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Risk Assessment of Genetically Engineered Microorganisms: From Genetic Reductionism to Ecological Modeling

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1. Introduction

Rapid developments in agricultural biotechnology in the 1980s have given rise to the first field tests of genetically modified plants and microorganisms. Public concerns over the unintended effects of releasing genetically engineered organisms (GEOs) have highlighted the importance of ecological risk assessment as a means of anticipating and managing possible untoward consequences.

Two modes of thinking have framed the discussion of risks associated with the release of GEOs into the environment. The genetic reductionist framework places greatest weight on understanding the foreign genes and the phenotypic characteristics of the host organism. The ecological framework is site specific and requires field testing of the GEO under the conditions of application. The former assumes a predictive theory between the genetic sphere and the ecological sphere, while the latter offers little credence to predictive risk assessment of GEOs and must accept the dismal conclusion that every ecological assessment experiment places the environment at risk.

The use of microcosms to test GEOs prior to release has been proposed as a bridge between the extreme positions of the genetic reductionists who defer to genetic knowledge for insuring the safety of released organisms and advocates of a radical empiricism who argue that risk analysis begins and ends in the field. An intermediate step of *microcosm analysis* has been proposed that could provide reliable and useful information about the survival, competitiveness and dispersal of genetically modified microorganisms released in the soil. This chapter examines the possibilities and limitations of microcosms, tradeoffs in microcosm structure between modeling actual conditions and gaining replicable and dependable results, and the problems of standardization.

2. Prospective versus Explanatory Risk Assessment

Two kinds of risk assessment can be distinguished which we can call retrospective and prospective. In retrospective risk assessment, an adverse event takes place and the role of the risk assessor is to ascertain what the cause was. Typically, industrial accidents are followed by investigations into the cause or causes of the event. Deciphering the cause of an accident like the chemical release in Bhopal, India is not an end in itself (with the exception of tort litigation). Rather the knowledge gained

is expected to make the technological system safer. The term "fault tree" analysis applied to technological risks describes a method of identifying all possible events leading to the hazard event. Fault tree analysis can be used to estimate the probabilities or explain the cause of an outcome (Krimsky and Golding 1991: 100). Retrospective risk assessment is about the past but is almost always directed toward the future.

Prospective risk assessment exclusively seeks to predict possible hazardous outcomes before they occur. Three major streams of prospective risk assessment are natural hazards research, studies of nuclear power plant safety, and chemical toxicology. The term "event tree" analysis describes a method used to estimate the probability of systems failure. In toxicology, the goal is to predict the health effects on humans, animals or plants of the consumption of or exposure to chemical agents. The fundamental problem of prospective risk assessment is the problem of induction, namely, how can we predict the future from our knowledge of the past. The prediction of natural hazards from actuarial data is a form of atheoretical inductivism where future probabilities are inferred strictly from past frequencies. Whereas the development of predictive risk assessment for technological systems and toxicological effects of chemicals on humans employs a combination of theory and empirical information (Krimsky and Golding 1992: 3-22).

Prospective risk assessment is induction with high stakes. The wrong estimate could mean thousands of birth defects, as in the use of thalidomide, to unacceptable deaths, such as those resulting from swine flu vaccine, or transplacental carcinogenesis that accompanied the administration of diethylstilbestrol (DES) to tens of thousands of pregnant women. Each system of prospective risk assessment is layered with methodological obstacles. Predicting birth defects, cancer risks or drug side effects usually involves one or more of the following methods: animal to human extrapolation; inferences from a small sample of humans to a large population; inferences from *in vitro* to *in vivo* conditions; extrapolating the effects of using large doses of a substance over a short period of time on a small number of animals to estimate the effects of small doses on large numbers of people over a long period of time. Despite fifty years of toxicological studies and assay development, the uncertainties of predicting human effects of drugs and chemicals on the basis of animal studies have not been solved. On the contrary, recent experiments have raised new questions about the use of toxicological testing methods on animals or cells to predict health effects on humans (Ames and Gold 1990).

3. Ecological Risk and Bioengineered Organisms

Since the early 1980s, the role of risk assessment for predicting changes in ecological systems began receiving special attention as the prospect of releasing genetically engineered organisms (plants, animals and microorganisms) into the environment seemed close at hand (Gillett 1986). The ecologists and molecular geneticists had, by and large, viewed the problem of predicting adverse outcomes of environmental releases from quite different perspectives. I have argued elsewhere that molecular biologists, by discipline, seemed more confident in the predictability of genotype to

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phenotype than ecologists and evolutionary biologists (Krimsky 1991).[1] Those trained in ecology and field studies generally believed that predicting the fate of GEOs on the basis of genetic information and *in vitro* experiments was based on false confidence, perhaps even a myth about the predictive power of genetic knowledge.

Predictive knowledge of GEOs became a central part of the debate over environmental release. The policy issues of immediate concern began to draw attention to the conflicting viewpoints of scientists schooled in different disciplines. First, there were disagreements over the need for risk assessment for GEOs. Since we create all sorts of hybrid plants in which unknown numbers of genes are exchanged across species and taxa, why all the tumult when we transfer a single known genetic locus.

Second, there are disagreements over the relevance and significance of historical ecological data for predicting the fate of GEOs. For example, some biologists were predisposed to use the accumulated knowledge of exotic introductions as a baseline for understanding what could happen when GEOs were introduced. Others argued that exotic introductions cannot inform the risk of GEOs since the latter are most frequently indigenous plants that have been modified in some small way, by virtue of the genome changes. Exotics, on the other hand, are significantly alien to the environment in which they have been released and so may face no counterbalancing or stabilizing mechanisms against untoward growth, competition or dispersal. Often cited examples of exotic introductions that have resulted in severe damage are the grasses of Eurasian origin introduced into the American west and kudzu introduced into the Southeastern United States.

A third area of disagreement centered on the dialectics of quantity and quality. According to one view, minor adjustments of the genome of plants and microorganisms are not likely to produce major ecological shifts between the organism and its environment. Writing in *Science*, Winston Brill, comparing microbes to chemicals argued that small changes to the latter may result in unexpected toxicological properties whereas, "by comparison, minor modifications obtained by breeding safe plants or mutating safe microbes do not yield progeny that become serious problems"[2] (Brill 1985a: 383). With respect to the ice minus example, one scientist compared the organism to a set of piano keys. Imagine one key removed. The piano will not sound like another instrument; it will simply be unable to play certain tunes well. The piano analogy breaks down when we consider that a key removed offers nothing positive to the player or composer while ice minus was expected to offer a practical benefit to farmers and its purpose included its ability to survive and function in the environment.

The notion that significant phenotypic changes would not result from single gene or several gene changes is not persuasive to some biologists who draw their examples from our knowledge of the natural history of microorganisms. Harvard biologist Fakhri Bazzaz counts himself among those who do not accept the view that the quantity of change is related to the quality of change: "It is conceivable that a small change in genetics will actually lead to a fairly large change in the behaviour, the ecological behaviour, of an organism, and in some cases that could have a detrimental effect on the ecosystems into which these organisms are introduced" (Bazzaz 1985: 55).

A fourth area of disagreement concerns the possible outcomes of transferring a foreign gene to an organism or moving a gene to a new locus in the same organism. The extreme reductionist argues that the gene would either do what it was designed to do or do nothing at all. Others cite pleiotropy as a realistic possibility, namely that single gene products can affect more than one trait, or epistasis, the capacity of one gene to modify the expression of another gene that is not an allele of the first. Looming behind these debates is the historical issue of emergence versus determinism and the conflict between mechanistic and interactionist paradigms of genetics (Lewontin et al. 1984). These alternative viewpoints about the role of genes is reflected in the uncertainties over risk assessment.

Each of the three categories of GEOs, namely, plants, animals, and microorganisms, offer some unique challenges for risk assessment. Of the three, however, microorganisms are least likely to be recalled or destroyed once released. For this reason, they are perceived by some to represent a heightened area of concern for intentional release.

4. Applications of Bioengineered Microorganisms

The most promising areas of application of genetically engineered microorganisms (GEMs) in the environment include: the use of genetically engineered microbes in mining or crude oil recovery operations; bioremediation of toxic materials in contaminated soils such as dioxin or PCBs; bacterial or viral insecticides; nitrogen fixing bacteria; the release of microorganisms as biosensors; and bacteria designed to reduce frost damage.

Given this broad range of application, is there a way to minimize the ecological risks of certain releases? Is there useful information that can be gained about risks prior to releasing organisms in the field? Will this information be of such a nature as to preclude catastrophic releases? Will it prevent or reduce releases of GEMs that may be ecologically harmful and costly but not catastrophic? Microbial ecologists have suggested that microcosm and greenhouse tests can serve this function as a means of screening out hazardous products.

How realistic is this process? These recommendations were advanced during the period "ice minus", a frost inhibiting microorganism, was approved for field testing. Since there is little chance that a released genetically modified microorganism can be recalled or destroyed once it enters the environment, the function of the greenhouse or microcosm test is to identify a potentially hazardous GEM that is not likely to show up in an analysis based exclusively on the foreign DNA, the host organism, and the history of its use.

There are plenty of skeptics around who argue that such laboratory or quasi-laboratory experiments cannot guarantee safety. An organism might pass the microcosm test while still exhibiting adverse effects. Since that is true of any screening assay or risk assessment, should the likelihood of false negatives serve as a reason to prohibit all releases of GEMs? This question is answered differently by different stakeholders. Hard line environmentalists who oppose the release of any GEOs argue that (1) there is a real possibility of a catastrophic effect and (2) the

potential benefits of the organism cannot justify those risks however remote. Similar arguments were used during the early developments of recombinant DNA research to effect a permanent moratorium on genetic engineering.

There may in fact be circumstances in which the risk of a catastrophic consequence from a released transgenic organism is more than idle speculation. Were that to be the case, then any risk assessment is a devil's gamble. A reasonable "precautionary principle" that avoids high consequence events even at low probability when there is no social imperative, is a prudent course of action. While ecologists and environmentalists considered the possibility of adverse outcomes, few, if any, mainstream scientists elevated those potentially adverse outcomes to the level of catastrophic consequences.

The first field test of a genetically engineered microorganism in the United States involved a strain of *Pseudomonas syringae* called ice minus because it was associated with protecting crops from ice damage from subfreezing temperatures. It took five years of regulatory and legal maneuvers before the tests were carried out in California (Krimsky and Plough 1988). The most extreme risk scenario raised about the test postulated that the ice minus bacteria might be wafted to the atmosphere in sufficient quantity to affect weather patterns, e.g., ice crystallization in the atmosphere. The U.S. Environmental Protection Agency (EPA) solicited consultation from atmospheric scientists who, based on theoretical calculations, dismissed the concern that field tests could induce an atmospheric perturbation. This left open the question of massive spraying of ice minus on thousands or tens of thousands of acres. In anticipation of large scale testing, the EPA collected data on the upward flux of bacteria sprayed on a field.

Radical shifts in weather patterns from anthropogenic causes could certainly be considered catastrophic. Nevertheless, global warming, while offering such a grim prospect, has not resulted in the mass mobilization against fossil fuels. Many of the examples cited of adverse consequences resulting from the release of non-native species (exotic introductions) while surely problematic or a nuisance, don't conjure up apocalyptic consequences. Insects like fire ants and plants like kudzu are popular examples of the unintended effects of exotic introductions. Fire ants were introduced accidentally while kudzu was brought to the United States intentionally. It is possible that the human and ecological effects they brought about could have been identified prior to their introduction by the appropriate risk analysis. In contrast, multitudes of new crops were introduced into agriculture without incident. Moreover, even the foreign introductions that have caused problems are not viewed as catastrophes, although no one questions the severity of problems like the introduction of brown snakes into Guam, rabbits into Australia or gypsy moths and kudzu in the United States (U.S. Congress 1993). Proponents of releasing GEOs argue that many of the most widely cited examples, kudzu notwithstanding, were unintended introductions.

5. Risk Assessment of GEMs

The release of GEMs into the environment offers a unique challenge to risk assessment because: the effects of microorganisms are not as obvious as those of

plants or animals; GEMs reproduce quickly and are impossible to recall; unlike nutrients, toxins and pollutants, microorganisms can reproduce and move about the environment on their own; and microorganisms exchange their DNA with other species quite readily adding to the complexity of risk assessment. Moreover, extrapolating from one microbial species to another or from tests conducted under one set of environmental conditions to another is often unreliable.

Two approaches have been suggested for assessing the risks of GEMs into the environment. The first approach would focus primarily on the source materials, that is the host organism and the foreign DNA. Based on what is known about the soil ecology of the host organism and the foreign protein transferred, it is presumed that one can make sound judgments about the phenotype of the recombinant organism and its relationship with its environment. For example, Miller (1991) maintained that genetically engineered microorganisms are not new because the transfer of DNA from unrelated organisms has been occurring since the origins of life. As a result, microorganisms have seen all possible combinations. Brill (1985b: 117) commented in a letter to *Science* that "a tremendous amount of gene transfer occurs naturally, not only among related genera, but also between unrelated microorganisms and even between kingdoms... What scientists create through genetic engineering is minuscule and ecologically insignificant compared to what occurs continually and randomly in nature." He also argued (Brill 1985a: 383) that indigenous microorganisms saturate natural habitats to which they are highly adaptive and that "the extra burden to the organism carrying new genes should decrease its ability to compete and persist." Campbell (1991) concurs that newly introduced GEMs are not likely to displace or outcompete the natural microbes. Also, since the genetic modifications on microbes are well characterized single gene additions or deletions, it is argued that the phenotypic changes can be accomplished with a high degree of safety.

In general, those people tied to the development of biotechnology are inclined to use the paradigm of crop breeding to evaluate the products of biotechnology while ecologists and environmentalists are drawn to the paradigm of exotic introductions.

Another line of argument, critical of selecting out GEMs as a special case, holds that we should not regulate an organism by the methods of its production but rather only by its properties per se (Miller 1994).[3] This issue arose during the debate over ice minus. One variant of ice minus was found in nature, while a second version, with virtually the same gene deletion, was produced in the laboratory by recombinant DNA techniques. There were no regulations on releasing large quantities of the ice minus strain cultured from the natural environment, while there were strict regulations for releasing the rDNA strain.

Ideally, one should only have to study the phenotype of an organism to assess risk. An organism with the same phenotype produced by different processes should be subject to the same risk estimate. A 1989 report of the Ecological Society of America, a group that has traditionally expressed caution over the release of genetically engineered organisms, stated: "We contend that transgenic organisms should be evaluated and regulated according to their biological properties (phenotypes) rather than according to the genetic techniques used to produce them" (Tiedje et al. 1989: 302). This idea certainly holds true for chemicals whose properties are independent of how the chemical is manufactured. However, in chemical risk

assessment we have seen the evolution of canonical toxicological tests. This has not been the case for the products of biotechnology; not only are microorganisms not as precisely defined as chemicals but they mutate in unpredictable ways. Until we have effective means for evaluating the phenotypes of transgenic organisms for human and ecological risk, regulators may have pragmatic grounds for screening organisms according to the methods by which genetic changes have been made (Krimsky 1995).

Ecologists and evolutionary biologists are dubious of *a priori* assumptions about the safe releases of genetically modified microbes such as the addition of foreign genes to an organism necessarily reduces its fitness. According to Sharples, evolutionary theory teaches us that "at least some genetic alterations improve the abilities of organisms to survive, reproduce, compete for resources, or invade new habitats" (Sharples 1987: 1330).

A second approach to risk assessment of GEMs seeks ecological data from simulated environments designed to model the complexity of the actual environment. These are generally referred to as microcosm or greenhouse experiments. Since these experiments are contained, there are no risks to the environment. The question is: Can these experiments really tell us anything about how a GEM will behave under natural conditions or do these tests offer a false sense of security. For example, will it be possible to use microcosm data to determine whether a genetically engineered microbe will outcompete its parental strain or spread to other niches beyond the desired agro-ecosystem, or in the case of microbial biodegradators, beyond the target site? How well does the microcosm replicate field conditions? What properties of GEMs can be measured in microcosms that are relevant to field releases? How can one be confident that the microcosm will yield consistent and reproducible results? How can we improve the reliability of the microcosm to predict the behaviour of GEMs in the field?

One recent experiment suggests that the answer may be clearly in the affirmative. Holmes and Ingham used microcosms containing the indigenous soil biota and plants to test the effects of releasing a genetically modified strain of *Klebsiella planticola*. The organism was modified with the gene to synthesize ethanol from organic waste. The engineered bacterium was introduced to enclosed soil chambers in which wheat plants were growing. The plants in the chamber with the genetically modified *Klebsiella* were killed while those in the control chamber remained healthy. The mechanism postulated to explain this effect is that the introduced microbe reduced the colonization of plant roots by mycorrhizae which makes the plants less competitive with weeds and more susceptible to disease. Also, in certain types of soil, plants died from ethanol produced by the GEM in the root system (Holmes and Ingham 1994).

This result refutes the conclusion that no significant ecological effects will result from the addition of a GEM to the soil. Moreover, the results may not be predictable from information about the foreign DNA and the host organism. Ecologists have argued that knowing the change in phenotype is not sufficient to predict the outcome of a release since it is the interaction of that phenotype with the environment that matters and that result usually requires a field test.

6. Microcosms and their Critics

Microcosms came into use in the 1970s for examining the fate and transport of chemicals introduced in the soil, such as pesticides or industrial toxic wastes (Draggon and Van Voris 1979). These early microcosms used standardized soil mixtures, often sterile soil, soil with no plants and no microorganisms. These systems were useful in examining the physical and chemical changes taking place and enabled researchers to standardize and replicate certain measurements (Metcalf 1975). They could use radio-labeling to trace the movement of chemicals without releasing radioactive materials in the environment (Cole et al. 1976; Gillett and Gile 1976).

When microcosms came into use for studying the fate of organisms in biological systems, the issue of their size, shape, composition and treatment became more salient. The notion of a microcosm offered by the U.S. National Research Council as "an intact, minimally disturbed piece of an ecosystem brought into the laboratory for study... that behaves ecologically like its counterpart in the actual field", establishes a standard of simulation that far exceeds the synthetic microcosms applied to chemical mobility which seek to control a few variables. Fredrickson et al. (1990) claim that microcosms can be useful to predict field effects even if they do not fully replicate the field; the key is in calibrating the microcosm with the field.

The lack of standardization of microcosms for risk assessment in biotechnology has presented some problems. The research literature reveals that the term microcosm applies to many sizes and shapes of experimental systems including test tubes containing 2 grams of soil, plastic trays (.05 x .3 x .5 m) and soil cores (.4 diam x .6 m).[4] The one exception is that the American Society for Testing and Materials (ASTM) developed a standard microcosm in 1987 for testing the fate and effects of xenobiotics. Without the standardization of microcosms for the assessment of microbial behaviour it is near impossible to compare risk assessment tests, to replicate experiments, and to build a body of dependable knowledge.

There are several things to consider in the development of microcosms for risk assessment of genetically engineered microorganisms. Do the microcosms reflect the native flora and fauna? Is the soil composition and physical structure comparable to the natural conditions in the field? Will the treatment of the microcosm during the test period replicate the conditions facing a GEM in the natural environment? The key to standardization is to establish uniform parameters of measurement, size, watering regimes, and assay methods for detecting organisms, while allowing sufficient flexibility in constructing the microcosm so that it comes as close as it can to replicating real field conditions.

The microcosm must be initialized to its natural environment. The most common way to accomplish this is to extract the soil from the location where GEMs will be released. A soil core microcosm (a cylindrical core) extracted from the site of interest is then brought into the laboratory for inoculation of genetically modified organisms (Gile et al. 1979).

There are still many problems with this methodology. By extracting the soil one can change its physical structure, for example, by compacting it. In removing the soil from its natural setting one changes the environmental parameters. Temperatures, water flow through the soil, plant roots, and insect population are likely to differ

between the soil core and its habitat of origin. The size of the core may also be a problem in cases where edge effects could be important in the growth or dispersal of microorganisms. The microcosms have high surface to volume ratios and surface boundaries which do not exist in the field may distort the results of microbial experiments.

Microcosms cannot address the effects of GEMs on large invertebrates, or the effects of vectored transport across large boundaries compared to the scale of the microcosm, or toxicity to certain large plants. Microcosms cannot replicate the results of air currents that may transport organisms or the use of large aerosol delivery systems. Cavalieri (1991: 571) notes: "Questions such as the persistence of the genetically engineered microorganisms in the field, its effects on non-target species, alteration in its host range, and its performance under different climatic conditions cannot be fully addressed in microcosm studies or small-scale controlled field tests."

The most serious criticism of microcosms comes from a critic of regulation, Winston Brill (1985a: 384) who claims they are irrelevant to field conditions "because different soils, soil treatments, and weather conditions can dramatically alter the growth rate, population, and persistence of a microbe, greenhouse or growth chamber experiments have little relevance to field results." The consequence of this argument is that releasing modified microorganisms in the field is the only viable screening method.

Several research efforts have responded to the challenge to improve the effectiveness of microcosm risk assessment. First, soil-core microcosms are allowed to equilibrate in the field, sometimes for as long as two months. This is to allow the soil in the microcosm to take on more of the qualities of the field soil before measurements are taken on the survival and dispersal of the organisms. Equilibration is limited to certain seasons. A second approach is to establish standards of reliability for the microcosm. Since water is an important factor in the dispersal of microorganisms, watering regimes that simulate actual field patterns will give a more accurate picture of microbial activity.

Another contribution to the role of microcosms in risk assessment is the development of a calibration standard. What confidence can scientists have that the microcosm results are replicable? How do we know that the introduced GEM is behaving oddly because of something peculiar to the microcosm rather than the GEM itself? According to Fredrickson et al. (1990: 194), "the majority of microcosm studies have made little or no attempt to field-calibrate the microcosm or relate findings to the field." Levy et al. (in Krimsky et al. 1995) have proposed a calibration method based on an internal standard. This involves using a mutant strain that provides a characteristic pattern of survival and spread in a given microcosm. Once the GEM is introduced, one can always refer back to the mutant strain and its pattern of behaviour to determine whether the microcosm is behaving in its expected fashion. In addition, the GEM can be introduced paired with the organism used as part of the internal standard. One can then compare the behaviour of the mutant strain with that of the GEM. In this sense, the microcosm can be calibrated with a mutant strain that has a characteristic pattern of behaviour.

6. Conclusion: The Expectation of Predictive Ecology

There is no way to demonstrate that an organism is safe. All one can expect to do from a methodological standpoint is to demonstrate either that (a) an organism is hazardous or (b) when tested against various hazard scenarios, the results falsify the conjectures that a hazard exists. The powerful legacy of Popperian philosophy (Popper 1965) has important implications for risk assessment in biotechnology, especially when we are a long way from canonical testing protocols.

If microcosms are to be useful as a screening mechanism for selecting our potentially hazardous microorganisms, we must be capable of using them to model falsifiable hypotheses of realistic risk scenarios. We must also accept, perhaps on faith, the notion that an organism which tests favourably against a series of risk scenarios deemed most probable by ecologists is less likely to turn up as a hazard than, ceteris paribus, an organism that is not subject to such tests.

We should not be trying to prove that an organism is safe. We should be trying to demonstrate it is hazardous. Once the hazard hypotheses are falsified, our confidence level in the safety of the organism will be heightened. Since there are practical limitations on the number of tests we can demand from companies, the selection of those tests is critical for risk assessment. Worst case scenarios with a remote probability may not be as useful as moderate risk scenarios with a higher expected probability for observing an effect. One might also use microcosms to test a variety of suggested principles such as: "microorganisms with added genes will be less competitive," or "a few genes will not transform a non-pathogen into a pathogen."

Predictive ecology is still in its infancy. The effort to standardize microcosms as screening assays for genetically engineered microorganisms with regard to hypotheses about survival, competitiveness, dispersal, and pathogenicity might advance the broader agenda in which prospective risk assessment can be applied to the ecological sciences (Krimsky et al. 1995).

It is useful to consider the theoretical limitations for using microcosms to predict the behaviour of GEMs in the natural environment. Does small scale provide a limiting factor and if so for what properties and what reasons? Is the issue complexity? Are small samples (intact soil cores) inadequate to represent the complexity of the actual ecological system? There are obvious limitations of microcosms in that we cannot put trees or animals in the microcosm. But what if we are trying to understand microbe to microbe interactions in a soil type? Are there system complexity issues that preclude the use of microcosms for predicting effects in the environment? Assuming the soil microenvironment is a random subset of the soil macroenvironment minus the large elements, will the absence of the larger elements affect the microbial behaviour?

Let us assume our soil core microcosm represents a random sample of the field area. However, the random sample may not reflect the heterogeneity of the soil ecology. We would need to know something about the variance of the parameter under consideration to determine how many intact soil cores are necessary for achieving results that reflect the heterogeneity of the field.

The fact that one system is used to model a larger system of higher degrees of complexity is not in itself a limitation provided we understand the role of complexity

in predicting the parameter of interest. Thus, while standardization of microcosms will be helpful in comparing and contrasting risk assessment data for GEMs, theoretical work is also needed that allows us to understand when microbial experiments in earth samples enable us to make inferences about similar experiments under actual field conditions.

The social response to the problem of managing the ecological risks of GEMs may be likened to the proverbial query about whether the glass is half full or half empty – it has an optimistic and pessimistic dimension. From the optimistic perspective, there has been a noticeable increase in the application of anticipatory ecological risk assessment in the form of greenhouse and microcosm studies. The field of ecotoxicology has embraced the issues of bioengineered organisms. There have been methodological advances in the use of microcosms for predicting ecological effects of field experiments.

Notwithstanding this progress in ecological modeling, a pessimistic perspective cannot be avoided as we observe a global retreat from the social commitment to anticipatory regulation. Nowhere is this more evident than in the United States. The U.S. Congress has abolished the 23 year old Office of Technology Assessment, which has produced many studies on bioengineered organisms and the environment. The U.S. system of regulation has moved toward a cost-benefit approach that places low priority on the protection of natural habitats per se and is moving rapidly toward a clear and present danger standard to justify regulatory intervention. Thus, at a time when a new biotechnology industry is advancing and scores of bioengineered organisms are being released, a new ideology is sweeping the dominant political culture of the governments of major industrial societies that sees little value in the investment of ecological risk assessment. If history is any guide, this could change dramatically if an untoward event were to take place from the release of a bioengineered organism.

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Notes

1. See especially Chapter 8, 'Debates over deliberate release: Disciplinary fault lines.' In: S. Krimsky, *Biotechnics and Society*, 1991.

2. Brill (1985a: 384) argued: "A program that aims to utilize, in agriculture, a plant, bacterium, or fungus considered to be safe but with several foreign genes will have essentially no chance of accidentally producing an organism that would create an out-of-control problem."
3. Miller (1994) highlighted the distinction between product and process regulation emphasizing the former: "We contend that transgenic organisms should be evaluated and regulated according to their biological properties (phenotypes) rather than according to the genetic techniques used to produce them."
4. In describing the types of microcosms Metcalf (1975: 243) states: "Laboratory model ecosystems or microcosms are potentially almost as diversified as the natural environment whose components are being modeled. Such systems range in complexity from petri dishes containing soil microflora and flasks containing microorganisms in water or nutrient medium to elaborately constructed and instrumented terrestrial chambers ... and model streams."

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