



“Where research places the community at risk, science must be accountable to the citizenry”

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Public must regulate recombinant research

The public controversy over use of recombinant DNA techniques has called into question one of the sacred cows of science: that the nature of basic research—the questions it asks, the form it takes, and the safeguards it requires—is best left up to the scientists who are most intimately connected with it.

When the Cambridge (Mass.) City Council held public hearings in June 1976 on Harvard's proposed moderate risk P3 laboratory designed primarily for recombinant DNA research, the long tradition of blind trust between citizen and scientist was severed. For some this portends to be a new politicization of science that threatens to weaken the U.S.'s lead in biological research. Others see this as a maturation of public participation—the citizen review process coming of age.

I want to review the process by which Cambridge citizens tackled this technical scientific controversy, discuss how I saw the issues while serving on the Cambridge Experimentation Review Board (CERB), and provide some of the reasoning behind the board's decision. Finally, I will discuss federal legislative requirements for regulating recombinant DNA technology.

Cambridge citizen review process

After two lengthy sessions of heated debate in the chambers of the Cambridge City Council on the risks and benefits of recombinant DNA research, a compromise decision was reached by the nine-member council to establish a citizen review board that would study the issues.

The city manager determined the composition of the committee. At the time, it was difficult to find individuals with extensive knowledge of microbiology who had not taken a public stand on the controversy. The manager consciously avoided choosing a committee of adversaries since, with such a group, there was no room for deliberation. He selected a board of eight Cambridge residents, evenly divided between men and women. By choosing a lay review board, the manager committed himself to the principle that those least likely to have vested interests in the research, or in the institutions in which the research was

being proposed, could best be trusted to render an objective opinion on the appropriate course between risks and benefits.

The citizen members included a physician (board-certified in infectious diseases), a philosopher of science, a fuel oil distributor, a structural engineer, a clerk, a nurse, a social worker, and a housewife.

The board visualized itself as a citizen jury whose responsibility it was to examine the controversy within the scientific community. CERB met twice weekly for three-hour sessions. It established a schedule whereby research opponents and proponents testified on alternate weeks. It drew in testimony from outside the local community through open-line telephone conversations. It called upon scientists to explain technical concepts, present simplified models of biochemical events, and draw upon analogies to foster understanding of the technology. In a five-hour marathon mock-courtroom session, board members served in a jurylike role, while advocates on both sides of the controversy presented arguments, cross examined one another, and responded to questions raised by the citizen board. The adversary format enabled board members to evaluate the responses of scientists to the critical issues.

In its final report CERB emphasized its self-image as a citizen court and cited the potential applicability of that model for other science policy debates: "The use of a 'citizen court' in areas of controversy within science that have significant bearing on public welfare is quite new and untested. It encouraged discussions among board members about where justification rests. At issue was whether proponents of the research must prove that it is safe beyond all reasonable doubt or whether the opponents must prove that if recombinant DNA research were undertaken there would be significant potential hazards."

Accountability to the public

What responsibility does science have to the lay public? Is it not of greater overall benefit to society to encourage autonomy

by scientists in the choice of research programs, rather than to call upon the public to certify a particular area of research?

It is important to keep clear the distinction between freedom of inquiry and the right to engage in experimental research. In the former, we recognize the established right of scientists as scholars to exchange freely in the market place of ideas. With experimental research, however, the scientist is doing more than creating theories and testing hypotheses. The scientist is intervening in nature. There is a specialized public interest established when elements of nature are modified, where laboratory containment is not possible, and where products of research—potentially hazardous to human society—are capable of self-replication.

Where there are areas of experimental research which cannot be carried out without placing the community at some risk, science must be accountable to the citizenry. In its report to the city, CERB proclaimed that: "Knowledge, whether for its own sake or for its potential benefits to humankind, cannot serve as a justification for introducing risks to the public unless an informed citizenry is willing to accept those risks. Decisions regarding the appropriate course between risks and benefits of potentially dangerous scientific inquiry must not be adjudicated within the inner circles of the scientific establishment."

Arguments against recombinant DNA research fall into four categories:

- Health hazards. These are specifically defined hazards associated with the creation of new pathogens or new niches for DNA that codes for toxins or oncogenic viruses.

- Species barriers. Humankind should not exploit the power of crossing species barriers between eucaryotes and procaryotes, and thus take into its own hands the future of evolution on the planet.

- Genetic engineering. Recombinant DNA techniques will eventually lead to baneful forms of genetic engineering, whereby the solution to social problems will be sought in the alteration of the human genome.

- Misplaced priorities. The benefits of the research can be obtained through less risky procedures. Furthermore, proponents, in discussing benefits, are asking the wrong questions and misplacing national priorities. For example, the claim that the research might provide some clues to the enigma of cancer simply places the emphasis on the individual and not on the social causes of cancer. The money to be allocated to this research is best spent in reducing the levels of environmental carcinogens.

The Cambridge review board, on the direction of the city manager, focused exclusively on the potential health hazards

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to the community. It left the other three arguments to another type of review process. Thus, in its recommendations CERB issued a plea that the social, political, and moral implications of the research be taken up in a national dialogue, with broad public participation.

NIH guidelines

After nearly one and a half years of study, NIH issued guidelines for recombinant DNA molecule research on June 23, 1976. The guidelines were written expressly for technical people by technical people, most of whom were intimately connected with the research. Public input was not commensurate with the magnitude of the public's investment as the bearer of potential risks.

The guidelines relativized the risk assignment for a range of experiments and provided a taxonomy of permissible genetic recombinations. Each potential donor of DNA was assigned a containment space consisting of a physical and biological containment parameter. This two-dimensional containment space can be represented by the matrix on this page. Included are a few examples for each containment coordinate. P1 to P4 represent increasing levels of physical containment, expressed in more elaborate laboratory facilities and procedures. EK1 to EK3 represent increasing degrees of biological containment, expressed in more attenuated strains of *Escherichia coli* as the host organism.

One of the technical issues that CERB did not tackle in its investigation was the scientific basis for the risk assignments. Why, for example, do experiments involving DNA from cold-blooded vertebrates receive containment coordinate EK2 + P2?

It was clear that NIH's relativized risk assignments were guided by some principles. Organisms that are known to exchange DNA with *E. coli* are considered low risk for recombina-

NIH guidelines on recombinant DNA research set containment levels

		Physical containment levels				
		P1*	P2*	P3*	P4*	Banned*
Biological host (<i>E. coli</i> strains)	safer	EK1	Class 1 bacteria naturally exchanging DNA with <i>E. coli</i>	Plants (no known pathogen)	Plant viruses	Venoms from insects and snakes, genes for botulinum toxin
		EK2		Cold-blooded vertebrates (frogs), plant viruses	Nonprimate mammals (cats), birds	Primates (monkeys), animal viruses
		EK3			Primates (monkeys), animal viruses	

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nant experiments. Donor species closer to humans on the phylogenetic scale were given higher risk assignments. Some donors were double listed. Primate DNA can be implanted into *E. coli* under EK3 + P3 conditions or under EK2 + P4 conditions. An EK2 and an EK3 host are substantively the same organism. EK2 becomes an EK3 when it has satisfied certain tests.

Critics raised a concern that the taxonomy of risk assignments was, to some degree, a reflection of the special interests of those researchers who did not want their pet projects assigned a containment coordinate that was too high. It is certainly not obvious that EK3 + P3 containment affords the same level of protection as EK2 + P4 containment. It is also not clear why recombinant experiments involving bird DNA are considered significantly more (potentially) hazardous than similar experiments involving frogs or insects.

These issues were never resolved in the Cambridge review process. CERB spent most of its time trying to understand the effectiveness of biological containment, the nature of laboratory procedures, and the possibilities of monitoring the escape of experimental organisms.

Biological containment

One of the strongest arguments against carrying out gene recombination experiments in Cambridge is that *E. coli* was selected as the host organism. Opponents cited *E. coli*'s survival capacity in a variety of niches: Many strains of *E. coli* are found to inhabit the human gut, and some varieties are capable of infecting humans.

There were also arguments advanced in favor of *E. coli*. Since the purpose of recombinant DNA technology is to determine the relationship between structure and function of segments of genes, it is essential to the researcher that the host organism offer a well-defined environment to the implanted DNA. Since no bacterium is better known than *E. coli*, it is clear why scientists were eager to initiate the experiments with it as host—at least until a safer organism is found whose genome is as well defined.

But the most important argument proponents offered was that they were not using any old variety of *E. coli*. The selected host was an enfeebled strain called K12. (EK1 is identical with K12. EK2 and EK3 are further attenuated forms.)

It was widely accepted that K12 could not be made pathogenic. Also cited were experiments that attempted to get K12 to colonize in humans, but which proved unsuccessful.

There were still many unanswered questions. The fact that a selected number of tries has failed to improve the survival advantage of *E. coli* K12 was not assurance that it could not happen. Moreover, all is not known about the nature of pathogenic organisms. Many of the arguments offered to CERB were

“There are too many stories of sloppy lab procedures. Lab workers may feel too intimidated to report grievances”

hybrids—a mixture of empirical results and a priori assumptions. Scientists disagreed about the interpretation of data and the projectability of data to novel situations.

One of the arguments presented I call the quantity/quality argument: “The chances are minuscule that by modifying the DNA of an innocuous bacterium by one tenth of one per cent, it could be changed into a pathogen.” We were also told: “It is extremely unlikely that man can create a bacterium that can be more virulent than those nature already has brought us.” Another argument, backed by evolutionary theory, claimed that by modifying the DNA of a bacterium we would in most instances reduce the survival advantage of that organism.

We not only had the difficult task of separating fact from speculation and from fiction, but also of judging when generalizations seemed justified. The fact is that many of the risks are unknown, and more data are required before any conclusive risk assignment can be made. These uncertainties were expressed by the director of NIH when he issued the guidelines. “In many instances,” he said, “the views presented to us were contradictory. At present, the hazards may be guessed at, speculated about, or voted upon, but they cannot be known absolutely in the absence of firm experimental data—and unfortunately, the needed data were, more often than not, unavailable.”

The taxonomy of risks established by NIH is thus a hypothesis, not a result. There are several distinct points where something could go amiss.

The NIH guidelines offer one approach for reducing the likelihood of such mishaps. To see this consider what the recombinant DNA technology is doing. There is a donor from which the investigator appropriates the DNA to be recombined. There is the host (*E. coli*) which accepts the gene segment. And there is the vector which serves as the vehicle for introducing the DNA into the host.

Proponents have asked us to accept the following claims: For all permissible combinations of donors, vectors, and hosts

- The modified *E. coli* will not receive a survival advantage.
- There will be no unsuspected emergent properties for the host; the newly transplanted gene will either be made to express itself, or do nothing at all.
- Segments of DNA capable of producing substances harmful to humans will not be implanted into *E. coli* inadvertently.
- Antibiotic-resistant genes will not be released into the environment.
- DNA segments implanted in *E. coli* which are ingested by the investigator will not conjugate with other varieties of *E. coli* in the investigator's gut.
- Even if the recombinant DNA were released to another organism in the human gut, the DNA would not transform that secondary organism to a pathogen.

Until the above statements are secured upon a solid bedrock of evidence, the public would be remiss in not taking appropriate precautions. The citizen review board in Cambridge was not satisfied that all the evidence was in. CERB viewed the major shortcoming of the NIH guidelines (aside from the fact that it only covered NIH-funded projects) to be in the area of laboratory monitoring.

Recommendations of CERB

A modest proposal for the introduction of any new technology is that there be a feedback system that signals us when something goes amiss. It was very disconcerting that the NIH guidelines placed such little emphasis on monitoring under laboratory conditions.

CERB was uncomfortable with the NIH guidelines for having given the principal investigator the major responsibility for overseeing laboratory safety. There was no assurance that such a principal investigator would require the highest standards of safety. There are too many stories of sloppy laboratory proce-

dures. And laboratory workers may feel too intimidated to report grievances to an institutional biohazards committee.

CERB called for more intensive monitoring and struck down the concept of self-regulation in favor of a local citizens biohazards committee. Throughout its investigation, CERB accepted the technical assignment of potential risks developed in the NIH guidelines. However, it sought more assurance on the credibility of claims about the effectiveness of attenuated strains, and the nontransferability of DNA fragments to other organisms.

The key elements of CERB's recommendations, subsequently incorporated into a city ordinance, are:

- All experiments undertaken at the P3 level of physical containment shall require an NIH-certified host-vector system of at least an EK2 level of biological containment.
- All modified organisms resulting from recombinant DNA experiments shall be tested for their resistance to commonly used therapeutic antibiotics.
- As part of an institution's health monitoring responsibilities, it should monitor for any survival and escape of the host organism.
- A city biohazards committee should be created to oversee all recombinant DNA research in the city.

In addition to its recommendations to the City Council, CERB called upon Congress to provide uniform federal guidelines covering all possible uses of the technology in research institutions and industry; to include health monitoring as part of the funding for any proposal that plans to use recombinant DNA techniques; and to fund research to determine whether host organisms that find their way to the human intestine can survive and escape under laboratory conditions.

At the present time, no set of guidelines or institutional structure is adequate to regulate all applications of the technology. Several bills are before Congress, and the likelihood is that some regulatory legislation will be passed.

Two critical issues must be considered in such federal legislation. The first concerns the options of local communities to impose more rigorous standards than what will be offered in federal legislation. The second concerns the appropriate forum to deal with the ethical and social consequences of the technology.

There are serious problems with having each local municipality or state establish its own regulations on how the research is to be undertaken. Unless it is clear that there are differences between municipalities or states that bear relevance to the substance of the regulations, local options could create disorder within scientific and industrial establishments. The impulse would be to move to that locality with the least stringent regulations.

I do think it appropriate, however, for local communities to be left with the two options—to have authority to exclude certain classes of research that the community deems too risky, and to have authority to establish local biohazards committees for overseeing recombinant DNA research in the city or town.

I would make an analogy with the siting of nuclear power plants, where those closest to the plant bear the greatest risk. If a community perceives risks with genetic research that it doesn't wish to bear, then it should have the option to exclude such research.

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Finally, we must as a nation begin facing up to the social and ethical consequences of recombinant DNA technology. It is not premature to establish a national dialogue to consider what, if any, limits should be placed on the research and what controls should be placed on its industrial and clinical applications. Thus far, these issues have been overshadowed by debates over imminent hazards.

Some of the more far-reaching applications are estimated to be only 10 to 50 years away. Some opponents of the research argue that there is a direct causal link between recombinant DNA in the 1970's and baneful forms of genetic engineering in the year 2050. I believe we have some options between the alpha and the omega. We must begin considering who is going to be accountable to the public for how this research is used.

Pharmaceutical companies are very keen to develop this technology, as it may allow them to produce certain hormones cheaply or make scarce blood factors or odd combinations of plants and insects where species properties are interchanged. All one has to do is to think back to the beginning of the petrochemical industry. We know that almost anything can be marketed. The production sector doesn't simply respond to demand; it creates it. Much of what has been marketed in the name of progress should never have left the research laboratories—PCB's (polychlorinated biphenyls), HCB (hexachlorobenzene), carcinogenic flame retardants, and DES (diethylstilbestrol), to name a few.

To deal with issues of regulation and technology assessment, the Cambridge Experimentation Review Board has recommended the creation of two national commissions. The first would be empowered to establish guidelines, health monitoring standards, and licensing procedures for all institutions undertaking the use of recombinant DNA technology. A second commission would consider the social and ethical implications of the use of the technology in research, as well as its industrial and clinical applications.

We are most fortunate in this historical episode to have had sufficient warning to address the full range of technical and social issues. Given that there are potential costs in not doing the research (opportunity costs) and potential risks in doing it, our first responsibility is to disclose fully the implications of the technology for the public, to define and empirically evaluate the unknown risks, and to set up appropriate forums for public participation.

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"If a community perceives risks with genetic research that it doesn't wish to bear, then it should have the option to exclude such research"

Dr. Sheldon Krinsky

Regulation no threat to free scientific inquiry

The essays of Dr. Chargaff and Dr. Davis epitomize the character of the dialogue on recombinant DNA research that has been taking place over the past several years. On one side, there are scientists calling for a slowing down of this research effort until society has had an opportunity to assimilate the full implications of the technology. On the other side are those who wish to push forward.

Representatives of the latter group of scientists divide the issues into a series of "what-can-go-wrong" arguments. Then, in the grand Cartesian tradition of science, they subject each of the component arguments to an analysis—mixing theory, fact, a priori assumptions, conjectures, analogies and intuitions—which demonstrates that the risks are vanishingly small.

In Chargaff's remarks there is a refreshing modesty about the limits of science and a keen sense of awareness of Homo sapiens' place in the intricate web of nature. Chargaff emphasizes our ignorance. Davis emphasizes our knowledge. At times there may be vagueness in the assessment of danger by those in opposition to the research. But this is accompanied by a rational skepticism. After all, the spokesmen for science have, on more than one occasion, led us through the murky paths of self-deception. Reason is all we have to guide us. But there is no monopoly over first principles or the acceptable strata of fact and theory relevant to the issue of risk.

I shall begin with some comments on Davis' interesting and provocative remarks. Specifically, I shall focus on three of his many arguments, in order that the presuppositions upon which they rest can be made explicit. Since I am not technically equipped to render a judgment on the empirical validation of these tacit propositions, I raise them for the general interest of the reader. My experience on the Cambridge citizen review board has made me aware of the divergence of opinion on key issues that bear upon the assessment of risk.

Consider the following argument by Davis:

- A mammalian donor cell has on the order of 10^6 gene equivalents.
- If there are any dangerous genes in the mammalian donor, they would be small in number.
- The probability is exceedingly low of randomly selecting a small quantity of dangerous genes from a normal tissue of a mammalian donor.
- Therefore, the probability of inadvertently transferring a dangerous gene segment to a host organism is exceedingly low.

Assuming that the premises in the above argument are correct, there is one presupposition that stands out: A gene that is benign in the donor will be benign in the host. There are two correlative statements to the above. The first is that there is an isomorphism between gene structure and gene product. If a gene segment G_x produces protein P_x in environment E_x , and if G_x is placed in environment E_y , then G_x will either produce P_x or not express itself.

Is it possible that there is a polymorphism rather than an isomorphism between gene structure and gene product? What is the likelihood that new and unspecified properties will emerge? Will there be more than one way of reading recombinant gene segments? Of course, even if there were emergent properties, these novel products might not be dangerous.

The second correlative statement is that the risk of human contact with recombinant genes is independent of the locus of contact. Suppose we consider an experiment in which soybean DNA is transferred to *Escherichia coli*. Do we have good reason to believe that the experiment will be safe beyond a reasonable doubt? After all, haven't humans been eating soybeans for many years with no reported deleterious effects?

Is the benign contact we have with soybean DNA through digestion (however that DNA is finally broken down) sufficient evidence that soybean DNA implanted on a plasmid, inserted into *E. coli*, and taken into the human gut will also be benign? In other words is the route of contact a factor in assessing risk?

In a second argument Davis claims that there is good evidence that natural recombinations are occurring in the human gut all the time. The example he cites refers to exchanges between bacteria. Can we assume that the evidence for procaryote to procaryote DNA exchanges implies anything about eucaryote to procaryote DNA exchanges?

In a third argument Davis implies that adding foreign DNA to an organism will ordinarily decrease its adaptability to its present environment. Furthermore, the more foreign the DNA is to the species, the more unlikely it is that the organism will improve its fitness. (This Darwinian analysis is reminiscent of the medieval view that God doesn't change since He is by necessity perfect and He could only change to something less perfect, which is a contradiction.)

The argument raises the issue of whether humankind can take a shortcut in evolution. Can we assume that any organism is already at its peak of suitability to its environment? Can human devices help evolutionary fitness? Is it a generally accepted result that by implanting higher-order genes to lower-order organisms we will almost certainly reduce the fitness of those organisms to their present environment?

Is the theory of evolution consistent with Davis' statement or does the theory entail it? It is, of course, possible for a general theory to be consistent with each of two statements that are mutually contradictory. Auxiliary assumptions play a crucial role in moving from general theory to particular statements. The question I raise is whether these auxiliary assumptions have been made explicit and appropriately validated.

Perhaps it will be acknowledged by experts that answers to the above questions are trivial, given the present state of knowledge, or that the answers are irrelevant to the question of risk. But the controversy itself should be nurtured and not swept under the rug. Public confidence can be established only when the issues are debated openly and honestly, even when those not privy to the technical knowledge awkwardly frame the questions.

Chargaff's remarks prompt me to say a few words on the subject of freedom of inquiry, since it has been raised as an argument against regulating recombinant DNA research. Opponents of regulation, waving the banner of freedom of inquiry, exhibit an acute blindness to the fundamental distinction between establishing limits on how scientific knowledge may be obtained and establishing limits on what scientific knowledge may be obtained.

Since it is the right and obligation of government to protect the public welfare, there can be no dispute about the principle

underlying limits on how knowledge may be obtained. Where the routes of inquiry place the public at risk or compromise human rights, science must be accountable to the public. We have guidelines protecting human subjects and for experiments with human fetuses. We regulate the use of radioactive materials in research. I am perplexed, therefore, when there is talk about the demise of science in connection with the prospect of licensing recombinant DNA research.

In his annual report of April 26 to the National Academy of Sciences, its president, Dr. Philip Handler, stated: "I view with great alarm the prospect of any law that would authorize government officials to determine what subject matter it is permissible to investigate as well as the manner in which research is to be conducted."

The issue is not whether we are setting a dangerous precedent by regulating recombinant DNA research. The question is whether the research technology is sufficiently hazardous to warrant regulation. Furthermore, we must ask who should regulate research—the investigators themselves, the agency that promotes it, or representatives of the public interest?

Support of limits on *how* scientific knowledge may be obtained in no way commits one to limits on *what* scientific knowledge may be obtained. For further elucidation, I divide the latter condition into two propositions:

- A duly constituted government has the right to prohibit the use of public resources for selected research areas. As regards this proposition, it is debatable whether the greater social good is achieved by having researchers define the priorities of basic research, as contrasted with a process involving broader public participation. An affirmative response to this proposition does not imply that the public interest should influence what is good science or what theories are acceptable.

- A duly constituted government has the right to prohibit entry into certain areas of knowledge, irrespective of where the funding originates. This proposition implies that there are areas of knowledge that may be termed dangerous. It raises the

question of whether there are absolute rights of scientific inquiry.

Freedom of scientific inquiry holds a high position in our architectonics of rights. The pursuit of scientific knowledge includes that general area of activity characterized by the search for explanations, the discovery of laws, the development of theories, the collection of data, and the promulgation of ideas. I am assuming, for the sake of simplicity, that in this proposition we are not dealing with any modes of inquiry or technologies that subject the public to appreciable hazards. What is alleged to be dangerous about this class of knowledge are the ideas themselves (their direct impact on society) or the use to which the knowledge may be put.

Let's not forget that freedom of scientific inquiry does not stand above our right to free speech. Although both rights are integral to a free society, they are not unlimited in scope. Where there is a clear and present danger, our right to free speech is limited. Likewise, one could imagine certain areas of knowledge which, if pursued, could place society in grave and imminent danger. I don't see how one can discount this possibility.

I share Chargaff's despair about the development of nuclear energy. I would gladly trade off the knowledge of nuclear science presently possessed by human societies for the opportunity to live without the anxiety of a nuclear holocaust or the rapid spread of radioactive materials.

The question over whether to proceed in a new area of potentially hazardous research is complicated by the fact that we live in a world of independent, competitive, and antagonistic nation states. Shall we give up claims to certain areas of inquiry while watching the research accelerate in other countries, or should we take the lead in learning where the hazards lie? Can we venture a sensible prediction on the overall balance of good and evil when we stand at the threshold of new knowledge? The fact that these questions raise many difficulties should not be an invitation to forgo one's social responsibility to examine the expected outcome of a new research program. □

Dr. Erwin Chargaff

Recombinant research may be just a waste

Having had the opportunity of seeing the contributions by Dr. Davis and Dr. Krimsky, I must emphasize that what I say here is not at all meant as a rebuttal. In the case of Krimsky's paper, there could be no thought of a rebuttal. Quite the contrary: I have the greatest admiration for the manner in which Cambridge citizens attempted to arrive at an informed opinion.

I am less certain that the decision they reached was correct. But what else could they do? How could a tiny group withstand the enormously powerful trend that seems to decree that whenever we have to choose between two evils we take both?

Also as concerns Davis' paper, no rebuttal is possible, but for other reasons. Positions have been taken and will not be given up easily. The arguments offered in favor of one or the other point of view are made to look like scientific ones, but in reality they are partly moralistic, partly political, and very often utilitarian. In times of extreme scarcity of scientific funds, only a molecular angel could resist the lure of easy and plentiful support for a fashionable project.

I hope I am wrong—I believe I am right—in expecting some very unpleasant mishaps. There is, of course, an even greater probability, namely, that nothing will happen, nothing good, nothing bad; that the enormous sums being spent on this kind of research simply will be wasted, with no other ill effects than

on the public purse; that the only consequence will be an outpouring of many thousands of papers of a quality similar to that of the contributions assembled in the recent issue of *Science*. To the extent that science has become a WPA (Works Progress Administration) for scientists, such a development may even be welcome.

One point has not, I believe, been stressed sufficiently. I have been brought up in the belief that one of the prerequisites for the validity of experimental science is that its findings be fully reproducible. I should say that this still is, to a large extent, true of physics, chemistry, and most other disciplines, but it no longer holds for many areas of molecular biology and especially for "gene" transplantation. One has only to look at many papers in this field to see how repugnantly unique and indescribably private much of the experimentation has become. I wonder how many of the specialized findings have been, or can be, duplicated. This has nothing to do with the honesty of the individual workers, which I have no reason to doubt. But it shows that we are dealing here with a new category, no longer confinable within the ancient boundaries of the natural sciences.

The present moral and scientific climate makes impossible an adequate discussion of the ethical problems raised by genetic engineering, of which there are plenty. The idiot laughter with