Controlling the risk in biotech.

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Controlling Risk in Biotech As more and more engineered organisms move from the lab to the environment, we cannot afford to be complacent about the risk. Better regulations are essential.

BIOTECHNOLOGY entrepreneurs envision a future where genetically altered bacteria digest oil spills and toxic waste, kill crop pests, and immunize wild animals against rabies. These organisms, say the biotechnologists, pose no unique hazards to health or the environment; they are as safe as their component parts--a natural bacterium and a gene taken from another organism.

This optimism brings to mind the early days of the synthetic-chemical industry. Like biotechnologists, chemical pioneers of the 1940s and 1950s saw great promise in new products that would be released into the environment. But government regulation of these chemicals was based on public health statutes that dated from the turn of the century. These statutes were not suited to deal with the thousands of synthetic chemicals introduced into agriculture and manufacturing. They did not address complex biological effects such as cancer and various chronic illnesses.

Finally, in the 1970s, the government enacted a series of new laws, including the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Toxic Substances Control Act (TSCA). Some laws required safety testing for all new chemicals, but exempted the tens of thousands of untested substances already on the market. Now, a generation after the chemical revolution, the country has to contend with 60 million tons of hazardous chemical wastes produced each year.

Could the biotech revolution prove equally destructive? If ecologists are right, our picture of the risks involved is no more complete than that of chemical risks 30 years ago. They assert that no one can predict the environmental effects of genetically engineered organisms, or GEOs, merely by knowing the host organism and the foreign genes. Before a new organism can be safely released, they say, it must be tested in a microcosm, and the dynamics of the ecosystem for which it is targeted must be carefully modeled. And while the probability of harm is small, the magnitude of any damage could be great. Introductions of GEOs might create new human diseases, spawn new plant or animal pests, or otherwise disrupt delicate ecological balances, just as introductions of exotic species--such as the gypsy moth and the citrus canker--have done in the past.

The risks of releasing new organisms will multiply as the biotech industry grows. Today only a handful of releases, sanctioned or unsanctioned, take place each year. But over the next three to five years, the Department of Agriculture (USDA) expects to receive over 200 applications for release of GEOs, including plants and animals. And the number of releases will skyrocket as small-scale field tests give way to commercial-scale manufacture and dispersion. As ecologist Martin Alexander has cautioned, if an undesirable event has a probability of occurring once in 1,000 uses of a given technology, the risk from a few uses would surely be low. Complacency should disappear, however, if 600 or 1,000 or more uses are envisioned.

As we stand at the threshold of a burgeoning biotechnology industry, it would seem prudent to take the ecologists' concerns seriously. Yet the U.S. regulatory system governing the release of GEOs is anything but prudent. It is modeled after the same controls that apply to the chemical industry--just as the first chemical regulations were based on earlier statutes. It does not take into account the unique properties of microorganisms, such as their ability to reproduce and mutate. It spreads oversight too thin and requires too little scientific review of proposed releases. It does not provide adequate safeguards against accidents. And it ignores important social and economic questions raised by environmental releases.

To prevent biotechnology from going down the same dangerous path as the chemical industry, we need a set of coherent, forward-looking regulations. Among other things, that will mean creating a single lead agency and making sure it has the technical and financial resources to do its job.

A Patchwork of Policies The current federal system for regulating environmental release is a loose patchwork of policies spread over five different agencies and at least ten different laws. The Food and Drug Administration regulates organisms intended for use in drugs, food additives, and medical devices. The National Institutes of Health (NIH) regulates the use of recombinant-DNA molecules developed with its funding. Workplace hazards connected with genetically engineered organisms come under the purview of the Occupational Safety and Health Administration. Veterinary products and organisms that could harm plants are governed by the USDA. Meanwhile, the Environmental Protection Agency (EPA) covers

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pesticides and new microbes not falling into other categories.

An interagency Biotechnology Science Coordinating Committee is supposed to tie the various threads of policy together, but so far it has been largely ineffective. With authority for regulating GEOs distributed among various agencies and covered by widely disparate laws, agencies use different definitions and risk assessment criteria, and confusion can arise over who regulates what product.

All the statutes under which new organisms have been lumped predate genetic engineering. For example, EPA regulates releases through FIFRA and TSCA. Both laws, particularly the latter, were intended for chemical substances, not self-replicating organisms. The laws neither address the special environmental and public health risks raised by the new industrial and agricultural uses for GEOs nor establish a program for better identifying those risks.

Some of the most glaring weaknesses of current regulation stem from TSCA. Unlike FIFRA, which requires that a firm obtain a license to manufacture a substance, TSCA is a notification statute. All a company has to do is inform EPA that it plans to manufacture a certain chemical or biological. Since the manufacturer does not even have to provide data attesting to the safety of its products, a notification system places the burden of proof on the regulator.

EPA has 90 days to review a TSCA submission. If it determines that a substance might pose an unacceptable risk, the agency may issue a set of rules applying only to that product. This rulemaking process is cumbersome and laborious, and it injects considerable discretion into regulatory decisions.

As more and more companies notify EPA that they intend to release organisms, the system will undoubtedly break down. The overburdened agency will be forced to use a "triage" system to determine which organisms deserve more careful scrutiny, and will be unable to review them on a case-by-case basis when the pace of submissions reaches 30 or 50 a year.

The role of the USDA presents another serious problem. No agency that is supposed to promote biotechnology in industry, commerce, and agriculture should be responsible for regulating its use in those sectors. Yet this is exactly the position that the USDA is in. The agency also lacks a coherent policy on engineered plants and organisms. And it has a poor record of encouraging citizens to participate in its decision making on biotechnology and of informing the scientific community how it plans to evaluate new products.

Bringing in Outside Experts The jerrybuilt framework that relies on FIFRA and TSCA does not take into account the complexity of weighing the risks of biological organisms designed for use in the environment. Scientists have yet to develop standard tests for genetically novel strains, like those used to determine whether a new chemical will cause mutations. And designing and implementing microcosm or field experiments can take years. As long as scientific uncertainty remains high, the experts within environmental agencies must be aided by a broad network of scientists in related disciplines.

Many scientists participated in debates over the first few GEO releases, either because of media attention or because a regulatory agency or a court of law had solicited their expertise. But as the review process becomes more routine, outside scientists will have less incentive to get involved.

Because scientists do not benefit professionally from troubleshooting new products, it is in the public interest for the government to provide financial incentives to attract outside reviewers. Unfortunately, while annual investment in U.S. biotechnology innovation from private, state, and federal sources totals nearly $5 billion, investment in expanding our knowledge of how these innovations affect the environment and public health is barely one thousandth of that figure.

In the future, the science of predictive ecology may advance far enough to make standard tests for GEOs possible. At that point, the need for broad review may diminish. For now, however, the more diverse the thinking about possible harm, the better our chances of identifying and avoiding it.

Unsanctioned Releases Even if the regulatory system were to do an adequate job of determining the safety of GEOs, its efforts would be meaningless without some guarantee that only safe organisms would reach the environment. Unsanctioned releases have already taken place in Montana, Nebraska, South Dakota, Texas, and California.

In addition, whole classes of release experiments are regulated inadequately or not at all. These include experiments in the private sector, university research, and large-scale fermentation. Some of these settings are inherently unsafe. In August 1987, for example, a biochemist working in his beachfront home in Kingston, Mass., was recombining the genes of sea organisms to create a new type of building material, when his house collapsed. Microorganisms, which the scientist maintained

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were not dangerous, escaped from his home. The investigator violated no law; private funds were involved, so he was not obligated to follow any guidelines. Since a harmful microbe can multiply and spread regardless of the type or size of organization conducting the test--or the source of funding--exemptions from the regulatory process make little sense.

It is not only in unregulated settings that accidents can occur. As the production of genetically altered organisms increases, so does the likelihood of unintentional releases. These can happen at any stage in an organism's lifecycle--from the laboratory to the production/fermentation facility, greenhouse, field test, and waste stream. Because many GEOs are designed to survive inside humans, laboratory workers can unwittingly serve as pathways for releasing the organisms and can themselves face potential health risks.

As for the possibility of a modified organism finding an environmental niche after "escaping" during a field test, again, the chances are slim--but any regulatory structure must be designed to handle a vastly greater quantity and diversity of such tests in the near future. When asked about the dangers of field tests, David Baltimore, head of the Whitehead Institute for Biomedical Research, has replied, "Would corn planted at the edge of the forest take over the forest?" Yet occasionally, introduced natural organisms do just that, causing widespread damage. Kudzu, for example, was imported to the Southwest for forage and erosion control, but has since become a major weed problem in forests and roadways.

If an organism did escape, the current regulatory regime would be unprepared to deal with the ecological upset that might ensue. No plans have been developed for containing damage. Nor are any serious research programs under way in this area.

While the regulation of GEOs during research and testing is merely inadequate, the regulatory framework for dealing with biogenetic waste is virtually nonexistent. The biotechnology industry brings with it a new form of waste that can live and multiply in the environment. Because it consists of living organisms, biological waste has the potential to spread disease. It could also transfer genetic material to organisms of different species, genera, and even families, fostering the creation of new pathogenic strains or compromising the ability of humans, animals, or ecosystems to protect themselves. The rapid spread of antibiotic resistance among bacteria in clinical settings is an obvious example of the ease with which certain kinds of genetic exchange take place.

However, the only regulations for treating biogenetic waste are NIH guidelines, which have no legal authority over industry, and FDA rules for sterilizing bioreactors. Most industrial fermentation plants may simply dispose of spent GEOs along with other untreated effluent.

A Socioeconomic Vacuum Just as important as an organism's environmental impact are its social and economic consequences. During the Reagan era, the administration directed regulators to consider the adverse economic effects that new regulations might have on business. Yet the government has always been reluctant to take this one step farther and consider the economic effects of actions proposed by industry. A product that will create inequities within the industrial community or that threatens social transformation leaves the regulators silent for lack of authority.

The assessment of biotechnology needs to be expanded beyond the narrow criteria adopted by the Reagan administration. An independent body should analyze the social, ecological, and economic impacts on all sectors, including small farmers, consumers, and the natural environment.

"Ice minus," the controversial organism developed by Advanced Genetic Systems in Oakland, Calif., sparked opposition from farmers in Tulelake, Calif., where it was slated for field testing. In addition to their concerns about possible environmental harm, the Tulelake farmers believed that the organism, designed to replace natural bacteria that raise the temperature at which frost forms on plants, might increase the land devoted to potato farming. The result, they feared, would be increased competition in what was already a low-profit-margin enterprise. Yet farmers' economic interests were largely ignored in the debate over safety, even though they could easily have been included and weighed against the new product's purported benefits.

Or consider the case of bovine growth hormone, which can now be produced using genetically engineered organisms. When injected into cattle, the hormone can increase milk production by up to 30 percent. But what economic impact will the hormone have at a time when milk surpluses are at record highs? The regulatory framework does not take such socioeconomic effects into account.

When an industry designs a new product for release into an environment where it will pose discernible risks, we must ask: What do we gain? What could we lose? What are we displacing? Does the new product fill real social needs? We cannot rely on industry to answer these questions for us. Advanced Genetic Sciences, for example, promoted ice minus as a substitute for chemical pesticides, even though pesticides have never been the

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method of choice for preventing frost damage. Meanwhile, other agrochemical and biotechnology companies are genetically engineering crops resistant to harmful side effects of pesticides--a practice that will expand and prolong the chemicals' use. Pesticides are the most profitable products of some of these corporations. Yet biotechnology could also be used to develop non-pesticide alternatives that would lessen farmers' dependence on a few big agrichemical companies.

With a powerful emerging technology, especially one with potential risks and large amounts of public funding, we cannot assume that the market will operate in the interest of the public without social guidance. The public sector should actively shape public policy, not allow it to be created by default. If weaning agriculture from chemical pesticides is a desirable goal, then public policies should help realize it.

In deciding what degree of risk is acceptable, regulators must begin to weigh the interests of industry against those of society at large. If the overall social and economic effects of a product are negative, any environmental risk that accompanies its testing or use should be deemed unacceptable. At present, no regulatory mechanisms exist for making such judgments or for answering communities' questions about social and economic impacts.

Toward a Sound Regulatory Process The present ambiguous and conflicting state of regulation satisfies no one. It creates confusion in the biotechnology industry, it does not adequately safeguard public health and the environment, and it largely excludes the public from the decision making. To deal with the coming wave of genetically engineered organisms, the system needs a top-to-bottom overhaul. The following proposals would help create a rational regulatory process:

Make EPA the lead agency. Designating one agency to oversee all environmental releases of genetically engineered organisms would help ensure careful review of the risks before a release was authorized. EPA should also be given greater authority over all large-scale uses of GEOs and empowered to regulate and inspect facilities to reduce the danger of accidental releases.

Amend TSCA. As applied to new organisms, the Toxic Substances Control Act is clearly inadequate. Instead of merely notifying EPA of a planned release, companies should be required to obtain licenses. As a prerequisite, the manufacturers--not EPA--should have to demonstrate an organism's safety and efficacy, as well as show that they are prepared to stem the worst impacts of a release. When a new technology is replacing an established one, the law should require end users to choose the least risky available technology to do a job. EPA should also have the latitude to request further information and testing on comparative risks.

Regulators also need to be able to penalize wrongdoers quickly and effectively--and the penalties should be high enough to discourage even small unauthorized releases. EPA should have the power to assess fines for violations without taking companies to court. This would shift the burden of bringing suit onto violators.

Give regulators more resources. The expansion of industry's genetic experimentation will place tremendous economic pressure on regulators to act quickly and without due care. With more funding, regulators would be able to provide better oversight within a timeframe that industry could live with. They would also be able to hire the necessary range of professionals--including soil ecologists and microbiologists--and keep them up to date on the latest developments in the field and techniques for evaluating them. Funding will need to grow with the industry, and could come in part from a tax on marketed products.

Set up advisory boards. Outside advisory boards could bring a fresh perspective to difficult technical, social, and economic problems in issuing permits. To prevent conflicts of interest, appointees to such boards would have to disclose any affiliations with, or equity interest in, biotech firms.

Encourage independent review. Funding must be available to bring the expertise of independent ecologists to bear on assessing the risks of new products. Publishing the name of an organism in the Federal Register and expecting scientists to divert themselves from busy schedules to examine the ecological consequences of a large-scale release is unrealistic. The government should contract out the review of new products to scientists in different disciplines, and the details of proposed field tests should be published in a variety of professional journals.

Involve the public. A public voice in the regulatory process is vital, since the experts' assessment of "acceptable" risks may differ dramatically from the views of the public that bears those risks. Such involvement can also benefit industry. For one thing, communities may be able to contribute useful information in the deliberations. For another, communities left out of the process are likely to oppose, and even obstruct, local releases.

Good precedents for involving local residents exist under other laws. The 1986 Superfund Amendments, for example, established the community's right to know the type and amount of toxic chemicals released into the

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environment by industry. This right could be extended to the storage and release of genetically engineered organisms. Communities should be informed about the potential risks of any release, as well as plans for monitoring the organism and stemming any damage it might cause.

Of course, the right to know should not infringe on manufacturers' legitimate trade secrets. But to prevent spurious claims, the burden of proof for trade secrecy must be on industry.

Public involvement need not be merely reactive. In Cambridge, Mass., for example, a citizens' review board played a constructive role in developing the city's regulations for recombinant-DNA experiments during the 1970s. Any EPA advisory boards should include representatives from public-interest and community groups.

Strengthen risk assessment. For every proposed release, the manufacturer should prepare an environmental impact statement before EPA issues a permit. Such studies should analyze worst-case scenarios and specify the assumptions used in developing them.

Monitor released organisms. EPA should carefully monitor the survival rate and dispersion of modified organisms in the environment. This monitoring would be both a precaution, in case the organism did harm, and a research tool to strengthen future risk assessments.

Increase safeguards. Because even a small release of a harmful organism could be devastating, regulators and biotech firms must do their utmost to prevent GEOs from escaping accidentally. Waste streams should be carefully regulated and monitored, and labs required to have barriers such as secondary containment chambers. Measures such as protective clothing and standardized lab practices can help prevent workers from unknowingly carrying GEOs out of their laboratories.

Expand the role of liability and insurance. To help protect public health and the environment, strict liability should apply to releases of genetically engineered organisms. In the case of hazardous chemicals, the Superfund law requires that plaintiffs show cause and effect between release and injury but does not require that they prove negligence. A similar provision for modified organisms would offer stronger public protection and force manufacturers to consider any release more carefully.

Companies that release genetically engineered organisms should have to carry enough insurance to cover any claims. This would give the insurance industry an incentive to help develop techniques for evaluating the risk of releasing new organisms.

Pursue international coordination. Environmental safety is a global, not a domestic, concern, since an accidental release of GEOs could harm food crops or human health worldwide. Whether through international scientific meetings and exchanges or through more formal international channels, issues concerning environmental releases must be addressed globally.

For example, the United States should prohibit multinational corporations based in this country from conducting field tests or other procedures abroad that have been prohibited at home. And scientific data about environmental safety must be widely shared to deter nations (especially in the Third World) from allowing ill-tested procedures within their borders for the sake of short-term economic gain.

If we fail to move on these fronts, or if we move too slowly, there is every danger that the painful history of the synthetic-chemical industry will repeat itself in the realm of biotechnology. The public became aware of chemical hazards--and the government responded to them--only after substantial damage to health and the environment had occurred. Regulators tried frantically to catch up after decades of neglect. But the nation's economy was already dependent on the firmly established industry.

It is too late to undo all the damage done by synthetic chemicals. But if we can introduce some foresight into the regulatory system, it is not too late to avert disasters from genetic engineering.