Risk Assessment Experiments for "Genetically Modified" Plants

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"There seems to be a view that the ecology of genetically engineered organisms is somehow different—more inscrutable perhaps, but certainly more dangerous—and that the intentional release of genetically engineered organisms poses more of a threat to the balance of nature than other kinds of organisms bred by man. This view is mistaken. While there are risks associated with the introduction of any novel organisms into a habitat, the ecology of genetically engineered organisms is exactly the same as the ecology of any other living thing."—M.J. Crawley

> "We used genetically engineered plants grown in natural habitats to compare the demography of transgenic and conventional lines of plants in a range of habitats throughout Great Britain in order to find out how ecological

performance is affected by genetic engineering."—M.J. Crawley, et al.2 rawley et al. recently reported the results of an elaborate risk assessment experiment2 comparing the long-term "invasiveness" of three crops in a variety of climatic conditions and habitats. The report was accompanied by an enthusiastic commentary by P. Kareiva³ who boldly pronounced it a "landmark paper." However, we suggest that the experiment and the commentary are illustrative in ways that their authors did not intend.

International organizations and professional groups have explored repeatedly the question of what are the correct assumptions about risk for the new biotechnology. The seminal issue has many nuances and manifestations, but at bottom, it is the question whether the use of the techniques of the new biotechnology, such as recombinant DNA (rDNA) technology, will require new paradigms—in governmental regulation, in planning and performing risk assessment, and even in the public psyche. The answer, which is negative, has before now been authoritatively settled.

Far from "bring[ing] one of the hottest debates about the use of genetically engineered plants in agriculture into the realm of rational discourse,"3 both the Crawley paper and the commentary may, in fact, revive and promote some obsolete misconceptions about the "new biotechnology" generally and risk assessment of "genetically engineered" crop plants specifically.

long history of "genetic engineering"

Traditional biotechnology is almost as old as agriculture itself. The "new biotechnology" differs from traditional methods by modifying the DNA of organisms in a manner that is more precise and predictable, and by greater latitude in the movement of genes between unrelated organisms. When it comes to crop

plants, separate analyses by the U.S. National Academy of Sciences (NAS, Washington, D.C.)4 and the U.S. National Research Council (NRC, Washington, D.C.)5 have not found differences between the environmental safety of old and new biotech-derived plants. In 1989, the NRC reported that "crops modified by molecular and cellular methods [i.e., the new biotechnology] should pose risks no different from those modified by classical genetic methods for similar traits" because "no conceptual distinction exists between genetic modification of plants and microorganisms by classical methods or by molecular techniques that modify DNA and transfer genes."

In fact, there exists broad consensus among scientists that the changes that result from rDNA technology are likely to be even safer than the random shuffling of characteristics that is inevitable with more traditional techniques. In the words of the 1987 NAS white paper, because "the new molecular methods are more specific, users of these methods will be more certain about the traits they introduce into plants than those using traditional methods."

Even plants that contain genes from different species or different genera-thereby transcending natural breeding barriers—are already commonplace to European and American farmers and consumers. They include sugarbeet, potato, tomato, pumpkin, oats, corn, and wheat.6

he determinants of risk

Among scientists, there is wide consensus that risk is primarily a function of the characteristics of a product (whether it is inert or a living organism) rather than the use of one or another technique of genetic modification.7 This consensus is based on both empirical data and extrapolations from general scientific principles. The extrapolations are based on our knowledge of the biological world and from our understanding of evolutionary biology. The empirical Henry Miller is at the Office of Biotechnology, U.S. Food and Drug Administration, Room 15-61, 5600 Fishers Lane, Rockville, MD 20816. Roger Beachy is at the Division of Plant Biology, Scripps Research Institute, La Jolla, CA 92037. Susanne L. Huttner is at the University of California Systemwide **Biotechnology** Research and Education Program, Los Angeles, CA 90024. The views expressed here are the authors' own, and not necessarily those of Bio/ Technology.

Arguably, more useful information would have been derived from exploring the question of how invasiveness is affected by the introduction of certain traits of interest. data are derived from our experience with genetics. Phenotypes are determined by gene expression within organisms, not by how the genes were introduced. For example, organisms expressing genes that confer antibiotic resistance are resistant, whether the genes were introduced by natural selection or in the laboratory by transformation, conjugation, transduction, transfection, or recombinant DNA manipulation. However, this view is inconsistent with the myth that there is something systematically similar and functionally important about the set of organisms whose only common characteristic is genetic manipulation with the techniques of the new biotechnology—a "horizontal approach" that values scanning across various organisms or experiments that use rDNA techniques.8

This issue has important implications for the planning and performance of risk assessment experiments. An overwhelming scientific consensus holds that long-standing principles and techniques for planning and performing risk assessment experiments are applicable to organisms modified with the newest techniques.^{1,9} Such experiments should focus on the relevant effects of introducing into plants certain traits that are known to be related to risk (for example, those that may affect persistence/invasiveness, weediness, or gene transfer), but they need not persist in testing and retesting the hypothesis that the use of recombinant DNA techniques, per se, alters those risk-related characteristics [vide infra].

The Crawley experiment

The experiment by Crawley and his coworkers was, according to Kareiva's commentary, "one of the most comprehensive population studies ever undertaken in plant ecology." In three climatically distinct sites and four habitats, the experiment compared the invasiveness of three variants of oilseed rape plants over three growing seasons: two varieties modified with recombinant DNA techniques to confer antibiotic or herbicide resistance and one "unmodified" variety. The results indicated no significant differences in invasiveness among the three varieties.

Kareiva cites the "landmark" Crawley experiment as a possible prototype for risk assessments, while we view it as an example of a well executed but poorly conceived risk assessment experiment. Some of its important limitations are, in fact, enumerated by Kareiva. The choice of experiment reflects the weakness of the original hypothesis to be tested, which was simply to find out how invasiveness "is affected by genetic engineering."2 Numerous analyses by professional, national, and international groups, including those of the NAS and NRC cited above had compellingly resolved the major aspects of the investigators' hypothesis years earlier.10 Crawley, himself, as quoted at the beginning of this paper, has written that "the ecology of genetically engineered organisms is exactly the same as the ecology of any other living thing."

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Arguably, more useful information would have been derived from exploring the question of how

invasiveness is affected by the introduction of certain traits of interest, under appropriate experimental conditions. Although the methodology was elegant and scientifically sound, the result was largely predictable—and scientists seldom perform scientific experiments of this magnitude when the outcome is virtually a foregone conclusion. It is not particularly interesting scientifically to conclude that transgenic plants with genes for resistance to an antibiotic or an herbicide are no more invasive than their "unmodified" parent, when they are tested in the absence of selection pressure from either substance in the test environment. And one observed difference, reductions in seed survival in the modified plants, cannot be attributed unequivocally to the genetic modification, because "maternal effects and other factors involved in the production of the different plant lines might have influenced the properties of the seeds."2

Finally, the results, such as they are, cannot be applied generally. All they enable scientists to say is that under the conditions tested, these particular variants of oilseed rape did not differ significantly from one another in their invasiveness. One can infer nothing about plants, or genetically engineered plants, in general. A prototype experiment, indeed!

Even in the absence of well-designed risk assessment experiments, concerns about the invasiveness of oilseed rape or other plants, merely because they are "transgenic," "recombinant," or contain a genetic combination unlikely to occur in nature, are unfounded. Such organisms can still afford a high degree of familiarity. 11 There is also no necessity to conduct risk assessment experiments to ensure confidence about the field testing of new plant varieties in general or those crafted with the newest genetic manipulation techniques in particular.

The Crawley experiment and Kareiva's disproportionate response to it raise the question whether the real purpose of the lavish study was rather more ecological public relations than scientific enquiry. In these times of constrained research resources, it might serve as a reminder of the importance of choosing experiments to yield the greatest amount of useful information.

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