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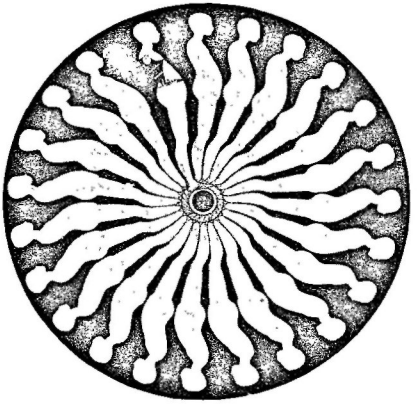

The Regulation of Genetic Engineering

STEPHEN BREYER AND RICHARD ZECKHAUSER

Genetic engineering has moved off the science fiction shelf and into the laboratories. The popular press, as well as scientific journals, report one interesting development after another. At the University of Wisconsin scientists have successfully synthesized a gene.[1] At Oxford they have changed the genetic nature of a mouse cell by injecting a deficient cell with healthy genetic material drawn from a chicken.[2] Ten years ago scientists proved the practicality of "clonal" reproduction—of creating asexually, from the cells of a single frog, an offspring that was the exact genetic duplicate of its one parent.[3] We also read that even now it may be technically possible to fertilize a human egg outside the human body and then implant it into the womb until birth; and we may see within our lifetimes the invention of an artificial womb that would nurture the fetus outside the mother's body.[4] These and other similar developments indicate that we are on the brink of a "genetic revolution"—the creation of new technology that could change society at least as profoundly as has the internal combustion engine, telecommunications, or atomic energy.

A growing number of scientists is urging Congress to learn from our past failures to control technology and to take steps to control this potential technological revolution even before it begins. The results of at least some genetic research, they argue, may prove a mixed blessing. What advantages might cloning bring that would warrant the risk that its very existence will lead to its abuse? Can one treat with equanimity the prospect of, say, 20,000 exact dupli-

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cates of General Franco? Artificial birth may allow some couples, now childless, to have natural children; but might not its widespread use, or perhaps even its existence, lead to basic changes in our concept of the family? And does not the experimentation needed to perfect it raise the deepest ethical problems? An ability to manipulate genes may eliminate inherited disease and perhaps end cancer; but might it not also produce fundamental change in the nature of a human being, in his values, in the values of our society?

These questions are disturbing to the point where Nobel Prize winner James Watson argued before Congress:

> Certainly to many our most sensible course of action would be to de-emphasize all those forms of research which would circumvent the normal sexual reproductive processes. If this step were taken, experiments on cell fusion would no longer be supported by federal funds or tax-exempt organizations. Prohibition of such research would most certainly put off the day [when cloning of human beings becomes a practical possibility]. Even more crucial would be to take steps quickly to make illegal, or reaffirm the illegality of, any experimental work with human embryos. With both these actions taken, our current value systems might survive somewhat longer.[5]

In a similar vein, a distinguished officer of the Life Sciences and Social Policy Committee of the National Academy of Sciences has written of "the need for institutional controls." In his view, it may be as wise to regulate "*certain* genetic technologies" as to attempt to prohibit "the development, testing and use of biological and nuclear weapons."[6] The increasing public concern over these issues has led Senator Mondale to introduce a Bill that would create a special commission to study regulatory possibilities in depth.[7] Congress has taken this matter very seriously.[8] Earlier this year, the Senate Subcommittee on Health chaired by Senator Kennedy held hearings on genetic engineering as part of its broader investigation into human experimentation.[9]

Indeed genetic research is now a major social issue. It warrants study and discussion not simply by scientists, but by lawyers, economists, and others interested in public policy. Yet such study is difficult to undertake for three reasons. First, the subject matter of "genetic engineering" is indefinite. To discuss it seems to require speculation about a near-limitless range of only dimly foreseen future possibilities—rather as if a Victorian were asked to discuss the social consequences of the automobile. Second, genetic engineering is inextricably entwined with a host of other medical and social issues such as heart transplantation, psycho-

surgery, experiments with human beings, and abortions. Third, regulation can take on a variety of forms, each with its own pattern of complexities. The government can forbid an activity directly (though this may not prevent it from taking place). Less absolutely, the government can encourage or discourage certain activities through taxes or subsidies. Liquor, tobacco, and perhaps empty beer bottles suffer levies that not only raise revenues but control behavior. Positive governmental incentives are provided for charities, education, and diggers for oil. Private institutional control mechanisms take on different forms: the free market, the ethics committee of a local hospital, and the approval or censure of one's professional colleagues.

The essential question that must eventually be answered is, which of these techniques, if any, should we rely upon to regulate development or use of which genetic discoveries? We cannot answer that question comprehensively, but we hope to make a beginning. We shall do so by asserting four general, rather controversial, propositions, which should indicate some of the properties of a proper answer.

1. *Neither theories of technology assessment nor public finance theory will provide much help in deciding whether, how much, or how money should be spent on genetic research.* Technology assessment has recently been described as

> a special type of policy assessment. [It] encompasses the first three steps of the policy making process . . .: (1) identifying possible outcomes . . .; (2) estimating the . . . probability of each . . . ; and (3) estimating the utility or disutility of each of the outcomes to the interested parties. . . . It generates data for the decision maker, who carries out the fourth step . . .: (4) weighing the [expected] utilities and disutilities to the interested parties and deciding if the policy alternative [under consideration] is better than other alternatives.[10]

This is, in effect, the public finance approach to research funding decisions. Roughly speaking, it consists of an effort to determine the possible outcomes of each research project, value the outcomes, compare the costs of achieving them, and fund accordingly.

Problems inherent in many applications of public finance theory are unusually severe, however, when applied to the funding of genetic research. For one matter, it will prove extraordinarily difficult to predict outcomes accurately. The number of possible outcomes is enormous and the individual probabilities that genetic re-

search will lead to disastrous or utopian results are small; when small probabilities are at stake, dramatic misestimates are likely. Could one estimate accurately in 1945, or even today, the probability that nuclear research will lead to destruction of the planet?

Even could we predict precisely the effect of research on an individual, we would not be helped much if the whole society is involved on some interactive basis. Thus social harm may result when many individuals each employ a genetic technique that each considers personally beneficial. Each family may want a more intelligent child, but it is not obvious what would happen if everyone's intelligence rose by 25 percent. It is obviously a good idea for some people to adopt children. But what would happen if all families adopted their children? Suppose some people choose to use "artificial reproduction measures." Suppose that all do. A crucial characteristic of these situations is that what one person does affects the welfare of the others. Since individuals' choices in the delicate area of social engineering may not be subject to control, prediction of the social benefit or harm that will result from a genetic innovation is made all the more complicated.

Even if the outcome could be identified, the problem of valuing it would be unusually severe. First, we may encounter something akin to a "change in tastes" problem. We cannot easily measure the future value of genetic engineering by its utility to a future generation if that generation's tastes, or values, are, in significant part, the result of genetic engineering. We may not wish to give up the automobile, but perhaps, were we with our present knowledge Edwardians, we should not choose to invent it. Nor would we choose to take a drug that would make us prefer turnips to steak, though, after taking it, we would not want to reverse the process.

Second, it is not clear to what extent the existing government has a duty or a right to take into account injuries or benefits to future generations, over and above the present desire of the average man to do so. Is there not, for example, a *moral* duty to avoid serious harm to the gene pool—harm that may not reveal itself for say, ten generations? Alternatively, to what extent ought we to risk defective babies now in order to create a better future?

Third, certain potential consequences of genetic engineering are of a sort that cannot be valued within any cost/benefit matrix. For example, does human creativity, our sense of dignity, our response to human suffering depend to some extent upon a feeling

of individual uniqueness? Will such treasured values diminish if men believe they are not random genetically but manifest a consciously determined genetic pattern? Alternatively, does our sense of security derive in part from the fact that loving nurture of parents is coupled ordinarily with genetic identity? To what extent will experiments that require abortion to eliminate mistakes desiccate our belief in the sacredness of human life? Would genetic mass production, even with an extensive product line, do the same? Scientific investigation cannot be expected to yield the answers to these questions. But even if it could, we would have no calculus with which to weigh the outcomes that would be identified.

Fourth, it is difficult to take into account the interests of all whom genetic engineering might affect. Even in the simplest case, where parents retain decision-making authority over the process of birth, it is the unrepresented fetus or infant who bears the major risk of error. On the positive side, if genetic research prevents a deformation, it is hard to value the gains to the beneficiary.

Fifth, if there are to be fruits of genetic research, we must know how they will be distributed. Physical integrity is not a traditional economic good; many citizens would be unhappy if it were to be wholly distributed on a market basis, particularly if the quantities available for purchase were significant. A world in which only the rich could purchase the avoidance of genetic abnormality might be worse than a world in which no one could do so.

We suspect that research funding decisions will be determined in part by differing intuitive reactions to these problems on the part of many different individual decision makers. And we despair of the possibility of developing a comprehensive decision-making framework that (with a few exceptions) could command near unanimity among funders as to which research projects are desirable and which not.

2. *Government prohibition of genetic research is not likely to be practical or desirable.* Genetic engineering will not descend upon us in a rush, but is more likely to insinuate its way into our midst bit by bit. Fundamental life science research has such practical objectives as the diagnosis and cure of inherited diseases, the treatment of infertility, and improved care for prematurely born infants. Even such a frightful-sounding experiment as the fusion

of the cells of a mosquito with those of a human being is more likely to produce a cure for cancer than to create a flying "mosquito man." Many such projects will offer apparently tangible benefits, whereas their possible harms will appear far more speculative. This makes it unlikely that those who would ban or severely restrict such research (even if they comprise the more farseeing among us) could generate the political force, or will, necessary to do so—particularly if such research also holds out long-range promise of, for example, healthier or brighter children. Moreover, such restrictive regulation would not be easy to enforce. Much research is done abroad, and where research is licensed by a government, much is done in secret. The Atomic Energy Commission was able to control atomic research through its monopoly over radioactive material. A monopoly over human eggs would be harder to achieve. At best we could slow the rate of genetic advance; we could not halt the march completely. At the same time, to restrict research severely impinges directly upon other strongly held principles. In science, the relation between experiment and free thought is familial. Although the pursuit of knowledge is not the *summum bonum* but only one good among many, one hesitates to impede it or to set a precedent that might be used to inhibit other socially controversial research. Indeed, the specter of government law enforcers in the research laboratory, university, or hospital is not to be taken lightly. The advocate of strict governmental control carries a heavy burden of persuasion.

3. *Federal agency-type regulation provides at best a very imperfect mechanism for controlling the potential harms inherent in genetic engineering.* To begin, political pressure to allow the use of a genetic discovery that benefits individuals while risking social harm can simply sweep aside agency restrictions, and the agency itself, in its wake. An agency is no more likely to be able to resist the pressure to allow use of an IQ-raising discovery than underdeveloped countries have been able to resist the automobile, despite the fact that the widespread use of either may prove socially harmful. Harms that are relatively easy to control—such as the creation of an army of "clones" or mosquito men—may not be realistic threats. Men have had the ability to change the race through selective breeding for many years and yet have steered clear of this treacherous area without regulatory constraint.

More importantly, the view that an "agency" of wise men or experts can determine what is in the social interest and then enforce its decision is naive. Agencies have proved inept at regulating in areas where values conflict, particularly if they lack precise Congressional instruction. One need only think of the Federal Communications Commission's efforts (or lacks thereof) to control children's television—which may, after all, have a far more pernicious social effect than most foreseeable genetic discoveries. Regulatory agencies also have difficulty in tailoring rules finely to take account of factual differences in roughly similar situations. The Federal Power Commission, for example, has proved unable to set economically proper utility rates. In fact, its well meaning regulatory efforts, when coupled with its need for broad administrable rules, have been in part responsible for an impending serious natural gas shortage. Indeed, we cannot be certain whether Food and Drug Administration rules designed to keep ineffective drugs off the market have on balance helped or hurt the consumer. Agency decisions reflect a host of political, administrative, and legal considerations, including not only the reasoned views of experts but also the interests of agency "clients" and those of its bureaucracy. Agency regulation, of course, may still prove necessary. But if so, some decisions, reflecting the dynamics of small-group decision making, will prove irrational. Some rules will seem insensitive to the need for special-case exceptions, and some actions will reflect an excessive eagerness to carry out the mandate the agency was given.

There is also the concern that the regulatory process might force to the surface certain issues and decisions that are better off submerged. Myths about the ways we conduct our lives can be most comforting. We believe that it is the physician's role to preserve life. Yet we are subliminally aware of situations where doctors have allowed "monster infants" to die. Such a practice is extraordinarily dangerous. It places unwarranted and unwanted ethical and medical responsibility in the hands of the doctor and entails risks of unjustified harm. But how would we want things different? Would we be better off asking a legislature to codify a set of standards to govern such situations? Would the result be more fair or rational? Can we not in some individual cases permit ethical decisions to kill, although we would forbid them were they to become elevated into the general consciousness through formulation of a legal principle?

4. *At present, and in the near future, some aspects of genetic research will call for informal, or decentralized, types of regulation.* Many hospitals, for example, now ask lay panels to review proposals to experiment with human beings. Such panels are sometimes criticized as "rubber stamps," but they can at least bring researchers to reveal the scope, details, and possible outcome of their work. "Sunlight," as Justice Brandeis reminded us, "is said to be the best of disinfectants." The lay committee can also make the researcher and the hospital aware of nonmedical reaction to their work, forcing them to take account of ethical and social considerations they might otherwise miss. And continued national discussion of genetic research—its medical and social aspects—can help to evolve standards which will influence experimenters and inform the judgment of lay committees. Professor Freund suggests that the "voluntary association," not the "criminal sanction," is the proper legal lens for viewing relations among patient, doctor, hospital, and perhaps the community in the experimental environment. When the subject is genetic research, some or all of these parties must consider themselves trustees for future generations as well.

The experience in the related field of heart transplantation is instructive. Dr. Barnard's initial success fostered a rash of operations around the world. Many of these seemed unwarranted in retrospect. Without any global regulatory procedure, a desirable feedback process operated swiftly. Moratoria on heart transplantation were soon imposed in a wide variety of institutions. The transplant procedure was quickly converted into an experimental process conducted only at a few outstanding research facilities. The lesson is straightforward. In the absence of regulation undesirable practices will spring up, but there exist strong natural forces that tend to contain and reverse them.

To point to the existence of alternative regulatory models is not to deny the need for more direct governmental intervention to deal with certain aspects or problems of life science research. Experimentation on human beings, for example, is a topic currently undergoing scrutiny in both the medical and legal communities. Legal safeguards, such as those designed to assure voluntariness, deemed applicable in the general case, will apply to genetic experiments as well.

Moreover, genetic and other life science techniques used must be safe for the patient. While the "safety" problem is one that

arises with most new drugs and new medical techniques, one must be particularly sensitive to the risk of injury to the fetus, who cannot look after himself.

Finally, the government must pay particular attention to how life science techniques, such as amniocentesis and genetic counseling, are distributed in society. One might claim that the distribution problem is no different here than when kidney machines or other life-saving techniques are at issue. But the popular if irrational association of genetics with fears of a "master race" or—to use an overworked word—"genocide" may make the need to distribute the benefits of such research evenly across all of society particularly pressing.

At this time, the outline of genetic engineering problems can be seen only dimly if at all. Proposals to institute formal regulatory procedures in this area, for example, to license or forbid varieties of genetic research, must be viewed with suspicion. On the other hand, it would surely seem appropriate for the federal government to stimulate increased study of, discussion of, and concern about, the problems of social and genetic engineering. But this would seem at present the prudent limit for governmental control.

NOTES

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2. —."Gene implant seen step to cell control." *Washington Post,* March 12, 1971.
3. Watson, J. "Moving toward the clonal man." *Atlantic,* May 1971, p. 53.
4. Grossman, E. "The obsolescent mother." *Atlantic,* May 1971, p. 39.
5. Watson, J. "Potential consequences of experimentation with human eggs." Testimony before the Twelfth Meeting of the Panel on Science and Technology of the House Committee on Science and Astronautics, January 28, 1971; reprinted in 117 *Congressional Record* No. 42, March 24, 1971.
6. Kass, L. The new biology: What price relieving man's estate? *Science 174:* 779, 1971, pp. 786-87.
7. *S. J. Res.* 71, 93rd Congress, 1st Session, 1973.
8. See, e.g., the bibliography and discussion of genetic policy issues in "Genetic engineering, evolution of a technological issue," *Report to the Subcommittee on Science, Research, and Development of the House Committee on Science and Astronautics,* 92nd Congress, 2nd Session, 1972.
9. Senator Kennedy is expected to introduce legislation in this area during this session of Congress.
10. Folk, H. The role of technology assessment in public policy. In Teich, A.H. (Ed.) *Technology and Man's Future.* 1972, pp. 246-47.

COMMENTARY

ROBERT S. KROOTH

Since I agree completely with Professor Breyer's and Professor Zeckhauser's views. I shall devote my comments to reviewing even more reasons why their opinions seem so unassailable, in the hope that I can help persuade anyone who is still on the other side of the question.

Like Professors Breyer and Zeckhauser, I too doubt the feasibility of suppressing research on genetic engineering. I have two reasons. First, as we all know, the scientific method usually involves formulating a theory, and by the use of logic developing predictions from the theory which can be tested. If the results of experiments do not agree with the predictions, the theory is modified or discarded in favor of a new one. New predictions are then developed and tested, and the theory may be revised again—in fact, many times. The process when relentlessly pursued becomes a dialogue between the scientist on the one hand and whatever he is studying on the other. It is this curious sense of conversation that is responsible for much of the excitement of experimental research. All this, I suppose, is obvious. What is a little less obvious is that no parliament can legislate the answers the scientist gets from the thing he is studying simply by legislating the questions the scientist is permitted, or not permitted, to ask. In a court of law, witnesses often give unexpected and apparently irrelevant responses to precisely phrased questions. Alas, so do most of the other elements in our universe. The less we know about what we are interrogating, the less we can predict what it will tell us. A scientist who is supposed to be studying virology may through no fault of his own obtain information bearing on genetic engineering. Then what? Does he destroy the record of the information? Suppose other people saw the data; what happens to them? Suppose the data convey information both on a proscribed subject and on a subject the scientist has been directed to study? Who decides how these factors shall be weighed in determining whether to suppress the information?

A popular European pastime over the last three decades has been sending geneticists to jail. Some members of my profession, who were associated with the Nazi regime in Germany, deserved it. Yet there were others who certainly did not. The job of a scientist of course is to report on the properties of the universe. But, since the scientist did not himself design the universe, he should not be held personally responsible for those properties. It is permissible in my view to proscribe certain experiments, especially if their execution

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endangers the public safety or violates some deeply felt value, such as the rights, welfare, or dignity of those participating as subjects. But I do not think it permissible to proscribe the acquisition of certain classes of information, provided the information is obtained by acceptable methods. Proscriptions of this sort would imply that the scientist knows the results and implications of unperformed experiments (in which case he would hardly perform them—law or no law). Alternatively, it implies that the scientist creates rather than transmits information. The same fallacy would arise if you sued the telephone company because someone conveyed bad news to you by phone. Few things are as overestimated by most educated people as the ability of scientists to control the character of the information revealed by their experiments.

A second reason why I do not think it feasible to suppress by law research which bears on genetic engineering is that increasing numbers of people no longer obey the laws which already exist. It is of course unlawful to rob, murder, or rape. Few proscriptions would appear to be less controversial than these. Yet each year, according to the United States Attorney General, more and more people indulge in the forbidden behavior to the point where the survival of our society is in peril. The failure of citizens to obey the laws makes people not only afraid of the cities and of one another; it also makes them afraid of science and, more generally, of the future. When the law is disregarded, we are at the mercy of events. We no longer believe that our destiny is guided, or even influenced, by the results of deliberation, or by adherence to previously established principles. In this atmosphere, there is an inevitable tendency to look ahead with apprehension and to discourage those who might bring about new occurrences or disclosures.

It is important, however, to distinguish between science—the acquisition of new information—and technology—the deliberate application of the information to human affairs. It is technology, I think, that we all chiefly fear. Few people have much confidence in our ability to control the use of scientific results. I myself have none. It seems to be so difficult to enact wise laws which restrain the technology, and it seems even harder to get the laws obeyed. Enforcement has been a key word. The idea appears to be that people will not obey the law unless they are compelled to. Everyone has to be put in the position where they have more to lose than they have to gain by breaking the law. The implication is that a law in and of itself has almost no force.

Well, as a geneticist, I happen to know of some state laws that are rarely broken, especially when one considers the number of opportunities for violation. One such law says that a man may not marry his mother, or a woman her father. These laws are the expression of some of the visceral beliefs of our culture. Apart from the prescribed penalties, those who break these laws run the risk not only of public condemnation (which is *much* more feared, I think, than condemnation by the courts or a regulatory agency). They also run the risk of self-condemnation. I suspect that laws of this kind are the only ones people can be relied on to obey. Perhaps for these reasons, self-regulation by peer groups, of the sort which Professors Breyer and Zeckhauser have described, may be more effective than even the most intimidating legislation.

So, to summarize my second reason, people who wonder about suppressing certain kinds of scientific research do so, I believe, because they despair of regulating by law the technology that might come from that research. But if we cannot regulate the technology (or anything else) by law, how can we imagine that we shall be able to use the law to regulate research? One day we may be able to control biomedical and other

technologies through the law, but the laws will have to be better than any so far passed or proposed. There will have to be laws like the one forbidding marriage between mother and son.

The Athenian legislator Solon said that if the laws are to be obeyed, "the law-makers must not be too much better than the people." In other words, the law must mirror the culture. Of course, not all of it will, but the rest is cosmetic and no one should really be surprised if that part of the law is frequently ignored. Professors Breyer and Zeckhauser touched on this matter when they wrote, "There is also the concern that the regulatory process might force to the surface certain issues and decisions that are better off submerged. Myths about the ways we conduct our lives can be most comforting." Apparently we are afraid to look in the mirror. In my view (and I suspect in theirs) the purpose of the law is to codify, not to comfort. Comfort should be available from other sources. What all this means in the case of the regulation of technology, especially biotechnology, is that if the laws are to be obeyed, the issues have to be expressed in language which shows their relevance to deep and emotional beliefs of the people. Toward that end, we of course require persons who can make technical questions more easily comprehended by everyone. However, we need something else as well. We need supremely gifted jurists and legislators who can figure out what our culture is.

No member of a crew is praised for the rugged individuality of his rowing.

EMERSON