairman, I appreciate the subcommittee's generous invitation to participate in these informal proceedings. And I am now most pleasantly surprised to find the Hon. Henry J. Hyde, my esteemed classmate, on the bench before me.

I think my presence illustrates the wisdom of your having established these proceedings as informal workships, for I could not have attended if specific legislation were under consideration. As a Federal judge charged with the duty of interpreting and applying statutes, I would consider unseemly and inappropriate any participation in their creation. The sole exception would involve testimony on statutes affecting the Federal judiciary, with respect to which I join the concerns of my fellow judges over absence of testimony from the judiciary. But that is another subject entirely, and in no way diminishes the value of these workshop sessions, which are open to the views of those having no particular position on any specific legislation.

My appearance, Mr. Chairman, is therefore not as a Federal judge but as a citizen, uninformed but concerned. In no manner do I here represent my court, the Federal judiciary, or the science liaison task force of the Federal Judicial Center, which I have the honor to chair.

A workshop opens the door to those of us whose microbiological knowledge would fit within a tiny DNA helix, and whose technical understanding of recombinant DNA research would be invisible under an electron mircroscope and too small to be cut by a restriction enzyme. In sum, Mr. Chairman, I am here out of the generosity of the subcommittee and because we who are not angels are willing to enter where angels fear to tread.

I have submitted a statement for the record and should here like to merely highlight some of its points.

Mr. THORNTON. Without objection your statement will be made a part of the record.

[The statement follows:]

STATEMENT OF

CHIEF JUDGE HOWARD T. MARKEY
UNITED STATES COURT OF CUSTOMS AND PATENT APPEALS

BEFORE THE
SUBCOMMITTEE ON SCIENCE, RESEARCH AND TECHNOLOGY

SEPTEMBER 8, 1977

I APPRECIATE, MR. CHAIRMAN, THE SUBCOMMITTEE'S GENEROUS INVITATION TO PARTICIPATE IN THESE INFORMAL PROCEEDINGS. MY PRESENCE ILLUSTRATES THE WISDOM OF YOUR HAVING ESTABLISHED THESE PROCEEDINGS AS INFORMAL "WORKSHOPS," FOR I COULD NOT HAVE ATTENDED IF SPECIFIC LEGISLATION WERE UNDER CONSIDERATION. AS A FEDERAL JUDGE CHARGED WITH THE DUTY OF INTERPRETING AND APPLYING STATUTES, I WOULD CONSIDER UNSEEMLY AND INAPPROPRIATE ANY PARTICIPATION IN THEIR CREATION. THE SOLE EXCEPTION WOULD INVOLVE TESTIMONY ON STATUTES AFFECTING THE FEDERAL JUDICIARY, WITH RESPECT TO WHICH I JOIN THE CONCERNS OF MY FELLOW JUDGES OVER ABSENCE OF TESTIMONY FROM THE JUDICIARY. BUT THAT IS ANOTHER SUBJECT ENTIRELY, AND IN NO WAY DIMINISHES THE VALUE OF THESE WORKSHOP SESSIONS, WHICH ARE OPEN TO THE VIEWS OF THOSE HAVING NO PARTICULAR POSITION ON ANY SPECIFIC LEGISLATION.

MY APPEARANCE, MR. CHAIRMAN, IS THEREFORE NOT AS A FEDERAL JUDGE, BUT AS A CITIZEN, UNINFORMED BUT CONCERNED. IN NO MANNER DO I HERE REPRESENT MY COURT, THE FEDERAL JUDICIARY, OR THE SCIENCE LIAISON TASK FORCE OF THE FEDERAL JUDICIAL CENTER, WHICH I HAVE THE HONOR TO CHAIR.

A "WORKSHOP" OPENS THE DOOR TO THOSE OF US WHOSE MICROBIOLOGICAL KNOWLEDGE WOULD FIT WITHIN A TINY DNA HELIX, AND WHOSE TECHNICAL UNDERSTANDING OF RECOMBINANT DNA RESEARCH WOULD BE INVISIBLE UNDER AN ELECTRON MICROSCOPE AND TOO SMALL TO BE CUT BY A RESTRICTION ENZYME. IN SUM, MR. CHAIRMAN, I AM HERE OUT OF THE GENEROSITY OF THE SUBCOMMITTEE AND BECAUSE WE WHO ARE NOT ANGELS ARE WILLING TO ENTER WHERE ANGELS FEAR TO TREAD.

THE FREEDOM TO LEARN

WRITTEN WELL BEFORE THE INDUSTRIAL REVOLUTION, AND ABOUT 170 YEARS BEFORE THE PRESENT SCIENTIFIC REVOLUTION, THE CONSTITUTION OF THE UNITED STATES GRANTS NO SPECIFIC POWERS TO THE CONGRESS RESPECTING SCIENTIFIC RESEARCH. EXCEPT FOR ART. I, SECTION 8, CLAUSE 8, CONCERNING EXCLUSIVE RIGHTS TO INVENTORS, THE CONSTITUTION NOWHERE VISUALIZES TODAY'S SCIENCE EXPLOSION OR THE TECHNOLOGICAL JUGGERNAUT OF RECENT YEARS. IF OUR FOREFATHERS WERE WRITING TODAY, HOWEVER, I THINK THEY WOULD INCLUDE, PROBABLY AS A PART OF THE FIRST AMENDMENT, "CONGRESS SHALL MAKE NO LAW ABRIDGING THE FREEDOM TO LEARN."

"SCIENCE," IN MY VIEW, IS BUT ANOTHER WORD FOR THE FREEDOM TO LEARN. "TECHNOLOGY" IS BUT ANOTHER WORD FOR THE USE OF LEARNING. AN ANALOGY MAY BE DRAWN TO THE FIRST AMENDMENT PROHIBITION AGAINST ABRIDGEMENTS OF FREEDOM OF SPEECH. AS THE COURTS, IN FREEDOM OF SPEECH CASES, HAVE DISTINGUISHED BETWEEN FREEDOM OF IDEAS AND FREEDOM OF ACTION, SO TOO, A DISTINCTION MAY BE DRAWN BETWEEN SCIENCE, CONSIDERED AS IDEAS, AND TECHNOLOGY, CONSIDERED AS ACTION. MAN

MUST REMAIN FREE, FOR EXAMPLE, TO RESEARCH CROWD REACTION TO STIMULI. HE CANNOT BE FREE TO FALSELY CRY "FIRE" IN A CROWDED THEATRE.

THE SUGGESTION, INDEED THE INSISTENCE BY SOME, THAT RESEARCH INTO RECOMBINANT DNA SHOULD BE PERMANENTLY STOPPED, IS DISTURBING, THOUGH NOT SURPRISING. THE SAME REACTION CONFRONTED GALILEO, PASTEUR, LISTER, THE RAILROADS, AUTOMOBILES AND FLUORIDATION. THOUGH PAST CONFRONTATIONS INVOLVED KNOWLEDGE ALREADY LEARNED AND RESISTENCE TO ITS SPREAD, THE PHENOMENON RESTS ON A FALSE NOTION, I.E., THAT THINGS CAN REMAIN AS THEY ARE. YOU MAY RECALL, MR. CHAIRMAN, THE STORY OF THE LITTLE OLD LADY WHO OBSERVED ASTRONAUTS ON THE MOON AND WHO SAID, "WHY DON'T THEY STAY DOWN HERE IN FRONT OF THEIR TELEVISION SETS, LIKE THE GOOD LORD INTENDED THEM TO." LIFE IS DYNAMIC, NOT STATIC. LIFE IS A MOVIE, NOT A SERIES OF STILL SLIDES. EVEN IF IT WERE DESIRABLE, IT IS IMPOSSIBLE TO SAY, "WE SHALL STOP HERE AND GO NO FURTHER." IT IS IMPOSSIBLE TO SAY THAT FOR OUR OWN COUNTRY, LET ALONE FOR THE ENTIRE WORLD. THAT IS TRUE OF THE LAW, OUR CULTURE AND OUR SCIENCE AND TECHNOLOGY. HENCE, ANY EFFORT TO ABRIDGE THE FREEDOM TO LEARN WILL FAIL, AND THE LAW IN GENERAL WILL SUFFER FOR HAVING ON ITS BOOKS A LAW UNENFORCEABLE.

THE CONSTITUTIONS'S PREAMBLE REFERS TO THE GENERAL WELFARE AND ART. I, SECTION 8, CLAUSE 1 PERMITS USE OF THE TAXING POWER TO PROMOTE THE PUBLIC WELFARE. "WELFARE" INCLUDES SAFETY, BUT IT INCLUDES MUCH MORE, AND MAY BE DRASTICALLY INJURED BY A LAW THAT SAYS, "THOU SHALT NOT LEARN." TO PARAPHRASE JUDGE LEARNED HAND,

WHO SPOKE OF JUSTICE, "YOU SHALL NOT RATION LEARNING." FURTHER, THE NINTH AND TENTH AMENDMENTS, RETAINING ALL POWERS NOT GRANTED TO THE CONGRESS AND NOW OFTEN DESCRIBED AS "THE FORGOTTEN AMENDMENTS," MAY BE VIEWED AS AN INDICATION THAT NO CONSTITUTIONAL POWER RESIDES IN THE CONGRESS TO FORBID ANY RESEARCH OR LEARNING.

IN TODAY'S WORLD, WHEN WE DESPERATELY NEED SCIENTIFIC AND TECHNOLOGICAL SOLUTIONS TO OUR PROBLEMS OF ENERGY, THE ENVIRONMENT, OVERPOPULATION--WHEN WE DESPERATELY NEED TO INCREASE THE BIRTH RATE OF DISCOVERY, INVENTION, AND INNOVATION--THIS IS NOT THE TIME TO ENCOURAGE MENTAL CONTRACEPTION AND TECHNOLOGICAL ABORTION.

IN DEALING WITH BIG BUSINESS, THEN WITH BIG GOVERNMENT, AND NOW WITH BIG SCIENCE, THE PEOPLE OF THE UNITED STATES HAVE A HISTORY OF SOLVING PROBLEMS ACCOMPANYING ADVANCES IN SCIENCE AND TECHNOLOGY. THROUGH THEIR REPRESENTATIVES IN THE CONGRESS, AND THROUGH BUSINESS AND INDUSTRY COMPETITION IN THE MARKETPLACE, OUR PEOPLE HAVE REFLECTED A BALANCED AND CONSIDERATE APPROACH NOT ALWAYS SHOWN BY THOSE CLOSEST TO THE PROBLEM. I HAVE EVERY CONFIDENCE THAT THEY WILL FIND SUCCESSFUL ANSWERS TO THE PROBLEMS ACCOMPANYING RECOMBINANT DNA RESEARCH. THOUGH I AM AN OPTIMIST, AND AWARE OF THE DEFINITION OF AN OPTIMIST AS ONE WHO FALLS OFF A 20 STORY BUILDING AND, AS HE PASSES EACH FLOOR ON THE WAY DOWN, SAYS, "WELL, EVERYTHING'S ALRIGHT SO FAR!", THAT STORY PRODUCES A LAUGH BECAUSE WE ALL KNOW THE RESULT AWAITING THE FALLING OPTIMIST, AND RECOMBINANT DNA RESEARCH, OR "CELL MATING" AS I CALL IT IN MY IGNORANT NEED FOR SIMPLIFICATION, IS RADICALLY AND INTRINSICALLY

NEW. IT IS ALSO NEW FOR HAVING ENTERED THE PUBLIC ARENA IN ITS EARLY RESEARCH STAGES. UNTIL RECENTLY, NOT EXCLUDING ATOMIC SPLITTING, THE PUBLIC HAS BEEN MORE OFTEN CONFRONTED WITH SCIENTIFIC DISCOVERIES SECRETLY ACHIEVED AND THEIR TECHNOLOGICAL PROGENY FULL-GROWN. I DO NOT DECRY THE EXISTENCE OR ACTIONS OF THOSE WHO HAVE BEEN CALLED, FAIRLY OR UNFAIRLY, "DISASTER MONGERS." THEY SERVE AN IMPORTANT EARLY-WARNING FUNCTION. THEIR CONCERNS CANNOT BE SAFELY IGNORED, BUT MUST BE CALMLY EVALUATED, AND IF THOSE CONCERNS BE UNFOUNDED THEY SHOULD BE CALMLY AND ADEQUATELY REFUTED.

BUT, TO PARAPHRASE BENJAMIN FRANKLIN, "THOSE WHO WOULD SEEK TOTAL SECURITY AND ABSOLUTE PREDICTABILITY, AT THE PRICE OF A LITTLE LEARNING, SHALL ENJOY NEITHER." WE MUST NOT TAKE COUNSEL OF OUR FEARS ALONE. THAT WAY LIES STERILITY, STAGNATION AND PARALYSIS. WHATEVER IS DONE TO CONTROL THE USE OF LEARNING MUST NOT STIFLE SCIENCE. IT MUST NOT STIFLE THE SEARCH. IT MUST NOT ABRIDGE OUR FREEDOM TO LEARN.

FEAR

MAN HAS ALWAYS LIVED WITH A FEAR OF THE UNKNOWN, BUT THE CONSEQUENCES OF RESEARCH ARE INHERENTLY UNKNOWN. IF RESULTS WERE KNOWN OR PREDICTABLE, THERE WOULD, OF COURSE, BE NO REASON TO SEARCH. I DO NOT BELITTLE THE UNPRECEDENTED NATURE OF RECOMBINANT DNA RESEARCH. IT DIFFERS IN KIND, NOT JUST IN DEGREE, FROM RESEARCH INTO THE INANIMATE WORLD, OR EVEN INTO LIVING ORGANISMS OF A SINGLE SPECIES. BUT THE PRINCIPLE OF WHICH I SPEAK IS NOT DIFFERENT. ONE PROMINENT WRITER HAS DECRIED RECOMBINANT DNA RESEARCH BECAUSE THE RESULTING CONSEQUENCES "ARE AS UNPREDICTABLE AS LIFE ITSELF." IF

LIFE ITSELF IS UNPREDICTABLE, AND IT CERTAINLY IS, THEN WHY SEARCH WE ALL FOR CERTAINTY? FOR ABSOLUTE PROTECTION? FOR A COMFORTING PREDICTABILITY? LIFE FOR EACH OF US IS A TERMINAL AFFLICTION, FULL OF JOYS AND SORROWS, FEAR AND COURAGE, HOPE AND DESPAIR. THE ONLY TWO CERTAINTIES ARE THAT LIFE IS UNPREDICTABLE AND THAT IT SHALL TERMINATE, WITH THE TERMINATION DATE ITSELF UNPREDICTABLE. PERHAPS THAT IS WHY SECTION 202 OF THE ATOMIC ENERGY ACT, AN ACT RELATING TO A FRIGHTENING SCIENTIFIC DEVELOPMENT IF THERE EVER WAS ONE, EMPLOYS A "MINIMIZE THE DANGERS" CRITERION.

MANY OF OUR FEARS ARE FRUITLESS. THERE IS NO PLACE TO HIDE FROM THE MAD OR UNSCRUPULOUS SCIENTIST, ANYMORE THAN THERE IS FROM THE MAD OR UNSCRUPULOUS DOCTOR, LAWYER, BAKER OR CANDLESTICK MAKER. WE LEARN OF THEIR MADDNESS AND UNSCRUPULOUS CONDUCT ONLY AFTER THE EVENT. THERE ARE NO GUARANTEES AND NO FREE LUNCH.

WE CANNOT BE FREE AND IRRESPONSIBLE, FOR THE OTHER SIDE OF THE COIN OF FREEDOM IS RESPONSIBILITY. I SOMETIMES WISH SOMEONE WOULD FORM THE AMERICAN CIVIL RESPONSIBILITIES UNION, FOR LIBERTY CANNOT LIVE AMONG IRRESPONSIBLE MEN. THE ONLY FREEDOM FROM RISK OF OUR BROTHER'S IRRESPONSIBILITY LIES IN A FATAL PARALYSIS, OR IN THE GRAVE. A FEAR OF EACH OTHER IS FATAL TO FREEDOM. PERHAPS THAT IS WHY OUR FOUNDERS PLEDGED THEIR LIVES, THEIR FORTUNES AND THEIR SACRED HONOR, NOT TO A HIGHER STANDARD OF LIVING OR TO SOME PRESSURE GROUP, BUT "TO EACH OTHER." AN EFFORT TO ASSURE TOTAL SECURITY AGAINST IRRESPONSIBILITY WOULD BE DOOMED TO FAILURE AND WOULD, ALONG THE WAY, DESTROY ALL FREEDOM, INCLUDING THE FREEDOM

OF RESEARCH. OF COURSE WE MUST TAKE SOME COUNSEL OF OUR FEARS, BUT ONLY AS TO THE METHODOLOGY OF OUR LEARNING AND HOW WE SHALL USE WHAT WE LEARN. WE MUST NEVER TAKE COUNSEL OF A FEAR OF LEARNING.

SCIENTISTS, UNTIL RECENTLY, HAVE ENJOYED THE LUXURY OF UNHAMPERED PURSUIT OF TRUTH. THOUGH IT MAY BE THAT SOME SCIENTISTS, LIKE THE REST OF US, MAY BE NAIVE AND OTHERS MAY BE ISOLATED FROM PUBLIC CONCERNS, I AM CERTAIN THAT THE MOST NAIVE AND ISOLATED SCIENTIST IS NONETHELESS FULLY AWARE OF ONE MONUMENTAL FACT--HE LIVES HERE TOO. THAT KNOWLEDGE NECESSARILY INFLUENCES HIS RESEARCH ACTIVITIES. THAT THE SCIENTIFIC COMMUNITY IS RESPONSIBLE IS ILLUSTRATED MOST DRAMATICALLY IN CONNECTION WITH RECOMBINANT DNA RESEARCH, WHERE THE HAZARDS AND CONCERNS WERE FORCEFULLY AND CANDIDLY BROUGHT TO PUBLIC ATTENTION BY THE VERY SCIENTISTS WHO WERE THEMSELVES DOING THE WORK, AND WHILE THEY WERE IN ITS EARLY STAGES.

THE EXPONENTIAL GROWTH OF KNOWLEDGE CONTINUES UNABATED. IN THE MIDST OF SUCH GROWTH, IT ILL BEHOOVES US EVER TO CRY "NO MORE." IT WOULD BE PARTICULARLY TRAGIC IF THE FEAR THAT PRODUCED THAT CRY WOULD HAVE BEEN OBVIATED BY A DISCOVERY ON THE NEXT DAY. WE WOULD NEVER KNOW WHETHER WE HAD STIFLED THE SEARCH ON THE VERY BRINK OF A GLORIOUS DISCOVERY, ON THE BRINK OF A BOON TO MANKIND AND ONE WHICH WOULD HAVE REMOVED ALL OUR FEARS.

MOREOVER, THOUGH "CELL MATING" IS THE CURRENT BIOLOGICAL RESEARCH TECHNIQUE OF INTEREST, IT IS ONLY ONE. THERE ARE, I UNDERSTAND, NUMEROUS OTHER STUDIES, RESEARCH PROGRAMS AND EXPERIMENTS UNDERWAY ABOUT WHICH ONE MIGHT ERECT A SCENERIO CONTAINING A SCARE

PER PAGE. TO INSERT THE DEAD AND DEADENING HAND OF GOVERNMENT REGULATION INTO EVERY LABORATORY IN THE LAND WOULD BE TO TAKE COUNSEL ONLY OF OUR FEARS.

REGULATION

LIKE ALL MAN'S ACTIVITIES, SCIENCE AND TECHNOLOGY, HAVE SOCIETAL RESPONSIBILITIES. LIKE WARS ARE TOO IMPORTANT TO BE LEFT ENTIRELY TO GENERALS, LIKE JUSTICE IS TOO IMPORTANT TO BE LEFT ENTIRELY TO JUDGES, SCIENCE AND TECHNOLOGY ARE TOO IMPORTANT TO BE LEFT ENTIRELY TO SCIENTISTS AND TECHNICIANS.

THERE IS NO RISK-BENEFIT DICHOTOMY APPLICABLE TO SCIENCES I.E., TO THE RIGHT TO LEARN. KNOWLEDGE LEARNED IS ALL BENEFIT AND NO RISK. NOT SO WITH TECHNOLOGY. THE POWER OF CONGRESS TO ADVANCE THE GENERAL WELFARE CLEARLY AUTHORIZES REGULATION OF THE USE OF KNOWLEDGE.

KNOWLEDGE IS USED IN A THOUSAND WAYS, ONE BEING ITS USE IN TRYING TO LEARN MORE, I.E., THE METHODOLOGY OF OUR RESEARCH. THE TECHNOLOGY OF CELL MATING KNOWLEDGE INCLUDES ITS POSSIBLE USE TO GROW CORN WITH SELF-PRODUCED NITROGEN AND THE MORE UNLIKELY USE, AT LEAST AT THE MOMENT, IN MAKING ALL MEN LOOK LIKE CLARK GABLE. THE TECHNOLOGY OF HOW WE ACQUIRE CELL MATING KNOWLEDGE RELATES TO WHETHER WE USE E. COLI OR A MORE CONTAINING BACTERIA AND WHETHER WE DO OUR RESEARCH IN A PI OR PIV LABORATORY. SO LONG AS ITS REGULATIONS DO NOT SUFFOCATE THE FREEDOM TO LEARN, I SEE NO CONSTITUTIONAL LIMITATION ON THE POWER OF CONGRESS TO REGULATE THE USE OF CELL MATING KNOWLEDGE OR THE MANNER IN WHICH THAT KNOWLEDGE IS ACQUIRED.

APART FROM ITS POWER TO REGULATE, THE WISDOM OF THE CONGRESS IN EXERCISING THAT POWER IN THIS PARTICULAR FIELD OF TECHNOLOGY IS ANOTHER MATTER. WHETHER REGULATIONS CAN BE DEVISED TO MINIMIZE DANGER WHILE PRESERVING THE FREEDOM OF RESEARCH SHOULD, I THINK, BE THE FUNDAMENTAL QUESTION BEFORE THIS SUBCOMMITTEE. I SHOULD NOT LIKE TO ENTER HISTORY, FOR EXAMPLE, AS THE CONGRESSMAN, LABORATORY DIRECTOR, OR AGENCY ADMINISTRATOR WHO SO SMOTHERED THIS PARTICULAR TECHNOLOGY WITH REGULATION AS TO HAVE DELAYED A CURE FOR CANCER BY 50 YEARS.

THE NIH GUIDELINES ARE NOT REGULATIONS. THEIR ONLY ENFORCEMENT POTENTIAL LIES IN THE CONTROL OF MONEY, AND THEY ARE LIMITED TO FEDERALLY FUNDED RESEARCH. QUESTIONS OF LICENSING, INSPECTION, AND FINES OR OTHER PENALTIES FOR NONCOMPLIANCE, ARE MATTERS FOR THE CONGRESS, IF IT SHOULD ELECT TO PROCEED WITH SOME FORM OF NATIONWIDE, ALL-ENCOMPASSING REGULATION.

AT THE MOMENT, THE IMPORTANT THING MAY BE TO PUBLICIZE THE GUIDELINES AS GUIDELINES. COMMERCIAL FIRMS AND THEIR LABORATORY WORKERS ARE NOT BENT ON SUICIDE. EARLY PUBLICATION OF KEPONE DANGERS MIGHT HAVE AVOIDED THE TRAGEDIES AT THE JAMES RIVER.

IT MAY BE WELL TO CONSIDER WHETHER PROTECTION OF THE FEDERAL GOVERNMENT, FROM THE ONUS OF HAVING SUPPORTED A TRAGIC RESEARCH EVENT, MIGHT REQUIRE THE FIXING OF RESPONSIBILITY FOR ALL RECOMBINANT DNA RESEARCH IN ONE AGENCY. EACH AGENCY HAVING A SPECIAL NEED FOR THIS RESEARCH COULD FUNNEL ITS REQUIREMENTS THROUGH THE SELECTED AGENCY. THE SECRETARY OF HEW FOUND IT NECESSARY TO FORM

AN INTERAGENCY COMMITTEE TO EXPLORE THE "PROBLEM" OF IMPLEMENTING THE GUIDELINES IN ALL AGENCIES. SHOULD THE INTERAGENCY COMMITTEE BE UNSUCCESSFUL, THE SCIENTIFIC COMMUNITY COULD FACE A SMORGASBOARD OF GUIDELINES FROM WHICH TO CHOOSE.

THE DUTY OF CONGRESS MAY BE, AT THIS STAGE, SIMPLY TO REMAIN INFORMED. ITS CONCERN FOR THE PUBLIC WELFARE, I.E., THE PROTECTION OF PUBLIC SAFETY WHILE MAINTAINING THE FREEDOM TO LEARN, MAY INCLUDE THE MAINTENANCE OF A PUBLIC PERSPECTIVE IN WHICH LEGITIMATE FEARS ARE MET WITH APPROPRIATELY LIMITED REGULATION AND UNFOUNDED FEARS ARE MET WITH CLEAR EXPLANATIONS. THE ROLE OF CONGRESS, IN MY VIEW, IS NOT MERELY A NEGATIVE ROLE. IT CAN AND SHOULD BE A POSITIVE AND CREATIVE ROLE, WHICH, WHILE KEEPING ONE EYE ON SAFETY, INCLUDES THE PROMOTION OF PROGRESS IN OUR ECONOMY, OUR AGRICULTURE, OUR HEALTH, AND SIMILAR CONCERNS.

THERE MAY BE A ROLE MODEL IN THE JOINT CONGRESSIONAL COMMITTEE ON ATOMIC ENERGY. THERE ARE DIFFERENCES BETWEEN RECOMBINANT DNA RESEARCH AND ATOMIC ENERGY RESEARCH, PRIMARILY IN THE U.S. OWNERSHIP OF ATOMIC FUELS. NONETHELESS, THE JOINT CONGRESSIONAL COMMITTEE IS AN OUTSTANDING EXAMPLE OF DEMOCRATIC CONTROL, EFFECTIVE AND YET NOT SUFFOCATING, OVER A MAJOR SCIENTIFIC DEVELOPMENT.

COMMUNICATION

CONGRESS CAN BE AN EFFECTIVE PARTNER IN SHAPING PUBLIC POLICY IN PACE WITH SCIENTIFIC DEVELOPMENT, AND IN CHANNELING THE MODERN MIRACLES OF SCIENCE TOWARD THE BENEFIT OF MAN. AS IN ANY PARTNERSHIP, HOWEVER, COMMUNICATION BETWEEN PARTNERS IS PARAMOUNT.

THIS SUBCOMMITTEE, THROUGH ITS PRESENT "WORKSHOPS," IS MOVING OUT TO INFORM ITSELF AND TO ENCOURAGE THE PARTNERSHIP COMMUNICATION OF WHICH I SPEAK. HARKENING AGAIN TO CONGRESSIONAL EXPERIENCE WITH ATOMIC ENERGY, THE ACT REQUIRES AGENCIES TO INFORM THE CONGRESS. THE JOINT COMMITTEE, HOWEVER, DID NOT RELY ON MERELY WHAT IT WAS TOLD, BUT HAS GONE OUT INTO THE FIELD, INTO THE DESERTS, INTO THE LABORATORIES, AND INTO THE URANIUM MINES, AND HAS TALKED WITH THE PEOPLE ACTUALLY DOING THE WORK. IT HAS MADE ITSELF FULLY INFORMED.

OPEN AND WIDESPREAD COMMUNICATION, HONEST AND CANDID, CAN, AND PROBABLY WILL SERVE AS THE MAJOR WEAPON AGAINST TRAGEDY IN RECOMBINANT DNA RESEARCH, AS IT WILL IN CONNECTION WITH OTHER SCIENTIFIC RESEARCH AND DEVELOPMENT.

LIKE THE SIX MILLION DOLLAR MAN, THE UNBIASED MAN, AND HENCE UNBIASED ADVICE, DOES NOT EXIST. THAT ADVISE MAY BE BIASED, HOWEVER, IS NEITHER FATAL NOT CAUSE FOR DESPAIR. THE KEY IS EVALUATION OF THE THING ADVISED, COMPARING AND WEIGHING IT AGAINST CONTRARY ADVICE. IT MAY BE USEFUL TO EVALUATE ALSO THE SOURCE, SO LONG AS SOURCE EVALUATION DOES NOT CONTROL ACCEPTANCE OR REJECTION OF THE THING ADVISED. IT IS ALSO EASY TO BLINDLY CREDIT EXPERT ADVICE, EVEN WHEN THE ADVICE GOES OUTSIDE THE ADVISOR'S EXPERTISE. BUT THE PUBLICITY SEEKER MAY, AFTER ALL, BE RIGHT AND THE EXPERT MAY, AFTER ALL, BE WRONG. SIMILARLY, BIAS AND SINCERITY ARE NOT ALWAYS MUTUALLY EXCLUSIVE. THE MOST SINCERE ADVISOR MAY HAVE A BIAS UNRECOGNIZED. EVEN SO, IF OUR EVALUATION FOCUSES PRIMARILY ON

WHAT IS SAID, AND FAR LESS ON WHO SAYS IT, THE CHANCES OF A SAFE AND SANE DECISION ARE INCREASED."

THOUGH COMMUNICATION MAY THUS BE DISTORTED BY ATTENTION-GETTING, LEADING TO OVERBLOWN ASSURANCE OR SCARE REPORTS IN NEWSPAPERS, COMMUNICATION MAY BE BOTH DISTORTED AND DESTROYED WHEN THE PARTNERS USE DIFFERENT LANGUAGES. SCIENTIFIC JARGON WILL NOT SIMPLY GO AWAY. IT HAS BEEN AROUND TOO LONG AND SERVES TOO USEFUL A PURPOSE AS A QUICK SHORTHAND FOR SCIENTISTS. NOR CAN DECISION-MAKERS IN THE CONGRESS, IN THE FEDERAL AGENCIES, AND ON THE BENCH, BE EXPECTED, AT THIS LATE STAGE, TO ACQUIRE A FACILITY IN "SCIENCOGRAPHY."

EVERY DISCIPLINE HAS ITS JARGON. IN THE LEGAL PROFESSION, WE HAVE ONLY COMPARATIVELY RECENTLY WAKED UP TO THE STUPIDITY OF THINGS LIKE "RES IPSA LOQUITUR." WE ARE NOW TRYING TO SAY, "THE THING SPEAKS FOR ITSELF." WE HAVE AN ORGANIZATION CALLED "SCRIBES," HOLDING SEMINARS AND DOING ITS BEST TO GET LAWYERS AND JUDGES TO SPEAK ENGLISH. PERHAPS WHAT IS NEEDED IS A SCRIBES ORGANIZATION FOR SCIENTISTS.

THE ENGLISH LANGUAGE IS MARVELOUSLY FLEXIBLE. I THINK IT CAN SAFELY BE SAID TO SCIENTISTS THAT, "IF YOU CANNOT DESCRIBE IN ENGLISH WHAT YOU WANT TO DO, DON'T DO IT." IN SO SAYING, I AM UTTERLY CONFIDENT THAT THE ENGLISH LANGUAGE IS PERFECTLY CAPABLE, THOUGH IT MAY REQUIRE A FEW MORE WORDS, OF DESCRIBING ANY SCIENTIFIC EXPERIMENT AND THE RESULTS INTENDED OR ACHIEVED. I AM SURE IT COULD BE IMPROVED, BUT I WOULD DESCRIBE DEOXYRIBONUCLEIC ACID AS "THE MOLECULE THAT CONTROLS HEREDITY."

IT MAY ALSO BE WELL IF EVERY LABORATORY HAD ON ITS STAFF AN ENGLISH MAJOR, WHOSE FUNCTION WOULD BE TO TRANSLATE EVERY SCIENTIFIC REPORT COMING OUT OF THE LABORATORY, AND INTENDED FOR ANY NON-SCIENTISTS, INTO CLEARLY UNDERSTANDABLE ENGLISH. THAT THE SUGGESTION MAY NOT BE TOO AFAR AFIELD IS ILLUSTRATED BY THE SUCCESS OF NEWSPAPER SCIENCE WRITERS, WHO ARE EVERY DAY CONVERTING SCIENCE LINGO INTO NEWSPAPER ENGLISH FOR THEIR READERS. ONE ENCOURAGING DEVELOPMENT IN THIS DIRECTION IS THE GROWING PRACTICE OF INVITING THE PRESS TO SCIENTIFIC MEETINGS.

COMMUNICATION IS A TWO-WAY STREET. IF WE ARE TO PIERCE THE WORD CURTAIN, THE DECISION-MAKERS IN THE CONGRESS, THE AGENCIES, AND THE JUDICIARY, MUST PLAY THEIR PART. I HAVE ELSEWHERE SUGGESTED THAT ALL LEGISLATION SHOULD BE ACCOMPANIED BY A "LANGUAGE IMPACT STATEMENT." THE INTERNAL REVENUE ACT HAS AN AVERAGE OF 51 WORDS PER SENTENCE. THE RECENT "SIMPLIFYING ACT" HAD AN AVERAGE OF 61 WORDS PER SENTENCE. IT WILL NOT DO FOR THE SCIENTIFIC COMMUNITY TO TRANSLATE ITS REPORTS AND ADVICE INTO ENGLISH, IF THE RESULTING PUBLIC POLICY IS SO CLUTTERED AS TO DEFEAT UNDERSTANDING. IN A SOCIETY IN WHICH IGNORANCE OF THE LAW IS NO EXCUSE--IN A SOCIETY ATTEMPTING TO LIVE FREE UNDER THE RULE OF LAW AND NOT OF MEN--CLARITY IN THE LAW IS A DESPERATE NEED.

IF EFFECTIVE COMMUNICATION IS TO BE ACHIEVED, IT IS INCUMBENT UPON THE CONGRESS, THE EXECUTIVE AND THE JUDICIARY TO REFUSE EVERY REPORT OR ADVICE NOT COUCHED IN CLEAR ENGLISH. THE ALTERNATIVE IS TO REMAIN INTIMIDATED BY JARGON AND VINCIBLY IGNORANT OF THE WHOLE TRUTH.

TOO OFTEN WE DECISION-MAKERS, AFRAID TO ADMIT WE DON'T UNDERSTAND, ACCEPT AND EVEN REPEAT THE SCIENTIFIC JARGON PRESENTED TO US, TRYING TO AT LEAST SOUND LIKE WE KNOW WHAT WE ARE TALKING ABOUT. THE PROCESS IS LIKE THE COLLEGE LECTURE, WHICH HAS BEEN DESCRIBED AS A PROCESS BY WHICH THE NOTES OF THE PROFESSOR BECOME THE NOTES OF THE STUDENT WITHOUT GOING THROUGH THE MINDS OF EITHER. THE CURE IS AN INTELLECTUALLY HONEST, "I DON'T KNOW. EXPLAIN IT TO ME IN ENGLISH."

ABSENT FULL UNDERSTANDING, THERE CAN BE NO COMMUNICATION. REPORTS AND ADVICE COUCHED IN SCIENTIFIC JARGON CAN NEVER FULLY ENTER THE MIND OF A COMMUNICATEE UNVERSED IN THAT JARGON. IT IS A MIRACLE THAT DECISIONS MADE IN SUCH AN ENVIRONMENT HAVE NOT THUS FAR PRODUCED VIOLENT TRAGEDY, THOUGH I AM SURE IT HAS PRODUCED NUMEROUS MINOR, UNRECOGNIZED TRAGEDIES.

SUMMARY

MR. CHAIRMAN, I SUPPOSE THE FOREGOING MIGHT BE SUMMARIZED IN THE FORM OF FOUR COMMANDMENTS:

(1) THOU SHALT NOT ABRIDGE THE FREEDOM TO LEARN.

(2) IF THOU REGULATE THE USE OF LEARNING, TAKE CARE THAT THOU SHALT NOT SMOTHER THE FREEDOM TO LEARN.

(3) THOU SHALT NOT TAKE COUNSEL ONLY OF THY FEARS.

(4) THOU SHALT COMMUNICATE OPENLY, WIDELY, CANDIDLY, COMPLETELY--AND IN THE SAME LANGUAGE.

HARKENING TO MY PLEA FOR SIMPLE ENGLISH, THOSE FOUR COMMANDMENTS MIGHT BE SIMPLIFIED AS:

(1) DON'T STIFLE SCIENCE.

(2) REGULATE TECHNOLOGY WITH CARE.

(3) DON'T LET FEAR CONTROL.

(4) COMMUNICATE IN ENGLISH.

YOU AND THE SUBCOMMITTEE, MR. CHAIRMAN, HAVE BEEN KIND IN INVITING ME AND GENEROUS IN LISTENING TO ME HERE TODAY. IF I HAVE ADDED LITTLE OF USE IN YOUR DELIBERATIONS, THAT RESULT WAS NOT INTENDED. I HAVE, IN OTHER CIRCLES, BEEN THOUGHT OF AS AN IRISHMAN WHO MAY NOT ALWAYS BE RIGHT, BUT WHO IS NEVER UNCERTAIN. HENCE, THE VIEWS EXPRESSED, THOUGH MINE ALONE AND ALWAYS SUBJECT TO CORRECTION, ARE TRULY FELT. I SHOULD BE GLAD, MR. CHAIRMAN, TO ATTEMPT ANSWERS TO ANY QUESTIONS YOU OR ANY MEMBER OF YOUR SUBCOMMITTEE MAY WISH TO ASK.

Mr. THORNTON. I would like to take this opportunity to point out that, while the tiny DNA helix is small as it appears today in itself, still I am told that the chromosomes for a human being, if it were stretched out lengthwise, would be 6 feet in length. So it might comprehend quite a large fund of knowledge.

Judge MARKEY. In my case it does not, Mr. Chairman.

The full statement refers to the fact that what I know couldn't even be cut by a restricted enzyme. And I think that is pretty small.

The Constitution of the United States, Mr. Chairman, in my view grants no specific powers to the Congress respecting scientific research. If our forefathers were writing today, however, I think they would include, probably as a part of the first amendment, "Congress shall make no law abridging the freedom to learn."

Science, in my view, is but another word for the freedom to learn. Technology is but another word for the use of learning. An analogy may be drawn to the first amendment prohibition against abridgments of freedom of speech. As the courts, in freedom of speech cases, have distinguished between freedom of ideas and freedom of action, so too, a distinction may be drawn between science, considered as ideas, and technology, considered as action. Man must remain free, for example, to research crowd reaction to stimuli. He cannot be free to falsely cry fire in a crowded theater.

The suggestion, indeed the insistence by some, that research into recombinant DNA should be permanently stopped, is disturbing, though not surprising. That phenomenon rests on a false notion, that is, that things can remain as they are. But life is a movie, not a series of still slides. Even if it were desirable, it is impossible to say, "We shall stop here and go no further." It is impossible to say that for our own country, let alone for the entire world. To paraphrase Judge Learned Hand, who spoke of justice, "You shall not ration learning."

In today's world, when we desperately need scientific and technological solutions to our problems of energy, the environment, overpopulation—when we desperately need to increase the birth rate of discovery, invention, and innovation—this is not the time to encourage mental contraception and technological abortion.

DNA is also new for having entered the public arena in its early research stages. Until recently, not excluding atomic splitting, the public has been more often confronted with scientific discoveries secretly achieved and their technological progeny full grown. I do not decry the existence or actions of those who have been called, fairly or unfairly, "disaster mongers." They serve an important early warning function. Their concerns cannot be safely ignored, but must be calmly evaluated, and if those concerns be unfounded they should be calmly and adequately refuted.

But, to again paraphrase, in this case Benjamin Franklin, "Those who would seek total security and absolute predictability, at the price of a little learning, shall enjoy neither." We must not take counsel of our fears alone. That way lies sterility, stagnation, and paralysis. Whatever is done to control the use of learning must not stifle science. It must not stifle the search. It must not abridge our freedom to learn.

Man has always lived with a fear of the unknown, but the consequences of research are inherently unknown. If life itself is unpredictable, and it certainly is, then why search we all for certainty?

Section 202 of the Atomic Energy Act, an act relating to a frightening scientific development if there ever was one, employs a "minimize the dangers" criterion. Of course we must take some counsel of our fears, but only as to the methodology of our learning and how we shall use what we learn. We must never take counsel of a fear of learning.

Like all man's activities, science and technology have societal responsibilities. Like wars are too important to be left entirely to generals, like justice is too important to be left entirely to judges, science and technology are too important to be left entirely to scientists and technicians.

There is no risk-benefit dichotomy applicable to science, that is, to the right to learn. Knowledge learned is all benefit and no risk. Not so with technology.

So long as its regulations do not suffocate the freedom to learn, I see no constitutional limitation on the power of Congress to regulate the use of cell mating knowledge or the manner in which that knowledge is acquired.

Whether regulations can be devised to minimize danger while preserving the freedom of research should, I think, be the fundamental question before this subcommittee. I should not like to enter history, for example, as the congressman, laboratory director, or agency administrator who so smothered this particular technology with regulation as to have delayed a cure for cancer by 50 years.

At the moment, the important thing may be to publicize the guidelines as guidelines. Commercial firms and their laboratory workers are not bent on suicide. Early publication of Kepone dangers might have avoided the tragedies at the James River.

The Secretary of HEW found it necessary to form an interagency committee to explore the "problem" of implementing the guidelines in all agencies. Should the interagency committee be unsuccessful, the scientific community could face a smorgasboard of guidelines from which to choose.

The duty of Congress may be, at this stage, simply to remain informed. Its concern for the public welfare, that is, the protection of public safety while maintaining the freedom to learn, may include the maintenance of a public perspective in which legitimate fears are met with appropriately limited regulation and unfounded fears are met with clear explanations. The role of Congress, in my view, is not merely a negative role. It can and should be a positive and creative role, which, while keeping one eye on safety, includes the promotion of progress in our economy, our agriculture, our health, and similar concerns.

There may be a role model in the Joint Congressional Committee on Atomic Energy. There are differences between recombinant DNA research and atomic energy research, primarily in the U.S. ownership of atomic fuels. The Joint Congressional Committee is an outstanding example of democratic control, effective and yet not suffocating, over a major scientific development.

Congress can be an effective partner in shaping public policy in pace with scientific development, and in channeling the modern miracles of science toward the benefit of man. As in any partnership, however, communication between partners is paramount.

This subcommittee, through its present "workshops", is moving out to inform itself and to encourage the partnership communication of which I speak.

Open and widespread communication, honest and candid, can, and probably will serve as the major weapon against tragedy in recombinant DNA research, as it will in connection with other scientific research and development.

Like the Six Million Dollar Man, the unbiased man, and hence unbiased advice, does not exist. That advice may be biased, however, is neither fatal nor cause for despair. The key is evaluation of the thing advised, comparing and weighing it against contrary advice. It may be useful to evaluate also the source, so long as source evaluation does not control acceptance or rejection of the thing advised. Even so, if our evaluation focuses primarily on what is said, and far less on who says it, the chances of a safe and sane decision are increased.

Communication may be distorted by attention-getting, leading to overblown assurance or scare reports in newspapers; communication may be both distorted and destroyed when the partners use different languages. Scientific jargon will not simply go away. It has been around too long and serves too useful a purpose as a quick shorthand for scientists.

Every discipline has its jargon. In the legal profession, we have only comparatively recently waked up to the stupidity of things like "res ipsa loquitur." We are now trying to say, "The thing speaks for itself." We have an organization called "Scribes", holding seminars and doing its best to get lawyers and judges to speak English. Perhaps what is needed is a Scribes organization for scientists.

The English language is marvelously flexible. I think it can safely be said to scientists that, "If you cannot describe in English what you want to do, don't do it."

It may also be well if every laboratory had on its staff an English major, whose function would be to translate every scientific report coming out of the laboratory, and intended for any nonscientists, into clearly understandable English. That the suggestion may not be too far afield is illustrated by the success of newspaper science writers, who are everyday converting science lingo into newspaper English for their readers. One encouraging development in this direction is the growing practice of inviting the press to scientific meetings.

Communication is a two-way street. If we are to pierce the word "curtain", the decisionmakers in the Congress, the agencies, and the judiciary, must play their part.

If effective communication is to be achieved, it is incumbent upon the Congress, the executive, and the judiciary to refuse every report or advice not couched in clear English. The alternative is to remain intimidated by jargon and vicinibly ignorant of the whole truth.

Too often we decisionmakers, afraid to admit we don't understand, accept and even repeat the scientific jargon presented to us, trying to at least sound like we know what we are talking about. The cure is an intellectually honest, "I don't know. Explain it to me in English."

Mr. Chairman, I suppose the foregoing might be summarized in the form of four commandments.

Harkening to my plea for simple English, those four commandments might be simplified as:

(1) Don't stifle science.
(2) Regulate technology with care.
(3) Don't let fear control.
(4) Communicate in English.

You and the subcommittee, Mr. Chairman, have been kind in inviting me and generous in listening to me here today. If I have added little of use in your deliberations, that result was not intended. I have, in other circles, been thought of as an Irishman who may not always be right, but who is never uncertain. Hence, the views expressed, though mine alone and always subject to correction, are truly felt. I should be glad, Mr. Chairman, to attempt answers to any questions you or any member of your subcommittee may wish to ask.

Mr. THORNTON. Thank you very much, Judge Markey, for an excellent statement.

I also would like to commend to staff the fine speech which you prepared, more of an essay on science and law, on the acceptance of your Jefferson medal at the New Jersey Patent Law Association—it is excellent work.

As a matter of fact, it fits in rather closely with some work that this subcommittee is doing on the development of a uniform patent policy. And should time permit later on in the proceedings, I would hope that we might address some of the implications of patent policy as a means of effectuating control of such things as DNA molecule research.

Mr. Hyde, do you have any questions of Judge Markey before we go to the other witnesses?

Mr. HYDE. Nothing specific, Mr. Chairman.

The Joint Committee on Atomic Energy, do we still have that?

Mr. THORNTON. It has been stripped of its authority. And I believe legislation has—I am not sure whether it has been signed into law to eliminate the committee or not. It may continue to have a statutory existence.

Mr. HYDE. That is what I thought. And Judge Markey was very favorably disposed toward the committee. And I frankly regret that it is in the descendancy rather than the ascendancy.

Just one other comment, Judge Markey, you mentioned, if you can't say it in English, don't do it. I know of several ideas that unfortunately the English language doesn't have an apt phrase for. And I will discuss those with you privately sometime.

I have no further questions.

Mr. THORNTON. However, I would like to follow that particular point by suggesting that that is indeed one of the great problems that we have in many areas of Government. And that is that people in a particular specialty tend to develop a vocabulary which is clear in meaning to the members of the profession, but which is very hazy and ill-defined to the members of the general public. Sometimes we see a brochure put out by an agency which was supposed to let municipalities know what might be useful in the way of new scientific research, and they described a hyperbolic queuing model for emergency vehicles. Well, I doubt that many small town mayors in Arkansas would know that what they were talking about was a means of associating the emergency vehicles as to be at the location which is most likely to be convenient to an expected disaster. So it looks like they could have said that clearer, that is, how to put the ambulances and the fire trucks where the action is expected to be.

Judge MARKEY. Mr. Chairman, we have every day in the paper here a section on gobbledegook, which we probably shouldn't mention in these halls because of the constant reference to the jargon employed by those of us in the Government. It is like shoveling sand against the tide to fight against the jargon of each separate group. But that doesn't destroy the need to make the fight. I think it is critical. I think we will be stumbling in the dark constantly unless something is done.

And at the risk of disputing for even 1 second Mr. Hyde's thought, I am sure that newly created science needs some definition. But I think there are analogies to be drawn, that there are ways and means of explaining it. We don't have to say deoxyribonucleic acid every time. We can say the molecule that controls heredity. It may not be totally accurate, but for the public, the nonscientist, it will be enough to understand. And that is where we need this communication in between.

Dr. SONNEBORN. May I make a comment on this?

I don't know whether you are familiar with this or not, but it is a fact that in the last decade, particularly in the universities, there have been many professors—Dr. Edsall, Dr. Glass, and I are among them—who teach science courses for students with no scientific background. They come right into the cold as it were, and they are amazed and delighted to find out that they can understand.

Mr. THORNTON. And on a scientifically related matter we frequently encountered, with a great deal of skepticism, some particular title of a scientific research, which may actually be for a very good purpose, but the title of which lends itself to a great deal of misunderstanding. Research which may be way out on the fringes should at least be labeled so that people can understand what is being looked into.

Judge MARKEY. That is part of the problem, Mr. Chairman—not to prolong it, I honor and respect the professors for letting the people take courses even though they had no scientific background before they took them. And that is great. But I think I am more concerned about the public, and particularly in relation to the ease with which a scare headline can be obtained.

A scare story, a scientific scare story, is almost guaranteed a headline. And when that is couched in highly technical jargon, it lends an aura of authenticity and believability to the report, which may or may not be valid. And, of course, the public, not having the guidance of professors in the university, would tend to believe it—were it to be given in plain English, if there were any way to do that, I think it would be a boon.

Mr. THORNTON. Thank you again, Judge Markey.

Our next witness is Dr. John Edsall, who is professor emeritus of biochemistry, of Harvard University.

Dr. Edsall, we are delighted to have you with us today. And your complete biography will be made a part of the record.

We are pleased to have your prepared statement, which without objection, will be made a part of the record at this point in the record.

[The biographical sketch and prepared statement of Dr. Edsall follow:]

DR. JOHN TILESTON EDSALL

Born in Philadelphia, Pa., November 3, 1902.

A.B. Harvard University, 1923; M.D. Harvard Medical School, 1928; and studied at University of Cambridge, England, 1924–26.

Instructor and Assistant Professor in Biochemistry, Harvard University, 1928–40. Associate Professor of Biochemistry, 1940–51. Professor of Biochemistry,

Member of National Academy of Sciences; American Academy of Arts and Sciences; American Philosophical Society; American Society of Biological Chemists (President, 1957–58); and American Chemical Society (Chairman, Division of Biological Chemistry 1948–49, 1950–51).

Foreign Member, Danish and Swedish Academies of Science.

Editor-in-Chief, Journal of Biological Chemistry, 1958–67. Editor, Proceedings of the National Academy of Sciences, 1968–72.

In charge of the Survey of Sources for the History of Biochemistry and Molecular Biology, American Philosophical Society Library, 1975– .

Guggenheim Fellow, California Institute of Technology 1940–41. Fulbright Lecturer, University of Cambridge, England, 1952 and in University of Tokyo, Japan, 1964. Visiting Lecturer, Australian National University, Canberra, 1970. Distinguished Visiting Professor, University of California, Los Angeles, February and March 1977.

Address: Biological Laboratories, Harvard University, Cambridge, Mass.

PREPARED STATEMENT OF JOHN TILESTON EDSALL

My name is John Tileston Edsall, and I am Professor of Biochemistry, Emeritus at Harvard University. I hold a medical degree, but have always been engaged in biochemical teaching and research. My research has dealt with the physical chemistry of amino acids, peptides, and proteins, including enzymes. I have worked particularly with blood proteins, and was much involved with the preparation of blood plasma fractions for clinical use during the Second World War. Since I became Emeritus I have been primarily concerned with historical studies on biochemistry and molecular biology, and with the relations of science and social problems. I have never worked experimentally on problems of molecular genetics, and am not doing laboratory work at all any more. I mention these points, in order to point out that I have no personal stake in research on recombinant DNA; whatever regulations are imposed on such research will not affect my personal plans or activities. As a member of the scientific community, with friends on both sides of the controversy over recombinant DNA, I do inevitably have some emotional involvement with the issue. I still believe, however, that I can view the matter with a reasonable degree of objectivity.

I would say at once that I am deeply concerned about various environmental hazards arising from technology. I was for instance an active opponent of government funding for the SST program, because of the human and environmental damage that such supersonic planes could inflict, without adequate compensating benefits. I am a strong supporter of more rigorous standards for the protection of occupational safety and health; in many cases—asbestos, PCBs, vinyl chloride, and other toxic substances—action to protect the workers and the public has come much later than it should have, and in many cases it is still gravely inadequate. These matters are more fully discussed in a report on "Scientific Freedom and Responsibility" (American Association for the Advancement of Science, Washington 1975) which I wrote on behalf of a Committee of the AAAS that was set up to deal with that broad subject.

In that report we discussed the moratorium on recombinant DNA research, imposed in 1974 by the scientists themselves before guidelines were worked out, and hailed it as an example of scientific responsibility in action. The NIH guidelines, and the stormy controversy that followed their promulgation, were still to come.

The problem of recombinant DNA research is quite different from the environmental hazards that I have mentioned above. Those were all strictly technological developments, unrelated to advance in basic science. Recombinant DNA research is in one sense a new form of technology, of small scale engineering. Its great interest, however, lies in the use of these new techniques to explore fundamentally new domains in basic genetics, and obtain quite rapidly answers to questions that might have been explored by other means, but far more slowly and cumbrously. Some of the practical benefits that might flow from such research have been widely discussed, such as the large scale production of important hormones and antibodies that could result from implanting the appropriate genes into bacteria, and growing them in very large batches. This is still speculative, though certainly possible. I would prefer not to make premature claims of such practical benefits. I believe rather that the most important consequence of this research for human welfare will come from the profound advancement that it can help to bring about in our basic understanding of life processes.

Practical consequences will certainly flow from that understanding, and I believe that they will be far greater than the particular procedures that we can now imagine. I would not claim, of course, that all the possible practical applications would be beneficent. Here as elsewhere knowledge can and probably sometimes will be misused; the eternal vigilance required for proper assessment and control of technology will be in demand, here as elsewhere. I do not believe that worries over possible misapplication of the research should serve as a basis for banning or retarding it. This point raises fundamental issues, to which I return later.

Fears of two kinds haunt the critics who oppose research on recombinant DNA, or who wish at least to see the guidelines imposed upon it made far more drastic than those of the NIH. There is the fear of producing new pathogenic organisms, and releasing them with resulting epidemics, of infectious disease or of cancer. Also there is a deeper anxiety on the part of many people; a fear that the very knowledge we attain may be more than the human race, in its present state of development, can wisely use; that we shall be tempted to misuse it, and that that misuse could lead to our destruction. They point to the history of nuclear weapons, in which a discovery made by basic scientists who sought to unravel the secrets of nature has led to a fantastic arms race, and to a threat of destruction that now hangs over all mankind. My distinguished friend and colleague, Dr. Robert Sinsheimer, Chancellor of the University of California at Santa Cruz, has suggested that there may be kinds of knowledge that we would be better off without; for instance, it would be a grave misfortune if we learned how to enable people live for 150 or 200 years—for if we know how to do it we would probably be impelled to make use of that knowledge, and the social consequences probably would be disastrous. I would not try to dismiss such fears lightly; critics like Sinsheimer have raised questions that deserve thoughtful consideration, and I will say more of that below.

First, however, I turn to the possible threat of epidemics from newly cloned organisms, bearing genes from higher organisms—genes that they never carried before. Here I must remind you that I am no expert in microbiology, or in the culture of living cells. In evaluating the NIH guidelines, I have to use my own general scientific judgment, corrected and fortified by consulting colleagues who are expert in those disciplines. After doing this I have come to the conclusion that the guidelines are soundly and adequately drawn. Indeed I think that the NIH authorities have, if anything, leaned over backward a bit, and have made the guidelines a little more stringent than was really required for the protection of the public. If they have done so, it was a sound procedure; far better, at this stage, to be too strict than too lenient. Those who drew up the guidelines did not start from scratch; we have the experience of a century of research on pathogenic microorganisms to guide us.

The design of laboratories, and the precautions that must be taken by the workers in them, to insure the containment of such organisms, have been worked out, over the years, with great effectiveness. In work on recombinant DNA, new stringent controls are introduced, most notably with respect to the use of mutant forms of the bacterium E. Coli K–12, which is itself a scarcely infectious form of the colon bacillus, even without mutation. The mutants that would be used in all experiments involving even a moderate estimated hazard have been so modified that they require special nutrients in order to grow; nutrients which they are almost certain not to encounter if by any chance they should escape from the laboratory. The level of protection afforded should be very high indeed.

Certain kinds of possible experiments, involving transfer of genes from pathogenic organisms to E. Coli K–12 as host, are entirely forbidden by the guidelines. Anyone who attempted to violate these guidelines would have to operate in secrecy, subject to severe penalties, and to probable ostracism by all his scientific colleagues, if he were found out. Even if some embittered enemy of the human race set out deliberately to create a new deadly disease-producing organism, he would almost certainly find the task close to impossible. The development of a really toxic bacterium or virus requires extraordinary adaptations; such as organism must fit into a very special kind of an ecological niche in order to survive, and to create a new one artifically would be a fantastically difficult trick.

Of course we cannot foresee in advance all the hazards of research on recombinant DNA—or on almost anything else. My own conclusion, however, is that the risks, if the NIH guidelines are observed, are extremely low, and are such as we accept freely in the living of our lives in general. Personally I am far more concerned about the hazards of the hundreds of thousands of chemicals that

are being produced, on an industrial scale. I have mentioned a few of them before, such as vinyl chloride and the PCB's; the total number is immense, and growing, and the controls are still gravely inadequate, though the Toxic Substances Control Act is a big step in the right direction. I am troubled that the outcry over the presumed dangers of recombinant DNA tends to distract us from concern over what I believe to be these far more real and present dangers.

I return now to the more basic fears that research on recombinant DNA has aroused; the fears that new knowledge, of certain sorts, may be inherently dangerous, and that we would be better off without it. Such fears have deep roots in the past; for instance it is written in the Book of Ecclesiastes that "He that increaseth knowledge increaseth sorrow". The spirit of most modern science, of course, has been directly contrary; scientists have generally held the advancement of knowledge to be an inherent good, even though some knowledge could be (and was) misused. This was the general temper of the times in the nineteenth and early twentieth century, at least in the industrial nations. Certainly it was the development of nuclear weapons that did more than anything else to shake this faith. The development of these weapons grew directly, and rapidly, from basic discoveries made by investigators who were not thinking of practical applications at all; and the consequences of those discoveries, if not brought under control, could destroy our civilization and more than cancel out all the benefits we have derived from the advancement of knowledge.

Inevitably this appalling problem haunts us, when we consider the possible applications of some dramatic new discovery in basic science. Yet I believe that nuclear weapons represent a very special case. The availability of weapons of such overwhelming power, in a world of sovereign states with no effective international control, produces powerful pressures that lead to an escalating arms race. We have not yet learned how to break that pattern, potentially disastrous though it is for all concerned. On the other hand there are no such military and psychological pressures to escalate the recombinant DNA race for nationalists advantage.

One can imagine the use of recombinant DNA in the attempt to produce new biological weapons, though it would probably be a relatively ineffective technique for anyone who wanted to do this; I have already indicated some reasons for this view. Any such experiments, of course, are banned in this country under the NIH guidelines, quite apart from our renunciation of biological warfare techniques. I doubt whether there would be real pressures anywhere to make such evil uses of recombinant DNA research. In this instance, therefore, I think. that there is no analogy with the problems raised by nuclear weapons; the fears that such weapons justly raise have no analogy for policy related to recombinant DNA.

I share some of Dr. Sinsheimer's concern about the possible applications of research on aging. If we learned how to double the present human life span, and keep people healthy to the age of 150 or so, many people would no doubt be eager to apply that knowledge; and I think, for reasons that I need not elaborate, that the social consequences would be highly undesirable and perhaps disastrous. (Incidentally I think that it is highly doubtful that we shall ever be able to do this, no matter how hard we try). If such techniques should ever be discovered, however, it is very likely that they will emerge from some quite different line of research, not from a program devoted specifically to the problems of aging. That is what usually happens in scientific research, and there is nothing much that we can do about it, unless we decide to shut down research entirely. We are not likely to do that. I believe that we shall have to take our chances that research will, from time to time, bring us face to face with some very knotty practical problems, and we must learn to cope with the consequences as best we can. The Congress, and people generally, are just beginning to grapple with the problems of technological assessment and control. With experience we shall learn to do a much better job on that, to look carefully before we commit ourselves to new large-scale enterprises. This will apply also to the practical consequences of recombinant DNA research.

The fact is, as Dr. Lewis Thomas[1] has emphasized in a recent thoughtful article, that we are still profoundly ignorant of the fundamentals of biology. The great advances of the last thirty years, in molecular genetics and in protein structure and function, are indeed extraordinary; we possess now a far deeper insight into many of the fundamental problems of biology than I would earlier

[1] Lewis Thomas "Notes of a Biology Watcher: the Hazards of Science": New England Journal of Medicine 196, 324–328 (Feb. 10, 1977).

have dared to believe that we would attain during my lifetime. I believe, however, that we are still only near the beginning; that what we have still to learn is vast, compared to what we know. I also believe—and I think that this is not just a romantic illusion—that deeper knowledge will in time lead to deeper wisdom; not merely to new techniques and gadgets that will make us healthier and enable us to grow more and better crops, but to a more profound understanding of how living creatures work, and of the conditions required for the good of life in general. Certainly there is no guarantee that increased knowledge in itself will make us wiser; we are sure to make mistakes and misapply some of the things we learn. Increased knowledge does not insure increased wisdom, but I do not believe that we shall ever attain the wisdom if we abandon the endeavor to attain the knowledge.

I therefore believe that any legislation, designed to regulate and control DNA research, should be so drawn as to encourage investigators to pursue such research, subject to due regulation under the present guidelines of the NIH, or closely similar regulations. The regulations, of course, will be subject to constant review and modification as we gain experience. I suspect that we may find that some of the restrictions may be safely relaxed within a few years; that is for experience to decide. I also believe that the body that is to administer and enforce the guidelines (which in future may be legal requirements) should be a part of the National Institutes of Health, perhaps affiliated also with the Center for Disease Control. It should of course contain, not only experts in science, medicine, and public health, but also representatives of the public, since research on recombinant DNA is a matter of great public concern, and can be conducted effectively only with proper understanding and support from the public. I also believe that the regulations should be generally applicable throughout the United States, and that local communities should not be entitled to impose more stringent requirements than those embodied in the national regulations. The problems raised by DNA research are national and international; the requirement of a variety of local rules in different places would complicate and confuse the enforcement of general national regulations. Finally I believe that, since this research will proceed in many countries throughout the world, it is essential to reach international understandings concerning the regulation of research in this area. I know that the authorities at the NIH are profoundly aware of the importance of this; I am sure that they will receive Congressional help and support in the development of a world-wide network that will both foster and regulate research that can do so much to enhance our understanding of life and how it works.

I thank you for the opportunity to present these views.

Mr. THORNTON. We ask you to please proceed.

STATEMENT OF DR. JOHN T. EDSALL, PROFESSOR EMERITUS OF BIOCHEMISTRY, HARVARD UNIVERSITY

Dr. EDSALL. I will deal with the major points here.

I should point out, to begin with, that I have never worked on recombinant DNA myself or even on closely related problems. I am a biochemist and physical chemist who has worked chiefly on proteins. So I don't have a personal stake in the matter. I am not going to do research in this field.

I am now emeritus, and I am working largely on the history of science. And I hope, therefore, that I can be perhaps a little more objective than some of the people who are involved in this field, although objectivity is very hard to obtain anyway.

I am, of course, much concerned about many serious environmental problems that arise from modern technology. But the problems of recombinant DNA research are quite different from most of these environmental hazards. Those were all strictly technological developments. They did not contribute to advances in basic science generally. But recombinant DNA research, though it is one sense a new

form of technology, a kind of small-scale engineering, is still fundamentally a great and powerful new method of finding out answers to questions that might have been explored by other means, very important questions in fundamental biology. But the other means would generally take us to the answers much more slowly than recombinant DNA research promises to do.

Various practical benefits have been suggested that may arise from this research. I won't try to go into them. You have certainly heard about them already from earlier testimony in these hearings. Practical consequences will certainly flow from increased understanding of fundamental biology. But I think the most important consequence for human welfare is going to come from the profound advancement that this research can help to bring about in our basic understanding of life processes.

Fears of two kinds hunt the critics who oppose research on recombinant DNA, or who wish at least to see the guidelines imposed upon it made far more drastic than those of the NIH. There is the fear of producing new pathogenic organisms, and releasing them with resulting epidemics, of infectious disease or of cancer. Also, there is a deeper anxiety on the part of many people; a fear that the very knowledge we attain may be more than the human race, in its present state of development, can wisely use; that we shall be tempted to misuse it, and that such misuse could lead to our destruction. They point to the history of nuclear weapons, in which a discovery made by basic scientists who sought to unravel the secrets of nature has led to a fantastic arms race, and to a threat of destruction that now hangs over all mankind.

My distinguished friend and colleague, Dr. Robert Sinsheimer, chancellor of the University of California at Santa Cruz, has suggested that there may be kinds of knowledge that we would be better off without; for instance, it would be a grave misfortune if we learned how to enable people to live for 150 or 200 years—for if we learned how to do it we would probably be impelled to make use of that knowledge, and the social consequences probably would be disastrous. I would not try to dismiss such fears lightly; critics like Sinsheimer have raised questions that deserve thoughtful consideration. But I still come out with quite different conclusions.

As to the possible threat of epidemics from newly cloned organisms bearing genes transferred from higher organisms, genes that they never carried before, how much of a danger is there? I must remind you that I am no expert in microbiology, or in the culture of living cells. In evaluating the NIH guidelines, I have to use my own general scientific judgment, corrected and fortified by consulting colleagues who are expert in those disciplines. After doing this I have come to the conclusion that the guidelines are soundly and adequately drawn. Indeed I think that the NIH authorities have, if anything, leaned over backward a bit, and have made the guidelines a little more stringent than was really required for the protection of the public. If they have done so, it was a sound procedure; far better, at this stage, to be too strict than too lenient. Those who drew up the guidelines did not start from scratch; we have the experience of a century of research on pathogenic microorganisms to guide us. The design of laboratories, and the precautions that must be taken by the workers in them, to in-

sure the containment of such organisms, have been worked out, over the years, with great effectiveness. In work on recombinant DNA, new stringent controls are introduced, most notably with respect to the use of mutant forms of the bacterium E. Coli K–12, which is itself a scarcely infectious form of the colon bacillus, even without mutation. The mutants that would be used in all experiments involving even a moderate estimated hazard have been so modified that they require special nutrients in order to grow; nutrients which they are almost certain not to encounter if by any chance they should escape from the laboratory. The level of protection afforded should be very high indeed.

Certain kinds of possible experiments, involving transfer of genes from pathogenic organisms to E. Coli K–12 as host, are entirely forbidden by the guidelines. Anyone who attempted to violate these guidelines would have to operate in secrecy, subject to severe penalties, and to probable ostracism by all his scientific colleagues, if he were found out. Even if some embittered enemy of the human race set out deliberately to create a new deadly disease producing organism, he would almost certainly find the task close to impossible. The development of a really toxic bacterium or virus requires extraordinary adaptations; such an organism must fit into a very special kind of an ecological niche in order to survive, and to create a new one artificially would be a fantastically difficult trick.

Of course we cannot foresee in advance all the hazards of research on recombinant DNA—or on almost anything else. My own conclusion, however, is that the risks, if the NIH guidelines are observed, are extremely low, and are such as we accept freely in the living of our lives in general. Personally I am far more concerned about the hazards of the hundreds or thousands of chemicals that are being produced, on an industrial scale; for example, vinyl chloride and the PCB's. The total number of such chemicals is immense, and growing, and the controls are still gravely inadequate, though the Toxic Substances Control Act is a big step in the right direction. I am troubled that the outcry over the presumed dangers of recombitant DNA tends to distract us from concern over what I believe to be these far more real and present dangers.

In addition to all this, as I mentioned before, there is the underlying concern of some people that certain kinds of knowledge may be inherently dangerous, quite apart from the technological applications that could follow from that knowledge. Such fears are deeply rooted in the past.

It is written, for instance, in the Book of Ecclesiastes that "He that increaseth knowledge increaseth sorrow." The spirit of most modern science, of course, has been directly contrary; scientists have generally held the advancement of knowledge to be an inherent good, even though some knowledge could be—and was—misused. This was the general temper of the times in the 19th and early 20th century, at least in the industrial nations. Certainly it was the development of nuclear weapons that did more than anything else to shake this faith. The development of these weapons grew directly, and rapidly, from basic discoveries made by investigators who were not thinking of practical applications at all; and the consequences of those discoveries, if not brought under control, could destroy our civilization

and more than cancel out all the benefits we have derived from the advancement of knowledge.

The analogy of nuclear weapons has been quoted by a number of people who warn us about the possible dangers of recombinant DNA. However, I think the suggested analogy does not really apply here.

The availability of nuclear weapons, of overwhelming power, in a world of sovereign states with no effective international control, produces powerful pressures for development of even more sophisticated weapons. These pressures lead to an escalating arms race. We have not yet learned how to break that pattern, potentially disastrous though it is for all concerned. On the other hand there are no such military and psychological pressures to escalate the recombinant DNA race for nationalistic advantage. Attempts might be made to direct recombinant DNA research to the production of new biological weapons; but I think such attempts would be relatively ineffective, for reasons I have already mentioned.

Any such experiments, of course, are banned in this country under the NIH guidelines, quite apart from our renunciation of biological warfare techniques as a matter of national policy. I doubt whether there would be real pressure anywhere to make such evil uses of recombinant DNA research. In this instance, therefore, I think that there is no analogy with the problems raised by nuclear weapons; the fears that such weapons justly raise are not, I think, relevant for policy-related to recombinant DNA.

As to Dr. Sinsheimer's warning concerning the possible dangers of research on aging, and the pressure to apply the acquired knowledge in a way that might be unfortunate, I don't believe that we can stop research in that general area Research that might lead to a breakthrough in the aging problem may come from some quite different direction, not from a program specifically devoted to studying the problems of aging. That is the way it usually happens in scientific research. And I think that is the way it is going to continue to happen, unless we decide to shut down research entirely, which I don't believe will or should happen.

I believe that we shall have to take our chances that research will, from time to time, bring us face to face with some very knotty practical problems, and we must learn to cope with the consequences as best we can. The Congress, and people generally, are just beginning to grapple with the problems of technological assessment and control. With experience we shall learn to do a much better job on that, to look carefully before we commit ourselves to new large-scale enterprises in the application of basic knowledge. This will apply also to the practical consequences of recombinant DNA research.

I would agree generally with the views of Dr. Lewis Thomas who, in a recent thoughtful article in the New England Journal of Medicine, emphasized that we are still profoundly ignorant of the fundamentals of biology. The great advances of the last 30 years, in molecular genetics and in protein structure and function, are indeed extraordinary; we possess now a far deeper insight into many of the fundamental problems of biology than I would earlier have dared to believe that we would attain during my lifetime. I believe, however, that we are still only near the beginning; that what we have still to learn is vast, compared to what we know. I also believe—and I

think that this is not just a romantic illusion—that deeper knowledge will in time lead to deeper wisdom; not merely to new techniques and gadgets that will make us healthier and enable us to grow more and better crops, but to a more profound understanding of how living creatures work, and of the conditions required for the good of life in general.

Certainly there is no guarantee that increased knowledge in itself will make us wiser; we are sure to make mistakes and misapply some of the things we learn. Increased knowledge does not insure increased wisdom, but I do not believe that we shall ever attain the wisdom if we abandon the endeavor to attain the knowledge.

Mr. THORNTON. I hesitate to interrupt—but before you come to the portion of this testimony where you summarize your conclusions, it is necessary now that I adjourn the meeting for a few minutes in order to answer a recorded quorum call and to make a vote, which I will do and then I will return.

We will be in recess for about 10 or 15 minutes.

[Short recess.]

Mr. THORNTON. The hearing will come to order.

At the time of our recess Dr. Edsall was about to give us some information, I think, concerning some guidelines we might use in drawing legislation in this area. Dr. Edsall, I would appreciate it if you would continue.

Dr. EDSALL. I have a few remarks to make on that.

I believe that any legislation that is designed to regulate and control recombinant DNA research should be drawn as to encourage the investigators to pursue such research, subject to due regulation under the present guidelines of the NIH, or something closely similar.

The regulations, of course, will be subject to constant review and modification as we gain experience. I suspect that we may find that some of the restrictions may be safely relaxed within a few years; that is for experience to decide. I also believe that the body that is to administer and enforce the guidelines (which in future may be legal requirements) should be a part of the National Institutes of Health, perhaps affiliated also with the Center for Disease Control. It should, of course, contain, not only experts in science, medicine, and public health, but also representatives of the public, since research on recombinant DNA is a matter of great public concern, and can be conducted effectively only with proper understanding and support from the public. I also believe that the regulations should be generally applicable throughout the United States, and that local communities should not be entitled to impose more stringent requirements than those embodied in the national regulations. The problems raised by DNA research are national and international; the requirement of a variety of local rules in different places would complicate and confuse the enforcement of general national regulations. Finally, I believe that since this research is proceeding, and will proceed, in many countries throughout the world, it is essential to reach international understandings concerning the regulation of research in this area. I know that the authorities at the NIH are profoundly aware of the importance of this; I am sure that they will receive congressional help and support in the development of a worldwide network that will both foster and

regulate research that can do so much to enhance our understanding of life and how it works.

Thank you for the invitation to appear at this hearing.

Mr. THORNTON. Thank you very much, Dr. Edsall.

Our final witness today is Dr. Tracy Sonneborn, who is professor emeritus of biology from Indiana University.

Your biographical materials will be included in the record, Dr. Sonneborn. And we are pleased to have you with us, and ask that you proceed at this time.

[A biographical sketch of Dr. Sonneborn follows:]

DR. TRACY SONNEBORN

T. M. Sonneborn is Distinguished Professor Emeritus of Biology at Indiana University. He is a past President of the Genetics Society of America and of the American Institute of Biological Sciences, and Honorary Member of the Genetics Society of Japan, and was one of the original members of the Committee on Science and Public Policy of the National Academy of Sciences. He is a Foreign Member of the Royal Society of London and holder of the Mendel Medal of the Czechoslovakian Academy of Sciences and the Kimber Genetics Medal of the U.S. National Academy of Sciences. He has taught genetics and done basic research in genetics for 50 years. Although not a molecular geneticist and not involved in recombinant DNA research, he convened in 1963 the first public forum in the USA on the ethical and social problems likely to arise from research in molecular genetics, published (1965) in book form under the title "The Control of Human Heredity and Evolution."

STATEMENT OF DR. TRACY SONNEBORN, PROFESSOR EMERITUS, BIOLOGY, INDIANA UNIVERSITY

Dr. SONNEBORN. One of the disadvantages of coming last is that there is nothing left to be said that hasn't already been said.

Dr. Edsall and the others have said many of the things that I wanted to talk about. So I think I am going to make it as brief as possible. Of the three topics I had intended to talk about concerning the implications for society and for science of science policy associated with recombinant DNA, public input and global aspects have already been discussed. So I shall say little about them, but more about the potential diversity of regulatory policies.

On public input, the issue, I think, is very clear. The advantages are on both sides, both for the scientists and for the public to inform each other and understand each other and be better prepared to accept in that way any public actions that are taken.

On the global aspects of safety policy, it has been pointed out many times that whatever risks exist in American research exist also outside of America. And the risk is based on three "ifs"—all big "ifs." If a harmful modification of a micro-organism were produced, if it escaped from any laboratory anywhere, and if it were viable and reproducible outside of the laboratory, then it could perhaps spread over the whole world. And obviously, the logic of that situation calls for a global policy ratified by national accords or for essential congruence of all national policies at a satisfactory safety level, however the congruence may be achieved.

I understand that your committee has developed information on what is going on in other nations. And I didn't know that until I came here. So I wanted to urge it, and to urge that there be communi-

cation with representatives of other countries on how they are managing the problem.

Now, on the question of permitting local deviations in either direction from the national standard, I would like to add just a few words to what Dr. Edsall said.

It seems to me that, in view of the global logic of the situation and the mounting evidence that approved bacteria-recombinant DNA combinations cannot spread or even survive outside of the laboratory, it is hard to see any justification for worry about any local hazardous conditions that could be very serious in that respect. To be sure, one can visualize a laboratory being on a fault and sliding and breaking open. But then what would happen? Well, if the laboratory had been following the NIH guidelines, using the proper organisms, the organisms would self-destruct. So I don't see that there is any great danger.

And I think the point is that these organisms as now constructed can be maintained in the laboratory only with, in our jargon of the laboratory, TLC, tender loving care.

Mr. THORNTON. I believe that is ordinary English.

Dr. SONNEBORN. Well, we have adopted it.

The implications of science policy for the safety of society, in view of the global issue, should be obvious. I won't develop that any further.

Regulatory policies for recombinant DNA research are obviously of critical importance for the scientists and for science, and indirectly for society. When last I heard, which I admit was several months ago, regulatory policies were being developed in many European countries. I don't know whether any of them have been enacted into law. You probably know much better than I.

However, regulation is being practiced through various mechanisms in different countries. In some it applies to both universities and industrial laboratories. I think different countries are likely to end up with somewhat different regulatory procedures and mechanisms, and heterogeneity may be either desirable or undesirable, depending upon the nature of heterogeneity.

Now, I am not particularly qualified to comment on the important question of whether different regulatory procedures are appropriate for recombinant DNA research of different kinds, for example, basic and applied; or for work that is going on in different kinds of laboratories, for example, in universities and industry and institutes. However, I can say that applications of recombinant research to industry, agriculture, medicine, and especially to human engineering, still seem so far away, in spite of the rapid pace of discovery, that regulatory policies for them could safely be deferred for a while.

Because my first hand experience and observation is almost completely limited to basic research and researchers in universities, I will only comment on regulation of basic recombinant research in universities.

Assuming that the objectives of regulatory policy are to achieve minimal interference with the research consistent with reasonable safeguards for the biosphere and society, I shall discuss only two points: That regulation of such research is most likely to achieve its purposes

if the system of regulation receives the allegiance of the scientists; and that the research will flourish best when the regulatory system does indeed interfere least with the research efforts of the scientists.

Basic researchers in universities are already subject to considerable regulation by the universities, by granting agencies, and by scientific journals, as I shall be glad to spell out in more detail if you would like.

Suffice it to say now that journals, through peer review, control the quality of what is published; and granting agencies, again through peer judgments, actually exert considerable control on the quality of research that is carried on, and on the kind of research that is carried on—and they do this through control of the purse strings, sometimes after a daylong inspection of the laboratory, and interrogation.

Basic researchers sometimes grumble and complain about regulations at all levels, and occasionally with good cause. But on the whole, those systems of regulation are perceived by the scientists as having reasonable pruposes and as being satisfactorily administered. In practice they have won the allegiance of the researchers. I believe that if the same qualities were perceived by the scientists in a Federal system of regulation of recombinant DNA research, it would likewise easily win their allegiance.

At present, however, as you doubtlessly know, very many of them are dismayed by and passionately opposed to some of the proposals under consideration in congressional committees. They perceive these regulations as unnecessary, cumbersome, unenforceable—a serious threat to the pursuit of this area of basic research, and another step toward comparable regulation of more and more areas of basic biological research, perhaps even of other basic sciences and eventually of thought control. Hopefully, at least the worst of these perceptions are wrong. Regardless of whether they are or are not, this is how they are widely perceived. Under such circumstances, allegiance of the researchers can hardly be expected.

What they will do if these proposals become law, I cannot predict. However, one of their options is to make the best of it, the best in their view involving, however, a considerable decline of momentum in the progress of the research. Another option is to change their area of research, which is readily done in universities, though I believe usually not in industrial laboratories. There are also other options. Options considered undesirable could be forestalled by allaying, if possible, the fearful perceptions of the researchers or by adopting regulatory mechanisms to which they can give allegiance because of confidence in their necessity, justice, and workability.

Basic research is a creative, imaginative process. It aims to identify fundamental phenomena and then to investigate them on the principle that one bomb on the arsenal is more effective than 1,000 that plow the fields. It requires intensive, prolonged, concentrated effort, and is driven by that intense curiosity without which man would not be man. Typically, a basic reesarcher is completely immersed day and night in his search for clues, solutions, interpretations. Such work flourishes best under conditions of serenity and minimal distraction. Anxiety is the enemy of creativity and productivity and seriously distracts attention from the work in hand. The closer regulatory policy can come to minimal conflict with the conditions for creative work,

the more the basic research will flourish and the more conceptual and practical benefits will flow from it for society. I thank you.

[The prepared statement of Dr. Sonneborn follows:]

PREPARED STATEMENT OF T. M. SONNEBORN

Please forgive me, Mr. Chairman and members of the subcommittee, if I repeat points made earlier in these hearings. What went on at them I don't know, because I was unable to be present. I am trusting that you will draw me out by questions if what I say misses the mark you have in mind.

I intend to discuss the implications for society and for science of three aspects of science policy associated with recombinant DNA issues: Public input; the global aspect of safety policy; and the potential diversity of regulatory policies.

1. PUBLIC INPUT

As is well known, recombinant DNA has raised a wide range of bright hopes and dark fears in the public—that great composite of varied and often conflicting interest groups, scientists among them, as I hardly need remind this subcommittee. The policy of providing this heterogeneous public with information and ample opportunity to express its opinion before legislation crystallizes has had and continues to have in my opinion and in that of many others, beneficial implications for both scientists and the rest of the public. Society, when informed and heard in time, is more likely to be satisfied with the eventually adopted policies. Scientists, when given opportunity to inform the public of the scientific situation, and to listen to the values and concerns of the public, should be better prepared to accommodate reasonably to legislation based on the total imput.

2. THE GLOBAL ASPECT OF SAFETY POLICY

Recombinant DNA research raises, as you know, a global issue. Many countries have the capacity to carry on this kind of research and are doing it. Whatever risks exist in American research exist also outside of America. If a harmful modification of a microorganism were produced, if it were viable and reproducible outside of the laboratory, and if it escaped from any laboratory anywhere—three big ifs—it could probably spread over the whole world. The logic of the situation thus calls for global policy ratified by national accords or for essential congruence of all national policies at a satisfactory safety level, however the congruence may be achieved. There has already been effective international communication on the problem, especially among scientists. For example, scientists from many countries, including Japan and both western and eastern European countries, were participants and/or observers in the public recombinant DNA forum held last March by our National Academy of Sciences. This and other avenues of consultation and exchange of information and views have led to considerable—but not complete—similarity between the Guidelines set up in different countries for the conduct of recombinant DNA research. The World Health Organization is, I understand, serving as a more formal means for international exchange of information in this area.

So far as I know, no country has adopted anl no other country has looked favorably on, the possibility of permitting local deviations in either direction from the national standard. This is understandable in view of both the global logic of the situation and the mounting evidence that approved bacteria-recombinant DNA combinatons cannot spread or even survive outside of the laboratory. Even in the laboratory, they can be maintained only by that essential laboratory ingredient, TLC, tender loving care.

The implication of science policy for the safety of society, in view of the global issue, should be obvious. I assume and hope that the appropriate committees of Congress are keeping informed of policies and actions taken in other countries, as is necessary if we are to integrate our policy into a global policy. It seems to me desirable for Congress to go even further anl try, in whatever ways seem appropriate and feasible, to consult and exchange ideas with representatives of other countries in trying to work out safe and flexible global policy subject to modifications as knowledge and experience increase. While I have great respect for the quality and variety of our own national human resources, it seems expedient to assume that neither we nor any other one nation necessarily has a corner on the market of wisdom in this area of science policy. It is obviously a matter in which all nations have a stake and are equally at risk, or not at risk, as the case may be.

3. THE POTENTIAL DIVERSITY OF REGULATORY POLICIES

Regulatory policies for recombinant DNA research are of critical importance for scientists and science and, indirectly, for society. When last I heard, several months ago, regulatory policies were being developed in many European countries. I do not know whether any of these policies have been enacted into law. However, regulation is being practiced through various mechanisms in different countries and in some it applies to both university and industrial laboratories. Different countries are likely, I think, to end up with somewhat different regulatory procedures and mechanisms. Such heterogeneity could be either desirable or undesirable, depending on the nature of the diversities.

I am not particularly qualified to comment on the important question of whether different regulatory procedures are appropriate for recombinant DNA research of different kinds, e.g. basic and applied, or in different laboratories, e.g. in universities, independent institutes and industry. However I can say that applications of recombinant research to industry, agriculture, medicine, and especially to human engineering still seem far enough away, in spite of the rapid pace of discovery, that regulatory policies for them can safely be deferred for a while. Because my first-hand experience and observation is almost completely limited to basic research and researchers in universities, I shall comment only on regulation of basic recombinant research in universities.

Assuming that the objectives of regulatory policy are to achieve minimal interference with the research consistent with reasonable safeguards for the biosphere and society, I shall liscuss only two points: that regulation of such research is most likely to achieve its purposes if the system of regulation receives the allegiance of the scientists; and that the research will flourish best when the reguance of the scientists; and that the research will flourish best when the regulatory system does indeed interfere least with the research efforts of the scientists.

Basic researchers in universities are already subject to considerable regulation by the universities, by granting agencies, and by scientific journals, as I shall be glad to spell out in more detail if you wish. They sometimes grumble and complain about it, occasionally with good cause; but on the whole these systems of regulation are perceived by the scientists as having reasonable purposes and as being satisfactorily administered. In practice they have won the allegiance of the reesarchers. I believe that if the same qualities were perceived by the scientists in a federal system of regulation of recombinant DNA research, it would likewise easily win their allegiance.

At present, however, very many of them are dismayed by, and passionately opposed to some of the proposals under consideration in Congressional committees. They perceive these regulations as unnecessary, cumbersome, unenforceable, a serious threat to the pursuit of this area of basic research, and another step towards comparable regulation of more and more areas of basic biological research, perhaps even of other basic sciences and eventually of thought control. Hopefully, at least the worst of these perceptions are wrong. Regardless of whether they are or are not, this is how they are widely perceived. Under such circumstances, allegiance of the researchers can hardly be expected.

What they will do if these proposals become law, I cannot predict. However, one of their options is to make the best of it, the best in their view involving, however, a considerable decline of momentum in the progress of the research. Another option is to change their area of research, which is readily done in universities, though I believe usually not in industrial laboratories. There are also other options: Options considered undesirable could be forestalled by allaying, if possible, the fearful perceptions of the researchers or by adopting regulatory mechanisms to which they can give allegiance because of confidence in their necessity, justice and workability.

Basic research is a creative, imaginative process. It aims to identify fundamental phenomena and then to aim investigation at it, on the principle that one bomb on the arsenal is more effective than 1000 that plow the fields. It requires intensive, prolonged, concentrated effort, and is driven by that intense curiosity without which Man would not be Man. Typically, a basic researcher is completely immersed day and night in his search for clues, solutions, interpretations. Such work flourishes best under conditions of serenity and minimal distraction. Anxiety is the enemy of creativity and productivity and seriously distracts attention from the work in hand. The closer regulatory policy can come to minimal conflict with the conditions for creative work, the more the basic research will

flourish and the more conceptual and practical benefits will flow from it for society.

Mr. THORNTON. Thank you very much, Dr. Sonneborn.

I want to compliment each of our witnesses for their very excellent presentations.

And without objection, your prepared statements will be made part of the record.

I think that it might be useful in concluding this set of hearings, if we explore again the paradox of a search for knowledge, individual rights of freedom of thought and the protection of societal goals.

It often requires a balancing between the individual freedoms and goals and societal goals.

You mentioned the fact that freedom of speech does not give you the right to cry "fire" in a crowded theatre.

Dr. Thomas Emerson, who is professor of law emeritus at the Yale Law School, defined to our committee a rationale in which he divided scientific research into that which was action and that which was not action, and said that the portion of research which dealt with ideas and the thinking process was protected in his view by the first amendment. It was only when it became action and carried forward into life itself that it lost the protection of the first amendment.

Of course, in recombinant DNA molecule research it can be argued that experimentation with the molecule which controls heredity—a phrase which I support the use of—that that is action, rather than being merely thought or speech. How would you address that issue, Judge Markey?

Judge MARKEY. Well, Mr. Chairman, I find myself in agreement with the witness who spoke of a distinction between thought and action or between ideas and action, or between the right to express and the place and time of the expression.

I view first of all the search for knowledge, as indicated to be part of the freedom to learn. I think the use of knowledge, which you can equate to action, is another question, after the knowledge is learned.

The place where they merge or begin to meet—and if there is any paradox—and I am not sure this is, with all due respect, but if there is, I am sure that that is the area in which it would fall. But I view that also as the use of knowledge. That is to say, the use of knowledge to acquire more knowledge.

Now, then, if a regulation—for example, if you say you can do this in a P4 laboratory, as the guidelines do, but you can't do it in a P1 laboratory, I see no problem with that. You have not stopped the doing, first of all, the search for knowledge. You simply say where it must be done—if that is a reasonable breakdown between P4 and P1, for example, I see no problem whatsoever and no real paradox. I think the manner or methodology used in learning—whether we use a very containing bacterium or whether we use E. Coli, not K–12, but right out of our gut—is again a method of learning, a choice of action, whether we use this or that is in my view an action. And I think again within the parameters indicated by Dr. Sonneborn, if a requirement, for example, that you must use *E. Coli* K–12 did not forestall the research, there would be no problem. And there, I think, is where the dichotomy arises. That is where the problem could arise.

If the scientists were to say, for example, in order for me to learn this I have to look at another less containing bacterium, you would then have the problem, have you then said, is your regulation now so confining as to in effect destroy the freedom to learn.

To make a silly example, if a scientist were to say, I want to see how all blue eyed people react to being hit with an automobile, and so I want to put 5,000 people into the situation and drive cars into them, we would say, absolutely not—thou shalt not. And with full justification. That is one side of the spectrum.

On the other hand, if we said, not matter how you do it you shall not learn how blue eyed people react to automobile accidents, I think we would be making a serious fundamental mistake.

As Dr. Edsall was talking I couldn't help thinking, as he referred to the dangers, in nuclear energy, whether used for weapons or otherwise, I couldn't help thinking, for example, that in our court we have had in recent times two cases involving the efforts of the Army Medical Corps to develop antiradiation drugs. Assumedly these drugs work, or at least they work to some extent. Wouldn't it be sad, for example, if something were to chop off this recombinant DNA research just prior to its having developed, "on the brink of," and we would never know because we stopped. But the next day this research might have developed a mechanism, cell mechanism or whatever, which would, for example, provide all human kind with insulation from radiation of any kind. That would be, I think, the saddest day ever. And whether that were achieved by a permanent, blanket stop or by a smothering, suffocating regulation, is hard to distinguish.

That is a long answer to a short question, Mr. Chairman, and I apologize. But you put your finger right on it when you raised the question as to whether there is a paradox between the freedom to learn and the protection of societal goals. It is not whether men have the freedom to look like Clark Gable or the ladies like Racquel Welch. It is the freedom to learn by acceptable methodology.

Mr. THORNTON. I think we should be free to do both. I appreciate the parallel. You are drawing a distinction there between a course of action. This distinction was drawn this morning by a suggestion that it was not only permissible to regulate biohazards, whether they be recombinanted DNA or pesticides or herbicides which have the potential for vastly changing our environment, and that it was not only a right but perhaps a duty to regulate such changes in man's environment. But it was very doubtful that there should be a right, and I think this is where we are—to affect thought, free ranging inquiry should be protected, and that the problem that is thrust upon us is how do we separate those two, where do we draw the line, and who is to make that decision. Is it the scientist only, or is this a proper role for the public to be involved in deciding? I think the general conclusion that many people expressed is that there is a proper role for the public here.

And the next question is, What kind of institutions may be needed in order to bring the public focus to bear on this middle ground where you are not dealing with either pure thought, or pure science, or with the regulation of biohazards but you are trying to ascertain and balance risk and ethical considerations in this middleground?

Judge MARKEY. Mr. Chairman, I would offer that regardless of the mechanisms and certainly the public must be present—so long as

whatever mechanism is adopted, it must be clearly understood that its function cannot stop the learning. That, of course, has been a part of the problem as I understand from limited reading in this particular research, because of certain scare reports and so on. As I mentioned in my presentation, in my statement, this whole question was raised by a responsible scientific community who are themselves doing the research. But nonetheless, if, as has happened and as some people have advocated, this body, this mechanism, whether involving the public or not, has the right or the right to say, "Thou shalt not learn this" or "that" or anything else, I think that would be a fundamental, serious mistake. I think their function should be limited strictly to how you shall use what you have learned in any of thousands of possible ways in our living, one of which is how you shall use it in learning something more, provided again that that does not stop the learning process.

Mr. THORNTON. Dr. Edsall, do you have any comment with regard to this issue area?

Dr. EDSALL. I think it is certainly important to get the public involved in issues of this sort. They are concerned, they have a right to be concerned. They need to have those things explained to them. It takes a lot of work on the part of the scientists, and of intermediaries like some of the scientific journalists, to try to put the issues in language that is sufficiently accurate and at the same time sufficiently understandable to the people at large. But I think this is an essential part of the whole enterprise. In my hometown of Cambridge, Mass., of course, there was a long debate over this. And the committee that was appointed by the city council to investigate this, a committee that was made up not of scientists at all but of members of the public (I think there was one medical man on it, but no professional scientists) really worked very hard indeed to understand the problems. They took lots of scientific testimony and worked on it for months, and finally came up with a very sensible and well-balanced report.

I am sure that this was a valuable experience for the people who took part, even though it took a lot of scientists' time in testifying for the committee. Also the scientists had to wait many months before they were allowed to go ahead with some of the experiments they wanted to do. Nevertheless I think this was an all-around valuable experience. I would be worried, however, if that sort of experience were to be repeated in hundreds of cities and towns all over the United States. This would consume an undue amount of time and effort on the part of the people involved. I think that, once having worked out reasonably good guidelines, we should settle down to operate on the basis of those guidelines, and should not always be trying to think up still more stringent regulations than before.

Mr. THORNTON. I appreciate very much your suggestion that should it be deemed necessary to enter into a statutory framework for regulations, that a uniform standard should be applied when the subject matter itself is uniform.

Dr. EDSALL. I should add, there are matters of local option, undoubtedly. Community regulations, such as zoning laws, would come into play here. A city government would not want to have a bacteriological laboratory for work on pathogenic organisms set up just anywhere in the city. They would naturally and reasonably impose some

limitations on the location of such laboratories. I certainly would not exclude that kind of local option; we already have it and I think it would naturally continue.

Mr. THORNTON. Of course we are stepping over the threshold question, whether it is desirable on anything other than an ad hoc basis, to regulate scientific inquiry by legislation? I would like to ask of the panelists whether they desire not to be faced with a multiplicity of local regulation that may be a driving force toward the achievement of a federal legislative framework, which may look good as an alternative to local regulation, but may look pretty bad in future years? Is there concern that it could be expanded to become a structure which regulates scientific reasearch across the board in a wide-ranging way? Does anyone have any comment concerning that?

Dr. SONNEBORN. My reaction to that is that I think it is much better to have one set of regulations than many. But having one does not exclude, it seems to me, the possibility of having it work through a local administration. As I understand it—and I may be wrong about this—I think one of the recommendations in the United Kingdom is that there should be a local public health or public safety officer in each institution, hired by the institution and responsible to the institution, but then the institution reports to a central agency. This man—or woman, or whoever it may be is always at one place and he gets thoroughly familiar with the local situation and is much better able to know what is going on than people who are making a circuit and stop by for one day or whether, and have a look. I think there is no necessary conflict between having a single set of Federal regulations and having the actual administration largely controlled locally.

Dr. MCCULLOUGH. I think what we are really trying to ask Dr. Sonneborn, you have said that you do not see any problem with a Federal regulation superseding local regulations because of the desirability of having some standard set of criteria that a scientist can become accustomed to if he moves around a university environment. But the question is, is this an alternative that the scientific community is willing to settle for in preference to local regulation that might over the long range be a hazard leading to more and more and more regulations of basic research, that is would basic research in the entire community be threatened by opening the door to a single set of regulations on DNA?

Dr. SONNEBORN. Of course I cannot speak for everyone.

Dr. MCCULLOUGH. How do you perceive that?

Dr. SONNEBORN. I think there is the possibility of a sort of compromise, and that is what I was trying to say. We have national regulations now in the NIH guidelines and that applies effectively to the university through the purse strings, really, and it seems to me and to many other scientists that what we need is to extend that to industry and that is it. Now, the responsibility for seeing that the guidelines are followed can be in local hands and then you do not have, as is often said, a bureaucracy built up to take care of it.

Dr. MCCULLOUGH. But then on the next *ad hoc* step should we apply and develop a set of guidelines for conducting research in all organisms which are dealing with pathogenic organisms?

Dr. SONNEBORN. This is a point I raised myself. It is a fear, there is no question about it. I think it all boils down to whether you have

confidence in the ability to administer properly. The scientists I think have done a pretty good job in regulating themselves in a good many other respects and I think they could handle this very well, for the reason that in this case altruism is synonymous with self interest. If there were an accident, if anything broke loose that could be traced to a recombinant DNA laboratory, that could be kaput for science, I would think. They must be conscientious and careful in control of their own.

Dr. McCULLOUGH. Then that same argument could be used with regard to experiment with lassa fever. We have a set of physical guidelines and controls for containment by the Biohazards Committee for anyone who wants to work with extremely pathogenic organisms. It should not be left up to the individual investigator in a university under that presumption to pursue his research on the basis of his concern for not wanting this to escape in a community, we should regulate that—or should we?

Dr. SONNEBORN. I suppose part of it boils down to the question of whether you can demonstrate a real risk to society. And that has been a question in this case, if guidelines are followed, it is questionable whether there is a risk. In the case of communicable disease laboratories, there is no dout but that there is a risk if they get out.

Mr. THORNTON. And yet this is the point, there has as yet been a Federal regulation of containment for lassa fever research. That has been left as a potential public health problem.

Dr. SONNEBORN. I think the implications are very clear, if you can do it for them, you can do it for recombinant DNA without any trouble and with much less hazard, the same way.

Judge MARKEY. Mr. Chairman, I suppose personal philosophy creeps in no matter what you do or say, and I do have, as many of us in this room do, a fundamental concern over regulation per se. I call it in my statement the "dead and deadening hand of Federal regulation" or regulation per se.

It seems to me that prior to a preemption in fact by a Federal set of regulations as to this research or any other, the burden of proof is on him who says—who raises the scare, who raises the need, who says, "We have got to have it," and I think that burden is a heavy one.

As has been indicated a moment ago, Mr. Chairman, in your own remarks, I do not know how many kinds of research are dangerous, but there are many.

Thousands and thousands of people ride in elevators, elevators which go very rapidly to the 105th floor in numerous buildings throughout this land. No one says, we have got to have a Federal regulation because we do not trust the fellow who built it, the people who maintain it, the man who is supposed to grease it, and so on and so on. As Dr. Edsall indicated earlier, we accept risk constantly. As somebody said it does not pay to get out of bed but you cannot stay in bed because most people die in bed. There is no end to that if you once enter that Pandora's box. And it seems to me, to answer Dr. McCullough's question, that the question of who is going to do what in the university to a great extent, any way, perhaps 99 percent rests on control, as Dr. Sonneborn indicated, by the purse, by the grant process.

The problem you would have if you had one, it seems to me, would be in the commercial laboratory and that is why I indicated, if NIH's guidelines are widely publicized, and if a commercial laboratory chose not to adopt them and went on their own and something happened, as a judge I would be charged of course with determining a reasonable standard of negligence. And I would immediately say, and I am fairly confident almost any judge I know would immediately say, "All right, where do I look to see what would be reasonable?" What would the reasonable man do who was conducting a laboratory doing this kind of research? And I am confident that I would probably end up by saying a reasonable man would have followed the NIH guidelines.

In the first place, they are the only ones we have. And since he did not do it, he is on his own. He chose that course of conduct on his part, and he was therefore unreasonable. And the negligence which resulted in this catastrophe is fully at his door.

The same is true of the need for insurance. I suspect that most insurance companies would say, "We are not going to insure your laboratory, General Electric or whoever, unless you adopt the NIH guidelines. If you do, we will insure you, if you don't, we won't." Now, that is all possible without any Federal regulation. I am not concerned, perhaps, over the question of local regulation. I think that there may be some antiscience as there was in Cambridge for a whole, but I think after five or six, let us say—I hope we do not have that many, but assuming five or six—the next village or city that attempted to say, "We are not going to have it here" would be confronted with that record and some member of the city council is bound to rise and say, "Aw, come one, fellows, that ground has been plowed, it did not get anywhere in Cambridge, it did not get anywhere here and it did not get anywhere there." And that movement, so to speak, from local areas, would die off.

As I indicated in my remarks lastly, Mr. Chairman, publicity, communication, public knowledge, could defeat any such efforts aborning. If, for example, this comittee in its report and others of standing were to come out and point up that these concerns have been met, they have been explained, there is not the fear we thought there was, I think that could forestall a lot of the concern for local regulation, local effort to stymie.

Mr. THORNTON. Dr. McCullough.

Dr. MCCULLOUGH. A problem that has been under discussion during the past few months related to this issue of control regulations has been the possibility of exercising control through the way in which patents are processed. Could you comment on what you might see as a mechanism of using the withholding of patents if there had not been compliance with the guidelines during the development of a particular idea in this area, or any research area, for that matter.

Judge MARKEY. First, Dr. McCullough, the moment you mention patents, of course you are talking about applied research, not basic research. There is no way that knowledge *per se* may be patented. There is not even room for question. You are talking about applied research. There have been, I am told, a number of patent applications already, relating to processes, relating to techniques, and relating to equipment useful in recombinant DNA research. I would hope that neither the committee nor the Congress would, for a moment, consider

withholding patents as you indicated, in this or any other area in the patent field, as a mechanism or a regulatory tool here. I say that for a number of reasons.

The primary one is based on the basic fundamental purpose of patents, which we tend to forget, and that is of course disclosure. The only reason for a patent and a patent system is disclosure.

Our forefathers knew from their experience with the guilds, from their experience with kings who gave out exclusive rights, et cetera, and their experience with secrecy, that they did not want trade secrets; they did not want new ways of doing things, new ways of production, hidden. And so they made a deal. They said if you will disclose it in accordance with the statute, we will give you a limited period—in the history of a country 17 years is a spit in the eye—for that short period we will recognize your exclusive right to keep others from doing what you developed. There is nothing new about that. Galileo was told by the city fathers, "Tell us what you are doing," and he said "All right, if you will give me some exclusive right, otherwise I will not." That is human nature and it has not changed, and so to say we will somehow forestall disclosure via the patents system, I think would be a very serious mistake.

You do raise another question, though, Dr. McCullough, if I may continue for a moment. Some of my friends in NIH who have not had as much experience as many of the other Federal agencies, who have given out purchase contracts and other things, have had in the past to deal with patent questions. And so at NIH that has raised some concern. And when I was asked, I said, "Where is the skin off your nose?" "How does it bother you?" "What is the difference if someone working in the laboratory, even under an NIH funded research program, should perchance develop a mechanism, the result of an applied research program which was patentable, how is it any skin off your nose if he has the right to exclude others?" "How does it hurt NIH if that happened?"

And, of course, there is no answer to that. There may be a feeling of pique, in that NIH money is used in the course of going through the program and this development. It would be nice if you say, "The taxpayers' money went to this and therefore the taxpayer should own it."

And that brings me to the general subject of Government patent policies. There are too many; there is no question about it. They are all different. If a good policy developed which would be uniform, I cannot see that that would be in any way harmful. I think it would be a good thing, particularly where we have diversified industry so widespread now, and industries work with different agencies of government, to have to deal with different kinds of patent policies. But there are only three possibilities when you begin to develop a patent policy business vis-a-vis the Government, and I would preface that with the anomaly represented by a Government-owned patent. The U.S. Government now is infinitely by far the largest owner of government patents in the world. But when you consider that a patent is merely the right to exclude others, there is something incongruous about the U.S. Government excluding its citizens from using an invention which "its citizens paid for."

The very purpose of acquiring the patent in the name of the Government in the first place is the idea that the taxpayers have

paid for it. And therefore you tell the taxpayer he can't use it. As a result of that anomaly, the Government has never sued a citizen for infringement of patent. I hope it never does.

There is one case where a patent infringement counterclaim was submitted and it was withdrawn. It would be a question if such a suit would stand. There is a case where the Government may use its Government-owned patents vis-a-vis other countries by exchange, having a U.S. patent enables the Federal Government to get a patent in, say, Germany, and therefore it has at least some trading material, vis-a-vis Germany. That could be done even though the U.S. patent were owned by the U.S. citizen, if that were to be desired.

But within our country at least there are three possibilities, as I indicated a moment ago. The Government may say, "We have no interest in patents," whether they resulted from a program or contract paid for by the Government. That is one possibility. But at the opposite end of the extreme, they can say, "We own all patents which developed in the course of our contract work." That is the other extreme. A middle ground, of course, is a licensed program. I know of no one anywhere in my 35 years dealing with patents that has suggested for a moment that the Federal Government should not have an absolutely free license to use any invention made in the course of a Government contract, Government-funded research or whatever, not only to make it itself, but of course, to have it made for it. In my view that is the way to go. That preserves the purpose of the patent system. I think it preserves every legitimate interest of the Government. At the same time it encourages technological development and marketing of this invention.

There have been numerous studies, Mr. Chairman, on what has happened to Government-owned patents and everyone thus far that I am aware of has come out with one simple answer: Absolutely nothing. That which is owned by everybody is owned by nobody. There is the ridiculous notion that a patent is a monopoly, all monopolies are bad, and therefore patents are bad.

Tht syllogism will not stand up, of course. If you think all monopolies are bad, I should like to know what your wife is doing tonight, and I will share your house and your car. The statute says that patent is property and shall be treated as such. That is the law passed by Congress. So much of what we are concerned with rests on the notion that a patent is a monopoly. I know of no product in this country, patented or otherwise, which is monopolized per se. For a quick example, the Polaroid cameras are thoroughly patented, but Kodak is very much alike, as is Minox, the Leica and all the rest of them.

So, Mr. Chairman, I think a lot of concern over whether or not the Government may own a patent is misplaced. I think that a wise policy would be one in the interest of all concerned. I have no personal interest either way, of course in this or in any other direction on this matter, but a wise policy would be a licensing arrangement and I say that also because the alterative is a secrecy situation.

If a researcher, an inventor working in a situation involving Government-funded work, does make an invention, if he knows that he cannot own it, he shall have no right to exclude others, nothing. Query: Why on Earth, being human, should he tell anybody about it? If he really

thinks it is valuable in his own human interest, the thing to do is just keep quiet about it until such time as, for example, he leaves the laboratory and a few years later come out with it in a small commercial laboratory anywhere and no one will ever know that it was developed under a contract. How much better to have it come forth in the course of the work done, even though funded by the Government and disclosed by patent?

That is a long and involved answer, Mr. Chairman, to a very short question. I am sorry. And I am sure if I had the gall, I would go on for a great deal longer.

Mr. THORNTON. I should like to say it is a very cogent summary of some of the issues that are involved in that particular area. And I do appreciate it. I think it might be useful to make sure that our reports and work concerning patent policy have the advantage of that discussion.

Dr. SONNEBORN. I have been meditating over this question and the question that seems to me quite obvious is this, that if the Government was not involved in regulating this research, it would be regulated by the scientists any way. And they would do it in a way that I think would be quite effective. So that I would agree, it seems to me safe that way.

Mr. THORNTON. There is an alternative, it seems to me, to the idea of having a Federal regulatory agency which is authorized to draw lines and issue rules and regulations as to how research shall be conducted.

And that pattern is one which has been described by two witnesses, both of whom are members and one of whom is the Chairman of the National Commission on Human Experimentation. That Commission, as presently constituted, is advisory, has conducted a great deal of inquiry, assimilation of data, and is charged with the duty of issuing reports and making recommendations as to how and under what circumstances experimentation on human subjects would be permissible. Ethically permissible. This is a different area, and one where statutes have been lacking. Statutory guidelines are not broadly in use at least. And yet we all know that experimentation on human subjects in prisons to test dangerous pathogens is wrong, and should not be allowed.

Now, is this a parallel that might be applied here? Can we approach it like that?

Dr. SONNEBORN. Do I understand—I don't know the situation—did I understand you to say that there are no laws on this, only an advisory Commission?

Mr. THORNTON. This particular commission is advisory only. There are laws concerning—doing things to human beings, yes, general laws of assault.

Dr. SONNEBORN. I mean of experimentation on human beings.

Mr. THORNTON. State laws.

Dr. MCCULLOUGH. There is the Helsinki Conference which established following the end of the Second World War, a series of perceptions in ethics and codes of conduct and that sort of thing which have, I believe, the impact of law, at least in the World Court they have had. If an individual departs too far afield from some of these areas which were discussed following the Second World War, they will find themselves in conflict with law which very frequently will bring them to

task. I am not sure of what question you are asking. The National Commission itself was established by law.

Dr. SONNEBORN. But does it have regulatory powers?

Dr. MCCULLOUGH. No; it does not.

Dr. SONNEBORN. Only advisory?

Dr. MCCULLOUGH. That is correct.

Dr. SONNEBORN. And it works.

Dr. MCCULLOUGH. At the moment we have heard two witnesses say that they have been pleased with the progress that the Commission has made, however, they feel that there are some aspects of the activity of the Commission that probably warrant further examination. They emphasized the fact that the interpersonal relationships on the committee probably contributed to its success. And they felt very, very pleased with the fact that it was an open public forum, access to all of the documents was available to anyone who was concerned, and this was a means of communicating on very sensitive subjects about which the public was concerned, and that was very effective within the limits of time and money and so on as a forum on subjects of this nature. It also places the Secretary of Health, Education, and Welfare in a position of having to be responsible, as they just do not make a recommendation and it disappears.

The law requires the Secretary to respond as to the disposition of that recommendation. If he accepts it, why he accepted it, and if he rejects it, why he rejected it. The concept has been discussed by some individual that perhaps some sort of an oversight advisory commission on research could constructively provide a forum for discussion and evaluation of the kinds of issues that have been the focus of attention at these hearings, the DNA recombinant molecule issue. If this kind of visibility was given to these kinds of issues, then perhaps some of the problems might be resolved without legislation and others might be clarified and considered in legislation. But no one can answer the question positively because the Commission does not terminate its activities until March and final evaluation can then be made.

Dr. EDSALL. The Commission on Human Experimentation gives advice and make recommendations. But if those recommendations are approved by the Secretary, do they then become official regulations?

Dr. MCCULLOUGH. The Secretary of Health, Education, and Welfare, for example, did promulgate regulations having to do with fetal research, which was their first task. I do not know the status of the other reports at the moment. I am not the person who has been following that precisely. But the intent is that researchers respond and in those instances where the Secretary has such research going on in his department, the regulations will be either modified or initiated in order to control the use of prisoners in research, psychosurgery, fetal research and that sort of thing.

Judge MARKEY. Is it all under the Secretary of HEW, or does he make recommendation to other branches of the Government?

Dr. MCCULLOUGH. At the present time the National Commission is reporting to the Secretary of HEW. Proposals are under consideration to establish a commission that would have responsibilities broader in scope.

Judge MARKEY. The reason I asked, I was impressed in attempting to read in the last 2 days before coming here, a little bit, with the fact

that there are so many agencies of Government dealing with recombinant DNA research.

I understand the Defense Department has a program, and HEW, of course, and NIH and a number of others. And that is somewhat disturbing. If you did set up a commission and it reported only to HEW, of course, then they would have to run around and get the concurrence of other agencies, which would delay matters.

Mr. THORNTON. Lest there be any misapprehension as to the status of laws which do relate to such things as broad as experimentation with human subjects, indeed human life, the right to liberty and the pursuit of happiness and prohibition against cruel and unusual punishment, et cetera, are embodied very deeply in our structure of laws, constitutional and moral and ethical considerations all involved in that particular protection. But the parallel was being drawn to a particular commission, which is a statutory commission but which does not have the authority to promulgate or issue regulations, but only to study, assimilate information and to report.

Judge MARKEY. Mr. Chairman, to return for just a moment to something that was hinted at a moment ago, and that seems to fit with what we have just been saying, if we are at the stage where we cannot trust scientists to be responsible and responsive in their laboratories, where we cannot trust each other, the game may be over anyway, and it may be that an effort to supply a guaranteed regulation to regulate all research in detail, and a guarantee of safety, would be (1) self-defeating; (2) would injure the law by adding laws unenforceable in effect; and (3) as I indicated, it would be self-defeating because if we have such irresponsible people, and you supply a regulation to say, "This is how you shall do it," the tendency then is to say, "This is how I will get around that." "That is required." "I don't have to do anything better than that, that is the minimum now; I can work up this or that to squeeze by it, squeeze around it," and so on. So that I keep coming out with the basic idea, we have to get to trust somebody one of these days. We started on that premise in this country. I am not naive enough to imagine that all men are good, not by any means. But somewhere we may get to the point where you say everything in life is either ordered or forbidden, and that is the end of freedom's ballgame.

Mr. THORNTON. If I may follow along that line of thought for just a moment, going back to the idea which has permeated these hearings, that it is appropriate and proper for Government to regulate biohazards, Dr. Edsall mentioned the many areas where this regulation is appropriate—the marketing or use of asbestos, vinyl chloride, and other toxic substances—clearly appropriate to regulate the use of biohazards and the marketing of such biohazards.

Clearly I think it has emerged from these hearings that as a matter of pure science it is inappropriate for Government to regulate thought processes, freedoms of thought, and freedom of inquiry. It may be that we are focusing upon this dilemma because of the conception of what recombinant DNA is. Is it a biohazard in its full range?

Is that what we are dealing with, something that is—even in the laboratory, a biohazard, and therefore falling within the area where Government regulation is proper?

Or is it part of the expansion of the field of knowledge which should be protected as a field of scientific inquiry?

So what is the nature of the particular thing that we are dealing with, recombinant DNA research?

Going a step beyond that question is whether, because it deals with a problem area as vital as life itself, and involves the creation or manipulation of new forms of life, it crosses another threshold which is not so much a biohazard as it is meddling in the order of things?

Does this add another dimension which moves it over into the area of being regulated? Now, I do not know the answer to that question. But I think that it is a question which is being asked, whether because of the nature of the research itself as opposed to its hazard it deserves special attention.

Dr. Sonneborn.

Dr. SONNEBORN. I hope it has been pointed out in some of the preceding hearings that we have been meddling for ages in life by the comparable creation of new organisms, by selection and certain breeding customs or practices, by mutagenesis and selection of mutations, and whatnot. That really is not a new threshold. And we are not any more, as far as I can see, creating a new order of life that is any different in principle from what we have been doing right along. We are not starting from scratch and saying, we are going to construct something out of nothing. You take something that is already an organism and slightly modify it. And that is exactly what we have been doing for years from the beginning of civilization. So I don't think that is a new threshold at all; it is just a new way to do that.

Judge MARKEY. May I add, even if it were, I can see no basic valid objection. I consider myself a very religious man. And yet I would dispute a cleric, for example, who said that we are fooling with the powers of God and that sort of thing. If we are learning things in the area of creation, He is letting us.

That was one of the pieces of paper I picked up, Mr. Chairman, which led me to make such a strong statement about predictability and so on. So I join the professor in saying clearly with hybrid corn and ad infinitum, we are doing it. But if we were not, I would certainly come down on the side of freedom to learn whatever it is.

To get back to your fundamental question earlier, Mr. Chairman, Query, regulating biohazards with respect to almost anything else has been so far—and with which I thoroughly agree—the power of Congress, of the Government to regulate biohazard. Thus far at least all of those have been hazards which have been sought to be projected into the public, sold, distributed and sprayed on crops, et cetera. Query: Might this be a guideline or a measuring stick here in the sense that we are talking about the scientists qua scientists inside his laboratory? He is not suggesting that he spew out any molecules, hazardous or otherwise. They are all inside. If we have guidelines such as we do, and say we have to have a P4 laboratory with a mechanism for cleansing the air that may escape from the laboratory, we have closed it off, we have surrounded the laboratory with a wall, protecting the public that way from this positive hazard of escape.

Within the laboratory I would fear any sort of regulation by which the Government says we are going to protect you, you researchers, from yourselves. I have very strong feelings, for example, on the air bags and the automobile belts which the Government has forced

on the American people. I understand people are required to spend some millions upon millions for a product which some 85 percent do not use and will never use. There is a fundamental question as to the extent to which the Government may go to make me protect myself. It has every right to keep me from hurting somebody else.

It is, I think—again, pointing in the direction of making everything in life either forbidden or ordered—to say, thou shalt protect thyself from this, that and the other thing. That is fundamental, I think, to our whole country, our whole scheme of our country. It gets back to the question of responsibility, of course. But the argument comes, of course, if I injure myself, I become a public charge, the ambulance comes, and that costs the public money; the implication being in a sense that the Government owns me, the society owns me, they have an interest in my health and well-being which I must protect. Incongruously, the same people who say that apparently have not suggested that we cease smoking by order. We did it once with prohibition of course, to, I think, an everlasting lesson. But we do, as you know, subsidize tobacco growers. So that once you start, I think you have to go the whole route. And if you are going to say we are going to regulate the researcher to protect himself from himself, you then, I think, have a very serious question of whether or not that is within governmental power.

Mr. THORNTON. Of course it has been pointed out that there are two major levels of concern. One is the problem of research, which we have been discussing. And the second is the application of that research to products, which presumably presents additional grounds for Government intervention.

The patent question relates to the application more than the research, because theoretically the researcher does not care whether he gets a patent or not, he is exploring for knowledge.

Judge MARKEY. He could not patent the knowledge any way, Mr. Chairman.

Mr. THORNTON. On the other hand, even in the application area, it has been pointed out that there are two subdivisions, one being where the unknown organism, the organism about which little is known, is proposed to be spewed out or released.

An example would be nitrogen-fixing bacteria, if it is developed, which could have profound impacts. What kind of study should be made to assure that we did not all of a sudden fix too much nitrogen, did not do too successful a job? Another example would be an organism which could be maintained in a laboratory environment to produce insulin. The culture bacteria itself would not be spewed out of the laboratory but the work product of the bacteria would be a useful medical tool. Obviously there is a difference between the standards for these kinds of things and all of these lead to shadings of regulatory authority. But I appreciated very much your response. Even if we are dealing with something as drastically different as crossing evolutionary barriers, which we are told we may be able to do, and whether this occurs in nature or not is not clear as some people say that there are instances where genes have been transferred from one form of life to another, from viruses to humans, or from humans to viruses and then to calves or swine or whatever. Your point, I think is very useful, that even if we are involved in this kind of thresholding information, that

still the tests should be based on judgments similar to those we make in regulating biohazards to protect the human kind.

Judge MARKEY. Mr. Chairman, not to put too fine a point on it, but to follow up, so to speak, the notion that we must not learn about anything and particularly here where there have been suggestions that we are invading the province of the Almighty, I cannot help but be reminded of the Scopes Trial in which we went through a great "sturm and drang" over whether it was appropriate to teach evolution, you remember. And I am not sure that the analogy is too far afield.

Dr. SONNEBORN. And it is still not over, either.

Judge MARKEY. I am sure that it will be met and I am not against it being met. But I think it has to be.

Mr. THORNTON. I would be remiss if I did not offer to translate for those people who may not be familiar with German the words "sturm and drang" into good college English.

Judge MARKEY. Thank you. I broke my own rules.

Mr. THORNTON. I think the concept is well enough known in the field of human development; the struggle that we go through in achieving a reasonable solution to problems, the storm and lightning and agony of travail—I am not sure I have given a good definition of it.

Judge MARKEY. That is perfect.

Mr. THORNTON. I do again have some pressure of time on the floor of the House. May I invite any concluding remarks that you, Dr. Edsall, might think appropriate or you, Dr. Sonneborn may wish to make.

Dr. EDSALL. I would like to say that if we have to have laws to regulate recombinant DNA research, it is a fact that I would regret. In the case of making pathogenic bacteria we have apparently gotten along primarily by the regulation by the bacteriologists themselves, their skill, their sense of responsibility, as well as the fact that they after all do not want to run unnecessary risks, themselves of getting infected. All of this seems to have worked very well without much in the way of legal regulations.

And certainly I would say that the hazards of lassa fever, for example, are probably greater than anything I see likely to turn up in the case of recombinant DNA. The only reason why I think maybe laws are required for recombinant DNA would be in the case of industrial research. And I think we have to think very carefully indeed before drawing those laws, because once you have a law on the books, it is frequently very hard to change it even when there is good sense that it ought to be changed.

Mr. THORNTON. Dr. Sonneborn.

Dr. SONNEBORN. My concluding statement is, I am just very grateful to be able to be here and to be instructed by my colleagues here and by you. It has been a marvelous experience for me. Thank you.

Dr. EDSALL. I want to join in that.

Judge MARKEY. As do I, Mr. Chairman.

Mr. THORNTON. It has been a fine experience for me, and on that note, I declare these hearings at an end.

Thank you very much.

[Whereupon, at 4:12 p.m. the subcommittee adjourned, subject to the call of the Chair.]

APPENDIX

May 10, 1977

Statement of the Association of American Universities on Federal Regulation of Recombinant DNA Research

Note:

The following statement represents the general views of the members of the Association and has been approved by the Executive Committee of the Association.

W. Robert Parks, President,
and President of
Iowa State University

The Association of American Universities (list of members attached) has been following various legislative proposals for regulation of recombinant DNA research with deep interest and concern because these universities are the sites of a substantial part of this research in the United States and because the issues involve important matters of principles. The Association recognizes the legitimate public interest in national standards ensuring both that any potential hazards of this research are averted and that its rich potential is realized. The universities comprising the AAU pledge their substantial collective experience to the development of mechanisms affording safety and productivity.

Need for Care in Drafting Legislation

Federal statutory regulation of basic research of the kind proposed is unprecedented and raises many complex issues of great significance not only to science but to the relationship between science and society. Therefore, the Association urges that great care be exercised in framing Federal legislation. The process must allow time for full exploration of issues, full analysis of alternatives and full presentation of various points of view.

Need for National Standards for Research with Limited Local Preemption

Our universities see as one area of prime importance the conditions under which States and localities may impose standards different from the Federal ones. The position of the Association is that for many reasons the standards should be

National. Any dangers or advances that might be generated will not be local, but National and international. Highly technical considerations must be weighed, and few localities can draw upon the necessary expertise. A maze of local standards would hamper research with no commensurate gains. On the other hand, States and localities should be able upon appeal to establish standards different from the National ones in order to meet the requirements of specific and unique local circumstances. The criteria for approval of such appeals should be clearly stated and should require a demonstration that the proposed modification is in fact necessary to protect human health or the environment in that locale.

Need for a High Level National Group and Emphasis on Accountable Technically Competent Local Groups

The second major issue is the administrative structure for administration of controls. The fundamental criteria for administrative mechanisms have not yet been spelled out in detail, and this is a clear prerequisite to the establishment of a sound structure. While the Association does not presume to specify what mechanism should be chosen, some criteria seem evident:

(a) A responsible official of the Executive Branch should be accountable to Congress for administration of standards;

(b) Administration of standards at specific research sites should be the responsibility of locally constituted, accountable groups which are technically competent to assess potential hazards;

(c) A high level formal National group composed of informed public figures and scientists should be available to inform the public, to serve as a link between the scientific, administrative and legislative worlds, and to review all major decisions;

(d) Technical advice from a group of scientists most highly respected for their eminence in relevant biological research must be available at the National level.

These criteria do not preclude use of the technical expertise available in the existing Recombinant DNA Program Advisory Committee and in the Center for Disease Control. They further suggest the need for a more broadly based National group. Finally, they suggest that a central, independent regulatory commission would fall short of meeting a set of carefully drawn criteria. Further in-depth discussion of this complex issue is clearly needed.

Other issues -- licensure, inspection and penalties, for example -- require careful discussion, but the two problems outlined above are from the standpoint of universities the central one.

The Association will continue to review proposed legislation, and stands ready to work with Congressional committees in developing appropriate regulatory legislation.

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STATEMENT ON EMPLOYEE PROTECTION SECTIONS IN DNA REGULATION

Submitted by request to the

House Committee on Science and Technology
Subcommittee on Science, Research and Technology

Prepared by

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May 13, 1977

The concept of "employee protection" as applied to the evolving regulatory legislation for recombinant DNA molecule research is a complex issue deserving wide discussion and consideration by many individuals. In the hope of stimulating such discussions, the following statement has been prepared describing the background of "employee protection" legislation, outlining its relationship to encouraging scientific responsibility, and suggesting further refinements for these protections.

Employee Protection Legislation

Several proposed DNA regulation bills now under consideration by the House and Senate congressional committees contain employee protection mechanisms which state, in general, that no employee may be fired or otherwise discriminated against on the basis of actions which he or she may have taken to "commence a proceeding" under the DNA regulation. This mechanism of employee protection has appeared in several other regulatory laws, most notably the Occupational Safety and Health Act (OSHA), the Federal Coal Mine Health and Safety Act, as well as numerous environmental regulatory bills. 1/

The employee protection mechanism is based on a concern of those persons supporting the need for government regulation that the force of the regulatory power depends to a large degree on the willingness of persons at the grass roots level to use and enforce it. In the example of the OSHA regulation, the concept of employee protection can be traced to the recognition of a need to protect those employees who call attention to an occupational hazard and who invoke the inspection authority of OSHA personnel in order

to correct such hazards. Such employees may often take such an action contrary to the intentions -- and perhaps direct orders -- of their employers, and thus face the risk of job termination, transfer, or other administrative discrimination as a result of their disclosure action. The intention of the employee protection mechanisms is to restrict the employer from exercising such discrimination and to provide a method of appeal to the affected employee should such discrimination occur. The indirect effect of this protection is to encourage employee participation in the regulatory process.

Employee disclosure of information about employer actions which run counter to governmental regulation is a difficult process to protect or encourage. The act of giving unauthorized information to outside groups -- even if such groups might be government agencies or a congressional committee -- is often viewed as an act of organizational disloyalty, and thus is liable to punitive actions by those persons holding positions of authority within the organization. Employee protection mechanisms are a deliberate attempt to intervene in this process of administrative reaction to organizational disloyalty. Such intervention is based on a belief that the employee disclosure action, even though it may be interpreted as organizational disloyalty, represents a "public service" and is thus an action to be protected by the representatives of the public.

Providing information about actions of an employer which potentially threaten the public interest is a generic process often called "whistle-blowing". The whistle-blower, the employee who takes the step of

disclosing information and countering organizational behavior, has been the subject of several case studies and conferences in recent years. 2/ Yet there is still very little known about common problems or common experiences of these isolated individuals. They are often identified as "trouble-makers" by their employers, and if unprotected they can experience serious risk and deprivation in their professional and personal lives.

How might a whistle-blower be involved in the DNA regulatory process? The following scenario suggests one possibility:

> A graduate at a prestigious university is working with his thesis adviser in a recombinant DNA experiment. The experiment is being conducted through NIH funding and is regulated by government standards. The laboratory in which the experiment is located has been classified as P-2 and the research procedures meet the appropriate regulatory guidelines.
>
> The thesis adviser, a respected molecular biologist, suggests that better research data might be obtained in the project through a short-term experiment which would regularly be classified as P-3 and require a more complicated, and costly, set of laboratory procedures. The biologist decides to do the new experiment in the P-2 laboratory without altering the research procedures because he believes that it would be a waste of time for this short-term experiment.
>
> The graduate student recognizes this decision as a regulatory violation and assumes that it may be of potential danger to the laboratory workers and possibly others. He notifies the lab director of the P-3 nature of the experiment. The director informs the student that it is none of his business and instructs him not to discuss it further.
>
> The student, concerned about the implications of this decision, discloses information about the P-3 experiment to the research projects manager at NIH. An investigative team from NIH proceeds to follow up the claim and contacts the laboratory director for further information.

> At this point (or any other point subsequent to the investigation), the student is dismissed from the laboratory on the basis of the disclosure action. He realizes that continuing his studies under his former thesis adviser would be unwise and withdraws from the research graduate program. The student may leave the research field completely, either through his own frustration or because of the influence and adverse reports of his behavior by his former adviser.

Before suggesting how the outcome of this scenario might be altered, it may be useful to review the relationship between scientific responsibility and whistle-blowing which has been under examination by the AAAS for several years. It is conceivable that legislated protections, coupled with an active encouragement of scientific responsibility by the professional societies, may nurture an environment more supportive of the individual scientist who discloses information in the public interest.

Whistle-blowing and Scientific Responsibility

The whistle-blowing studies mentioned earlier describe the individual case histories of 20 employees who chose to disclose information about illegal or improper actions of their employers. It is worth noting that of this number, four cases, or 20%, involved individual scientists or engineers who believed that by making such disclosures they were acting on the basis of their professional or social responsibilities.

In response to one of these early whistle-blowing cases, which involved two scientists specializing in the biological effects of radiation, (John W. Gofman and Arthur Tamplin) the AAAS first began a formal inquiry into the relationship between scientific responsibility and whistle-blowing. A committee established by the AAAS in December 1970 reviewed

several mechanisms which would enable the Association and other scientific societies to further implement ethical codes designed to encourage scientific responsibility in the public interest. A report of this group, published in 1975, noted:

> We believe that some form of due process should be an essential part of any employer-employee agreement or contract, to protect the employee from arbitrary action by the employer, allegedly based on professional or personal misconduct. A minimum requirement for such due process would involve a hearing by a board, including independent members, with the right of appeal to some reasonably neutral but professionally qualified higher authority. Codes of professional ethics are likely to be ineffective unless some type of due process is provided for the resolution of disputes. Without this, scientific freedom is likely to be abridged. We therefore strongly recommend that all employment contracts involving scientific or professional employees include such provisions for the review of disputes through hearing and appeal processes. Provision for neutral or third-party participation is important, particularly when issues of public interest are involved. 3/

A new AAAS Committee on Scientific Freedom and Responsibility, appointed in 1976, has begun to further refine the meaning of due process in whistle-blowing or other "conflicting loyalties" cases involving scientists or engineers. This Committee is studying whether the professional scientific societies have the means to offer such protections to their members when situations arise involving conflicting loyalties between the demands of their profession, the public interest, and the demands of an employer, or whether such situations of conflicting loyalties can be resolved only through legislative protections.

Dr. Frank von Hippel of Princeton University, one of the thirteen Committee members, has examined the impact of legislative employee

there needs to be an appeal mechanism coupled with the restrictions, providing a direct method of recourse for the employees who may experience such discrimination. This appeal mechanism should not preclude the employee from going directly to the courts if he or she wishes to do so, but it should furthermore not make the courts the only source of appeal. As the experience of the OSHA protections indicates, there may also be a need for a screening mechanism to filter out from all claims of discrimination these cases which directly involve disclosure actions by the employee.

In previous employee protection mechanisms, the Secretary of Labor has been designated as the source of appeal for those employees who believe that they have experienced discrimination as the result of a disclosure action.

(2) The legislative history of the DNA regulatory act (if not the Act itself) should specify which government agency is charged with implementing procedures for the employee protection section. It is suggested that these procedures, if they are to be prepared by an agency other than the one preparing the regulations for the remainder of the Act (presumably HEW), should be integrated into the final complete set of regulations and should be distributed simultaneously to the regulated organizations.

(3) The regulations regarding employee protection against discriminatory actions should be posted in the research laboratories governed by such regulation or should be otherwise distributed to the laboratory employees.

(4) The agency designated as the source of appeal for discriminatory actions should be directed to report annually on the number of cases of alleged discrimination received by its offices, and should further report on the final resolution of these cases.

Furthermore, there are several areas of uncertainty surrounding these legislated protections for employees who "commence proceedings" under the regulation. For example, although it is clear that these protections apply to employees in the private sector, it is unclear whether government employees, or persons working on government funds, are also protected against discriminatory actions by their employers if they should initiate a disclosure proceeding under the regulation. This point, of course, might be critical to those persons working in national laboratories or working on government grants.

Secondly, there appears to be some uncertainty about the meaning of the term "to commence a proceeding under the Act". While it is clear that this term applies to actions such as testifying before a congressional committee or a government agency, it is uncertain whether information disclosure alone to public officials or private media, in the interest of commencing a proceeding, would be similarly protected against discriminatory retaliation.

As noted earlier, the AAAS Committee itself has not yet resolved the question of whether legislative employee protections are the most effective mechanism for resolving situations involving conflicting loyalties between

the profession, the public, and the employer. However, it can be recognized that such legislation is a cornerstone on which other actions developed by the professional societies themselves might be based, in order to both encourage and protect those scientists and engineers who speak out about a potential danger to public health and safety. The initial efforts of the biological scientists who first brought public attention to the complex questions imbedded in recombinant DNA research have been justly praised and held up as an impressive example of scientific responsibility. It is now time, however, to continue that process of concern for public welfare within the scientific community and to implement protections for those scientists and engineers who risk employer retaliation for disclosures of actions potentially damaging to public health or safety.

REFERENCES

1. The bills identified by the Committee which contain employee protection mechanisms include: Occupational Safety and Health Act of 1970 (P.L. 91-596, section 11c); Federal Coal Mine Health and Safety Act of 1969 (P.L. 91-173, section 110b); Federal Water Pollution Control Act Amendments of 1972 (P.L. 92-500, section 507); Safe Drinking Water Act (P.L. 93-523, section 1450i); Toxic Substances Control Act of 1976 (P.L. 94-469, section 23); Resource Conservation and Recovery Act of 1976 (P.L. 94-580, section 7001); and the proposed Clean Air Act Amendments of 1976, S. 3219, section 36.

2. Ralph Nader, Peter Petkas, and Kate Blackwell. Whistleblowing. Grossman, New York, 1972. See also Charles Peters and Taylor Branch. Blowing the Whistle. Praeger, New York, 1972.

3. Scientific Freedom and Responsibility. A Report of the AAAS Committee, prepared for the Committee by John T. Edsall. AAAS, Washington, D.C. 1975. p. 37.

4. Frank von Hippel, "The Defense of Professional Freedom and Social Responsibility". Invited Talk, Annual Meeting of the American Association for the Advancement of Science, February 21, 1977.

5. Morton Corn, Assistant Secretary of Labor, Memorandum for the National Advisory Committee on Occupational Safety and Health: Discussion of OSHA's Program for Discrimination Investigations. November 15, 1976.

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ARTHUR R. WHALE
GENERAL PATENT COUNSEL
ASSISTANT SECRETARY

June 7, 1977

Representative Ray Thornton
Subcommittee on Science, Research
and Technology
2321 Rayburn House Office Building
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Dear Mr. Thornton:

The enclosed memorandum is submitted for inclusion in the record of the hearings held by your Subcommittee May 25-6 on recombinant DNA legislation. This memorandum, in effect, supplements the testimony of that of our Dr. Irving S. Johnson at your earlier hearings, when the subject of the handling of confidential information was deferred to this later time.

You will note that my comments are confined to the disclosure question. It seems to me there is an unfortunate misunderstanding of the importance of protecting against premature disclosure because of adverse effects of such disclosures on the commercialization of inventions originating in corporate and university laboratories. This concern applies whether the research has been privately financed or funded by the government.

The misunderstanding arises from two assumptions which, I suggest, are wrong. First, it is assumed in some quarters that universities are not interested in patenting the results of their research investments. This is wrong, and demonstrably so, because of the importance of patents in attracting the corporate investments in development and production efforts to commercialize a university-originating invention. Mr. Latker has ably made this point in his presentation to the Subcommittee.

Second, it is assumed that the exemptions of trade secrets from disclosure under the Freedom of Information Act provide the corporate sector with the protection it needs against premature disclosure. I believe this misconception will dissipate, wherever it is held, on a consideration of the court decisions, agency practices and the practical problems facing agencies in making the determinations of trade secret status for information in their possession.

In this memorandum I have concentrated on the Freedom of Information Act problems. My conclusion urges that any legislation prescribing the licensing and registration of facilities and projects should provide positive protection against disclosure of information submitted to comply with statutory requirements. The exception, of course, is where the information must be released pursuant to the demands of public health and safety. Such provisions for protection should be as specific as possible, in view of a court decision which holds that a general statutory safeguard is inadequate.

The concerns I express are consistent with those contained in the reports of the President's Biomedical Research Panel and the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, a pair of studies commissioned by the Congress.

Since a high percent of requests for information under the Freedom of Information Act come from competitors trying to learn what their competitors are doing (over 90% in the case of the Food and Drug Administration), and because the approach I suggest would clearly provide for disclosure where the public health or safety was involved, I see no public interest served by placing in jeopardy the confidentiality of research and development efforts of corporate and university laboratories willing to invest in these undertakings. On the contrary, the threat of premature disclosure to competing laboratories,

which in turn would in most cases defeat the prospects for patenting and destroy much of the incentive for commercialization, would seem contrary to the public interest.

Please let me know if I can be of any help in further discussion of this important subject.

Very truly yours,

A. R. Whale

ARW:mfm

cc: Gail M. Pesyna, Ph. D.
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Enclosure

MEMORANDUM ON DISCLOSURE OF CONFIDENTIAL INFORMATION UNDER RECOMBINANT DNA STATUTE

Requirements for early disclosure of confidential information to a government agency is a common feature of several recombinant DNA bills now before the Congress. While these bills treat recombinant DNA research mainly in terms of public health and safety, their failure to provide positive protection against agency disclosure of confidential information to competitors of the corporate or university innovator would produce serious and unintended consequences.

Such disclosures would occur in the following ways:

1. In applications for licensing of facilities,
2. In registration of research protocols,
3. Through inspection by Federal authorities,
4. Through release of information to Federal advisory committees and their consultants,
5. Through exposure of information in research protocols to non-employee members of biohazards committees, and
6. Through various reporting requirements.

This memorandum addresses the points of primary concern in the disclosure problem and suggests how they can be minimized.

Effects of Premature Disclosure

Except for their contribution to scientific knowledge, the results of recombinant DNA research are useless standing alone. They require the

investment of significant sums to convert them to products available to benefit the public. This is true whether the initial work is done in university or in corporate laboratories.

Premature public disclosure in present context refers to the disclosure of confidential information, for example, in facility applications and research protocols, to an agency that would then be requested to make the information available to other parties under the Freedom of Information Act. Such release would render virtually impossible the prospects for patenting in the United States, where filing must be done within one year from a public disclosure, for the research protocol would be presented before work was undertaken, and consequently, before patentable subject matter could be reasonably identified. Prospects for patenting abroad would be even more limited, because the laws of many important countries have no such grace period within which to file after public disclosure. The market lead time for the innovator would therefore be denied.

The adverse consequence of the lack of opportunity to patent falls both on university research and commercial laboratory research, whether financed privately or by the government. The virtual identity of interests between the university and the corporation in this regard is often misunderstood.

Where patents can be obtained, they offer a means for safeguarding

the investment of the corporation and the university in their research investments. If the investment is immediately dissipated by premature disclosure of details sufficient to show competitors the route to a successful end, much of the advantage of the innovator is lost and, accordingly, so is much of the incentive to invest in future work. To the extent the corporation enjoys a limited exclusive period, either by patenting its own work or receiving at least a limited exclusive license from government-financed research executed in the corporate laboratory, the corporation secures the necessary lead time and the opportunity for recovering investments and returning profits.

With the university, the prospects for patenting offer the opportunity for the university to interest a licensee of its choice to commercialize the invention. Norman J. Latker, Patent Counsel for the Department of Health, Education and Welfare, outlined the experience at HEW with the disposition of rights to HEW-funded research in testimony before a House subcommittee.[1] In his remarks, Mr. Latker traced the Department's failure to convert the research it sponsored into usable commercial products under the Department's patent practices prior to 1969. He pointed out that the subsequent practice of granting rights to the Department's contractors had produced dramatic

1. Testimony by Mr. Latker before the Subcommittee on Domestic and International Scientific Planning and Analysis, House Committee on Science and Technology, September 29, 1976.

results in terms of the investment of risk capital in the commercialization of products from Department-sponsored research.

Mr. Latker clearly identified the problem and the necessity for supporting the commercialization of agency-sponsored R&D. In his view "the research and development agencies should be under a heavy obligation to assure availability of patent protection when private resources are needed to achieve commercialization."

In summary, regardless of the source of the capital underwriting the research, the availability of patent protection is of the highest importance if the research is to be productive in the public sense. However, prospects for patenting would be essentially eliminated by premature disclosure of the type that would occur under recombinant DNA legislation that does not specifically provide for the confidential treatment of this information.

Exemptions Under FOIA

It is sometimes mistakenly assumed that subsection (b)(4) of the Freedom of Information Act (FOIA) provides adequate safeguards against disclosure of trade secrets and would operate to protect against the premature public disclosure discussed above.[2] Subsection (b)(4) says, with respect to the requirement for public disclosure of information in agency files, that such requirement "does not apply to matters that are... trade secrets and commercial or financial information obtained from a

2. 5 U.S.C. 552 (1967) (amended 1974).

person and privileged or confidential." This is the so-called trade secret "exemption" of FOIA.

While the underlying rationale for the Freedom of Information Act may have been laudatory, in practice it has been shown to serve mainly as an avenue by which competitors obtain confidential data indirectly from the originator. The cases and commentaries, as well as the practical problems facing the agencies involved, indicate clearly that the safeguards are illusory.

The Washington Post reports the unhappiness of former Food and Drug Commissioner Alexander M. Schmidt at the way the FOIA was working at FDA.[3] He said that about 90% of the requests for documents constituted "industrial espionage - companies seeking information about their competitors - and not the public's right to know." To a similar end is an article appearing in the Wall Street Journal.[4] Again the conclusion is expressed that an overwhelming percentage of the requests for information have nothing whatsoever to do with the public's examination of the actions of its government but are directed to legislatively sanctioned industrial spying.

Indeed, there is widespread misunderstanding of the Act itself with respect to the nature of the exemptions that are ostensibly provided by subsection 552 (b)(4). For example, the exemption was never intended to be a true "exemption." In the legislative report accompanying the Senate

3. Washington Post, July 27, 1976, at A4.
4. Wall Street Journal, May 9, 1977, at 1.

version of the FOIA amendments, there appears the following statement:

> Congress did not intend the exemptions in the FOIA to be used either to prohibit disclosure of information or justify automatic withholding of information. Rather, they are only permissive. They merely mark the outer limits of information that may be withheld where the agency makes a specific affirmative determination that the public interest and the specific circumstances presented dictate... that the information should be withheld.[5] (Emphasis supplied)

While it is true that the Senate version of the FOIA was not adopted by the Congress, there appears a similar interpretation in the House report of its version, which differed little in this regard. The following statement is contained in the House report:

> This milestone law guarantees the rights of persons to know about the business of their government. Subject to nine categories of exemptions, whose invocation in most cases is optional, the law provides that anyone may obtain reasonably identifiable records or other information from federal agencies.[6] (Emphasis supplied)

It is particularly instructive to note the summary of a meeting between Representative John E. Moss and Representative Barry Goldwater, Jr., concerning the exemptions under FOIA. This summary concerns the impact of the exemptions on energy R&D activities in the private sector:

> We agreed that any lack of predictable protection of the private sector's proprietary information

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5. S. REP., 93rd Cong., 2nd Sess. 854.
6. 3 U.S. CODE CONG. & AD. NEWS 6269 (1974).

> under the existing Freedom of Information Act exemption from mandatory disclosure for such information (5 USC 552 (b)(4)) could seriously inhibit private sector cooperation and participation with ERDA to the detriment of the national energy research and demonstration program.
>
> Mr. Moss acknowledged Mr. Goldwater's conclusion, based on an independent staff legal analysis, that protection under exemption (b)(4) is neither predictable nor adequate because of recent court interpretations of the exemption.[7]

Representative Moss was the father of the Freedom of Information Act. His observations reflect his serious concern for the interpretation of the exemption as well as a recognition of its inadequacy as a source of reliance on an agency's treatment of confidential information.

The leading case on interpretation of FOIA is National Parks and Conservation Association v. Morton.[8] There the tests as to the application of the exemption are said to be (1) whether the government's ability to obtain information in subsequent inquiries is likely to be affected by the knowledge that it may be made public, and (2) whether release of the information obtained by the government agency might cause substantial harm to a competitive position. Although an argument can be made that the second test would justify retention of trade secrets in confidence against a request under FOIA, the cases and commentators, not the least of whom is Representative Moss, have found this not dependably true in practice.

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7. 121 CONG. REC. H12379 (Dec. 11, 1975).
8. 498 F. Supp. 965 (D. D. C. 1974).

Illustrative of the problem is Petkas v. Staats, a Court of Appeals decision from the District of Columbia, home base for FOIA litigation.[9] There the court overturned an agency assurance of nondisclosure even though the information had been supplied on the condition that it would not be disclosed. The court said the obligation would not be enforced and remanded the case for examination under the tests laid down in the National Parks case.

One commentator examined the law and practice in implementing the FOIA "exemption" and concluded as follows:

> Presently, the status of proprietary information within government possession is uncertain. Prior agreements between the recipient agencies and the supplying businesses, whether formal or informal, statutorily premised or discretionally given, no longer serve as a valid assurance that business interests will be considered. Confidential treatment, determined under the more exacting standards of trade secret law, depends upon an intricate and individual evaluation of data not now covered by existing agency guidelines. A business concerned with safeguarding valuable information has little alternative but to resort to litigation for a judicial determination of the matter. As has been shown, even this avenue may be of limited value. It is apparent, therefore, agencies must develop adequate evaluative procedures which encompass fairness for all interests involved, and give due regard to the property interests protected by due process.[10]

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9. 501 F. 2d 887 (D. C. Cir. 1974).
10. Gazarek, Would Macy's Tell Gimbel's: Government-Controlled Business Information and the Freedom of Information Act, Forwards & Backwards, 6 LOYOLA UNIV. L. J. 594, 621 (1975).

This article also alludes to the varying interpretations of what constitutes a trade secret, a determination that compounds the difficulties encountered in relying on an "exemption." But even if the agency agrees that specific subject matter constitutes a trade secret, the exemption under FOIA is at best fragile.

It is pertinent, for example, that the legislative history of the Government in the Sunshine Act notes in a discussion of the FOIA exemptions that the Freedom of Information Act "permits but does not require the withholding of information."[11] This, indeed, is consistent with both precedents and practice under FOIA.

The same conclusion, as well as reference to the adverse effects thereof, with respect to the problems of the university in seeking grants and in soliciting commercial interest for university-developed inventions likewise emerges strongly from a pair of congressionally-sponsored studies.[12] The President's Biomedical Research Panel expressed its concern in this manner:

> The Panel is seriously concerned that the unpredictability of government protection for intellectual property rights, owing to the uncontrolled and unconditioned disclosure of research information under current court interpretation of the Freedom of Information Act, is likely, in the Panel's view, to stifle industry interest in developing potentially important research innovations.[13]

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11. 3 U.S. CODE CONG. & AD. NEWS 2191 (1976).
12. Commissioned under Title III of the Health Research and Health Services Amendments of 1976 (P. L. 94-278).
13. DHEW Publication (OS) 76-513, at 16.

Similarly, The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, a group of entirely different composition, examined the question independently and urged that information "the disclosure of which would adversely affect future patent or other valuable commercial rights" be protected from disclosure under FOIA.[14]

Much of the concern of these groups arose from the Court of Appeals' decision in Washington Research Project, Inc. v. Department of Health, Education and Welfare.[15] There the court placed the burden of demonstrating the trade secret character of the information requested on the agency. The information was contained in research protocols submitted as part of requests for grants from HEW. The lower court had ordered release of the grant applications which included the research protocols. In affirming, the Court of Appeals declared that the exemption relied upon applied to trade secrets and that there were no trade secrets in a "noncommercial scientist's design." The court said further that "it defies common sense to pretend that the scientist is engaged in trade or commerce."

The basis for the court's decision was therefore on the ground that the appellant had failed to bring himself within the FOIA exemption by virtue of his employment rather than the nature of the subject matter - and despite

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14. DHEW Publication (OS) 77-0003, at 37.
15. 504 F. 2d 238 (D. C. Cir. 1974).

the fact that the interests of his university employer in preserving confidentiality were fully as legitimate as would have been those of a corporate employer.

Practical Difficulties Under FOIA

Finally, there are the practical aspects of the handling of trade secrets under FOIA in the face of requests for disclosures. Whether or not the exemption from disclosure is regarded as permissive, the agency in possession of the information submitted by companies or universities engaged in recombinant DNA research would inevitably find it impossible to comply fairly with the administrative requirements of FOIA. The threshold question of determining what information constitutes a trade secret poses a problem in itself. Additionally, this decision must be made within ten days of the request for disclosure.[16] Accordingly, within ten days the agency must locate the material requested, evaluate it for trade secret content, advise the originator of its decision to disclose (if it had previously agreed to do so, possibly as a condition of disclosure to the agency) and advise the requester of its decision.

It must be remembered as well that the determination of trade secret status in this field of high technology should be made by individuals in the agency who are trained in the technology and who would, therefore, be removed from more productive duties for this undertaking. The

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16. 5 U.S.C. 552 (a)(6)(A).

burden on the agency would be, in the usual case, virtually an impossible one to discharge justly within the time allowed.

The agency is, in fact, in the middle. It stands subject to suit from the requester if it denies access to information and suit from the originator if it discloses trade secret information. Of course, once the information is disclosed to a requester, usually a competitor of the originator, the harm to the originator has been done; whatever might be gained by litigation would inadequately compensate for the loss of the originator's trade secrets.

It is, of course, possible for the originator who learns in time of the prospective delivery of his information to a requester under FOIA to go to court to prevent disclosure. He could try to persuade the court that the documents are, indeed, entitled to trade secret status. But for the court to reach its decision it would need the time, patience and expertise to evaluate the documents in camera, one by one. The likelihood of a fair disposition of the issue by this route is understandably small. If the suit was initiated by a disappointed requester to whom the agency had refused to give up information, the agency-defendant could not be expected to discharge the defense of its position with the greatest vigor, for it has nothing more at stake than the enmity of the originator. And if the originator intervened in the litigation, the issue is still at the mercy of an overburdened court.

Legislative Solution

The criminal statute prohibiting disclosure of confidential information by Federal employees, 18 U.S.C. 1905, is of uncertain comfort with respect to disclosure under FOIA. Indeed, section 1905 would, if involved at all, apply only after disclosure and after the damage had been done. Also, section 1905 only applies "unless otherwise provided by law." Since FOIA is another law, it is an easy interpretation to find that section 1905 does not prevent disclosure under FOIA. Indeed, in M. A. Shapiro and Company v. Securities and Exchange Commission the court explicitly held that section 1905 "does not prevent disclosure of information that is authorized to be disclosed under other laws" and that, accordingly, "there is nothing in Section 1905 of Title 18 that prevents the operation of the Freedom of Information Act" - -i.e., disclosure under FOIA.[17]

On the other hand, there are many such "other" statutes that prohibit disclosure of confidential information;[18] and where they do, the penalties of 18 U.S.C. 1905 can be invoked for unauthorized disclosure by federal employees. Subsection (b)(3) of FOIA similarly provides an "exemption" against disclosing information protected by another statute.

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17. 339 F. Supp. 467, 470 (D. D.C. 1972).
18. Atomic Energy Act of 1954, 42 U.S.C. 2011, 2161-2166; Civil Rights Act of 1964, 42 U.S.C. 1971, 2000e-5(b) and 8(e); Federal Election Campaign Act, 2 U.S.C. 431, 437g(a)3; Consumer Product Safety Act, 15 U.S.C. 2051, 2055(a)(2); Occupational Safety and Health Act of 1970, 29 U.S.C. 651, 664.

A good example is the Federal Nonnuclear Energy Research and Development Act of 1974.[19] The inclusion of protection for confidential information was intended specifically to circumvent the unpredictability of the protection ostensibly afforded by the fourth "exemption" of FOIA. Indeed, Senator Fannin stated in connection with the House-Senate Conference Committee's action on the bill:

> The conferees took this action because... under existing law, primarily the Freedom of Information Act, "holdings" have made government protection of trade secrets and other proprietary information completely unpredictable... Out action here is intended to remedy that situation for ERDA.[20]

Again, in the Federal Aviation Act of 1958, as amended, there is specific language prohibiting release under FOIA where the Administrator has determined the information contains trade secrets, privileged information or confidential commercial or financial information.[21]

In approaching a statutory solution, however, attention should be given Robertson v. Butterfield, a 1974 Court of Appeals decision from the District of Columbia.[22]

In that case appellees had requested certain reports in the files of the Federal Aviation Administration. These reports consisted of analyses

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19. 42 U.S.C. 5901, 5916.
20. 121 CONG. REC. H12379 (Dec. 11, 1975)
21. 49 U.S.C. 1301, 1357(d)(2).
22. 498 F. 2d 1031 (D.C. Cir. 1974).

made by employees of FAA with respect to the operation and maintenance performance of airlines. The FAA Administrator had denied disclosure as being "not required in the interest of the public." The lower court referred to the Federal Aviation Act of 1958, in which there is provision for withholding such reports.[23]

The Court of Appeals interpreted the lower court's decision as relying on subsection 552 (b)(3) of FOIA, although the decision did not specifically so state. This exemption goes to the disclosure of matters "specifically exempted from disclosure by statute." The issue before the Court of Appeals, therefore, was whether the Federal Aviation Act of 1958 was, under these circumstances, such a "statute" as to bring the denial for disclosure within subsection (b)(3).

The Court of Appeals held that it was not. The court reasoned that the exemption of subsection (b)(3) applied only where the statute that was asserted to exempt disclosure "[specified] the documents or categories of documents it authorizes to be withheld from public scrutiny." This, declared the court, the Federal Aviation Act failed to do.

Accordingly, a statute affording positive protection for confidential information associated with recombinant DNA, whether submitted as part of a voluntary request for approval of facilities and projects or as mandatory

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23. See note 21.

compliance with other provisions of a recombinant DNA statute, should denominate with care the categories of information to be withheld from disclosure under FOIA. Such a categorization, for example, might generally take the form of the several types of information enumerated at the beginning of this Memorandum. It would also state, of course, that any such statutory exemption would be subject to overriding considerations of the public health and safety.

In summary, there is strong precedent and sound rationale for including statutory language in a recombinant DNA bill that would give positive and dependable protection for research and development information submitted pursuant to requirements of a statute. The public interest will not be served by leaving the matter to the vagaries of an FOIA exemption, particularly where the agency responsible for the decision concerning disclosure would have to expend high priced and precious talent to make reasonable judgments required by the FOIA approach. But, more important, FOIA has been shown to be inadequate and undependable; reliance on the trade secret "exemption" will not inspire full disclosure.

The concerns about premature disclosure affect both the commercial organization and the university. Specific statutory language that would qualify the statute under subsection (b)(3) would avert much litigation from both requesters of information and originators of information that would otherwise be invited by any decision the agency might make. Only

through such a positive declaration in the statute will the prospects for patenting by industry and universities be preserved and the essential step of commercialization be encouraged in this advancing frontier of medical science.

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