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THE ECONOMIC IMPLICATIONS OF REGULATION BY EXPERTISE: THE GUIDELINES FOR RECOMBINANT DNA RESEARCH

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THE ECONOMIC IMPLICATIONS OF REGULATION BY EXPERTISE: THE GUIDELINES FOR RECOMBINANT DNA RESEARCH

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The debate over recombinant DNA research raises a number of important issues of public policy. Receiving most attention has been the direct question about the social value of the research, considering its potential benefits and risks. Equally important, but receiving somewhat less attention, are a series of more general issues that, while illustrated by the debate over recombinant DNA research, are likely to recur in other contexts with increasing frequency. First, to what extent can and should society constrain and direct scientific research? Second, in making decisions that require the use of highly technical information that is possessed by a very restricted group, to what extent can society make decisions that are technically informed without in the process delegating the authority to make nontechnical judgments and evaluations to an unrepresentative technical elite?

Although the guidelines issued by the National Institutes of Health (NIH) have been subjected to public review and are being

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supplemented and amended by political jurisdictions ranging from city councils to the U.S. Congress, the essential feature of the approach that has been taken to date to control recombinant DNA research is professional self-regulation. The molecular biologists who do this research have established the grounds for debate. Specifically, most of the discussion has focused on classifying the range of recombinant experiments according to the direct risk they pose to humans and assigning to each class a set of safety rules, ranging from outright bans to good laboratory procedures under normal circumstances. Moreover, for the most part implementation of the guidelines is left to the scientists who are in charge of the research. The NIH guidelines provide no enforcement mechanisms other than the requirement that grants from NIH be given only to institutions that agree to abide by them.

Although government organizations at all levels have attempted to review most of the features of the guidelines, government actions thus far have been primarily to consider enforcement mechanisms that would cause all researchers, including those not supported by NIH, to abide by the guidelines or face stiff penalties. NIH is not a regulatory agency, and has neither the resources nor the mandate to engage in the kind of enforcement activities that are practiced by agencies such as the Food and Drug Administration (FDA) or the Occupational Safety and Health Administration (OSHA). Consequently, the obvious first step for legislative and regulatory authorities is to add teeth to the guidelines. Meanwhile, the underlying conceptual model that molecular biologists initially applied to the problem has

remained largely untouched by the process of public review.

REGULATING TECHNICALLY COMPLEX ACTIVITIES

Recombinant DNA research, like so many problems of technical assessment, is a public policy issue and a candidate for regulation for two reasons. First, the federal government provides most of the financial support for molecular biology. Consequently, the public naturally will ask what it is buying, and whether particular lines of research deserve more or less public financial support. Second, the public must bear most of the risks of experimental accidents. Even if an experiment is not financed from the public treasury, citizens still have a stake in the safety practices surrounding a dangerous experiment, since an accident can lead to significant uncompensated losses to persons who play no part in the decision to undertake the experiment and, therefore, whose welfare may not be fully taken into account by whomever makes that decision.

The Role of the Expert

A necessary input to rational policy decisions about sophisticated new technical developments is an assessment of the procedures and outcomes of the various ways the new technique can be used. Most activities at the frontiers of human knowledge, including recombinant DNA research, are fully understood only by highly trained experts. These experts must be involved in the public decisionmaking process if policy decisions are to be sensible. The problem for public policy makers is to devise a mechanism for gathering the relevant technical

information and checking its authenticity and completeness without at the same time delegating to the experts too many aspects of the decision that do not depend on technical expertise.

The dangers in delegating too much authority to the technical expert are more complex than are generally recognized. In the debate over recombinant DNA research, the delegation problem receiving most attention is the direct stake in terms of financial and professional gains that molecular biologists have in the outcome. Certainly this issue is relevant. The biologists who do this research have years of professional training, substantial financial support, and the prospect of receiving professional awards and prestige hinging on the decision whether DNA recombinant research will be permitted. But this argument can cut both ways. The public's perception of the riskiness of the research, not the actual risk, will determine the amount and nature of research that will be allowed. Because of the technical complexity of the problem of assessing the risks, public decision-makers are likely to be somewhat uncertain about the technical information that is supplied by the experts, even if in reality the information is accurate and complete. If so, a few unnecessary safety precautions that ease public uncertainty may be a small price for the experts to pay in light of the personal gains to be captured by those who engage in the research. Thus, if the research is fundamentally safe but its safety is difficult to prove, the personal stake that scientists have in the issue may well lead to unnecessarily cautious safety standards as an expedient.

Nevertheless, the public uncertainty over risk assessments

by experts is a natural, rational response to the disparities in incentives faced by experts and by the public at large. Experts control the information on which risk assessment is based, and they are likely to be willing to run greater risks than would be acceptable to the public at large. An obvious factor contributing to this difference is the personal stake of the experts in continuing the research that requires their expertise. But there are other factors operating as well.

One of the values of research is the excitement of acquiring new knowledge, regardless of its immediate or prospective usefulness. Whether the specific project is unraveling the genetic code, searching for life on Mars, discovering the essence of physical matter, or comprehending more completely the behavior of complex social systems, the act of expanding the frontiers of human understanding is, to some at least, of considerable interest in its own right. Research is, then, a form of consumer good. Individuals can be expected to differ according to the value they place on increasing human knowledge for its own sake, without considering its practical benefits, just as they differ in their tastes for other purely consumptive activities. Consequently, the costs that people are willing to bear in order to pursue new knowledge will differ from person to person.

People who have chosen to do research on any particular topic are not likely to be representative of society at large in terms of their tastes for that research. First, technical experts understand more of the ramifications of new knowledge, and hence can derive more consumptive value from research than nonexperts. Second,

anyone who pursues a particular line of scholarly research does so in part because it seems especially interesting to that person. Molecular biologists are a self-selected group. Far more people have the ability and motivation to become molecular biologists than actually do so; others become physicists, lawyers, and even economists. These decisions reflect individual tastes for particular kinds of knowledge, and it stands to reason that molecular biologists will find genetic experiments more interesting than will people who do other kinds of research or who have selected careers that do not involve research. Third, biologists engaged in hazardous research are also self-selected in terms of attitudes towards risk. Just as individuals exhibit different tastes for consumptive activities and occupations, so, too, do they differ in the amount and type of risk that they are willing to accept. If a particular line of work, whether using recombinant DNA techniques or lumberjacking, is of greater than average risk, people who enter that line of work are likely to be, on average, either more risk-taking, or more optimistic in their beliefs about aspects of the field that are still incompletely understood, than are people in general.

For the preceding reasons, the public at large is likely to be less than fully reassured if a particular group of technical experts claims that their line of work is sufficiently nonthreatening to society to be worth pursuing. What is safe enough to people in one line of work is unlikely to reflect an evaluation of risks and benefits that is representative of the values of other members of society.

An additional problem of self-regulation arises if more than one area of expertise is relevant to the policy decision. If a particular expert group regulates its own activities, it faces the same problem with respect to other groups of experts that society faces with respect to it. If other groups are consulted, the self-regulated group loses autonomy and authority, but if it decides to handle all aspects of the problem itself, it will be likely to make errors of analysis in reaching its conclusions. From society's point of view, the quality of the ultimate decision regulating the activities of experts will obviously be lower if relevant parts of the analysis underpinning the decision are overlooked or flawed, while informational inequities make it difficult to consult the affected experts without inadvertently delegating authority to them.

The discussion so far has produced several reasons why citizens may want public officials to intervene in the self-regulatory activities of a particular technical elite. These arguments can be generalized to a simple proposition. The social desirability of a public policy decision depends upon both the quality of the technical information on which the decision is based and the extent to which the decision is representative of the tastes and values of the affected individuals. In certain arenas of public policy, one can acquire better and more complete technical information on one aspect of the problem only by sacrificing some of the quality of other types of information and/or the representativeness of the outcome.

Measuring the extent to which a particular decision is unrepresentative of the decision that a society would make if all

members were fully informed is, of course, impossible, since the hypothesized cause of an unrepresentative procedure is the unavailability to all but the expert of the very information that would be necessary to make the measurement. Nevertheless, the logic of the preceding arguments leads to some qualitative predictions that can be tested. First, activities in which experts are already involved are likely to be regulated less tightly than are activities that have been well-defined and considered by the experts and that objectively have equal potential risks and benefits but that have not yet been undertaken. In spite of the fact that precise regulation of ongoing activities is easier to devise because more information is available about it, looser regulations will be applied to areas of ongoing activity, all other things being equal, because experts already will have made personal decisions about and commitments to the ongoing activities. Second, an unrepresentative procedure is prone to overlook entirely or to analyze erroneously issues that call for the use of the tools of another discipline.

AN EVALUATION OF THE GUIDELINES

The NIH guidelines and the justifications accompanying them appear to exhibit these two characteristics of an unrepresentative outcome. The purpose of this section will be to offer some evidence for this proposition.

Inconsistencies in the Guidelines

The validity of the first prediction regarding inconsistencies

in the guidelines that are related to the pattern of ongoing work remains for the molecular biologists to determine, but to an outsider the results are suspicious. The NIH Guidelines contain several examples of either unequal treatment of roughly similar risks, or equal treatment of apparently quite different risks. A few examples illustrate the point.

First, the controls on recombinant experiments involving insect DNA are essentially no more than standard good laboratory procedures, while substantially more stringent controls have been placed on experiments involving DNA from lower vertebrates and higher plants. The rationale for this and other differences in controls according to the species from which DNA is taken is that the less related is the DNA to human genes, the less is the risk to humans. Neither the guidelines nor any biological literature of which we are aware provides support for the proposition that this principle should extend to distinctions between insects and trees. Moreover, risks other than the problem of direct threats to humans should be considered. Humans and other species could be affected indirectly if hybrid cells entered and altered food or disease chains at any point. Thus, the distinction between insect DNA and other species subject to tighter controls seems without any real scientific foundation. What is clear is that Drosophila DNA has been used in some of the pioneering efforts in recombinant research, and that one user of it served on the committee that wrote the first draft of the guidelines.

Second, the literature on the comparative properties of different hosts and vectors for recombinant DNA experiments suggests

that some are more dangerous than others. The text and appendices of the guidelines contain several informative comparative analyses of alternative source-host-vector systems. For example, SV40, a virus that is known to cause cancer in animals, is generally regarded as less safe than polyoma virus; furthermore, B. Subtilis, although less well studied than E. Coli, is regarded as likely to prove safer than the latter; and lambda bacteriophage, although less manipulable by experimenters, is regarded as likely to prove to be safer than the plasmids that are commonly used as vectors. The general principle involved in these safety judgments is that experiments are likely to be safer if none of the elements involved in affecting the DNA recombination have a known niche in man or a closely related species. Nevertheless, in each of the three cases cited above, the controls proposed in the NIH guidelines do not distinguish between the more and less risky alternatives.

The principal basis for the decision to treat these alternatives equally is that more is understood about the genetics of the more risky alternatives, which is a result of the fact that the more risky alternatives have been more extensively used in experiments in molecular biology. Consequently, research on the characteristics of the alternatives would have to proceed for several years before most of the interesting recombinant experiments involving them could be performed. Thus, the decision to have equal treatment of more and less risky alternatives is primarily one of expediency. Of course, the decision has the unfortunate long-term consequency that it provides no incentive for molecular biologists to develop alternative

sources, hosts, and vectors that promise to be safer or to use these alternatives if they are developed.

The value of standards as incentives is illustrated by a recent example. The level of biological containment prescribed for the most dangerous experiments that the guidelines permit could not be achieved at the time the guidelines were originally proposed. Consequently, if some of the most interesting experiments were to be performed, a new host had to be developed that was satisfactory for experimental purposes but weaker than those then in use. Roy Curtis, III and his colleagues at Alabama succeeded in developing a weakened strain of E. Coli literally within months of the development of a demand for it.

The point of the preceding example is that the guidelines should be regarded as more than a set of controls for existing experiments. They also set up incentives that will affect the future course of research in the field. The failure to provide incentives to develop less risky hosts, vectors, and sources of DNA reduces the chance that they will be developed or that they will be extensively used if they are developed. In short, today's guidelines not only affect the safety of current experiments, they indirectly affect the safety that can be achieved in the future. There is no evidence that this particular long-term affect of the system of controls that NIH has proposed was taken into consideration.

The preceding discussion, of course, must be regarded as raising a series of questions, rather than constituting an indictment of the guidelines. Not being molecular biologists, we cannot be

certain of purely technical issues in this highly complex field. With regard to the second prediction -- that important issues not within the range of expertise of the perpetrators of the guidelines would be overlooked or dealt with incorrectly -- the guidelines do exhibit conformance with expectations.

The Technical Orientation of the Guidelines

The major sins of omission of the guidelines have to do with their purely technical character. Essentially, the guidelines define the laboratory practices, physical layout, and biological containment required for the experiments that are permitted. Numerous other issues that bear crucially on the type and amount of research that will be undertaken, and the attendant hazards that society will face, have been largely overlooked in the debate about recombinant DNA research.

One such omission is a comprehensive analysis of problems of human error. The guidelines specify certain training requirements and laboratory practices (e.g., no pipetting by mouth) for laboratory workers in labs in which recombinant DNA research is taking place. As Paul Berg has observed, the regulations regarding physical containment in facilities at containment levels up to and including P-3 are dependent upon the absence of human errors and outright risky shortcuts that are known to take place in laboratories. Consequently, most molecular biologists regard the biological containment regulations as far more important than those regarding physical containment. Even here, however, human error is a distinct possibility, owing to

mistakes such as confusing samples or, in the dark of night when no one else is watching, simply taking a short-cut. Undoubtedly human error can never be eliminated; however, the guidelines do not inventory the range of possible human errors that might be especially dangerous, and in so doing miss whatever potential exists for using the guidelines to avoid or ameliorate them.

The debate over recombinant DNA research has also avoided examining the possibility of using budgetary allocations among types of research as a mechanism to alter the direction and safety of recombinant research. The risk to society from recombinant DNA depends on the nature of the research projects carried out in this field, which in turn depends upon budgetary allocations by NIH and the National Science Foundation (NSF), the agencies that provide most of the financial support for molecular biology. Consequently, one mechanism for altering the societal exposure to risky experiments is to allocate more of the budget for research in molecular biology to other types of genetic research and to the safer varieties of recombinant research. In addition, budgetary allocations could be increased for developing safer host-vector systems. Historically, research scholars have been the dominant force in selecting the lines of research to be pursued and, therefore, the way that NIH and NSF spend their research budgets. As a result, taking a more instrumental view of budgetary allocations represents something of a break with tradition that would weaken the influence of molecular biologists in determining the directions of further research in their field. As the same time, the use of budgetary incentives may be a

more effective mechanism in the long run for reducing the riskiness of research than is direct regulation of the laboratory environment.

Another omission from the discussion about recombinant DNA experiments is a serious, comprehensive treatment of the problems of enforcing the guidelines. The only federal enforcement activities that are contemplated in the guidelines are the threat of the loss of NIH financial support if the guidelines are violated and the creation of an oversight committee to inspect laboratories in which recombinant research is carried out. The committee would include nonbiologists from the local community.

These provisions constitute a very mild enforcement system. The nature of the oversight committee makes suspect its ability to identify violations of the guidelines other than very gross ones. Moreover, the threat that a violation will lead to suspension of all NIH support to a university provides a strong incentive for a basically friendly oversight committee to avoid reporting violations, since members of a university community are unlikely to want to see the university placed in financial jeopardy. And even if a violation is reported, NIH is not likely to carry out the threat to cancel all of its grants to a major research institution without considering the motivation and severity of the violation. Of course this creates opportunities for politically expedient decisions that undermine the guidelines. The source of this problem is that a penalty system that imposes the same punishment, regardless of the offense, does not make much sense. Certainly, a failure to abide by the most stringent containment standards for the most hazardous experiments should be

dealt with more stringently than even a premeditated avoidance of some feature of the standards for an experiment with minimal adverse consequences. Yet any attempt to make decisions depend on severity and motivation converts NIH to a judicial authority without any of the normal legal safeguards of regulatory processes.

Some of the ramifications of the issues not raised by the guidelines or to a significant degree in the debate about recombinant research are, of course, not within the existing ambit of authority of NIH. Without legislative action, NIH could not make a major change in its budget or impose a complex penalty scheme on violators of the guidelines. But it is reasonable to ask NIH and the community of molecular biologists to recognize the importance of dealing with these issues, to address them seriously, and to propose actions that Congress and other governmental units might take. The principal issue in the early interventions by state and local governments, such as California and Cambridge, Massachusetts, has been the problem of enforcement, rather than the adequacy of the guidelines. This is a rational public response to the cursory attention that has been given to enforcement thus far. Whether the guidelines can be effectively enforced at reasonable costs, both in dollars and in loss of freedom of inquiry, remains an open question.

Benefit-Risk Analysis

The primary sin of commission in the debate about recombinant DNA research and the desirability of the guidelines has been the simplistic and largely inappropriate use of benefit-risk analysis

to evaluate the research. In debating the value of their research in terms of benefits and risks, the molecular biologists have overstepped the bounds of their technical expertise, with the result that crucial aspects of a valid benefit-risk analysis are omitted or incorrectly treated in the discussion. The following are but a few examples to illustrate the point.

The principal benefits that are cited in the discussion about the value of recombinant DNA research, in addition to the overall contribution to human knowledge that the research will produce, are several commercial uses of particular kinds of recombinations. Among the specific possibilities mentioned are the production of insulin, hemoglobin and other body chemicals, the development of a cure for viral cancer, and the creation of plants that use atmospheric nitrogen. Among the issues missing from the benefit discussion are: (1) an assessment of the probability that any of these possibilities will be commercially attractive, (2) an estimate of the amount of time it will take for knowledge to be sufficient to make these objectives technically possible, (3) an estimate of the costs of the research that must be done before society will know whether commercial use of DNA recombination is worthwhile, and (4) the design of a comprehensive program of research that would contribute to the achievement of these public health and agricultural objectives. Each of these is essential to calculating the net expected benefits of the program. To apply the benefit-risk model to a line of research requires developing a research program that maximizes the difference between the expected benefits and costs of the activities. Some of

the necessary component parts of the analysis are developing a calculus for comparing costs and benefits that are separated in time (e.g., how are risks and costs borne by the current generation to be compared to benefits and risks experienced several decades in the future?), estimating the probabilities associated with uncertain events so that expected values of their benefits and costs can be calculated, and relating each component of a program to the potential benefits. Nowhere in the discussion of the benefits of recombinant DNA research is there discussion of how current and proposed research projects will contribute to capturing these benefits, and whether the guidelines and the NIH research budget set up the proper incentives for molecular biologists to pursue the lines of research that will make the greatest contributions to achieving these objectives. Nor is any discussion to be found on the relationship of alternative safety standards, including those set by the guidelines, to the cost of acquiring the knowledge that is needed to commercialize DNA recombinations. Nor is there an analysis of how alternative safety standards affect the kinds of benefits that ought to be pursued most vigorously and, consequently, the particular lines of basic research that ought to be emphasized.

Another essential element to a benefit-risk analysis is to explore the alternative uses of the same resources and the alternative means to satisfying the same ends. Presumably a ban on recombinant DNA research would cause molecular biologists who do this work to switch to other kinds of genetic research. While the gross cost of this switch would be the knowledge that can only be attained through

recombinant DNA research, the net cost would be less since, presumably, other lines of genetic research would progress more rapidly. A question that requires answering in a benefit-risk analysis is what benefits from other lines of research by molecular biologists are being sacrificed or delayed by devoting significant resources to recombinant DNA research.

Of course, the potential benefits of recombinant DNA research may also be reachable by other means. A precise statement of the benefits that might accrue from recombinant DNA research is that it may contribute to disease treatment, food production, and several other objectives, just as other lines of research may also make contributions in the same areas. A valid benefit-risk analysis would estimate the extent to which some expenditures on recombinant DNA research would increase the chance that society will capture these benefits for a given total expenditure on all paths to the same ends. For example, is a better way to reduce the death rate from cancer to seek cures for viral cancer through recombinant DNA research, or to expand research on environmental causes of cancer? Or, if in the long run insulin supplies are likely to run short, how should emphasis be divided among recombinant DNA studies, research on other synthetic process, or expansion of supplies from animals?

Related to the question of the selection of a comprehensive research strategy for achieving the objectives mentioned in justifying recombinant DNA research is the question of the best timing for various activities that might contribute to the attainment of these ends. In particular, one alternative to an immediate, up or down

decision on DNA recombination is to delay all or part of it. The discussion about the costs and benefits of further delays in pursuing this research has focused on the costs -- postponing for the period of the delay the date at which the benefits will be reaped and losing national prestige if scientists in other countries produce successful research before Americans do. But the delay in benefits is trivial, indeed, if they are in any case unlikely to accrue for decades. On the other side, delay can be especially valuable if an activity has some chance of causing a catastrophic, irreversible event and if further investigation of methods to reduce the chance and impact of the event is likely to pay off in a relatively short period of time. At least two issues in the debate about recombinant DNA suggest that these conditions do apply in this case. One is the possibility that research that is as informative as the research now under way could be performed in a few years if attention were focused on developing safer sources, vectors, and hosts. The other is the disagreement among molecular biologists as to whether there is a natural barrier to DNA recombinations between prokaryotes and eukaryotes.

In any situation involving risks which have unknown dimensions, one potential benefit of a research project is to acquire more information about risks without actually having to be exposed to all of them. Because technical experts disagree about the potential hazards of recombinant DNA, one criterion for evaluating current research ought to be the extent to which its results will contribute to society's ability to comprehend and minimize the risks of further

research. An unfortunate feature of benefit-risk analysis is that its practitioners tend to think in terms of adopting an optimal long-term solution to the problem of decisionmaking under risk, as if guns were being held to the heads of decisionmakers to make final decisions on the basis of current information. But if some research activities are known to avoid risks that are endemic to other activities but, at the same time, to contribute to the information upon which further risk assessments will be made, it may make sense to pursue the former activities even if their direct contribution to ultimate societal objectives is less than that which the latter activities are likely to make.

Is Benefit-Risk Analysis Appropriate?

Perhaps more fundamental than the preceding issues concerning the requirements of a valid benefit-risk analysis is whether DNA recombinant research ought to be evaluated in this way at all. To approach the problem with this frame of reference is to adopt the view that research is primarily an investment to achieve normal economic ends. If so, the first immediate question is whether government should be involved at all in commercializing molecular biology. If, as seems likely, hybrids created from recombinant DNA research are patentable, is it plausible that drug companies and other private firms lack sufficient incentives to develop hybrids and, therefore, that government must be the principal source of support for this research? Moreover, if these companies do lack sufficient incentives, is it not more appropriate that government should subsidize corporate

research in this area on the grounds that private industry is more likely to pursue cost-minimizing programs that are more closely directed to achieving commercialization than is the scholarly research community?

The principal consequence of selecting research projects on the basis of their returns as investments is that the basis for selecting them must be other than the scientific interests and curiosities of the researcher. A project can be of scientific interest because it requires a display of virtuoso technique, because it resolves a technical dispute that has no practical consequence, or because, after the fact, it turns out to have provided some new insight that was completely unanticipated. In these respects, research is more like a novel or a work of art than like a capital investment, and these features are likely to be ignored if research is to be regarded as another form of investment.

Society may commit public funds for research for numerous reasons: it may value more knowledge for its own sake, it may regard research as a necessary cost of maintaining a system of higher education (without the possibilities for research, could as many good medical schools be operated?), or it may be governed by a winning political coalition that includes the research community, along with the beneficiaries of tax shelters, and that succeeds in redistributing income in favor of itself. Whatever the reason, the resulting structure of research will be quite different if projects are not selected strictly on the basis of their ex ante likely contribution to some particular instrumental end. In particular, the system of

diverse, independent research scholars who individually control their selection of research topics and collectively determine how research dollars shall be spend, which projects are most interesting, and what proposals should be publicly supported, is not consistent with an instrumental, investment-oriented, "Big Science" model of research. Moreover, the relationship between society and research is far different in the two systems. In the science-as-art model, society may retrospectively alter financial support for research on the basis of several performance indicators -- the state of the system of higher education, the amount of interesting new scientific information being reported, and the spin-offs of basic research for practical ends -- but the main issue with regard to the selection of future research projects is whether they conflict seriously with other activities that contribute to society's welfare. This model is very close to the model of personal behavior in a free society; scientists are free to pursue whatever lines of inquiry they find interesting as long as they avoid direct harm to others.

Recombinant DNA research takes on a different light when viewed against the science-as-art template. First, a particular activity that constitutes a relatively tiny part of research in general and that is a source of anxiety for large numbers of people, for whatever reason, is likely to lose public financing. Second, if the risks associated with a particular line of research are real, but nevertheless offset by potential benefits, the mechanism of undertaking the research is likely to be quite different than the customary academic research mode. In particular, government will

seek ways to do as little of the risky research as possible while capturing maximal instrumental benefits, to control research methods very closely, and to become more deeply involved in making ex ante judgments about the instrumental value of research proposals. Third, regardless of one's feelings about the ethical aspects of assigning burdens of proof, if the instrumental benefit of a line of research is not regarded by nonexperts as worth the risks that they perceive, the scientific community will bear the burden of proof in reducing uncertainties about the extent of the risks involved.

CONCLUSIONS: THE FUTURE OF DNA RECOMBINANT RESEARCH

Public policy making on recombinant DNA will be influenced by many factors other than the ones discussed above. Certainly if Congress perceives a significant risk in recombinant DNA, it will move to adopt more stringent controls than are likely to arise from a self-regulatory process administered by an agency with no enforcement authority. But other realities will also influence the outcome. Perhaps the most important is that not all of the research -- or even most of it -- is likely to take place in American nonprofit research institutions. This means that regulations based upon the role of the federal government as the principal source of research funds for the nonprofit sector may deal with only the tip of the iceberg, particularly on a global scale.

Institutions are already in place that deal with the kinds of hazards associated with recombinant DNA research. For example, OSHA and the Environmental Protection Agency (EPA) can enter the arena

without further legislative mandate, and almost surely will if they perceive recombinant DNA research to be risky and, in particular, if private industry begins to pursue this research with vigor. Moreover, if private industry is subjected to significant regulation in this area, universities will not be far behind. It did not take long for OSHA and the Equal Employment Opportunities Commission to include universities within the ambit of the regulatory policies that they pursue.

The first choice facing the government is whether to support recombinant DNA research. Although public officials may believe that society would be better off if the research did not take place, they really cannot accomplish this objective on a world-wide scale. Consequently, the decision about financing must be partly strategic -- how can the federal government provide financial support in such a way that the resulting research is least threatening? Several considerations come to mind in this regard. One, as discussed in this paper, is to support research on the development of containment systems and source-host-vector combinations that are safer than those that are currently available. Another is to be far more generous in supporting the less risky lines of recombinant DNA and other research in molecular biology research than in supporting more risky projects. Still another is to attract as much of the research and commercial development into the public sector as possible by being perhaps unnecessarily lavish in providing funds to create the optimal research environment for essentially any legitimate molecular biologist. This would maximize the extent to which knowledge about molecular biology is in the public domain, and therefore minimize private incentives

to do the work by reducing the likelihood that private research would produce proprietary information. It would also give the government greater control in directing the lines of genetic research that are pursued.

A second area of decisionmaking involves the selection of a system of controls on recombinant DNA research. An immediate step is to establish regulations regarding commercial uses of recombinant DNA before the first commercial use emerges. The nature of these regulations will affect the incentives private industry has to pursue this research; obviously a ban on commercialization backed up by criminal penalties represents an extreme action that would immediately stop most private research in the field. Alternatives include licensing and inspection procedures through an agency such as FDA, EPA, or OSHA. Serious examination of the problems of preventing severe accidents with commercial quantities of recombinant DNA hybrids will contribute to more than the development of a regulatory policy that is probably inevitable. It will also shed additional light on the nature of the risks of this research in general and upon the likelihood that extensive commercialization is a real possibility.

With regard to scholarly research, Robert Sinsheimer's proposal to limit federally supported research to government-owned facilities deserves serious consideration. First, a few large government facilities are much easier to control than a diffuse system of small laboratories with differing designs and procedures. Second, such a system relieves universities of bearing most of the risks of the actions of their molecular biologists. Third, in

government facilities it will be easier to develop a coherent system of monitoring the performance of containment systems for the purpose of reevaluating risks and altering standards and procedures. Fourth, because government regulation must be accompanied by complex administrative procedures to satisfy Constitutional protections of due process, regulatory rules and standards are difficult to change. Government laboratories need not be subjected to these formalities and, consequently, can change safety procedures quickly in response to new information and contingencies.

In order to make rational decisions on recombinant DNA, policy makers will need expert analysis and advice. To avoid some of the problems of inadvertant delegation of control to the experts, policy makers should consider assembling a panel of near experts whose training will enable them to comprehend the technical issues but whose professional pursuits do not involve recombinant DNA methods, and who thus suggest by self-selection that they are, on average, more representative in their tastes and risk assessments regarding recombinant DNA research than are the experts. The job of this group would be to translate and evaluate the technical case of the experts, and to raise further questions that may have been overlooked in the debate.

In sum, federal policy should be based upon the notion that a well-designed program can redirect the focus of research in ways that reduce societal risks. At the same time, the federal government should probably abandon at least for the present, establishing policy towards recombinant DNA on the basis of future commercial spinoffs.

Instead, for a while the focus should remain on guaranteeing that as much of the research as possible will take place in carefully controlled environments and will contribute both to advancing basic knowledge about genetics and to reducing the uncertainties and risks surrounding research in this area.

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