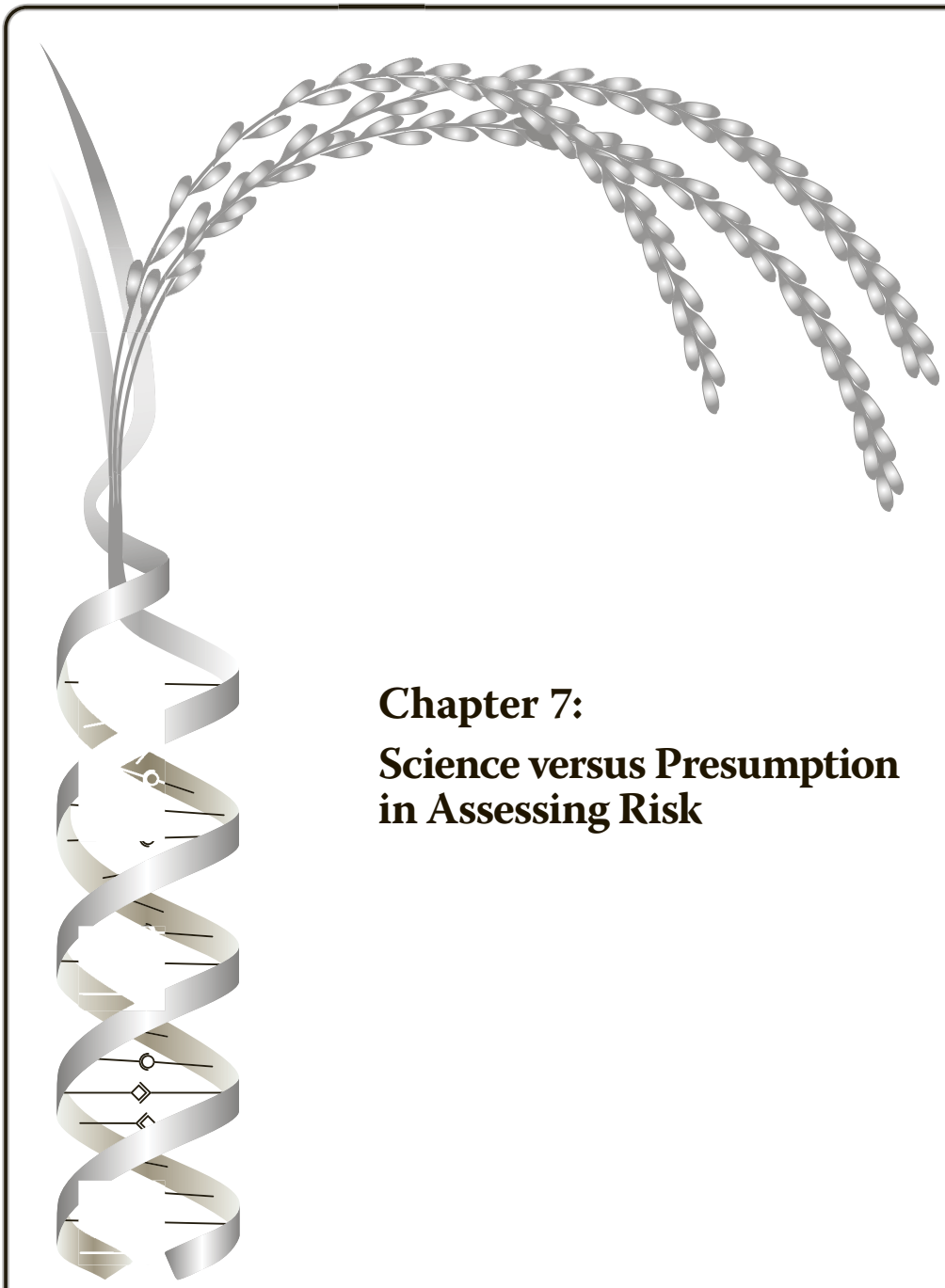

Chapter 7:

Science versus Presumption in Assessing Risk

Chapter 7: Science versus Presumption in Assessing Risk

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Consumers benefit in a myriad of 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 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

[322] This manuscript builds on earlier, shorter papers by the same authors: Miller, H. and Conko, G. *The Protocol's Illusionary Principle*, Nature Biotechnology, 2000, 18, 360-61, 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.

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 how the precautionary principle can systematically weaken 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 U.S. National Academy of Sciences,[323] the American Medical Association,[324] the Institute of Food Technologists,[325] and the United Nations' Food and Agriculture Organization and World Health Organization[326] 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

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[323] NAS, *Introduction of Recombinant DNA-Engineered Organisms into the Environment: Key Issues*, Washington, DC: Council of the U.S. Academy of Sciences/National Academy Press, 1987.

[324] AMA, *Report 10 of the Council on Scientific Affairs (I-00): Genetically Modified Crops and Foods*, Chicago, IL: American Medical Association, 2000, available at: http://www.ama-assn.org/ama/pub/article/2036-3604.html.

[325] IFT, *IFT Expert Report on Biotechnology and Foods*, Chicago, IL: Institute of Food Technologists, 2000.

[326] WHO, *Strategies for Assessing the Safety of Foods Produced by Biotechnology: Report of a Joint FAO/WHO Consultation,* Geneva, Switzerland: World Health Organization, 1991.

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]." [327]

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." [328]

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." [329]

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 chapter two, still other novel plant varieties are produced with somaclonal variation techniques or

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[327] NRC, *Field Testing Genetically Modified Organisms: Framework for Decisions*, U.S. National Research Council/ National Academy Press Washington, D.C., 1989.

[328] *National Biotechnology Policy Board Report* National, Institutes of Health, Office of the Director, Bethesda, MD, 1992.

[329] IFT, 2000.

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 couch grass. 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.[330] 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

[330] IAEA, *Officially Released Mutant Varieties: The FAO/IAEA Database*, Vienna, Austria: Joint FAO-IAEA Division, International Atomic Energy Agency, December 2000.

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, the Department of Agriculture requirements for paperwork and field trial design make field trials with gene-spliced organisms 10 to 20 times more expensive than the same experiments with virtually identical organisms that have been modified with conventional genetic techniques.[331] 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 percent 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." [332]

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.[333] 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,

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[331] Miller, Henry I., *Policy Controversy in Biotechnology: An Insider's View,* R.G. Landes Company, Austin, TX, 1997.

[332] Seibert, Jerry, *Regressive EPA Policy: Guest Opinion*, California Farmer, June 1997.

[333] Maltsbarger, Richard and N Kalaitzandonakes Study reveals hidden costs in IP supply chain, 2000, http://www.biotech-info.net/hidden_costs2.html, accessed 17 February 2001.

as well as the most diverse agricultural production system in the nation – involving more than 250 mainly minor-use-pesticide crops."[334]

Although the handful of large agribusiness companies involved in agricultural biotechnology have actually benefited 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 have 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.[335] 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 *un*regulated. 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.

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[334] Seibert, 1997.

[335] FAO, *Evaluation of Allergenicity of Genetically Modified Foods: Report of a /WHO Expert Consultation on Allergenicity of Foods Derived from Biotechnology,* Food and Agriculture Organization, Rome, Italy, January 2001.

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 cholera epidemic, which afflicted more than 1.3 million people and killed at least 11,000 between 1991 and 1996.[336]

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.[337]

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

[336] Anderson, Christopher, "Cholera epidemic traced to risk miscalculation," *Nature*, Vol.354, November 28, 1991, p. 255.

[337] ACSH, *Endocrine Disrupters: A Scientific Perspective,* American Council on Science and Health New York, NY, July 1999.

(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 U.S. 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 U.S. 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."[338]

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 maybe 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

[338] Schmidt, Alexander, Testimony before the Senate Labor and Human Resources Committee, 1974.

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. 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 little 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."[339] 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,

[339] Keeney R.L., "Mortality risks induced by economic expenditures," *Risk Analysis*, 2000, 147:148. See also Catalano R. "The Health Effects of Economic Insecurity," *American Journal of Public Health,* 1991; 81:1148.

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.[340]

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."[341] 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?"[342]

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 U.S. 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.[343] Thus, the WTO ruled in favor of the U.S. 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

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[340] Wildavsky, "Public Policy," Chapter 6 in Bernard D. Davis, Ed. *The Genetic Revolution: Scientific Prospects and Public Perceptions*, The Johns Hopkins University Press, Baltimore, MD, 1991, pp. 77-104.

[341] EC, *Communication from the Commission on the Precautionary Principle*, COM, 2000, Commission of the European Communities, Brussels, Belgium, February 2, 2001.

[342] Byrne, David, "Food Safety: Continuous Transatlantic Dialogue is Necessary," *European Affairs*, Vol. 1, No. 2, Spring 2000, pp. 80-85.

[343] WTO, *EC Measures Concerning Meat and Meat Products (Hormones): Report of the Appellate Body*, World Trade Organization, Geneva, Switzerland, January 16, 1998.

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 an 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 also will 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,[344] 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

[344] Kershen, Drew L., *Genetic Enhancements Can Reduce Food Company Legal Risks. Legal Backgrounder,* Washington Legal Foundation, Washington, DC, September 7, 2001.

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, the 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 to more effectively 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 benefiting 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.[345] 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.

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[345] Barton, John, John Crandon, Donald Kennedy, and Henry I. Miller, "A Model Protocol to Assess the Risks of Agricultural Introductions," *Nature Biotechnology*, Vol. 15, No. 9, September 1997, pp. 845-848.

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 foot 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,[346] 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.[347] This document, intended to clarify the 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

[346] Barton, Crandon, Kennedy, and Miller, 1997.

[347] FDA, "Statement of Policy: Foods Derived From New Plant Varieties," *Federal Register*, Vol. 57, May 29, 1992, pp. 22,984-23,005.

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 on 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 rulemaking 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 U.S. 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.[348] 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.[349] 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 regulations, 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 20-year old commitment not to discriminate against gene-spliced products are unfortunate. The long-term result will be 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.

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[348] FDA, "Premarket Notice Concerning Bioengineered Foods," *Federal Register*, Vol. 66, January 18, 2001, pp. 4,706-4,738.

[349] Miller, Henry I., *Political Angles at the FDA*, Washington Times, December 7, 1998, A19.

The 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 U.S. 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."[350]

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."[351]

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

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[350] Keating-Edh, Barbara, Testimony before the National Biotechnology Policy Board, *1992 National Biotechnology Policy Board Report*, National Institutes of Health, Bethesda, MD, 1992.

[351] *National Biotechnology Policy Board Report*, National Institutes of Health, Office of the Director, Bethesda, MD, 1992.

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.