HOOVER INSTITUTION
ON WAR, REVOLUTION AND PEACE

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Mr. John Morrall
Office of Information and Regulatory Affairs
Office of Management and Budget
NEOB
Room 10235
725 17th Street, NW
Washington, DC 20503

Dear Mr. Morrall:

I appreciate the willingness of Dr. John D. Graham and his colleagues at OIRA to accept comments on OMB's March 28,2002 Draft Report to Congress on the Costs and Benefits of Regulations.

By way of introduction, I am a former FDA reviewer, manager and office director. From 1979-1993, I had responsibility for various aspects of biotechnology product review and policy-making, and I was the founding director of the agency's Office of Biotechnology, 1989-1993. While a government official, I often represented the FDA or the U.S. Government at international conferences or on panels related to biotechnology. As a fellow at Stanford University's Hoover Institution since 1994, I have studied domestic and international regulation of biotechnology. I have published widely on various aspects of biotechnology, including three books and more than 400 articles. I am a member of the US delegation to the Codex group on biotech foods.

The gist of this analysis is very simple: Biotechnology regulation in the United States – primarily at the Department of Agriculture's Animal and Plant Health Inspection Service (APHIS), Environmental Protection Agency (EPA) and Food and Drug Administration (FDA) are unscientific, un-cost-effective, damaging to American innovation and to consumers' ability to choose among products in the marketplace, and harmful to the environment. In addition, flawed U.S. domestic regulation vitiates the ability of U.S. negotiators, in forums such as the Codex Alimentarius Commission, to insist upon science-based regulation internationally.

Not only does this regulatory approach – which focuses specifically on products made with the most precise and predictable techniques -- violate the principle that the degree of regulation should be commensurate with the perceived degree of risk posed by a product or activity, but as discussed below, they are arguably *inversely* related to risk. The approach to regulation taken by domestic regulatory agencies conflicts not only with scientific consensus and common sense, but also with official USG statements of the principles that should guide regulatory policy.

Those who are skeptical about the safety of plants, animals and microorganisms crafted with the newest gene-splicing techniques (and food and other products derived from them) – few of whom reside within the scientific community – gloss over a fundamental point: Neither biotechnology nor genetic engineering is new, and consumers, government and industry all have extensive – and positive -- experience with them.

A primitive form of biotechnology -- the application of biological systems to technical or industrial processes -- dates back at least to 6000 B.C. when the Babylonians used specialized microorganisms in fermentation to brew alcoholic beverages. And genetic engineering can be dated from man's recognition that animals and crop plants can be selected and bred to enhance desired characteristics. In these applications, early biologists and agriculturists selected for desired physical traits, with poorly understood changes in the organisms' genetic material occurring concomitantly.

Putting it another way, "nature" didn't give us seedless grapes, the tangelo (a tangerine-grapefruit hybrid) or fungus-resistant strawberries: plant-breeding – by farmers, biologists and breeders -- did.

During the past half-century, better understanding of genetics at the molecular level has added to the sophistication of the genetic improvement of all manner of organisms. The genetic engineering of wheat for human consumption – an important component of the "Green Revolution" – was recognized in 1970 with the awarding of the Nobel Peace Prize to Dr. Norman Borlaug.

These applications of "conventional" biotechnology, or genetic engineering, represent scientific, technological, commercial and humanitarian successes of monumental proportions. However, the techniques used for these earlier successes were relatively crude and recently have been supplemented, and in many cases replaced by "the new biotechnology," a set of enabling techniques which make possible genetic modification at the molecular level. The prototype of these techniques, variously called recombinant **DNA** technology, genetic modification (GM) or "gene-splicing," is a more precise, better understood, and more predictable method for altering genetic material than was possible previously.

Thus, all that has changed since the demonstration of gene-splicing in the early 1970s is the *technology* of biotechnology. The new technology is at the same time more precise and predictable than its predecessors and yields more versatile and predictable products. The desired "product" of gene-splicing may be the engineered organism itself — for example, bacteria to clean up oil spills, a weakened virus used as a vaccine, or a papaya tree that resists disease — or it may be a biosynthetic product of the cells, such as human insulin produced in bacteria, or oil expressed from seeds.

An authoritative 1989 analysis of genetic technologies by the United States National Research Council summarized the scientific consensus: "With classical techniques of gene transfer, a variable number of genes can be transferred, the number depending on the mechanism of transfer; but predicting the precise number or the traits that have been transferred is difficult, and we

cannot always predict the [traits] that will result. With organisms modified by molecular methods, we are in a better, if not perfect, position to predict [their traits]."

As discussed extensively in the attachments to these brief summary comments, other aspects of scientific consensus include:

O The newer molecular techniques for genetic improvement are an extension, or refinement, of earlier, far less precise ones;

O Adding genes to plants or microorganisms does not make them less safe either to the environment or to eat;

O The risks associated with gene-spliced organisms are the same in kind as those associated with conventionally-modified organisms and unmodified ones;

O Regulation should be based upon the risk-related characteristics of individual products, regardless of the techniques used in their development; and

O The evaluation of gene-spliced food does not require a fundamental change in established principles of food safety; or a different standard of safety.

Our experience with gene-spliced plants alone – let alone with other genetically improved organisms over millennia – is impressive. They have for several years been grown worldwide on more than 100 million acres annually (approximately three-quarters of that in the United States), and more than 60 percent of processed foods in the United States contain ingredients derived from gene-spliced organisms. There has not been a single mishap that resulted in injury to a single person or ecosystem. Thus, both theory and experience confirm the extraordinary predictability and safety of gene-splicing technology and its products – especially compared to the less precise and predictable techniques of "traditional" biotechnology.

However, gene-spliced products – in field testing, in the food supply and in other commercial applications – have been regulated in a discriminatory, unscientific and burdensome fashion, by USDA/APHIS, EPA's Office of Pesticides and Toxic Substances, and FDA's Center for Food Safety and Nutrition. These hugely intrusive and expensive oversight regimes have violated one of the basic tenets of regulation – that the degree of oversight should be commensurate with risk. In fact, arguably, oversight has been *inversely* related to risk.

U.S. regulatory agencies have for more than a decade and half applied to biotechnology regulation what might be called "The Emperor's New Clothes" school of rule-making. No matter how unscientific, unwise, unnecessary or anti-innovative the regulatory proposal, the process attains legitimacy as regulators negotiate step after bureaucratic step according to specified rules – holding public meetings, publishing announcements in the *Federal Register*, analyzing public comments, and so forth – with everyone pretending that the evolution and substance of the document makes sense. Although the regulations have attained legitimacy of sorts, by being produced according to the required process, the resultant policy has been profoundly contrary to

the public interest. (If OMB were to calculate cost-benefit as it has done in the past, the cost of these regulations per premature death, or ecosystem damage, prevented, the cost would be astronomical, inasmuch as the denominator approaches zero.) The fundamental assumption that underlies the regulatory approach of USDA, EPA and FDA – namely, that scientific justification can be found for oversight regimes focused on the "pseudo-category" of organisms or other products modified by gene-splicing techniques -- is flawed and contrary to a broad-based and long-standing scientific consensus *(vide supra)*.

It should be emphasized that with the abovementioned elements of scientific consensus transgressed – as they are in fundamental ways at USDA, EPA and FDA – one *cannot* arrive at a paradigm that makes sense and offers meaningful protection against bona fide risks. In other words, in spite of regulators' remonstrations to the contrary, one cannot adopt a scope of regulated products that is absurd, apply a "scientific process" to their evaluation, and hope to emerge with a result that has integrity.

Moreover, it should be noted that the chosen scope of the document is incompatible with the part of the United States' federal framework that is supposed to guide regulatory approaches to products derived from gene-spliced organisms. That guidance is contained in a 1992 statement of policy from the White House Office of Science and Technology Policy, "Exercise of Federal Oversight Within Scope of Statutory Authority: Planned Introductions of Biotechnology Products into the Environment," which describes "a risk-based, scientifically sound approach to the oversight of planned introductions of biotechnology products into the environment that focuses on the characteristics of the ... product and the environment into which it is being introduced, not the process by which the product is created. Exercise of oversight in the scope of discretion afforded by statute should be based on the risk posed by the introduction and should not turn on the fact that an organism has been modified by a particular process or technique."

In short, official U.S. dictates unequivocally that merely the use of gene-splicing techniques is not an appropriate trigger for oversight – and yet federal oversight commonly employs that trigger, for expansive (and expensive) regulatory regimes.

It is clear that the scientific community does not consider gene-spliced organisms or components of such organisms to be a meaningful category. Consider, for **example,** some of this year's Gordon Research Conferences and the individual sessions within them. There is one in June on Bacterial Cell Surfaces. None of the sessions addresses gene-spliced organisms specifically; rather, they are concerned with subjects like "protein secretion, -- and "cell-cell communication," whether gene-spliced or not. Similarly, the July conference on Microbial Toxins and Pathogenicity does not designate special sessions for gene-spliced organisms or sub-cellular constituents, although gene-splicing is used routinely for the research described in sessions like "Bacterial Cell Biology and Pathogenesis" and "Bacterial and Host Gene Regulation during Infection." Finally, during the dozens of presentations at the February 2003 conference on Chemistry and Biology of Peptides, not one is limited to the "category" of gene-spliced peptides. This should be instructive: proteins, cells, and foods produced solely by gene-spliced microorganisms are not meaningful categories.

The existing regulatory policies for biotechnology products at APHIS, EPA and FDA are wasteful in terms both of direct and indirect costs. These regulations are not only hugely expensive to comply with – field trials of a gene-spliced plant can be 10-20 times more expensive than trials with a virtually identical plant crafted with less precise, less predictable techniques; and EPA-regulated plants must undergo pesticide registration – but the bureaucracies created to implement this regulation are massive. One need only search for "biotechnology" on the agencies' web-sites to identify the vast, and arguably unnecessary, bureaucracies. (There is no evidence that the regulatory mechanisms in place to oversee "traditional" biotechnology would not also have been sufficient for products made with the more precise and predictable gene-splicing techniques.)

In summary, the regressive, overly burdensome and unscientific policies toward biotechnology at U.S. regulatory agencies have damaged innovation, destroyed entire sectors of R&D (e.g., microbial, "biorational" pesticides) and inhibited others (e.g., agricultural biotechnology, except for a handful of commodity crops), and encouraged similarly flawed regulation internationally. Because these approaches are becoming progressively entrenched at organizations such as the agencies of the United Nations, they will be difficult to rationalize, but if irreparable, long-term repercussions are to be avoided, APHIS, EPA and FDA must be instructed to revise their policies along the lines of the 1992 OSTP policy statement cited above and to adopt regulatory policies that make scientific and common sense. The perpetuation of the status quo will continue to inhibit innovation, reduce consumer choice, and make a mockery of the ideal of science as the basis for public policy.

I have attached several reprints and a reprint that address specific issues and individual agencies' regulation, in order to support and further illustrate the points herein.

Thanking you again for the opportunity to submit comments, I am

Sincerely yours,

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attachments

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SCIENCE VERSUS PRESUMPTION IN ASSESSING RISK'

by Henry I. Miller And Gregory Conko

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Consumers benefit in myriad ways from the development of new technologies and products, including lower prices, greater choices, and improved quality. But the possibility that a given innovation will pose risks to public health or the environment cannot be ignored; therefore, the challenge of government regulation is to permit beneficial new products to undergo testing and enter the marketplace, while limiting or mitigating serious hazards. How to accomplish this most effectively and efficiently has been the subject of much deliberation and debate.

Environmental and public health activists long have clashed with scholars and risk-analysis professionals over the appropriate regulation of various risks. Underlying the controversies about various specific technologies and products – such as chlorinated and fluoridated water, pesticides, hormones in livestock, and recombinant DNA-modified (gene-spliced) foods – has been a fundamental, almost philosophical, question: How should regulators, acting as society's surrogate, approach risk in the absence of certainty about the likelihood and magnitude of potential harm?

Traditional regulatory approaches for many classes of new products have focused on an evaluation that considers both the magnitude and likelihood of plausible health or environmental harms on one hand, and expected benefits on the other. That assessment would then, at least in part, dictate the choice of an oversight regime. That regime would then be applied to individual products: Those whose harms are expected to exceed benefits are judged to pose an unreasonable risk and are not permitted to enter the market, whereas products whose benefits are expected to exceed harms are permitted. But foresight is imperfect, and disproportionate harms from marketed products do sometimes occur. Ostensibly in order to reduce the likelihood and impact of such occurrences, for more than a decade proponents of a highly risk-averse approach to regulation have advocated the use of the "precautionary principle," which they argue will reduce the risk of such harm.

There is no widely accepted definition of the precautionary principle, but its most common formulation is that governments should implement regulatory measures to prevent or restrict

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[1] This manuscript builds on earlier, shorter papers by the same authors: Miller, H. and Conko, G. The Protocol's Illusionary Principle. Nature Biotechnology 18, 360-61 (2000); and Miller, H.I. and G. Conko. The Perils of Precaution: Why Regulators' "Precautionary Principle" Is Doing More Harm Than Good. Policy Review, June-July 2001, 25-39.

actions that raise even conjectural threats of harm to human health or the environment as long as there is incomplete scientific evidence as to the potential significance of these dangers. Its advocates argue that such a "precautionary approach" to risk regulation is necessary for many new technologies and products (and even for many that are decades old). However, support for precautionary regulation is perhaps nowhere more zealous than in the case of recombinant DNA technology, or gene splicing (also sometimes referred to misleadingly as "genetic modification," or "GM") applied to agricultural, food and environmental products. Whether the term "precautionary principle" is used or not, this risk-averse approach provides the foundation for much of the current regulation of gene-spliced products. For that reason, the subject warrants extensive discussion.

The use of the precautionary principle is sometimes represented euphemistically as "erring on the side of safety," or "better safe than sorry" – the idea being that the failure to regulate risky activities sufficiently could result in severe harm to human health or the environment, and that "over-regulation" causes little or no harm. But this latter assumption is highly misleading.

Although potential risks should be taken into consideration before proceeding with any new activity or product, whether it is the siting of a power station, the introduction of a new drug into the pharmacy, or the consumption of food from gene-spliced plants, the precautionary principle overemphasizes the potential for technologies to pose unique, extreme, or unmanageable risks. What is missing from precautionary calculus is an acknowledgment that even when technologies introduce new risks, very often they confer net benefits – that is, their use reduces many other, far more serious and costly hazards. Examples include blood transfusions, MRI scans, and automobile seat belts and air bags, all of which offer immense benefits and only minimal risk.

Unnecessary delay in granting marketing approval for these and other technologies denies consumers access to products that could substantially reduce the risk of injury, or even death; this is a common side-effect of the application of the precautionary principle. Thus, the use of the precautionary principle often distorts the risk equation, heightens risk, and actually causes harm to public health and the environment. The oversight of recombinant DNA technology used for agriculture and food production offers a vivid example of the how the precautionary principle can systematically victimize science, technology, public health, the environment and innovation.

This paper first describes the general scientific consensus regarding the risks associated with recombinant DNA-modified, or gene-spliced, organisms and the implications of that consensus for the regulation of organisms in the field, and of food in the marketplace. Next, the paper examines the potential for poorly conceived regulation actually to increase risk, paying particular attention to the potentially risk-enhancing danger of existing precautionary regulatory policies. It concludes with a discussion of scientifically defensible, risk-based frameworks for the regulation of products that involve the use of recombinant DNA technology.

SCIENCE AND THE RISKS OF RECOMBINANT DNA TECHNOLOGY

The creation of the first recombinant DNA-modified organism in 1973 marked the advent of a promising new technique for the development of new medical, agricultural, environmental, and

industrial products. Soon afterward, scientists and policymakers began to consider possible approaches to the oversight of the testing and use of recombinant DNA-modified organisms and products derived from them. During the last 25 years, dozens of scientific bodies, including the US National Academy of Sciences (NAS 1987), the American Medical Association (AMA 2000), the Institute of Food Technologists (IFT 2000), and the United Nations' Food and Agriculture Organization and World Health Organization (WHO 1990) have analyzed the oversight that is appropriate for gene-spliced organisms and arrived at remarkably congruent conclusions:

- The newer molecular techniques for genetic improvement are an extension, or refinement, of earlier, far less precise ones;
- Adding genes to plants or microorganisms does not necessarily make them less safe either to the environment or to eat;
- The risks associated with gene-spliced organisms are the same in kind as those associated with conventionally-modified organisms and unmodified ones; and
- Regulation should be based upon the risk-related characteristics of individual products, regardless of the techniques used in their development.

An authoritative 1989 analysis of the modern gene-splicing techniques published by the NAS's research arm, the National Research Council, concluded that "the same physical and biological laws govern the response of organisms modified by modern molecular and cellular methods and those produced by classical methods," but it went further, observing that gene-splicing is more precise, circumscribed, and predictable than other techniques:

> "Recombinant DNA methodology makes it possible to introduce pieces of DNA, consisting of either single or multiple genes, that can be defined in function and even in nucleotide sequence. With classical techniques of gene transfer, a variable number of genes can be transferred, the number depending on the mechanism of transfer; but predicting the precise number or the traits that have been transferred is difficult, and we cannot always predict the [characteristics] that will result. With organisms modified by molecular methods, we are in a better, if not perfect, position to predict the [characteristics]" (NRC 1989).

The same principles were emphasized in the comprehensive report by the United States National Biotechnology Policy Board, which was established by the Congress and comprised of representatives from the public and private sectors. The report concluded:

> "[t]he risks associated with biotechnology are not unique, and tend to be associated with particular products and their applications, not with the production process or the technology per se. In fact biotechnology processes tend to reduce risks because they are more precise and predictable. The health and environmental risks of not pursuing biotechnology-based solutions to the nation's problems are likely to be greater than the risks of going forward." (National Biotechnology Policy Board Report 1992) .

An analysis of food safety published in 2000 by the Institute of Food Technologists addressed

regulatory approaches to gene-spliced foods and specifically took current regulatory policies to task. The report concludes that the evaluation of gene-spliced food "does not require a fundamental change in established principles of food safety; nor does it require a different standard of safety, even though, in fact, more information and a higher standard of safety are being required." It went on to state unequivocally that theoretical considerations and empirical data do "not support more stringent safety standards than those that apply to conventional foods." (IFT 2000).

Yet, despite the broad consensus of the scientific community about the essential similarities of old and new methods for genetic improvement, and the importance of the new techniques to science and commerce, only recombinant DNA-modified organisms are, as a class, subjected to lengthy, mandatory premarket regulatory review. For gene-spliced plants, both the fact and degree of regulation are determined by the production methods – that is, the use of gene-splicing techniques, per se, triggers extraordinary premarket testing requirements for human health and environmental safety, regardless of the level of risk posed.

Dozens of new plant varieties produced through hybridization and other traditional methods of genetic improvement enter the marketplace and food supply each year without any scientific review or special labeling. Many such products are from "wide cross" hybridizations in which large numbers of genes – including even entire chromosomes or whole genomes -- are moved from one species or one genus to another, and incorporated randomly into the host genome, yielding a plant variety that does not and cannot exist in nature. Some "wide crosses" can be produced through ordinary sexual reproduction. Others are the result of in vitro techniques of protoplast fusion and embryo rescue, which overcome physical or genetic barriers to the development of fertile progeny. Many varieties of plants derived from wide crosses – which under any reasonable definition may be said to be "genetically engineered" or "genetically modified" -- are consumed widely and routinely in the United States, Europe and elsewhere; they include wheat, corn, rice, oat, tomato, potato, rice, pumpkin and black currant. As discussed in George Bruening's paper in this volume, still other novel plant varieties are produced with somaclonal variation techniques or by treating plant cells with radiation or chemicals to produce random genetic changes that give rise to new traits.

Although all of these breeding techniques have the potential to create unexpected agronomic, environmental or health effects, in most cases the products of the relatively imprecise "traditional" methods of genetic modification are subject to no governmental premarket regulation whatever. Consider, for example, the relatively new manmade "species" *Triticum agropyrotriticum*, which resulted from the combination of genes from bread wheat and a grass sometimes called quackgrass or couchgrass. Possessing all the chromosomes of wheat and one extra whole genome from the quackgrass, *T. agropyrotriticum* has been independently produced in the former Soviet Union, Canada, the United States, France, Germany, and China. It is grown for both animal feed and human food. At least in theory, several kinds of problems could result from such a genetic construction that introduces tens of thousands of foreign genes into an established plant variety. These include the potential for increased invasiveness of the plant in the field, and the possibility that quackgrass-derived proteins could be toxic or allergenic. But regulators have evinced no concern about these possibilities, and these plant varieties, which are

certainly "genetically modified," are not subject to review.

Another striking example of the inconsistency of government regulatory policy involves induced-mutation breeding, which has been in common use since the 1950s. The ionizing radiation and toxic chemicals used to induce random genetic mutations most often kill the plants (or seeds) or cause detrimental genetic changes. But on rare occasions, the result is a desirable mutation – for example, one producing a new trait in the plant that is agronomically useful, such as altered height, more seeds, or larger fruit. In these cases, breeders have no detailed knowledge of the nature of the genetic mutation(s) that produced the useful trait, or of what other mutations might have occurred in the plant **(IAEA** 2000). Yet the approximately 2,250 mutation-bred plant varieties from a range of different species that have been marketed over the last half century have been subject to no formal premarket regulation whatever, although several – including two varieties of squash and one each of potato and celery – were found to have dangerous levels of endogenous toxins and were banned from commerce.

Why are novel genetic constructions crafted with these older techniques exempt from regulation from the dirt to the dinner plate, from the turf to the tongue? Why don't regulatory regimes require new genetic variants made with older techniques to be evaluated for increased weediness or invasiveness, and for new allergens or toxins that could show up in food? The answer is based on millennia of experience with genetically-improved (but pre-gene-splicing) crop plants: Even the use of relatively crude and unpredictable genetic techniques for the improvement of crops and microorganisms poses minimal – but, as noted above, not zero – risk to human health and the environment. Plant breeders routinely use a number of well-established practices to identify and eliminate plants that exhibit unexpected adverse traits prior to commercial use, and there is widespread consensus that regulation need be no more stringent than post-marketing surveillance for any problems. And, echoing the quotations above from the 1989 National Research Council study, scientists agree that the same practices are appropriate and sufficient to ensure the safety of plants developed with recombinant **DNA** techniques.

Paradoxically, only the more precisely crafted, gene-spliced crops are exhaustively, repeatedly (and expensively) reviewed before they can enter the field or food supply. Throughout most of the world, gene-spliced crop plants, such as herbicide-tolerant soy and canola, and insect-resistant corn and cotton, are subject to lengthy, hugely **expensive** mandatory testing **and** premarket evaluation, while plants with similar properties but developed with older, less precise genetic techniques are exempt from such requirements. In the *T. agropyrotriticum* example above, the wheat variety containing tens of thousands of newly-introduced genes from a wild plant species not previously found within the food supply is subject to no governmental strictures or review at all when it is field tested or, ultimately, enters the food chain. However, if a single gene from couchgrass (or any other organism) were introduced into wheat by means of recombinant DNA techniques, the resulting variety would be subject to extraordinary, hugely expensive, redundant regulatory regimes.

This inconsistent approach to the introduction of new plant varieties violates both a fundamental principle of regulation – that the degree of regulatory scrutiny should be commensurate with risk – and the legal dictum that similar situations should be treated in similar ways. It is contradicted

by common sense, in that regulators have adopted an approach in which there is *inverse* proportionality between risk and the degree of scrutiny. Only the more precisely crafted and more predictable gene-spliced organisms are subjected to extensive and expensive testing and monitoring (and in some places, labeling) regimes. No traditional food derived from a "conventionally-modified" plant variety could pass such testing regimes, in the field or prior to entering the food supply.

What does this regulatory inconsistency mean in practice? If a student doing a school biology project takes a packet of "conventional" tomato or pea seeds to be irradiated at the local hospital x-ray suite and plants them in his backyard in order to investigate interesting mutants, he need not seek approval from any local, national or international authority. However, if the seeds have been modified by the addition of one or a few genes via gene-splicing techniques – even if the genetic change is merely to remove a gene – this would-be Mendel faces a mountain of bureaucratic paperwork and expense (to say nothing of the very real possibility of vandalism by anti-technology activists, because the site of the experiment must be publicized). The same applies, of course, to professional agricultural scientists in industry or academia.

In the United States, Department of Agriculture requirements for paperwork and field trial design make field trials with gene-spliced organisms 10-20 times more expensive than the same experiments with virtually identical organisms that have been modified with conventional genetic techniques (Miller 1997). By EPA's own radically conservative estimates, the regulatory costs of its Plant-Incorporated Protectants regulation will raise the average expense per "permit submission" for testing a new plant from $200,000 to $500,000 – a 150 per cent increase, only because the field trials employ a more precisely constructed and more predictable plant variety! Don Gordon, president of the Agricultural Council of California, has predicted that the EPA's regulatory approach will have profound impacts on companies' ability to perform R&D: "...research and development of 'plant pesticides' will continue; but, only a few very large companies will have the resources necessary to cope with this new and costly bureaucratic process" (Seibert 1997).

Agricultural economists have studied the spectrum of indirect, non-regulatory costs of segregation and identity preservation that are required when regulatory policies focus on recombinant DNA technology. Richard Maltsbarger and Nicholas Kalaitzandonakes at the University of Missouri-Columbia, for example, analyzed several case studies of segregation of high-oil corn and concluded that the sum of "coordination, segregation and opportunity costs" is in the range of 16 to 27 cents per bushel, an amount that is significant (Maltsbarger and Kalaitzandonakes 2000). Moreover, they note that the analyses were developed assuming a five percent allowable threshold of contamination from other varieties or hybrids, and that costs would be much higher if lower thresholds were mandated.

These kinds of regulation-related burdens will disproportionately affect California, which "has a heavy burden of existing and emerging plant pests, as well as the most diverse agricultural production system in the nation – involving more than 250, mainly minor-use-pesticide crops" (Seibert 1997).

Although the handful of large agribusiness companies involved in agricultural biotechnology have actually benefitted from such extensive and expensive regulatory regimes (*vide infra*) – buying up small competitors unable to endure inflated regulatory costs – academic researchers, the ultimate engine for innovation, have been among the most severely affected victims of excessive, ill-conceived regulation. Operating on small budgets, their ability to perform field trials of recombinant plants and microorganisms has been markedly restricted.

Some regulators remonstrate that such rules constitute a scientifically defensible regulatory algorithm that does indeed focus on such risk-related characteristics as weediness, pathogenicity, toxicity, and potential for outcrossing. And many of these rules might seem reasonable if considered narrowly – that is, if one ignores the flawed scope of what is encompassed by the oversight regime. But that scope – the inclusion of gene-spliced plants while excluding all others – is so flawed and inappropriate that it invalidates the approach.

Another similar example of an inappropriate choice of the scope of oversight invalidating an approach to regulation is the United Nations' recent attempt to ensure that potentially allergenic gene-spliced foods will be detected before consumers can be exposed to them. One of the theoretical concerns that has been raised about foods derived from gene-spliced plants is that consumers might experience allergic reactions to novel proteins, or to known allergens in an unexpected milieu (such as if a gene coding for a peanut protein were transferred to a potato). A panel of consultants to the United Nations' Food and Agriculture Organization and World Health Organization has proposed a protocol for the testing of such foods (FAO 2001). Intended to guide testing in order to determine the allergenic potential of gene-spliced foods, it poses questions – such as, is the source of the introduced gene allergenic, and does the gene product resemble known allergens – in a neat little flow chart.

Considered in a vacuum, it may seem to be a reasonable approach; the questions are scientific, after all, and the algorithm has a certain logic. However, it ignores the realities of the development and commercialization of new plant varieties, and the way that foods derived from them traditionally are regulated – or to be more precise, the way that they are unregulated. Consider the example of *Triticum agropyrotriticum* described above, in which a new manmade "species" was created by combining all the genes from both bread wheat and a wild grass species known as quackgrass.

Conceivably, such a genetic construction that introduces tens of thousands of foreign genes more or less at random into an established plant variety could pose a serious risk that novel proteins could be toxic or allergenic. But regulators have never shown concern about these risk-related issues, nor would new plants created in this way be subject to this new FAO/WHO proposal. Thus, although it might enjoy a patina of scientific respectability, the FAO/WHO allergenicity protocol is compromised by adopting a scope that simply makes no scientific sense. When asked why the consultants didn't remedy the inappropriate choice of scope, one of the experts on the panel responded candidly that although they were, of course, aware of the flaws, they were specifically directed by UN administrators not to address them.

If those crafting regulatory approaches to novel plant varieties were genuinely interested in

reducing risk, surely greater precaution would be appropriate not to gene-splicing but to the cruder, less precise, less predictable "conventional" forms of genetic modification. Instead, regulators have chosen to set the burden of proof far higher for gene-splicing technology than for conventional plant breeding. This regulatory approach is inconsistent with the scientific consensus about the risks associated with gene-spliced organisms, and it misallocates regulators' resources. **A** more scientifically defensible, rational approach is necessary if regulators are to achieve the dual goals of reducing overall product risk and efficiently allocating public resources.

THE DANGER OF PRECAUTION

All technologies pose potential risk. In order to reduce net risks most effectively, the degree of regulatory scrutiny applied to individual products should be commensurate with the degree and type of risk being addressed. For example, different innovations in automobile design can (and should) elicit highly disparate regulatory responses: the new electric/internal combustion engine hybrid cars can be regulated in much the same way as conventional vehicles, but a nuclear-powered car with a plutonium-containing reactor would need to be approached quite differently.

The fundamental flaw in precautionary-style regulation is that it too narrowly focuses on the risk of innovation, while ignoring the impact of the *absence* of innovation. This distorted approach to risk distracts consumers and policymakers from many known, significant threats to human health and diverts limited public health resources from those genuine and far greater risks. Consider, for example, the environmental movement's misguided crusade to rid society of all chlorinated compounds.

By the late 1980s, environmental activists were attempting to convince water authorities around the world of the possibility that carcinogenic byproducts from chlorination of drinking water posed a potential cancer risk. Peruvian officials, caught in a budget crisis, used this supposed threat to public health as a justification to stop chlorinating much of their country's drinking water. That decision contributed to the acceleration and spread of Latin America's 1991 to 1996 cholera epidemic, which afflicted more than 1.3 million people and killed at least 11,000 (Anderson 1991).

Activists have since extended their anti-chlorine campaign to so-called "endocrine disrupters," or "endocrine modulators," asserting that certain manmade chemicals mimic or interfere with human hormones (especially estrogens) in the body and thereby cause a range of abnormalities and diseases related to the endocrine system.

It is well documented that the demonstration that a chemical administered at high doses causes cancer in certain laboratory animals does not prove that it can cause cancer in humans under normal circumstances – both because of different susceptibilities and because humans are ordinarily subjected to far lower exposures to synthetic environmental chemicals. The American Council on Science and Health and others have explored the endocrine disrupter hypothesis and found that, while high doses of certain environmental contaminants produce toxic effects in laboratory test animals – in some cases involving the endocrine system – humans' actual

exposure to these suspected endocrine modulators is many orders of magnitude lower. No consistent, convincing association has been demonstrated between real-world exposures to synthetic chemicals in the environment and increased cancer in hormonally-sensitive human tissues (ACSH 1999).

Moreover, humans are routinely exposed through their diet to many estrogenic substances (substances that have an effect similar to that of the human hormone estrogen) found in many plants. Dietary exposures to these plant estrogens, or phytoestrogens, are far greater than exposures to supposed synthetic endocrine modulators, and no adverse health effects have been associated with the overwhelming majority of these dietary exposures.

Furthermore, there is currently a trend toward lower concentrations of many contaminants in air, water, and soil – including several that are suspected of being endocrine disrupters. Some of the key research findings that stimulated the endocrine disrupter hypothesis originally have been retracted or are not reproducible. The available human epidemiological data show no consistent, convincing evidence of negative health effects related to industrial chemicals that are suspected of disrupting endocrine systems. In spite of that, activists and many government regulators continue to invoke the need for precautionary (over-) regulation, and even outright bans, of various products.

Anti-chlorine campaigners more recently have turned their attacks to phthalates, liquid organic compounds added to certain plastics to make them softer. These soft plastics are used for important medical devices, particularly fluid containers, blood bags, tubing and gloves; children's toys such as teething rings and rattlers; and household and industrial items such as wire coating and flooring. Again invoking the precautionary principle, activists claim that phthalates might have numerous adverse health effects – even in the face of significant scientific evidence to the contrary. Some governments have taken these unsupported claims seriously, and several formal and informal bans have been implemented around the world. Whole industries have been terrorized, consumers denied product choices, and doctors and their patients deprived of lifesaving tools.

Biased ***Decision-Making***

The European Union is a prominent advocate and practitioner of the precautionary principle, particularly with respect to gene-splicing, incorporating it explicitly into various regulations, standards and agreements. In the United States, where the precautionary principle is thought of (if it is thought of at all) as a concept advocated by the radical environmental movement and used by national regulators as political cover for trade barriers, regulatory agencies have not incorporated that precise term of art into law or official policies. That does not prevent many US regulatory agencies from commonly practicing excessively precautionary regulation, however, and the regulation of such products as pharmaceuticals, food additives, synthetic pesticides and other chemicals, and gene-spliced plants and microorganisms, is without question "precautionary" in nature. The primary distinctions between precautionary regulation in the United States and the use of the precautionary principle in Europe are degree, areas of application (reflecting diverse prejudices about certain products, technologies, and

activities), and semantics.

The precautionary principle can distort the process of selecting a regulatory approach for a new technology or product by amplifying a systematic bias that exists normally in regulatory decision-making. Regulators routinely face an intrinsically asymmetrical incentive structure in which they are compelled to address the potential harms from new activities or products, but are free to discount the hidden risk-reducing properties of unused or under-used ones. The result is a lopsided decision-making process that is inherently biased against change and therefore against innovation.

This asymmetry arises from the fact that there are two basic kinds of mistaken decisions that a regulator can make. First, a harmful product can be approved for marketing – called a Type I error in the parlance of risk analysis. Second, a product potentially beneficial to society may be rejected or delayed, can fail to achieve marketing approval at all, or may be inappropriately withdrawn from the market – a Type II error. In other words, a regulator commits a Type I error by permitting something harmful to happen, and a Type II error by preventing something salutary from becoming available. Both situations have negative consequences for the public, but the outcomes for the regulator are very different.

Examples of this Type I-Type II error dichotomy abound in both the US and Europe, but it is perhaps illustrated most clearly in FDA's new drug approval process. A classic illustration is the FDA's approval in 1976 of the swine flu vaccine – generally perceived as a Type I error because, although the vaccine was effective at preventing influenza, it had a major side effect that was unknown at the time of approval. A small number of patients suffered temporary paralysis from Guillain-Barré Syndrome. This kind of mistake is highly visible and has immediate consequences: Regulators are the focus of criticism from the media, self-styled public-interest groups and the Congress. Because regulatory officials' careers might be damaged irreparably by the good-faith but mistaken approval of a high-profile product, their decisions are often made defensively – in other words, to avoid Type I errors at any cost.

Former FDA Commissioner Alexander Schmidt aptly described the regulator's plight:

> "In all our FDA history, we are unable to find a single instance where a Congressional committee investigated the failure of FDA to approve a new drug. But, the times when hearings have been held to criticize our approval of a new drug have been so frequent that we have not been able to count them. The message to FDA staff could not be clearer. Whenever a controversy of a new drug is resolved by approval of the drug, the agency and the individuals involved likely will be investigated. Whenever such a drug is disapproved, no inquiry will be made. The Congressional pressure for negative action is, therefore, intense. And it seems to be ever increasing" (Schmidt 1974).

Type II errors in the form of excessive governmental requirements and unreasonable decisions can cause a new product to be "disapproved," in Schmidt's phrase, or the approval to be delayed. Unpredictable, arbitrary delays in getting products to market are a source of "financial risk," and are, therefore, anathema to innovators. These delays discourage research and development,

lessen competition, inflate the ultimate price of the product, and diminish the number of products that get to market.

Consider, for example, the FDA's precipitate response to the 1999 death of a patient in a University of Pennsylvania gene therapy trial for a genetic disease. The cause of the incident had not been identified and the product class (a preparation of the needed gene, encased in a viral delivery system, that would be administered to the patient) had been used in a large number of patients with no fatalities and serious side effects in only a few percent of patients. Nevertheless, apparently wanting to be perceived as reacting vigorously to a Type I error, regulators halted not only the trial in which the fatality occurred, but all the other gene-therapy studies at the same university, and similar studies at other universities and in industry. By these actions, by publicly excoriating and humiliating the researchers involved, and by imposing new reporting and monitoring requirements on all gene therapy investigations, the FDA has dampened enthusiasm for the entire field of gene therapy, among both investigators and venture capitalists.

Although Type II errors can dramatically compromise public health, they seldom gain public attention. Often, only the employees of the company that makes the product and a few stock market analysts and investors are knowledgeable about unnecessary delays. And if the regulator's excessive risk-aversion precipitates a corporate decision to abandon the product, cause and effect are seldom connected in the public mind. Naturally, the companies themselves are loath to complain publicly about a mistaken FDA judgment, because the agency has so much discretionary control over their ability to test and market products. As a consequence, there may be no direct evidence of, or publicity about, the lost societal benefits and the culpability of regulatory officials.

Exceptions exist, of course. A few activists, such as the well-organized AIDS advocacy groups that closely monitor the FDA, scrutinize agency review of certain products and aggressively publicize Type II errors. Congressional oversight should provide another critical check on regulators' performance, but as noted above by former FDA Commissioner Schmidt, only rarely does it focus on Type II errors. Type I errors make for better Capitol Hill theater, after all, with patients who have been injured, and their family members, prominently featured. And even when such mistakes are exposed, regulators frequently defend Type II errors as erring on the side of caution – in effect, invoking the precautionary principle – as they did in the wake of the University of Pennsylvania gene therapy case. Legislators, the media, and the public too often accept this euphemism uncritically, and our system of pharmaceutical oversight becomes progressively less responsive to the public interest.

The FDA is not unique in this regard, of course. All regulatory agencies are subject to the same sorts of social and political tensions that cause them to be castigated when hazardous products make it to market (even if those products produce net benefits), but to escape blame when they keep beneficial products from being available to consumers. Adding the precautionary principle's bias against new products into the public policy mix further encourages regulators to make Type II errors in their eagerness to avoid Type I errors.

For regulators of gene-spliced plants, assessing the risk portion of the risk-benefit calculation is

easy, because both theory and empirical evidence indicate that the risks of the techniques, per se, are negligible. What one is left with, then, is essentially the intrinsic risk of the host plant – with which there is generally considerable experience – taking into consideration any newly-added traits. But leaving aside the risk, the benefit – or, alternatively, the risk-reducing – portion of the calculation has seemingly been ignored, as noted above a common failure of precautionary regulation. For example, some of the most successful of the gene-spliced crops, especially cotton and corn, have been constructed by splicing in a bacterial gene that produces a protein toxic to predatory insects, but not to people or other mammals. Not only do these gene-spliced corn varieties repel pests, but grain obtained from them is less likely to contain *Fusarium,* a toxic fungus often carried into the plants by the insects. That, in turn, significantly reduces the levels of the fungal toxin fumonisin, which is known to cause fatal diseases in horses and swine that eat infected corn, and esophageal cancer in humans. When harvested, these gene-spliced varieties of grain also end up with lower concentrations of insect parts than conventional varieties. Thus, gene-spliced corn is not only cheaper to produce but is more esthetically acceptable and a potential boon to public health. Moreover, by reducing the need for spraying chemical pesticides on crops, it is environmentally and occupationally friendly.

Other products offer agronomic, nutritional and environmental advantages. Gene-spliced herbicide-resistant crops have permitted farmers to adopt more environment-friendly no-till farming practices. Crops now in development with improved yields would allow more food to be grown with less water and on less acreage, conserving more land area for wildlife or other uses. Genes have been isolated that enable plants to resist soil salinization, which lowers yields; and to hyperaccumulate heavy metals when grown in toxic waste sites. And recently developed plant varieties with enhanced vitamins, minerals, and dietary proteins can dramatically improve the health of hundreds of millions of the malnourished populations of less developed countries.

These are the kinds of tangible environmental and health benefits that invariably are given Iittle or no weight in precautionary risk calculations. But it should be emphasized that even in the absence of such monumental benefits, both potential and current, regulators' estimation of risk in the risk/benefit calculation is far from what scientific consensus would dictate.

Wealthier Is Healthier

In addition to the direct negative societal impacts caused by the loss of beneficial products, government over-regulation implemented in the name of the precautionary principle poses some indirect and subtle perils. Money spent on implementing and complying with regulation (justified or not) exerts an "income effect" that reflects the correlation between wealth and health, an issue popularized by the late political scientist Aaron Wildavsky. It is no coincidence, he argued, that richer societies have lower mortality rates than poorer ones.

Wealthier individuals are able to purchase better health care, enjoy more nutritious diets, and lead generally less stressful lives. Conversely, the deprivation of income itself has adverse health effects, including an increased incidence of stress-related problems, including ulcers, hypertension, heart attacks, depression and suicides. To deprive communities of wealth, therefore, is to enhance their risks.

It is difficult to quantify precisely the relationship between the deprivation of income and mortality, but academic studies suggest, as a conservative estimate, that every $7.25 million of regulatory costs will induce one additional fatality through this "income effect" (Keeney 1990). The excess costs in the tens of billions of dollars required annually by precautionary regulation for various classes of consumer products would, therefore, be expected to cause thousands of deaths per year. Arguably, all the regulations and policies, the new boxes on the organization charts, boards and panels, data bases, websites, newsletters, studies and reports (including this one) that impose costs on the public and private sector all exert this income effect. These are the real costs of "erring on the side of safety," which amount to what John Graham, the head of the regulatory office in the Bush administration's Office of Management and Budget, has referred to as "statistical murder." The expression "regulatory overkill," thus, may not be not empty rhetoric.

Instead of precautionary regulation, Wildavsky advocates a strategy of "resilience," in which society accumulates knowledge about risks in a process of trial and error. Research, development, and marketing of new products should be encouraged, and regulators permitted to restrict such activities only upon a showing of bona fide evidence of potential harm, not mere speculation or pseudo-controversy generated by vocal activists. Such a strategy allows society to take maximum advantage of the risk-reducing benefits of new technologies, while building the resources necessary to cope with the inevitable harms that result both from the unanticipated risks of new products and from the risks posed by the absence of beneficial technologies. In other words, risk-taking, not risk avoidance, improves overall safety and health (Wildavsky 1991).

Legal Uncertainty

During the last few years, skeptics have begun more vigorously to question the theory and practice of the precautionary principle. In response to those challenges, the European Commission (EC), a prominent user and abuser of the precautionary principle, in 2000 published a formal communication to clarify and to promote the legitimacy of the concept. The EC resolved that, under its auspices, precautionary restrictions would be "proportional to the chosen level of protection," "nondiscriminatory in their application," and "consistent with other similar measures." The Commission also avowed that EC decision-makers would carefully weigh "potential benefits and costs" (EC 2000). The Commission's Health Commissioner, David Byrne, repeated all of these points in an article on food and agriculture regulation in the journal *European **Affairs.*** In it, he asked rhetorically, "How could a Commissioner for Health and Consumer Protection reject or ignore well founded, independent scientific advice in relation to food safety?" (Byrne 2000).

Byrne himself should be able to tell us: The ongoing dispute between his European Commission and the United States and Canada over restrictions on hormone-treated beef cattle is exactly such a case. The EC argued that the precautionary principle permits restriction of imports of US and Canadian beef from cattle treated with certain growth hormones. **A** scientific committee assembled by the WTO dispute resolution panel found that even the scientific studies cited by the EC in its own defense did not indicate a safety risk when the hormones in question were used

in accordance with accepted animal husbandry practices (WTO 1998). Thus, the WTO ruled in favor of the US and Canada because the scientific evidence clearly favored their position. Nevertheless, the EC continues to enforce restrictions on hormone treated beef, a blatantly unscientific policy that belies the Commission's protestations that the precautionary principle will not be abused.

The European Commission and individual countries of Europe have long applied the precautionary principle to the regulation of the products of recombinant DNA technology, or gene-splicing. By the early 1990s, many of the countries in Western Europe, as well as the EC itself, had erected unscientific and unnecessarily strict rules regarding the testing and commercialization of gene-spliced crop plants. In 1999, the Commission explicitly invoked the precautionary principle in establishing a moratorium on the approval of all new gene-spliced crop varieties, pending approval of an even more strict EU-wide regulation.

Notwithstanding the EC's promises that the precautionary principle would not be abused, all of the stipulations enumerated by the Commission have been ignored or reinterpreted in its regulatory approach to gene-spliced (or in their argot, "genetically modified" or "GM") foods. Rules for gene-spliced plants and microorganisms are inconsistent, discriminatory, and bear no proportionality to risk.

The European Commission's abuses demonstrate that clarifications and promises are of little use in the absence of an enforceable commitment to act in a rational, responsible way. Remarkably, although the European Commission characterized its 2000 communication on the precautionary principle as an attempt to impart greater consistency and clarity, it specifically declined to define the principle, adding naively, "it would be wrong to conclude that the absence of a definition has to lead to legal uncertainty." Although reliance on regulatory agencies and courts to define and elaborate statutory policy is not unusual, this failure to define what purports to be a fundamental principle makes confusion inevitable; it leaves innovators' legal rights and regulators' legal obligations hostage to the subjective judgment of governments or individual regulators (or, perhaps, even trade officials or other politicians).

As it is being applied, the precautionary principle seldom provides either evidentiary standards for "safety" or procedural criteria for obtaining regulatory approval, no matter how much evidence has been accumulated. In effect, regulators are given carte blanche to decide what is "unsafe" and what is "safe enough," with no means to ensure that their decisions actually reduce overall risk or that they make any sense at all. The precautionary principle tends to make governments less accountable because its lack of definition allows regulators to justify any decision.

Ultimately, such legal uncertainty poses very real societal costs. Not only are consumers denied the opportunity to use beneficial new products, but the high cost of arbitrary and lengthy regulatory reviews can discourage smaller companies and academic researchers from proceeding with products that are expected to be of marginal profitability (or that "merely" offer the possibility of information of purely scientific information). Furthermore, the cost of excess regulation will also be reflected in the market prices of those products that do eventually make it

to market. In effect, ill-conceived regulation imposes upon them a punitive tax. And in the case of recombinant DNA technology and gene-spliced plants, this penalty can be quite substantial.

Finally, as pointed out by law professor Drew L. Kershen (Kershen 2001), another completely different kind of risk must be considered: potential legal liability to food-producing companies that attempt to make their products "gene-splicing-free." In response to some of the various pseudo-controversies that have engulfed gene-spliced crops and foods, many food companies have considered avoiding gene-spliced crops altogether in their feed or food supplies, and several have actually done so. Kershen cites the example of Gerber, which in 1999 announced that its baby food products would no longer contain any gene-spliced ingredients, and that it would attempt to shift to organic crops that are grown without synthetic pesticides or fertilizers. However, these crops generally contain higher levels of mycotoxins, which cause illness and death in animals and cancer in humans, than either conventional or gene-spliced crops. Kershen argues that such a strategy, therefore, creates the potential for claims of liability from damage (cancer) by consumers. Under a claim of strict products liability, Kershen says they could allege a manufacturing defect based on contamination in the baby food, and also a *design* defect, "because Gerber knew of a baby food designed (made) with less risky ingredients [but] purposefully chose to use the riskier design – i.e. Gerber chose to use non-GMO ingredients knowing that these have a higher risk of mycotoxin contamination."

Kershen cites violation of environmental regulations as another legal risk to food producers who choose systematically to reject gene-spliced crops. He describes that under pressure from fast-food companies such as McDonald's and Wendy's, potato grower J.R. Simplot and potato-processors have imposed requirements on farmers not to use any gene-spliced plants, and that by doing so, potato processors "are putting themselves at legal risk of being held accountable for their growers' environmental [non-]compliance." This risk arises from the fact that through "technology-forcing" regulations, EPA often intentionally imposes over-stringent regulatory standards for pesticides, on the theory that companies will be forced to invest in research and development that will provide innovative ways to meet the standard. Thus, potato growers who have difficulty meeting these standards could "argue to the EPA that their potato processors have contractually forced them to use more pesticides than necessary by requiring non-GMO varieties of potatoes," instead of EPA-approved gene-spliced crops that do not require chemical pesticides.

ALTERNATIVES TO "PRECAUTIONARY" REGULATION

As discussed above, precautionary-style regulation fails to protect public health or the environment because it over-emphasizes the risks of the testing and use of new processes and products, while it ignores possible net reductions of risk; thereby, it diverts attention and resources from potentially greater harms that may result from forgoing beneficial new technologies. In order more effectively to reduce the overall risks of agricultural practices and to enhance food safety, the regulation of new plant varieties should focus on, and be triggered by, the risk-related characteristics of new products, not on the techniques used in creating them. Below, we discuss an approach to regulation that is, in contrast to the precautionary principle, scientifically defensible and risk-based, that links the degree of oversight with the degree of risk,

and that is sufficiently flexible to be adaptable to various views of regulation.

Plants in the Field

Several years ago, the Stanford Project on Regulation of Agricultural Introductions developed a widely applicable regulatory model for the field testing of any organism, whatever the method(s) employed in its construction. By enabling accurate, scientific determinations of the risks posed by the introduction of any type of organism into the field, this regulatory model enables governments to promote enhanced agricultural productivity and innovation, while protecting valuable ecosystems. It offers regulatory bodies a highly adaptable, scientific method for field-testing potential agricultural crops or other organisms. The approach is widely applicable whether the introduced organisms are "naturally" occurring, non-indigenous "exotics," or have been genetically improved by either old or new techniques. It offers an easily adaptable route to comprehensive, cost-effective regulation, thereby benefitting academic and industrial researchers, as well as government regulators.

In January 1997, the project assembled a group of approximately 20 agricultural scientists from five nations at a workshop held at the International Rice Research Institute (IRRI), Los Baños, Philippines (Barton, Crandon, Kennedy, and Miller 1997). The purpose of the IRRI Conference was to seek consensus on a broad, science-based approach that would evaluate all biological introductions, not just the introduction of gene-spliced organisms. There was already abundant evidence that severe ecological risks can be associated with "exotics," or, in a more descriptive term we prefer, non-coevolved organisms (NCOs).

As part of the pilot project, the IRRI Conference participants initially selected the particular crops to be evaluated, or stratified, and then enumerated the risk-related characteristics, or traits, to be considered in order to estimate overall risk. Organisms to be included in the stratification were selected to ensure that the final list would be diverse as to the type of crop, economic significance, and complexity of risk analysis. The stratification process required the group to reach consensus about the weighting of various factors that determine risk. Consensus was reached without serious difficulty on the most important factors. The participants agreed upon the following list of risk-based factors that would be integral to a model algorithm for field-testing and commercial approval of all introductions:

- Ability to colonize
- Ecological relationships
- Human effects
- Potential for genetic change
- Ease/difficulty of risk-management

Each organism was assessed for all five factors, which enabled the group to come to a global

judgment about the organism's risk category. Most of the common crop plants addressed were found to belong in negligible-risk Category 1, while some organisms were ranked in low but non-negligible-risk Category 2. One plant (cotton) was judged to be in Category 1 if it were field tested outside its center of origin, and Category 2 if tested within its center of origin.

It cannot be over-emphasized that in the evolution of this "Stanford Model," the factors taken into account in the analysis were indifferent to either the genetic modification techniques employed, if any (e.g., conventional breeding techniques vs molecular methods of manipulation); or to the source(s) of the cultivar's genetic material (e.g., combining DNAs from phylogenetically distant organisms).

In other words, the group's analysis supported the position that the risks associated with field testing a genetically altered organism are independent of the process by which it was modified and of the movement of genetic material between "unrelated" organisms. The Stanford Model suggests the utility and practicality of an approach in which the degree of regulatory scrutiny over field trials is commensurate with the risks – independent of whether the organisms introduced are "natural," exotics, or have been genetically improved by conventional methods or modified by gene-splicing techniques.

Regulators' treatment of field trials within the various categories could range from complete exemption or a simple "postcard notification" to a regulatory authority, to case-by-case review, or even prohibition (such as experiments currently with Food and Mouth Disease Virus in the United States). Different national regulatory authorities might choose different regulatory requirements for the various risk categories; as discussed in the original paper (Barton, Crandon, Kennedy, and Miller 1997), the model is sufficiently flexible that the stringency of regulation may vary widely, according to the preferences and needs of particular regulatory authorities – but always within a scientific framework. Under such a system, some currently unregulated introductions of traditionally-bred cultivars and exotics considered to be of moderate or greater risk would likely become subject to review, whereas many currently reviewed gene-spliced organisms would likely become exempt. The introduction of such a risk-based system would rationalize significantly the regulation of field trials, and would reduce the regulatory disincentives that currently impede the use of in vitro genetic manipulation technologies for the benefit of agricultural development.

Plants in the Food Supply

In 1992, the Food and Drug Administration published a notice in the *Federal Register* describing its official policy regarding foods derived from new plant varieties (FDA 1992). This document, intended to clarify FDA's position on the regulation of recombinant DNA technology and gene-spliced plants, explained that the "regulatory status of a food, irrespective of the method by which it is developed, is dependent upon objective characteristics of the food and the intended use." The policy reminded plant breeders and food producers that they had "an obligation under the [Federal Food, Drug and Cosmetics Act] to ensure that the foods they offer to consumers are safe and in compliance with applicable legal requirements." However, it treated gene-spliced and other foods no differently, and required scrutiny by regulators only when the products raised

specific safety concerns. Thus, the agency's approach was consistent with the consensus of the scientific community regarding the regulation of gene-spliced products. This approach was widely applauded as regulation that made sense, relied on scientific principles, protected consumers, and permitted innovation.

To guide developers of new plants how to satisfy regulatory requirements, the FDA policy defined certain potentially hazardous characteristics of new foods that, if present, required greater scrutiny by the agency, and which could result in additional testing and labeling, or exclusion from commerce. In other words, characteristics related to risk – not simply to the use of one technique or another – would trigger heightened regulatory scrutiny. According to the FDA's 1992 announcement, such characteristics include the introduction of genes that code for proteins (or mediate the synthesis of other added substances, such as fatty acids and carbohydrates) that differ substantially in structure or function from other substances typically found in the food supply. Heightened scrutiny by regulators would also be required if the genetic change altered a macronutrient (such as a new variety of citrus lacking vitamin C), caused a potent allergen to be presented in a milieu in which a consumer would not expect it (a peanut allergen in a potato, for example), or enhanced levels of a natural toxicant.

Thus, the FDA's 1992 policy appeared to codify a risk-based approach to the oversight of new plant varieties. However, at the same time, and without the benefit of rule-making or formal notification to industry, the agency created a "voluntary consultation procedure," in which producers of gene-spliced plants were expected to consult with the agency before marketing their products. Without exception they did so. Currently, thousands of food products in US supermarkets contain gene-spliced whole foods or ingredients that have been regulated under the FDA's formal 1992 policy and informal consultation procedure. None has ever been shown to cause harm to human health.

In January 2001 the agency proposed to make mandatory the voluntary consultation procedure. If issued as a final rule, this would require developers of new plant varieties prepared with gene-splicing techniques – but virtually no others – to notify the FDA and supply large amounts of information before the plants could be marketed (FDA 2001). The data requirements of the new policy are excessive, and the review process subjects food producers to the political and bureaucratic vagaries of the federal review process (Miller 1998). The FDA lists nine categories of obligatory information whose level of detail is far greater than would be required (or could possibly be met) for food products made with less precise, less sophisticated techniques. Consider the example of *Triticum agropyrotriticum* described above, a non-gene-spliced "species" created by combining all the genes from bread wheat and a wild grass called quackgrass. New genetic constructions such as this are, as a class, exempt from all premarket regulation, while new gene-spliced varieties are, as a class, subjected to a ***de facto*** premarket approval requirement.

The reversal of the FDA's scientific and risk-based approach to food regulation and the abandonment of a twenty-year old commitment not to discriminate against gene-spliced products is unfortunate. The result will be, in the long-term, reduced use of a promising technology, diminished choices for farmers and consumers, higher food prices, and lower overall food safety.

California, an important agricultural state but one that does not grow significant amounts of commodity grain crops – which have been the primary focus for gene-splicing improvements by big agribusiness companies – will disproportionately bear the burden of these limitations; in other words, regulation makes the application of gene-splicing techniques too expensive to be used widely on the fruits, nuts and vegetables widely grown in California.

FDA explained its 2001 decision to change policy in part by the expectation that many future gene-spliced plant varieties could contain substances that are not known to have been previously present in the food supply. Even if this were the case, however, such eventualities were foreseen under the official 1992 policy, and they would elicit agency review. It is the consensus of the scientific and professional communities that the FDA could address recombinant DNA-modified plants generally within its existing rules and require premarket notice, consultation or review only for those specific new plant varieties that raise risk-related concerns. This would represent a more constructive approach to the regulation of new plant varieties, one that would not punish or discourage innovation.

In summary, regulation should focus on real risks and should not be triggered by the use of one technique or another. This approach has provided effective oversight for thousands of new biotechnology products, including foods, drugs, vaccines and diagnostic tests. There was no reason – except politics – to make, or even to consider, such a change. The erstwhile, risk-based FDA policy toward gene-spliced and other novel foods had worked admirably. It involved the government only in those extraordinarily rare instances when products raised safety issues. The result was eight years of unprecedented opportunity for farmers, food producers, and consumers.

Public Attitudes Regarding Regulation

Representatives of the biotechnology industry have played an important role in the development of this excessively precautionary regulatory system – but it has not been a positive one. In the late 1980s and early 1990s, when the US Department of Agriculture, Environmental Protection Agency, and Food and Drug Administration were considering their options for the oversight of the products of recombinant DNA technology, industry representatives actually requested heightened regulatory scrutiny for gene-spliced agricultural and food products, ostensibly in order to bolster public confidence in gene-spliced foods. (However, there was virtually no public resistance at that time, and industry leaders admitted privately that excessive regulatory requirements were a strategy to create market-entry barriers to competitors' performing research and development.) In spite of two decades of excessive, precautionary regulation by federal agencies having been accompanied by ever-increasing public concerns and resistance about gene-spliced food, the industry lobbied in favor of the most recent change in FDA policy.

Although efforts should be made to reassure the public that gene-splicing techniques are in fact safer than more "traditional" methods of genetic modification, excessive regulation is not an appropriate way to do so. The application of an intentionally excessive degree of government regulation to quell public apprehension – a rationale invoked by FDA for its new policy – is neither a legitimate use of government power, nor likely, ultimately, to reassure consumers. As

the president of a national consumer organization testified to a panel convened by the National Institutes of Health (NIH):

> "For obvious reasons, the consumer views the technologies that are *most* regulated to be the *least* safe ones. Heavy involvement by government, no matter how well intended, inevitably sends the wrong signals. Rather than ensuring confidence, it raises suspicion and doubt" (emphasis in original, Keating-Edh 1992).

The NIH panel agreed, concluding, "Intense government oversight tends to confirm public perceptions that biotechnology processes pose significant and unique dangers that should be feared" (National Biotechnology Policy Board Report 1992).

Societal oversight of risks is complex, to be sure, but when crafting regulatory approaches to mitigate them, regulators and legislators should be guided primarily by science, economics, law, and a respect for Constitutional rights, not by government's perceptions of public perceptions, which are mercurial and doubly subject to error and misinterpretation.

Several subjective factors can cloud thinking about risks and influence how non-experts view them. Studies of risk perception have shown that people tend to overestimate risks that are unfamiliar, hard to understand, invisible, involuntary, and/or potentially catastrophic – and vice versa. Thus, they overestimate "threats" they cannot readily see, such as electromagnetic radiation and trace amounts of pesticides in foods, with a degree of uncertainty and fear sometimes verging on superstition. Conversely, they tend to underestimate risks whose nature they consider to be clear and comprehensible, such as using a chain saw or riding a motorcycle.

These distorted perceptions complicate the regulation of risk, for if democracy must eventually take public opinion into account, good government must also discount heuristic errors or prejudices. Edmund Burke emphasized government's pivotal role in making such judgments: "Your Representative owes you, not only his industry, but his judgment; and he betrays, instead of serving you, if he sacrifices it to your opinion." Government leaders should ***lead,*** by making decisions that are rational and in the public interest even if they are unpopular at the time. This is especially true if, as is the case for most federal and state regulators, they are granted what amounts to lifetime job tenure in order to shield them from political manipulation or retaliation. In the area of biotechnology regulation, as discussed above, regulators have failed Burke's test of earning the public trust.

CONCLUSIONS

History offers compelling reasons to be cautious about societal risks, to be sure. These include the risk of incorrectly assuming the absence of danger (false negatives), overlooking low probability but high impact events in risk assessments, the danger of long latency periods before problems become apparent, and the lack of useful remediation opportunities in the event of an adverse event. Conversely, there are compelling reasons to be wary of excessive precaution, including the risk of too readily detecting a non-existent danger (false positives), the financial cost of testing for or remediating low-risk problems, the opportunity costs of forgoing net-

beneficial activities, and the availability of a contingency regime in the event of adverse events. The challenge for regulators is to balance these competing factors in a way that reduces overall harm to public health. This kind of risk balancing is often conspicuously absent from precautionary regulation, of which there are few more conspicuous examples than oversight of recombinant DNA technology.

It is also important that regulators take into consideration the ambient level of restraint generally imposed by society on individuals' and companies' freedom to perform legitimate activities such as scientific research. In the Western democratic societies, we enjoy long traditions of relatively unfettered scientific research and development, except in the very few cases where bona fide safety issues are raised. Traditionally, we shrink from permitting small, authoritarian minorities to dictate our social agenda, including what kinds of research are permissible and which technologies and products should be available in the marketplace.

Application of the precautionary principle in a number of areas has resulted in unscientific, discriminatory policies that inflate the costs of research, inhibit the development of new products, divert and waste public- and private-sector resources, and restrict consumer choice. The excessive, discriminatory and poorly conceived regulation of recombinant DNA technology applied to agriculture and food production is a prominent example. Further encroachment of the precautionary principle into this and other areas of domestic and international health and safety standards will create a kind of "open sesame" that government officials could invoke fearlessly whenever they wished arbitrarily to introduce new barriers to trade, or simply to yield to the vocal demands of a radical, anti-technology constituency.

The controversies over gene-splicing applied to agriculture and food production are, for the most part, pseudo-controversies. The science is clear. The public policy implications of continuing to apply flawed regulatory paradigms are clear. The appropriate approaches to regulatory oversight are clear: Risk-based approaches to oversight are available. All that is uncertain is whether we will find the political will to go where science, common sense and the public interest dictate.

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RISK ASSESSMENT

The protocol's illusionary principle

Henry I. Miller and Gregory Conko

In an editorial last month, this journal pointed out that the biosafety protocol recently completed in Montreal "violates a cardinal principal of regulation — namely, that the degree of scrutiny should be commensurate with risk." We think it important to examine in a bit more detail the antiscientific, if nonetheless increasingly popular, basis on which this deeply flawed protocol was conceived.

The protocol is founded on a "precautionary approach" to regulation, as described in the 1992 Rio Declaration on Environment and Development: ". . .lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation." The precautionary approach and precautionary principle are neologisms coined by opponents of technology who wish to rationalize banning things they don't like, such as gene splicing, cellular phones, oil exploration, and carbon dioxide emissions. This bogus "principle" dictates that every new technology must be *proven* safe before it can be used. An ounce of prevention is certainly desirable, but because nothing can be proved totally safe—at least, not to the standard demanded by antitechnology extremists—the precautionary principle creates prodigious obstacles to the development of new products.

Consider, for example, that bizarre speculations by activists about weather patterns being altered by a frost damage-mitigating "ice minus" *Pseudomonas syringae* bacterium once caused the US Environmental Protection Agency (EPA; Washington, DC) to delay approving a small-scale field trial of the microorganism. Precaution, in this sense, shifts the burden of proof from the regulator, who once had to demonstrate that a new technology was likely to cause some harm, to the innovator, who now must demonstrate that the technology will not. Regulatory bodies are free to arbitrarily require any amount and kind of testing they wish. Perhaps the finest — and certainly the most significant — post-Montreal example of the arbiti-ary and capricious application of the precautionary principle to agbiotech was the decision by the German government in February to block the commercial-scale cultivation of Ht-corn by the biotechnology company Novartis. This action came one day before it was expected to be approved for commercaial use by the Ministry of Agriculture, which specifically cited the need to respect the precautionary principle and called for more research into the crop plant's potential hazards.

Thus, rather than creating a uniform, predictable, and scientifically sound framework for effectively managing legitimate risks, the biosafety protocol establishes an ill-defined global regulatory process that permits overly risk-averse regulators to hide behind the precautionary principle in delaying or deferring approvals. Witness the regulatory feeding frenzy spawned by unscientific approaches to biotechnology regulation in Europe and at the US EPA. The result has been the virtual disappearance of gene-spliced foods from the shelves of European markets, hindrance of agbiotech research at US universities, and the near-elimination of once highly touted research on microbial pesticides and bioremediation.

Focusing mainly on the possibility that new products may pose theoretical risks, the precautionary principle ignores very real, existing risks that could be mitigated *or* eliminated by those products. If the precautionary principle had been applied decades ago to innovations like polio vaccines and antibiotics, regulators might have prevented occasionally serious side effects by delaying or denying approval of those products, but that precaution would have come at the expense of millions of lives lost to infectious diseases. Instead of demanding assurance of safety that approaches absolute certainty, the goal should be to balance the risk of accepting new products too quickly (Type I error in the parlance of risk assessment) against the risks of delaying or foregoing new technologies (Type II error). And because individuals' tolerance for risk is so heterogeneous, regulators should be open to the exercise of greater informed choice by the end users of technology.

More than one billion people in the world now live on less than a dollar a day, and hundreds of millions are severely malnourished. By increasing the efficiency of agriculture and food production, recombinant DNA technology can significantly increase the availability and nutritional value of foods and reduce their cost. But the application of the precautionary principle will stall progress and exact a substantial human toll. The huge stakes both in human and commercial terms demand that within the flawed regulatory paradigm agreed upon in Montreal, regulators create scientifically sound, risk-based frameworks for the regulation of recombinant organisms.

The seeds of risk-based regulation can be found within the biosafety protocol agreement itself. Annex II contains a guide to what the protocol considers adequate risk assessment. It properly focuses on the biological characteristics of the individual products, but leaves much discretion to regulators about the framework for risk analysis. Therefore, risk analysis of recombinant DNA-manipulated (and other) organisms could be conducted within a methodological framework that depends on the stratification of organisms into risk categories according to the consensus judgments of independent scientific experts.

One example of this approach has already been described[1]. A workshop conducted by the authors of that paper and attended by agricultural experts from six nations demonstrates that such risk categorization is feasible. In that exercise, the criteria used in the stratification included pathogenicity, invasiveness, possibility of impact on wild gene pools, weediness, center of origin, and risk to humans. Most of the crop plants evaluated were found to be in the "negligible risk" category (therefore requiring little or no regulatory oversight), and the rest were in the "low but nonnegligible risk" category (which might require only notification to a regulatory authority or a minimal safety review).

The advantages of this methodology are that it is highly flexible and that it may be used by regulatory bodies with various functions and philosophies of risk. Because the majority of organisms subject to the protocol will be plants, and most of these will be of negligible risk, this risk-based approach obviates the need for unnecessary or extensive case-by-case review and thereby eliminates an important source of regulatory disincentives to the use of recombinant DNA techniques for agriculture.

Although a risk-based review mechanism of this type would be an important first step toward scientific risk analysis, an oversight system should also include incentives to reward optimal decision making and should hold regulators accountable for both Type I and Type II errors. Although even the most carefully crafted institutional reforms cannot guarantee optimal risk assessment and risk management, formal institutional recognition that there is a trade-off between moving too quickly and too slowly can help to achieve net risk reduction and to promote overall social benefit.

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Opinion

ENVIRONMENTAL PROTECTION, IN NAME ONLY

BY HENRY I. MILLER

A proposal to create a senior scientist position at the U.S. Environmental Protection Agency is winning support from Congress. In June, a National Academy of Sciences panel recommended creating the position to bolster EPA's use of science, and at a House subcommittee hearing this summer, U.S. Rep. Vernon Ehlers (R-Mich,) announced that he was preparing legislation to create the deputy-level (agency head) science position. "Scientists need more clout," he said.

But EPA needs more than Ehlers' remedies, which are like trying to stop a charging rhino with a pea shooter. In fact, a similar strategem failed miserably earlier in the tenure of EPA chief Carol Browner. What has never been addressed is the fundamental problem that adherence to scientific principles in the formulation of policy has long been alien to EPAs "corporate culture."

An expert panel commissioned by then-€PA administrator William Reilly reported in 1992 that:

• "The science advice function—that is, the process of ensuring that policy decisions are informed by a clear understanding of the relevant science—is not well defined or coherently organized within EPA."

• "In many cases. appropriate science advice and information are not considered early or often enough in the decision making process."

• While "EPA should be a source of unbiased scientific information, EPA has not always ensured that contrasting, reputable scientific views are well-explored and well-documented." And most damning of all, that

• "EPA science is perceived by many people, both inside and outside the Agency, to be adjusted to fit policy. Such 'adjustments' could be made consciously or unconsciously by the scientist or the decision-maker."

EPA AND SCIENCE

In an effort to elevate **EPA's** scientific profile, in 1989the agency had brought on board former National Institutes of Health deputy director William Raub as the senior science advisor. Raub was known to be a smart, savvy, and collegial scientific administrator. Nonetheless, the **EPA** *staff* proceeded to make his life miserable. From the beginning, they ignored him when they could. When they couldn't, they sent him drafts of important documents too late for a meaningful review—often just days before a court-ordered deadline for an agency action. Instead of disciplining those responsible, **EPA** administrator Browner excluded Raub from her inner circle and finally replaced him in 1995 with a less-threatening lower-level EPA staffer.

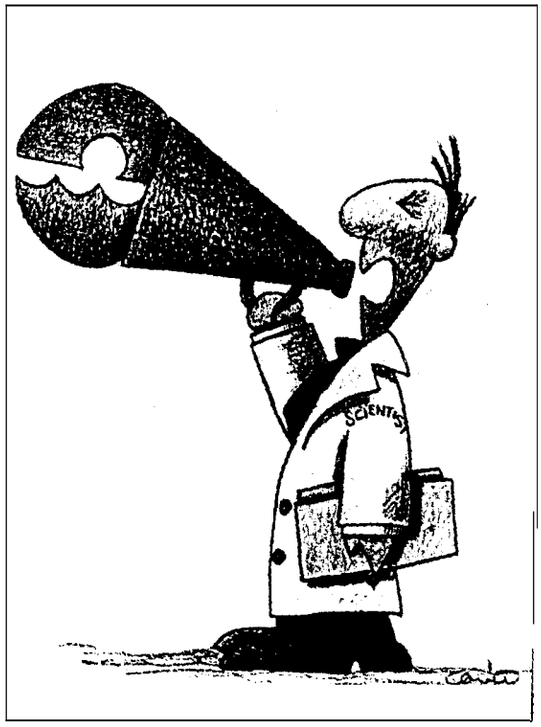
The tradition continues. Under mounting pressure from environmental groups to ignore the recommendation of the agency's own scientists, Browner last December scrapped a science-based standard for chloroform in drinking water. In 1998, EPA had proposed raising the Maximum Contaminant Level Goal for chloroform in drinking water from zero to 300 parts per billion. This recommendation had resulted from a thorough review by EPA scientists of toxicological data on human exposure to chloroform going back 20 years, and took into account the principle contained in the agency's draft cancer guidelines that there are thresholds below which toxins are essentially harmless. But the recommendation was to become the victim of political sabotage, and the agency instead retained a "zero tolerance" rule. In April of this year, however, a federal court rejected EPA's proposed standard, saying that the proposal was contradicted by the agency's own review

[illegible science"

EPA

that EPA's draconian new air quality standards were arbitrary and capricious and had to be revised. In May of this year the U.S. Supreme Court agreed to rule on EPA's deliberately disregarding the cost of its regulations as required by the Clean Air Act. As argued in an amicus brief filed July 21 by a public policy research institution and 40 prominent economists, the EPA should "consider explicitly the full consequences" of regulatory decisions, including costs, benefits, and any other pertinent facts.

Superfund, the program directed at clean-up of toxic wastes, is a continuing disaster. After he left EPA. agency chief William Reilly admitted as much, saying that unscientific assumptions about risk "have driven clean-up costs to stratospheric levels and, together with liabilities associated with Superfund sites, have resulted in inner-city **sites** suitable for redevelopment remaining derelict and unproductive." The result has been "to impose a drag on urban redevelopment in the inner city, and to push new industry to locate in pristine, outlying **sites."**



EPA AND BIOTECHNOLOGY

Finally, the EPA has attacked biotechnology on several fronts. Consistently adopting unscientific approaches, agency oversight focuses on the most precise and predictable techniques of biotechnology while ignoring genuinely hazardous products. These policies have been a drag on innovation. A regulation under the Toxic Substances Control Act focused only on the most precise techniques of the new biotechnology, for example, has halted most research into gene-spliced microorganisms that might be used to clean up oil spills and toxic wastes.

And the agency is expected any day to issue a final regulation that requires the testing as pesticides of gene-spliced crop and garden plants such as corn, cotton, wheat, and marigolds that have been modified for enhanced pest or disease resistance. The policy fails to

[illegible]

thetic, toxic chemicals and genetic approaches to enhancing plants' natural pest and disease resistance.

EPA's policy is so potentially damaging and outside scientific norms that it has galvanized the scientific community: Eleven major scientific societies representing more than 80,000 biologists and food professionals published a report warning that the EPA policy would discourage the development of new pest-resistant crops and prolong and increase the use of synthetic chemical pesticides; increase the regulatory burden for developers of pest-resistant crops; limit the use of biotechnology to larger developers who can pay the inflated regulatory costs; and handicap the United States in competition for international markets.

"Science at EPA," a voluminous book published last year by Resources for the Future, a Washington, D.C.-based think tank, carefully dissects eight major regulatory programs of the past two decades. It makes the case that the science behind the policy often gets distorted or ignored: "EPA for a variety of reasons is unwilling, unable, and unequipped to address and acknowledge *the* uncertainties in the underlying science."

Why this sellout of citizens' interests? It is an example of the "bootleggers and Baptists" parable of regulation, first described by economist Bruce Yandle. In the South, Sunday closing laws make it illegal to sell alcohol on Sunday. These laws are maintained by an inadvertent coalition of bootleggers and Baptists. The Baptists (and other religious denominations) provid the public outcry against liquor on Sunday, while th bootleggers (who actually sell liquor illegally o Sunday at inflated prices) quietly persuade legislatur and town councils to maintain the closing laws th make their exorbitant profits possible.

Environmental regulation is similar. The "Baptist are the coalition of government regulators and rac cal environmental groups that promote unnecessa regulation, allegedly on grounds of safety concer the "bootleggers" are the big agribusiness compan that profit when their competition is stifled by exc

been closely allied with EPA, particularly dur Carol Browner's tenure, and have been the recipi of generous grants from the agency. Some of the agribusiness companies have benefited from El excesses that can create market entry barriers to sn er competitors. This arrangement reeks of conf of interest.

Many of EPA's regulatory programs are unscie and illogical and afford little or no protection to hu health or the environment. They have unaccep huge costs and divert resources from other legit public and private sector endeavors. They breed deserved cynicism about government's motives. (the only environment that benefits is that of the bu crats themselves.

Fixing EPA will require much more sweepir fundamental changes than are currently being disc These could range from the creation of an ombu panel with the power to impose sanctions on EF cials who collaborate on unscientific policies to c tling EPA and redistributing its few essential func less scientifically challenged agencies.

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MANAGEMENT & TECHNOLOGY

SCIENCE VIEWPOINT HENRY MILLER AND GREGORY CONKO

Cloudy horizons in a brave new world

GM product regulations could deprive scientists, farmers and food companies of research tools – and consumers of choices in the marketplace

These are tough times for agricultural and food biotechnology, but its regulators are active and thriving This is no coincidence

In Europe, there is widespread public and political opposition to importing grains grown from genetically modified seeds. Governments have imposed moratoriums on commercial scale cultivation of plants GM foods have been banished by big supermarket chains Vandalisation of field trials by envlronmental activists is frequent – and largely unprosecuted In the US as well, regulators have imposed strict, unscientific rules on agricultural and food research that hinder product development.

But the regulatory ***coup de gruce*** has been delivered by the United Nations. In late January, under the 1992 Biodiveisity Treaty agreement was reached in Montreal on a UN-sponsored "biosafety protocol" – that is, regulations that will erect trade barriers against agricultural products developed with gene splicing techniques.

Six important agricultural exporting countries known as the Miami Group – that includes Canada and the US – had threatened to walk out of the negotiations because their farmers rely extensively on GM crop plants and export them widely In the words of Tim Galvin, a US negotiator, "no deal is better than a bad one".

If only they had stuck to that principle. Walking away from this anti-competitive, anti-consumer agreement would have been preferable to the result an arbitrary, one size-fits-all regulatory system for GM products based solely on the way they are developed, regardless of how safe or dangerous individual products may be

Unnecessary and unpredictable regulation invariably discourages use of a technology, so this situation is a prescription for disaster The regulations will deprive scientists, farmers and food companies of research tools. and consumers of additional choices in the marketplace.

More than 1,000 scientists from around the world recently signed a declaration supporting the use of agricultural biotechnology, reflecting the scientific consensus that the regulation of GM techniques should be based on the biological characteristics of individual products, not on the methods used to develop them. And, in spite of opposition from antibiotech activists, tens of thousands of food products from GM organisms have been consumed routinely and safely for more than 15 years. But GM's ideological opponents, joined now by the UN. have chosen to ignore these facts.

The agreement has less to do with legitimate concerns about the environment and more to do with trade protectionism and anti-science fearmongering. The regulations are based on the "precautionary principle", the conviction that every new technology should be proven absolutely safe before people can use it. This erects an almost insurmountable barrier against new products because nothing can be proved totally safe – at least, not to the standard demanded by anti-technology extremists.

Focusing only on the possibility that new products may pose theoretical risks, the precautionary principle necessarily ignores the fact that new products often reduce or eliminate existing risks.

GM techniques, for example, can significantly increase the availability and nutritional value of foods, and reduce their price, thus alleviating the huge problem of global malnutrition. Applying the precautionary principle to these advances will exact a substantial human toll.

Biotechnology is burdened with an ill-defined global regulatory process that permits risk-averse, incompetent or corrupt regulators to hide behind the precautionary principle.

In this way, what George Orwell called "vague fears and horrible imagnings" can be elevated above scientific evaluation, even when the products in question are obviously safe and will benefit the environment and human health

Such harmful regulation could easily have been opposed on principle But rhe Miami Group nations ultimately capitulated They were more interested in striking a deal that would appease both the environmental movement and the agribusiness industry

Under the deal, food crops intended for processing such as raw corn, soya beans and canola (rape seed) are still subject to unscientific regulatory hui dles but are exempt from the case-by-case approval mechanism that governs other products

In protecting some US and Canadian farmers, however, the Miami group sacrificed the interests of academic researchers, small and innovative companies, and consumers .

Now corn and soya bean farmers, for example, will know nhead of time whether a shipment of their gram will be accepted overseas, but a new variety of iron-fortified rice to be field tested at a university field station, or a pest resistant strain of millet to be grown by village farmers, will be delayed by gratuitous) regulatory reviews

What was needed, but lacking, n Montreal was the political will o insist on policies that make scientific sense and protect consumer choice.

The only winners from these new rules are government egulators, who will enjoy iew-found power and resources, und anti-science extremists, who iave succeeded in reducing the iew biotechnology to a mere hadow of its potential Those vho negotiated this agreement iave made a mockery of free trade and, in a noral, if not legal ense, committed rimes against iumanity

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Letters to the Editor

Regulatory Gangs Maul Biotech

On your May 2 editorial page you ran an editorial on the vicissitudes of agricultural biotechnology and an article by Jerome Groopman that explained the gradual nature of progress at the cutting edge of medical biotechnology (specifically, in human gene therapy). Neither of these cautiously optimistic pieces mentioned critical public policy developments—including some that are imminent—that will determine the pace, and even the viability, of biotechnological innovation:

• USDA regulations have made experiments with gene-spliced plants ten- to twentyfold more expensive than the very same field trials with virtually identical organisms crafted with older, less precise techniques. As a result, research and development have been only a fraction of their potential, and consumers have thereby been deprived of the benefits of gene-spliced plants such as sunflowers modified to yield a more healthful cooking oil and more nutritious vegetables and grains.

• The EPA has attacked biotechnology on several fronts. A regulation under the Toxic Substances Control Act has halted most research into gene-spliced micro-organisms that might be used, for example, to clean up toxic wastes.

• The EPA is expected any time to issue a final regulation that requires review as pesticides of the testing of gene-spliced crop and garden plants, such as corn, cotton, wheat and marigolds. that have been modified for enhanced pest- or disease-resistance. This policy is so potentially damaging and outside scientific norms that 11 major scientific societies representing more than 80,000 biologists and food professionals published a report warning that the EPA policy would discourage the development of new pest-resistant crops and prolong and increase the use of synthetic chemical pesticides; increase the regulatory burden for developers of pest-resistant crops; limit the use of biotechnology to larger developers who can pay the inflated regulatory costs; and handicap the U.S. in competition for international markets.

• Under pressure from anti-technology extremists and the Clinton administration, the FDA plans soon to repudiate both its well-tested, niuch-praised policy on new plant varieties—which is applied irrespective of whether the plant arose from gene-splicing or "conventional" genetic engineering methods—and its 20-year-old commitment not to discriminate against gene-spliced products generally. Within a few months, according to senior FDA officials, the agency expects to announce a new requirement that all gene-spliced foods come to the agency for pre-market evaluation.

• The "Cartagena biosafety protocol," finalized in January under the auspices of the United Nations' Convention on Biological Diversity, introduces a global scheme for regulation of biotech products that violates a cardinal principal of regulation: the degree of scrutiny should be commensurate with risk. The protocol is certain to hobble the work of academic researchers and small, innovative companies, ultimately delaying or denying the benefits of the "gene revolution" to much of the world.

• Three panels of the Codex Alimentarius Commission, the United Nations agency concerned with international food standards, are working toward holding biotechderived food and food ingredients to standards that are unscientific, far beyond those that any other products can or should meet, and that will prevent their competing successfully.

• On the basis of a single fatality last year in a gene therapy clinical trial, vast new Draconian requirements are being piled on every aspect of gene therapy research, from record-keeping and inspections to animal studies and the clinical trials themselves. Not only the FDA, which has primary jurisdiction. but the NIH and the National Bioethics Commission are getting into the act.

Is cautious optimism warranted? Irrational, excessively burdensome regulation can undo all manner of advantages enjoyed by a new technology, including wide applicability, limitless ingenuity and ample resources. Therefore, as someone who was a midwife at the birth of the new biotechnology a quarter-century ago and has watched it grow, I'm more inclined toward reckless pessimism.

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The Attempt to Uproot Biotech Foods

U.S. Trade Representative Robert Zoellick may be "strongly considering" filing a WTO complaint about European countries' unwillingness to accept U.S. agricultural biotechnology products ("U.S. Officials Courts African Allies For Brewing Biotech-Food Fight," Feb. 20), but he is being outflanked at the deliberations of the Codex Alimentarius Commission, the joint food standards program of the United Nations, whose ongoing task force on biotech foods will meet in Japan this month.

During the *two* years of negotiations by the U.N. group, dominated by European countries and NGOs, which are permitted full participation, it has purposefully ignored scientific principles and the basic axiom that the degree of regulatory scrutiny should be proportionate with risk. It has also disregarded the scientific consensus that the new biotechnology, or gene-splicing, is a refinement of older techniques of genetic modification, and the group is moving deliberately toward circumscribing only food products made with gene-splicing for various Draconian and even bizarre regulatory requirements. They include long-term monitoring for adverse health effects and batteries of tests for composition, genetic stability, toxins, allergenicity and so on. No food modified by less precise, less predictable traditional techniques—which comprise virtually the entire diets of Europeans and Americans—could (or should) meet these standards.

This wrong-headed regulation will impair the competitiveness of these products in the marketplace and limit their use—which is precisely the agenda of many of those on the task force. Agricultural biotechnology is regarded as an icon of American technological and economic success and supremacy, and our trade competitors intend, therefore, to punish it.

The prospect of unduly burdensome Codex standards for gene-spliced foods is ominous—both for the prospects of the technology itself and for U.S. hopes of WTO relief from European protectionism—because members of the World Trade Organization will, in principle, be required to abide by those standards. In other words, with these measures in place, a country that wishes to block trade in gene-spliced foods for any reason can defend against challenges of unfair trade practices simply by remonstrating that it's deferring to Codex.

If the current Codex approach is adopted, the costs of biotechnology R&D will be greatly (and unnecessarily) inflated. The result will be essentially irreversible constraints on innovation and trade, in a field in which U.S. companies lead the world. It is moot whether there exists a level playing field if it is knee-deep in mud. No agreement at all would be a far better outcome than one whose flaws are as manifest and pernicious (and permanent) as in the Codex standards.

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HENRY I. MILLER

Good Intentions *Are* Not Enough

During two years of deliberations by the Codex Alimentarius Commission's Ad Hoc Intergovernmental Task Force on Foods Derived from Biotechnology, the Europeans and some nongovernmental organizations have trampled United States interests. The participants — including the U.S. delegation — have willfully ignored scientific principles and the basic axiom that the degree of regulatory scrutiny should be proportionate to risk. They have also disregarded the scientific consensus that the new biotechnology, gene-splicing, is a refinement of older, traditional techniques of genetic modification. They have moved deliberately toward circumscribing gene-spliced food products for various Draconian and even bizarre regulatory requirements that will impair the competitiveness of these products in the marketplace and limit their use.

The regulation of foods derived from the new biotechnology must make scientific and common sense.

Derailing the development of gene-spliced foods is precisely the agenda of many of those on the task force, and the reason is clear. As Wellesley College political scientist Robert Paarlberg has observed, the products of agricultural biotechnology have been "developed mostly in *U.S.* laboratories, widely adopted by U.S. farmers, and pushed out onto the world market by U.S. companies with the support of the *U.S.* government" [italics added]. In other words, agricultural biotechnology is an icon of American technological success and supremacy, and our trading partners intend, therefore, to punish it.

The Codex task force is en route to codifying various procedures and requirements more appropriate to potentially dangerous prescription drugs and pesticides than to new, improved varieties of tomatoes, potatoes, and strawberries. These standards include long-term monitoring for adverse health effects and batteries of tests for composition, genetic stability, toxins, allergenicity, and so on. None of the foods modified by less precise, less predictable traditional techniques — which constitute virtually the entire diet of Europeans and Americans — could (or should) meet these standards.

The prospect of unduly burdensome Codex standards for gene-spliced foods is ominous — both for the prospects of the technology itself and for U.S. hopes of World Trade Organization relief from European protectionism — because members of WTO will, in principle, be required to abide by those standards. In other words, the standards will provide cover for unfair trade practices, because with these measures in place, a country that wishes to block trade in gene-spliced foods for any reason can defend against charges of unfair trade practices simply by remonstrating that it's deferring to Codex.

These unscientific regulations and standards will harm the environment and public health by stifling the development of innovations that can increase agricultural productivity and supplant agricultural chemicals. Experts at the United Nations and in academia have warned that the greatest single threat to the planet's environment comes from the world's burgeoning population and its demand that ever more land be brought into food production. Yet an important answer — developing more-productive plant varieties — will be blocked by hugely expensive regulation of gene-spliced techniques.

Although efforts should be made to reassure the public that gene-splicing techniques are in fact safer than more-traditional methods of genetic modification, excessive regulation is not the way to do so. As the president of a U.S. national consumer organization testified a decade ago to a federal investigative panel, "For obvious reasons, the consumer views the technologies that are *most* regulated to be the *least* safe ones. Heavy involvement by government, no matter how well intended, inevitably sends the wrong signals. Rather than ensuring confidence, it raises suspicion and doubt."

Regulation should focus on real risks and should not be triggered by the use of one technique or another. If the current Codex approach is adopted, the costs of biotechnology R&D will be greatly (and unnecessarily) inflated. The result will be essentially irreversible constraints on innovation and trade. It is moot whether there exists a level playing field, if it is knee-deep in mud. No agreement at all would be a far better outcome than one whose flaws are as manifest and pernicious (and permanent) as in the Codex proposals.

The U.S. delegation to Codex must adopt a position that is clear and unequivocal: The regulation of foods derived from the new biotechnology must make scientific and common sense. The stakes are too high for rational regulatory policy to be compromised either by protectionism or by bureaucratic irresoluteness. ●

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Guest Comment

On NRO

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The Big Fed Freeze

Feds freeze out frost-fighting bacterium

By Henry I. Miller

The green was rolling in for winter growers of lettuce in the desert areas of Arizona and California — and then along came freezing December weather that stunted crops. The result has been the worst lettuce shortage in 15 years and prices have gone through the roof. The Los Angeles Unified school district, which usually gets lettuce for *42* cents a pound, was paying $1.90 last week.

Frost damage causes losses to American farmers of billions of dollars annually. A 1990 freeze in California caused about $800 million in damage to agriculture and resulted in the layoff of 12,000 citrus-industry workers, including pickers, packers, harvesters, and salespeople. Two winters ago, one largely agricultural California county lost more than 85 percent of its citrus crop. Peaches and other crops are regularly threatened in the Southeastern United States.

The techniques available to limit the frost damage are pathetically low-tech. They include burning smudge pots, which produce warm smoke; running wind machines to move the frigid air; and spraying water on the plants to form an insulating coat of ice. The only possible high-tech solution, a clever application of biotechnology, was frozen out by federal regulators.

In the early 1980's scientists at the University of California and in industry tried a new approach to limiting frost damage. They knew that a harmless bacterium which normally lives on many plants contains an "ice nucleation" protein that promotes frost damage. In the presence of the bacterium, therefore, ice forms more readily — that is, at higher temperatures.

The scientists sought to produce a variant of the bacterium that lacked the ice-nucleation protein, reasoning that spraying this variant bacterium (dubbed "ice-minus") on plants might prevent frost damage by displacing the common, ice-promoting kind. Using very precise biotechnology techniques called "gene splicing," the researchers removed the gene for the ice nucleation protein and planned field tests with ice-minus bacteria.

Then the government stepped in, and that was the beginning of the end.

The Environmental Protection Agency (EPA) classified as a ***pesticide*** the ubiquitous and obviously innocuous ice-minus bacterium, which was to be tested in northern California on small, fenced-off plots of potatoes and strawberries. The regulators reasoned that the naturally occurring, ubiquitous, "ice-plus" bacterium is a "pest" because its ice-nucleation protein promotes ice-crystal formation. Therefore, other bacteria intended to displace it would be a "pesticide." This is the kind of convoluted reasoning that could lead **EPA** to regulate outdoor trashcans as a pesticide because litter is an environmental "pest."

At the time, scientists inside and outside the EPA were unanimous about the safety of the test. (As an official at the Food and Drug Administration at the time, I wrote that agency's opinion, which emphasized the high degree of safety and the potential importance of the product.) Nonetheless, the field trial was subjected to an interminable and burdensome review just because the organism was gene-spliced (and even though it contained no new genetic material, but had merely had part of one gene deleted).

It is noteworthy that experiments using bacteria with identical traits but constructed with older, cruder techniques require no governmental review of any kind. When tested on less than ten acres, bacteria that aren't gene-spliced and even highly toxic chemical pesticides are completely exempt from regulation. Nor is the government involved in the use of vast numbers of the "ice-plus" organisms in snowmaking at ski resorts.

Even after the EPA finally granted its approval for testing the "ice-minus" microorganisms in the field, the agency conducted elaborate, expensive, intrusive — and predictably worthless — monitoring of the field trials. (Monitoring for what, one wonders — the harmless bacteria mutating into pit bulls?)

While the ice-minus bacteria proved safe and effective at preventing frost damage, further research was discouraged by the combination of onerous government regulation, the inflated expense of doing the experiments and the prospect of huge downstream costs of pesticide registration. The product was never commercialized, and plants cultivated for food and fiber throughout much of the nation remain vulnerable to frost damage.

Thus, we have federal regulators to thank for the absence of an innovative, high-tech approach to preventing damage from the inevitable winter and spring cold snaps — and for lettuce prices of several dollars a head.

The EPA's treatment of the frost-protection organism is a microcosm of how errant, irresponsible regulators wreak misery on average Americans. The pity is that they are seldom held accountable.

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http://www.nationalreview .com/comment/comment-miller040402.asp

Letters to the Editor

Science vs. the U.N.'s Luddites

There is much to applaud about the view of agricultural biotechnology in the U.N.'s report, "Making New Technologies Work for Human Development" ("Politically Incorrect U.N.," Review & Outlook. July 12), but the rhetoric is hollow.

The U.N.'s repeated insistence upon excessive, unscientific biotechnology regulation will slow agricultural research and development, promote environmental damage and bring famine and death to millions in developing countries.

In Montreal in January 2000, delegates to the U.N.-sponsored Convention on Biological Diversity negotiated a "biosafety protocol" for the regulation of international movement of gene-spliced, or genetically modified (GM), organisms. It was based on the bogus "precautionary principle," which dictates that every new technology—including, in the case of gene-splicing, a refinement of less precise technologies—must be proven safe before it can be used. The precautionary principle creates prodigious obstacles to the development of new products. Precaution, in this sense, shifts the burden of proof from the regulator, who once had to demonstrate that a new technology was likely to cause some harm, to the innovator, who now must demonstrate that the technology will not. Under this new standard of evidence, regulatory bodies are free to arbitrarily require any amount and kind of testing they wish.

The biosafety protocol establishes an illdefined global regulatory process that permits overly risk-averse, incompetent or corrupt regulators to hide behind the precautionary principle in delaying or deferring approvals. We have already seen many examples of the arbitrary and capricious application of the precautionary principle to agricultural biotechnology that are directly related to the Montreal protocol. One of the most egregious was the decision by the German government to block the commercial-scale cultivation of gene-spliced, insect-resistant corn by the biotechnology company Novartis. This action came only one day before it was expected to be approved for commercial use by the Ministry of Agriculture, which specifically cited the need to respect the precautionary principle and called for more research into the crop plant's potential hazards.

Another recent example of the U.N.'s malign influence is a task force of the 165-member Codex Alimentarius Commission, the joint food standards program of the U.N.'s World Health Organization and Food and Agriculture Organization, which last year began discussions of issues related lo biotechnology and food. Since then. the group has moved deliberately toward circumscribing only food products made with gene-splicing for various Draconian and even bizarre regulatory procedures and requirements that will impair the competitiveness of these products in the marketplace. The motivations for this anti-social policy-making vary. The Europeans—especially the European Commission and France—want to stop gene-spliced products because they are mostly made by U.S. companies, and the radical environmental non-governmental organizations (NGOs), which are permitted *to* participate in Codex meetings, are ideologically opposed to new technology.

The Codex task force is en route to codifying various procedures and requirements more appropriate to potentially dangerous prescription drugs or pesticides than *to* gene-spliced tomatoes, potatoes and strawberries. They include long-term monitoring for adverse health effects and batteries of tests for genetic stability, toxins, allergenicity, and so on—requirements that foods produced with conventional genetic techniques could not (and should not) meet. Among the most insidious is something called "traceability," an array of technical, labeling and record-keeping mechanisms to keep track of a plant "from dirt to dinner plate," so that consumers will know whom to sue if they get diarrhea from gene-spliced prunes, and providing, in the words of the anti-biotech European Commission delegate, "a tool governments can use to remove products from the market."

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FDA planjeopardizes food biotech

Although prone to overregulation and frequent misjudgements, the FDA has had remarkable success at overseeing food biotechnology. For the past eight years, the agency's official policy has treated gene-spliced and other foods the same, and required scrutiny by regulators only when the products raise specific safety concerns. This approach has been widely applauded as regulation that makes sense, protects consumers, and permits innovation.

However, under pressure from anti-technology extremists and the Clinton administration. in April 2000 the agency announced a change in policy that reverses both its scientific approach to food regulation and a twenty-year old commitment not to discriminate against biotechnology-derived foods and pharmaceuticals.

The new approach is tantamount to singling out only cars with advanced engineering for a punitive tax and, in addition, imposing a lower speed limit on them. The result will be, in the long-term, international bureaucracies meddling where they don't belong, disuse of a stunning new technology, diminished choices for farmers and consumers, and higher food prices.

Thousands of biotech foods in US supermarkets have been regulated under the FDA's 1992 policy on products from "new plant varieties", which applied irrespective of whether the plant arose by gene-splicing or conventional genetic engineering methods. It defined certain potentially hazardous characteristics of new foods that, if present, required greater scrutiny by the agency, and which could have resulted in additional testing and labeling, or banishment from commerce. Thus, the agency's approach conformed to the fundamental principle that the degree of scrutiny should be commensurate with risk. Likewise, it was consistent with a widely held scientific consensus that "conventional" and new biotechnology are essentially equivalent, and that the highly precise gene-splicing techniques, in fact, yield a better characterized and more predictable product.

At the same time that the official FDA policy treated biotech foods no differently from others, the agency maintained a "voluntary consultation procedure". in which producers of biotech foods were expected to consult with the agency before marketing their products, and without exception they did so. The major change in the new FDA policy would require the producers to notify the FDA four months before marketing a gene-spliced food and provide the agency with data that affirm the new food's safety.

What's so wrong with codifying essentially what was previously voluntary, but standard, practice? Plenty.

First, the data requirements of the new policy are excessive. The FDA lists nine categories of obligatory information whose level of detail is far greater than would be required (or possible) for food products made with less precise, less sophisticated techniques.

Second, the new policy reverses the FDA's twenty-year-old guiding principles for oversight of biotechnology - that regulation should focus on real risks and should not turn on the use of one technique or another. These tenets have provided effective oversight for thousands of new biotechnology products, including foods, drugs, vaccines and diagnostic tests.

Finally, the FDA's abandonment of a scientific approach to biotech regulation has far-reaching implications, both geopolitical and temporal, as I saw first-hand in March during a meeting in Japan of a task force of the UN's food standards organization, the Codex Alimentarius Commission, The change of policy at the FDA - which was then impending - strikingly altered the dynamics of the negotiation.

The FDA has for decades been considered a world leader in biotech regulation and could be relied upon in international forums to defend scientific principles and vigorously advocate its own risk-based approach. Faced with initial antagonism to

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the US position from other countries and NGOs (which is not unusual at international negotiations on regulatory issues) the US delegation commonly would set the tone by insisting on adherence to scientific principles and explaining the scientific basis for its own regulatory policy.

What was anomalous at the Codex task force meeting was that the US delegate, senior FDA food regulator Robert Lake, never mentioned the FDA's own risk-based approach. He never cited the important principle that the degree of regulatory scrutiny should be commensurate with risk. Nor did he invoke the scientific consensus about the essential equivalence between old and new biotech.

Instead, the US followed the lead of the European Commission and France, both vehemently anti-biotech. and agreed to work toward Draconian and unscientific standards for gene-spliced foods. The result will be the creation of overt obstacles to the use of gene-splicing techniques in food production and agriculture, and also vagueness in regulatory definitions and concepts, ensuring that regulators can be as arbitrary and capricious toward biotech products as they wish. The prospect of unscientific, overly burdensome Codex standards for gene-spliced foods is ominous, because members of the World Trade Organization will, in principle, be required to follow them, and they will provide cover for unfair trade practices.

The impending deterioration in domestic regulatory policy - that is. the changes just announced - tied the hands of the US delegation in Japan, and will continue to do so in other international forums that are addressing biotech food regulation. These include two other Codex panels and the Paris-based Organization for Economic Cooperation and Development. International regulation is destined to become biotech food's *bête noire*.

A particular irony is that the FDA's announcement of a new policy that will compromise the United States's position in international negotiations was accompanied by a statement of support from Alan Larson, Under Secretary of State for Economic, Business and Agricultural Affairs Perhaps reflecting the long-standing "special relationship" between the United Kingdom and United States, his remarks were a remarkable combination of Orwellian newspeak and Clintonian mendacity. He spoke of the policy representing "sound science", when it represents exactly the opposite. He defended new regulatory requirements although admitting that there exists "strong scientific evidence that biotech foods are as safe as other foods". He claimed that the new measures "are primarily aimed at reinforcing public confidence", although as pointed out by the head of a national consumers' group, "For obvious reasons, the consumer views the technologies that are *most* regulated to be the *least* safe ones. Heavy involvement by government, no matter how well intended, inevitably sends the wrong signals Rather than ensuring confidence, it raises suspicion and doubt."

Thus, we have a US Under Secretary of State who has gone out of his way to endorse a transparently unscientific, unwarranted, unintelligent domestic regulatory policy that will irretrievably damage the application of the newest, most precise techniques of biotechnology to agriculture and food production. This blatantly political policy direction, sanctioned at the highest levels of the US government, represents commercial suicide: Overregulation is the great equalizer that most damages the leader in a technological field; and in agricultural and food biorechnology. that leader has been the United States.

In this case, it also represents scientific suicide as well. New regulations increase the paperwork and costs of product development, and are in effect a punitive tax on potential innovators. Their greatest effect will be to hobble the work of academic researchers and small, innovative companies, ultimately blunting the benefits of the "gene revolution" in the United States and around the world.

The long-standing, risk-based FDA policy toward gene-spliced and other novel foods worked admirably. It involved the government only in those extraordinarily rare instances when products raised safety issues. For others, market forces were permitted to work their magic, the result of which was eight years of unprecedented choice for farmers, food producers and consumers. The policy also encouraged strong *FDA* advocacy for scientific regulation internationally, which has now ended with dire consequences.

Food production has low profit margins and cannot easily absorb the costs of gratuitous regulation, domestic or international. The overregulation of gene-spliced foods will prevent its wide application to food production, deprive farmers of important tools for raising productivity, and deny to food manufacturers and consumers greater choice among improved, innovative products.

The Bush administration deals a blow to biotechnology—and itself

Henry I. Miller

A persistent criticism of the Bush administration, according to polls, is that its policies too often favor the interests of big business over those of consumers. Although these criticisms of "deregulatory" policies usually have been dubious at best, on July 19 the US Environmental Protection Agency (EPA; Washington, DC) issued a regulation that is genuinely anti-consumer, anti-environment, and anti-farmer. The only beneficiaries will be a handful of big agribusiness companies and the regulators themselves.

The subject of the regulation, the use of recombinant DNA techniques to enhance the intrinsic pest resistance of crop and garden plants, offers a safe, viable alternative to chemical pesticides; but the testing and commercialization of these plants have been systematically obstructed since 1994, when EPA first proposed to regulate them as though they were dangerous chemical pesticides. EPA remonstrates that it is regulating not new plant varieties, but only the introduced pesticidal protein, which it now calls by the neologism "plant-introduced protectant" (PIP). However, that is a distinction without a difference, similar to suggesting that US states enforce emission standards not for automobiles, but for engines and exhaust systems.

Innovative, recombinant DNA-modified varieties have already demonstrated their commercial, environmental, and public health benefits. An example is recombinant "*Bt* cotton," which differs functionally from other varieties by the presence of a single protein from the bacterium *Bacillus thuringiensis* (*Bt*). The protein, made by a gene transferred to the cotton plant by recombinant DNA techniques, is toxic to certain insects but not to humans or other mammals. The use of toxin is not new: For decades, preparations of live *Bt* bacteria have been sprayed onto plants by home gardeners and commercial farmers, with an admirable record of both safety and effectiveness.

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Bt cotton is used to control the cotton and pink bollworm and the tobacco budworm, which together account for a quarter of all losses due to pest infestations and cost US farmers more than $150 million annually. In 1999, states that had a high rate of adoption of *Bt* cotton showed a significant reduction in the need to treat fields with chemical pesticides. Treatments were cut from an average of three treatments per acre to about one and a half. *Bt* cotton has eliminated the need for more than 2 million pounds of chemical pesticides since it was introduced in 1996.

Federal regulation of recombinant plants is inconsistent and discriminatory, and bears no proportionality to risk

In purely economic terms, the aggregate advantage to cotton farmers nationally—the net value of crops not lost to pests, savings in pesticides, and so on—is in the range of $100–150 million per year. But the economic benefits pale beside the environmental advantages. Three of the chemicals that must be used in much greater amounts on conventional, non-Bt cotton—endosulfan, methyl parathion, and profenos—are thought to have negative effects on birds, fish, and other aquatic organisms.

By diminishing chemical pesticide usage, the adoption of *Bt* cotton also reduces occupational exposures to the toxic chemicals by workers who mix, load, and apply the pesticides, and who perform other activities that require their presence in the field. Moreover, as the amount of pesticides applied is reduced, the level of runoff into waterways is reduced, a major problem in many farming regions.

Federal regulation of recombinant plants is inconsistent and discriminatory, and bears no proportionality to risk. In fact, there is arguably ***inverse*** proportionality to risk, in that the more precisely crafted and more predictable recombinant organisms are subjected to far more stringent regulation than more crudely crafted, less predictable organisms. This violates a cardinal principle of regulation: that the degree of regulatory scrutiny should be commensurate with risk. The EPA holds the new technology to an inappropriate standard, requiring hugely expensive testing of recombinant DNA-modified crop and garden plants, such as cotton, grapes, and tomatoes, as though they were highly toxic chemical pesticides—a policy that has been repeatedly condemned by the scientific community. The agency has imposed requirements that could not possibly be met for products of conventionally bred crop plants, and its policies fail to recognize that there are important differences between spraying synthetic, toxic chemicals, and genetic approaches to enhancing plants' natural pest resistance.

There is a broad and longstanding scientific consensus about the continuum between conventional and new biotechnology. As a 1992 *Nature* editorial states, "no conceptual distinction exists between genetic modification of plants and microorganisms by classical methods or by molecular techniques that modify DNA and transfer genes"?. Scientists worldwide agree that the process of adding novel genes .to plants does not make them less safe either to the environment or for humans to eat. And yet transgenic varieties are singled out for particular scrutiny, while dozens of varieties produced through hybridization and other traditional methods of genetic improvement enter the marketplace each year without scientific review or special labeling. Many of the latter products are from "wide crosses"—hybridizations in which genes are moved from one species or one genus to another to create a plant variety that does not and cannot exist in nature. For example, *Triticum agropyrotriticum* is a new synthetic "species" that resulted from the combination of genes from bread wheat and a grass sometimes called quackgrass or couchgrass. Possessing all the chromosomes of wheat and one extra whole genome from the quackgrass (containing tens of thousands of genes), *T. agropyrotriticum* has been independently produced in the former Soviet Union, Canada, United States, France, Germany, and China, and is grown for both human

food and animal feed. The inconsistency of EPA's policy is illustrated by the fact that if a single gene from quackgrass were introduced into wheat by recombinant DNA techniques, the new plant would be subject to the EPA's draconian review and licensing process for pesticides.

EPA's policy is so potentially damaging and outside scientific norms that it has galvanized the scientific community, which has repeatedly and unequivocally condemned the agency's approach[3,4]. Dozens of major scientific societies representing more than 100,000 biologists and food professionals have warned that the EPA policy discourages the development of new pest-resistant crops, prolongs and increases the use of synthetic chemical pesticides, increases the regulatory burden for developers of pest-resistant crops, expands federal and state bureaucracy, limits the use of biotechnology to larger developers who can pay the inflated regulatory costs, and handicaps the United States in competition for international markets[3,4].

As predicted, the EPA's policy has already caused extraordinary mischief: namely, the recall of corn products found to contain minuscule amounts of a recombinant corn variety call StarLink, which unlike other commercial varieties contains a *Bt* toxin called Cry9C. This bacterial protein, introduced into corn with recombinant DNA techniques, was approved by EPA for animal feed but not for humans because, although Cry9C does not resemble known allergens, it was not immediately degraded in digestion tests. (Most food allergens are not readily digested, so the EPA wanted more data before concluding that consumers could not be allergic to the protein.)

However, the food products in question are actually far less likely than thousands of other products on the market to cause allergic or other health problems. More than 20 million Americans report that they are allergic to peanuts, and about 125 deaths a year are attributed to food allergy. Fava beans, a fixture of upscale restaurant cuisine in North America and Europe, can be life-threatening to persons with a relatively common hereditary enzyme deficiency. Unlike those foodstuffs, however, even after exhaustive testing, no allergic reactions, toxicity, or any other problem has been demonstrated for Cry9C or any substance similar to it.

The ripple effect of this StarLink nonproblem is monumental, and growing. Because EPA classified the Cry9C as a pesticide, the US Food and Drug Administration (FDA; Rockville, MD) was forced to recall the hundreds of products found to contain minute traces of it. (EPA sets pesticide tolerances — zero in the case of Starlink — and the FDA enforces them) "Contamination" with StarLink's Cry9C has been found in corn exported to Japan, which annually imports about 16 million tons of US feed corn (worth around $2 billion) and has a policy of "zero tolerance" for the banned variety (considering violations to be criminal). The Japanese Ministry of Agriculture, Forestry, and Fisheries finally accepted a baroque US plan for testing corn exports to ensure that they are free from StarLink.

The just-finalized regulation concerned with recombinant plants is not the first instance in which biotechnology (and society) has been a victim of EPA's wrongheaded policymaking. In 1997, the agency issued a regulation under the Toxic Substances Control Act, the effect of which has been to halt most research into any "new" microorganism defined inexplicably as one containing combinations of DNA from unrelated sources — that might be used, for example, to degrade oil spills or clean up toxic wastes. Under this regulation — for EPA "newness" is synonymous with risk, and because recombinant DNA techniques can easily be used to create new gene combinations with DNA from disparate sources — these techniques "have the greatest potential to pose risks to people or the environment," according to the agency's tortured logic. However, as described above, a broad scientific consensus holds that the genetic technique employed is irrelevant *to* risk, as is the origin of a snippet of DNA that may be moved from one organism to another; what matters is its function.

The new EPA regulation is only one symptom of the rot within the agency, but it is a serious one. It ensures that the potential of biotechnology applied to agriculture and food production is tarnished — as is the health of the environment, not to mention the reputation of the Bush White House

The final regulation on recombinant DNA-modified plants emerges at a time when the Bush administration is still operating with a skeleton crew, one that includes a scientifically illiterate EPA chief, Christine Todd Whitman, and her deputy, Linda Fisher, a former Monsanto senior executive who continues to promote industry's interests at the expense of the public interest. The vast expense of EPA's policy — actually a kind of punitive tax — acts as a market-entry barrier to seed and biotechnology companies undertaking recombinant DNA research, so big agribusiness–companies and the US Biotechnology Industry Organization (BIO) have lobbied tirelessly for it.

Little can be done in the short run to remedy this public policy debacle. Even a direct order from the President to revise the policy and undertake remedial rulemaking would likely be ignored by tenured bureaucrats — and would take years, in any case. Getting the current regulation written and published took more than seven years — even with EPA and the Clinton White House strongly behind it.

EPA's inept treatment of biotechnology is not an anomaly. The agency has been widely criticized for being inefficient and unscientific. When the Office of Management and Budget analyzed the cost effectiveness of a panoply of regulations throughout the federal government, of the 30 least cost-effective regulations on the list, no fewer than 17 had been imposed by EPA. This impression of inefficiency is reinforced in an analysis by Washington, DC–based Resources for the Future of eight major EPA regulatory programs of the past two decades. Resources for the Future concluded that the science behind the policy often gets distorted or ignored: "EPA for a variety of reasons is unwilling, unable, and unequipped to address and acknowledge the uncertainties in the underlying science."

EPA Administrator Whitman should now be put on notice that she is on probation and that another major blunder will result in President Bush "accepting her resignation," as the euphemism goes. And Ms. Fisher should depart now, before she does further damage.

The new EPA regulation is only one symptom of the rot within the agency, but it is a serious one. It ensures that the potential of biotechnology applied to agriculture and food production is tarnished — as is the health of the environment, not to mention the reputation of the Bush White House.

1 US National Research Council Field testing genefically modified organisms Framework for decisions (US National Research Council. National Academy Press, Washington. DC. 1989)
2 Editorial Nature 356. 1–2 (1992)
3 Appropriate oversight *for* planls with inherited traits from resistance to pests A report from eleven scientific societies (Institute of Food Technologists. Chicago, IL. 1996)
4 Council on Agricultural Science and Technology The proposed EPA pesticide rule (CAST, Issue Paper No 10, October 1998)

Regulation Is the Biggest Pest of All

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Agriculture in northern California, one of the region's major industries, is under threat from an insect called the glassy-winged sharpshooter. These leaf-hoppers carry Pierce's disease, a lethal bacterial infection of grapevines, citrus, and other plants, for which there is no cure. They have migrated from Mexico and are now causing millions of dollars in damage annually to California's vineyards.

But the worst is yet to come: the infestation currently threatens the San Joaquin Valley's 800,000 acres of table, raisin, and wine grapes, and involvement of the premier wine-making regions of Napa and Sonoma cannot be far off.

The meager weapons available to attack the sharpshooter include inspecting plants shipped from areas known to be infested by the insects and spraying chemical pesticides; scientists are also experimenting with a wasp that preys on the glassy-winged sharpshooter. In the long run, however, these methods will likely fail. As Dale Brown, president of the Napa Valley Grape Growers Association, acknowledges, **"genetic resistance is where we want to go." But this definitive solution has been made hugely expensive and impractical by regulatory obstacles erected by the Environmental Protection Agency (EPA).**

To introduce or enhance resistance to Pierce's disease in grapevines, one logical approach is to transfer genes that confer resistance into grapes from distantly related, noncommercial grapes that possess natural immunity. But conventional grape breeding is a notoriously slow process, and attempts to use more-sophisticated and efficient gene-splicing techniques have run afoul of EPA regulatory policies.

The EPA treats any plant that has been modified with gene-splicing techniques to enhance its pest or disease resistance as though it were a chemical pesticide. This policy flaunts the widespread scientific consensus that gene-splicing is more precise, circumscribed, and predictable than other techniques and that foods from the new, insect-resistant gene-spliced plant varieties have lower levels of contamination by toxic fungi and insect parts than those from conventional varieties. Thus, these gene-spliced varieties not only increase yields and make better use of existing farmland but are a potential boon to public health. Moreover, by reducing the need for spraying chemical pesticides on crops, they are environmentally and occupationally friendly. Yet the EPA holds gene-spliced plants to an extraordinary standard, even requiring hugely expensive testing as though they were pesticides. **These policies are, in effect, a punitive tax on a superior, and badly needed, technology.**

Dozens of major scientific societies have condemned the policy, warning that it will discourage the development of new pest-resistant crops, prolong and increase the use of synthetic chemical pesticides, increase the regulatory burden for developers of pest-resistant crops, expand federal and state bureaucracy, limit the use of biotechnology to larger developers who can pay the inflated regulatory costs, and handicap the United States in competition for international markets.

All these predictions have come true. California is already reaping what the EPA regulators have sown; they should now be held accountable.

— *Henry I. Miller*
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Precaution without principle

Henry I. Miller and Gregory Conko

Remember the admonition not to believe a bureaucrat who claims that "I'm from the government and I'm here to help you?" Well, government regulators now have a more subtle, updated version of that assertion: a wolf in sheep's clothing called the "precautionary principle". It has already laid waste to several industries and boasts a body count in the tens of thousands. It is now being used *to* cripple public sector and academic researchers as well as the biotechnology industry.

Although a widely accepted definition of the "principle" does not exist, its thrust is that regulatory measures should prevent or restrict actions that raise even conjectural threats of harm to human health or the environment, although there may be incomplete scientific evidence as to their potential significance. Several European countries have used the precautionary principle to justify paralyzing restrictions on agricultural and food biotechnology, and the European Commission (EC) has invoked it *to* justify a moratorium on the approval of new recombinant DNA-modified products'.

Use of the precautionary principle is sometimes represented as "erring on the side of safety". But we believe the way it is typically applied to research and development and to commercial products can actually increase risk.

Potential risks should be taken into consideration before proceeding with any new activity or product, whether it is the choice of site for a power station or the introduction of a new drug into the pharmacy. But advocates of the precautionary principle focus primarily on the possibility that technologies could pose unique, extreme, or unmanageable **risks.** What is missing from the precautionary calculus is an acknowledgment that even when technologies introduce new risks, most confer net benefits; that is, their use reduces many other, far more serious hazards. Examples include blood transfusions, magnetic resonance imaging (MRI) scans, and automobile air bags, all of which offer immense benefits and only minimal risk.

The real danger of the precautionary principle is that it distracts consumers and policymakers from known, significant threats to human health and often diverts limited public 'health resources from those genuine and far greater risks. Consider, for example, the environmental movement's misguided crusade to rid society of all chlorinated compounds.

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By the late 1980s, environmental activists were attempting to convince water authorities around the world of the possibility that carcinogenic by-products of chlorination made drinking water a potential cancer risk. Peruvian officials caught in a budget crisis used this supposed threat to public health as **a** justification to stop chlorinating much of their country's drinking water. That decision contributed to the acceleration and spread of Latin America's 1991-1996 cholera epidemic, which afflicted more than 1.3 million people and killed at least 11,000 (ref. **2).**

Anti-chlorine campaigners more recently have turned their attacks *to* phthalates, liquid organic compounds added to certain plastics to make them softer. These soft plastics are used for important medical devices, particularly fluid containers, blood bags, tubing, and gloves; children's toys, such as teething rings and rattlers; and household and industrial items, such as wire coating and flooring. Waving the banner of the precautionary principle, activists claim that phthalates could have numerous adverse health effects—even in the face of significant scientific evidence to the contrary[3]. Governments have taken these unsupported claims seriously, and several formal and informal bans have been implemented around the world. Industry has been stymied, consumers denied product choices, and doctors and their patients deprived of lifesaving tools.

During the past few years, skeptics began more intensively to scrutinize the precautionary principle. In response to those assessments, the EC, a prominent user and abuser of the precautionary principle, last year published a formal communication to promote the legitimacy of the concept[4]. The EC resolved that, under its auspices, precautionary restrictions would be "proportional to the chosen level of protection," "non-discriminatory in their application," and "consistent with other similar measures." The commission also avowed that EC decision makers would carefully weigh "potential benefits and costs." But all of these stipulations have been flagrantly ignored or abused in the commission's regulatory approach to recombinant DNA-modified—or in their argot, "geneticallymodified" (GM)—foods.

Dozens of scientific bodies, including the UK's Royal Society, the US National Academy of Sciences, the World Health Organization, and the American Medical Association have analyzed the oversight that is appropriate for gene-spliced organisms and arrived at remarkably congruent conclusions: The newer molecular techniques for genetic improvement are an extension, or refinement, of earlier, far less precise ones; adding genes to plants or microorganisms does not make them less safe either to the environment or *to* eat; the risks associated with recombinant DNA-modified organisms are the same in kind as those associated with conventionally modified organisms; and regulation should be based upon the risk-related characteristics of individual products, regardless of the techniques used in their development.

Notwithstanding the EC's promises that the precautionary principle would not be abused, regulators treat recombinant DNA-modified plants and microorganisms in a discriminatory and inconsistent fashion, and without proportionality to risk. Both the fact and degree of regulation turn on the use of certain production methods—that is, on whether recombinant DNA techniques have been used—regardless of the level of risk posed by individual products.

For example, recombinant herbicide-tolerant crop plants, such as soybeans and canola, are subject *to* lengthy, hugely expensive mandatory testing and pre-market evaluation, whereas plants with virtually identical properties but developed with older, less precise genetic techniques are exempt from

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such requirements. In the United States, Department of Agriculture requirements for paperwork and field trial design make field trials with gene-spliced organisms 10–20 times more expensive than the same experiments with virtually identical organisms that have been modified with conventional genetic techniques[5].

The real-world impacts of this wholly disproportionate approach are instructive. If a student doing a school biology project takes a packet of ''conventional," but genetically improved, tomato or pea seeds to be irradiated at the local hospital and plants them in his backyard in order to investigate interesting mutants, he need not seek approval from any local, national, or international authority. However, if the seeds have been modified by the addition of one or a few genes by recombinant DNA techniques, this would-be researcher (or equivalent highly skilled agricultural scientists) faces a mountain of bureaucratic paperwork and expense.

Not only does this discrimination flaunt the scientific consensus about the essential continuity between the traditional and molecular genetic improvement of plants, but it also ignores the fact that recombinant DNA technology is more precise and predictable and the modifications far better characterized than with other techniques. Logical application of the precautionary principle to situations of scientific uncertainty would dictate that greater precaution apply to the cruder, less precise, less predictable "conventional" forms of genetic modification. Instead, by torturing the precautionary principle, regulators have chosen to set the burden of proof far higher for recombinant DNA technology than for conventional plant breeding. And, as the EC's moratorium on new product approvals demonstrates, even when that extraordinary burden of proof is met through unprecedented amounts of testing and evaluation, regulators frequently declare themselves unsatisfied.

Remarkably, although the EC characterized its communication on the precautionary principle as an attempt to impart greater consistency and clarity, it specifically declined to define the principle, adding naively that "it would be wrong to conclude that the absence of a definition has to lead to legal uncertainty." Although reliance on regulatory agencies and courts to define and elaborate statutory policy is not unusual, this reluctance to define what purports to be a fundamental principle makes confusion and mischief inevitable, leaving innovators' legal rights and regulators' legal obligations subject to the wholly subjective and sometimes nefarious judgment of governments or even individual regulators.

As it is being applied, the precautionary principle provides neither evidentiary standards for "safety" nor procedural criteria for obtaining regulatory approval, no matter how much evidence has been accumulated. In effect, regulators are given carte blanche to decide what is "unsafe" and what is "safe enough", with no means to ensure that their decisions actually reduce overall risk or that they make any sense at all. Contrary to the claims of its supporters, the precautionary principle tends to make governments less accountable, not more so, because its lack of definition allows regulators to justify any decision.

In spite of the assurance of the European Union and other advocates of precautionary regulation to the contrary, regulators of biotechnology applied to agriculture and food production seldom consider the potential risk-reducing benefits of new technologies. For example, the use of recombinant DNA-modified plants with enhanced pest or disease resistance has reduced farmers' use of chemical pesticides, reducing runoff into waterways, and the exposure of workers who manufacture, transport, and apply these chemicals. It has also permitted farmers to more widely adopt environment-friendly, no-till farming practices. And recently developed rice varieties enhanced with pro-vitamin A and iron could drastically improve the health of hundreds of millions of the malnourished in developing countries. These are the kinds of tangible environmental and health benefits that have been given little or no weight in precautionary risk calculations.

But benefits aside, the safety of this new technology is not really in doubt. Both theoretical and empirical evidence shows the extraordinary predictability and safety of gene-spliced organisms. Recombinant DNA-modified plants are now grown worldwide on more than 100 million acres annually, and more than 60% of processed foods in the United States contain ingredients derived from recombinant organisms. There has not been a single mishap resulting in injury to a single person.

For anti-biotechnology activists, the deeper issue is not really safety at all. Often, the controversies over the testing and use of gene-spliced organisms — and in particular, the metastasis of the precautionary principle — stem from a social vision that is not just strongly anti-technology, but one that poses serious challenges to academic, individual, and corporate freedom.

In the western democratic societies, we enjoy long traditions of relatively unfettered scientific research, except in the very few cases where bona-fide safety issues are raised. (An example with contemporary relevance is the ban on research using live foot-and-mouth disease virus in the mainland United States.) Traditionally, we shrink from permitting small, authoritarian minorities to dictate our social agenda, including what kinds of research are permissible and which technologies and products should be available in the marketplace. Thus, for remarkably well-behaved recombinant DNA technology, a refinement of earlier techniques, it is beside the point whether the purpose of investigating a new plant variety or microorganism is to test a scientific hypothesis or a marker gene, to produce a more elegant rose, to offer a marginal improvement for purposes of downstream processing, or to improve the lot of malnourished children.

It is precisely the anti-technology nature of the precautionary principle that makes it the darling of many non-governmental organizations. Greenpeace, one of the principal advocates of the precautionary principle, wrote in its 1999 Internal Revenue Service filings that the organization's goal is not the prudent, safe use of recombinant DNA-derived foods or even their labeling; rather, they demand nothing less than these products' "complete elimination [from] the food supply and the environment.@' Many of these groups do not merely proselytize for illogical and stultifying regulation or outright bans on product testing and commercialization; they advocate and carry out vandalism of field trials.

Carolyn Raffensperger, executive director of the Science and Environmental Health Network, a consortium of radical groups, asserts that the precautionary principle "is in the hands of the people," as illustrated, according to her, by violent demonstrations against economic globalization, such as those in Seattle at the 1999 meeting of the World Trade Organization[7]. "This is [about] how they want to live their lives," says Raffensperger.

In our view, it's really about how a small, vocal, violent **group** of radicals wants to dictate to the rest of us how we should live our lives. In other words, the issue here is freedom and its infringement by ideologues who disapprove, on principle, of a certain technology. But bullies should not be permitted to use untruths, conspiracy, and violence to oppose legitimate research into technologies that can improve our safety and well-being. We should no longer allow extremists to dictate the terms of the debate.

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