

From Asilomar to Industrial Biotechnology: Risks, Reductionism and Regulation

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The international meeting held in February 1975 at the Asilomar Conference Center in Pacific Grove, California, set in motion the first scientific evaluation of genetically modified organisms. It left a legacy that remains influential decades later when the world is faced with the prospect of a cornucopia of new products derived from gene-splicing technology. Unlike the initial concerns over the risks of recombinant-DNA molecule technology (r-DNA), which was the centrepiece of the early controversy during and for several years after the 1975 Asilomar meeting, the contested issues today are about the social, environmental, economic, and ethical consequences of creating products from the progenitor technology. The public's attention has turned from the risks of r-DNA in basic research to the risks of biotechnology primarily in agriculture and the pharmaceutical industry.

In this paper, I focus on the cultural, political and epistemological components of risk analysis for genetically modified organisms (GMOs) and their impact on the regulation of the biotechnology industry. The guiding questions are: (1) in what ways did the Asilomar '75 framework for risk assessment set the stage for the social management of biotechnology in the United States during the start of its industrial development? and (2) what role did genetic reductionism play at Asilomar '75 and how did it shape the regulatory and legal development of biotechnology?

I argue that, beginning in 1980 with the election of Ronald Reagan, a changing political climate took hold in the United States, which gave rise to a neo-conservative government along with its cultural and economic manifestations. This helped to fuel and reinforce an epistemology of scientific reductionism. In short, this neo-conservative political ideology supported the breakdown of traditional sector boundaries between universities and industry, which led to the adaptation of science toward private rather than public agendas.

The belief structure of neo-conservatives is rooted in the economic theories of Friedrich Hayek and Milton Friedman. Hayek wrote in his book *The Constitution of Liberty* that we

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know what freedom is but there is no generally acceptable view of what justice is (Hayek, 1960). Therefore, he concluded, it was desirable to build the economy of a society on the concept of freedom. Injustice resulting from the market, he argued, would have to be dealt with in some secondary way, such as by appealing to the sentiments of philanthropy. In neo-classical economics, 'freedom' is understood to mean 'consumer sovereignty'. Micro-economics is the theoretical grounding for public policy in the extreme neo-classical view, where a 'value-free' calculus of utility based on the corpuscular view of rational individuals (*homo economicus*) became the intellectual currency for describing economic behaviour and justifying policy. The reductionism of economics and the reductionism of science functions synergistically. Globalization, the strategy to eliminate trade barriers among nations, is the path towards an international consumer society, where individual state planning becomes secondary to removing any impediments to the transfer of consumer products, capital, and labour.

Through a historical narrative process, I shall draw connections between the new conservative agenda of individualism, free markets, technology transfer, and 'junk science' with the scientific agenda of genetic reductionism, intellectual property, and corporate-academic alliances. The confluence of these agendas helps to explain and rationalize biotechnology regulatory policies in the United States. One can see evidence of a naïve and overzealous reductionism reflected in risk assessment, patent law, global harmonization, and environmental regulation.

Cultural Context of Asilomar

In the American context, the 1970s was the decade in which government responded to the political activism and social learning that took place in the 1960s. The birth of the environmental movement is generally set at 1970 when the US Environmental Protection Agency was created, Earth Day had its beginning, and technology assessment through environmental impact analysis was introduced into federal programmes. A new sensibility toward government ethics followed the post-Watergate era. Revelations about immoral human experiments involving radiation and psychotropic drugs led to a new system of accountability for clinical researchers. Comprehensive new laws were passed to protect the air, water, land and work place from toxic poisons. The US Congress created the non-partisan Office of Technology Assessment in 1972 as its advisory arm to help policy makers, and the public, understand the expected and unexpected ways that new technology affects human health and the global environment.

Young biologists were schooled in the 1960s during the peak of the anti-Vietnam war movement and became aware of the perils of atmospheric testing. Their professors spoke about the role of physics in the nuclear arms race and the role of chemists who developed defoliants that were aurally sprayed over vast acreages of Southeast Asia (Westing, 1984). They completed graduate school during the negotiations of the Biological Weapons Convention, signed in 1972. The state signatories pledged to prohibit the stockpiling, development and use of biological warfare agents (Wright, 1990, pp. 370–376).

The 1970s was a decade in which government regulation was sought to restrain the excesses of corporate polluters, to protect workers from occupational disease, and to prevent the despoliation of the planet's natural resources. Biologists came of age in the shadow of physicists who were in the ascendancy among the sciences in receiving government research grants. Physics brought the allies victory in World War II with radar,

electronics and atomic energy. In the aftermath of the war, many physicists were profoundly affected by the first use of the atomic bomb on civilian populations and the spiralling nuclear arms race that escalated during the Cold War. In the 1960s, groups of scientists formed organizations like *Science for the People*, and *Scientists and Engineers for Social and Political Action*, which criticized American domestic and foreign policies and connected capitalism with the new military–industrial complex.

Biologists had not generally been identified with war research, but they had been implicated in unethical human experiments such as the infamous Tuskegee Syphilis study. One of the most far-reaching government oversights of science came in the 1970s through the requirement that all experiments on human beings had to be vetted for safety, informed consent, and ethical cogency by an independent committee set up by each institution that received any federal funding. Biologists also had to comply with new regulations that protected animals from abuse and excessive pain in laboratory experiments. Federally funded institutions were required to establish animal care committees during the 1970s. Experimental science became accountable to third parties (other than the sponsor and the principal investigator) in human subjects' protection, animal care, the use of radioactive materials, and the disposal of toxic chemicals.

Those who entered the academic world in the late 1960s and early 1970s were part of a social milieu that did not shy away from raising questions about the ethics of science. The birth of the bioethics movement contributed to that sensibility. There were periods prior to the 1975 Asilomar meeting (called Asilomar II) when risky science was discussed. Articles written in the late 1960s discussed the possibilities of genetically modifying human beings. Shapiro, Beckwith and Eron, of Harvard Medical School, held a news conference to raise public awareness about their work in isolating a gene and its implications for eugenics (Shapiro *et al.*, 1969).

Concerns were also raised about the hazards of tumour viruses, and on 24 January 1973, a group of scientists met at the Asilomar Conference Center to discuss laboratory hazards of working with tumour viruses (Krimsky, 1982, pp. 58–69). Paul Berg and James Watson participated at the meeting. It was a risk that seemed very real to the scientists working with a class of viruses that were known tumourigenic agents for certain mammalian species although little was known about the infectivity of humans. It was not just the laboratory workers, though, who were at risk. Once exposed to a virus, they could potentially infect people in the community in which they lived and worked. The discussion turned from informed consent of the lab worker to informed consent of the community. This led to the dilemma of widening the circles of informed consent. Would any of the at risk population have a right to informed consent before any potentially risky experiments were performed? A unanimous outcome of the first Asilomar meeting (known as Asilomar I) was the proposal that there be epidemiological studies of laboratory workers to determine whether they were at risk from experiments involving tumour viruses. These studies, however, were never implemented.

As Gottweis (1998, p. 77) points out, 'risk' is not an objective entity.¹ There is a cultural selection process that takes a proposed risk and elevates it on the public agenda. It is like throwing some seeds on the earth. Some will germinate and some will not. The conditions have to be optimum. The same is true with assertions about risk, whatever the so-called evidentiary basis for the claims. The public is continuously faced with risk claims, but not all claims result in a social response. For example, in the late 1960s, human genetic engineering was discussed in popular magazine articles. Jonathan Beckwith's initial call

for a national dialogue on the social and ethical dimensions of new discoveries in genetics, when he and his colleagues isolated a gene, did not lead to much beyond a week's worth of media attention (Beckwith, 1970, 2002). And the concern about the infectivity to lab workers from mammalian tumour viruses also did not lead to a national debate over the risks and benefits of this research. One can argue, however, that each of these events further sensitized the biological community as it became poised for the next breakthrough. The build-up of social receptivity to risk is a key. Some people have introduced the metaphor of the 'tipping point' to explain how a series of small risk claims gains the gravitas to initiate a mass social response (Gladwell, 2000).

Perhaps the first event that ignited the fuse of the r-DNA controversy occurred when a graduate student working in Paul Berg's lab at Stanford University attended a scientific meeting to discuss her project of transporting animal virus genes into bacteria. Janet Merz recalled the concerns of one member of the conference that there might be risks associated with transporting animal tumour virus DNA into bacteria. She reported these discussions to Berg. At first, Berg seemed unconcerned about the risks, but after speaking with other colleagues, he too began to take the potential risks more seriously (Krimsky, 1982, pp. 24–38).

It was not until the 1973 Gordon Conference on molecular genetics that scientists took a collective action beyond private discussions to alert their colleagues about the potential hazards of inserting viral DNA into bacteria. The Gordon Research Conferences brought together investigators in specialized areas of science to discuss recent advances in their fields and new directions for research. Named after its founder Neil E. Gordon, a member of the chemistry department of Johns Hopkins University who initiated the first meeting in 1931, the Gordon Conferences have grown to accommodate dozens of meetings annually in different fields of specialization. At the 1973 meeting in molecular biology, scientists had learned that Stanley Cohen and Herbert Boyer had developed a simpler more efficient way of creating hybrid organisms. That discussion appeared to have 'tipped the balance', convincing some scientists to take the risks of gene splicing more seriously, especially when it became clear to the elite scientists that these experiments could be done by every 'pick and shovel' molecular geneticist. The scientific elites were faced with the question: do we trust our science with everyone?

A second meeting of biologists held at the Asilomar Conference Center in California in 1975 (Asilomar II) focused on the risks of transferring genetic material across species. In retrospect, Asilomar II was an illustration of 'precautionary thinking' applied to the biological sciences. The potential risks posed by the gene transfer experiments were hypothetical. There was surely no definitive evidence of a biohazard—merely a build-up of circumstantial evidence. The risks were theoretically plausible but empirically unknown.

From the earliest events leading up to Asilomar II, scientists were always acting on the presupposition that the concerns raised by their colleagues regarding risky experiments would be addressed internally within the relevant quarters of the scientific community. The antipathy that biologists had toward external regulation was as much a part of their ethos as their firm belief that they would not allow biology to be misused for destructive ends. During the peak period of the r-DNA controversy in the mid-1970s, Harvard biologist Mathew Meselson, who had discovered restriction enzymes in 1968 and became a leading advocate of the biological and chemical weapons conventions, stated in a NOVA documentary that any science could be used for malevolent purposes in a 'Hitlerian society'.

In an open democratic society, however, misuse of science could come about from unethical individuals through error or by unanticipated outcomes.

Asilomar II proved to be successful for the community of molecular biologists for several reasons. First, biologists could proudly say that they provided an early warning before any risky experiment was performed, especially one that might cause harm to laboratory workers. They could cite many examples in the fields of physics and chemistry where society learned about the effects after human casualties were reported—as in radiation hazards and the industrial release of chemical neurotoxins and carcinogens.

Second, the Asilomar organizers kept a group of dissident scientists (that is, members of *Science for the People*, and iconoclast opponents of allowing gene splicing in densely populated university settings) at bay while bringing the majority of biologists to a consensus on an approach for managing the unknown risks. After Asilomar, fewer scientists remained critical of gene splicing experiments. The differences among molecular biologists became more polarized. A smaller number of dissidents were more easily marginalized. James Watson, who shared the Nobel Prize for discovering the structure of DNA, used his authority to characterize opponents of r-DNA as ‘kooks, shits and incompetents’ (*Chemical & Engineering News*, 1977, p. 26).

Third, Asilomar II was successful from the perspective of the molecular geneticists because it kept the federal government from passing any legislation that would regulate r-DNA experiments. The clarion call was that regulation would damage the vitality of American science. This anti-regulatory response to science was carried over years later to the gestating biotechnology industry. In this case new academic–industry collaboration spoke with a single voice warning that regulations for the nascent life sciences industry would curtail research and industrial innovation.

Social Construction of r-DNA Risk Management

One of the notable outcomes of Asilomar II was the approach its organizers took in assessing and managing potential and conjectural risks. During the intense period of dialogue that took place within the broader scientific community prior to and during Asilomar II, several public responses to the potential risk of r-DNA research began to emerge. First, experiments that rearrange DNA in living organisms should be prohibited. No molecular geneticists could be identified with this position. Second, only r-DNA experiments in a few well controlled high containment facilities should be performed. This was a position taken by a few geneticists and many more scientists who were not familiar with the new technology. It was generally considered impractical in a field ready to explode. At the time there were only a handful of level 4 biological laboratories in the United States. There was a rush to build biological level 3 facilities to accommodate new rules for r-DNA research formulated by the National Institutes of Health (NIH). Third, experiments should only be performed under new standards of risk management that would provide sufficient margins of safety to scientists, cleaning staff, students and laboratory technicians. This third strategy was adopted quite early in the process.

A small group of molecular biologists formed a committee (referred to as the Berg Committee after its chair Paul Berg) with the imprimatur of Philip Handler, then President of the National Academy of Sciences, to define the problem of r-DNA risk and to propose a mechanism to address it. Out of that committee came the idea of convening an international conference of scientists involved in this new field of research. This became

known as Asilomar II and took place in February 1975. Among the recommendations of Asilomar II was that the leadership of the NIH convene a committee of scientists who would be responsible for drafting guidelines for the American scientific community on the safety of engaging in gene transplantation experiments.

The approach taken by the Asilomar II participants to manage r-DNA research involved three elements: physical containment, biological containment, and human behaviour. The purpose of physical containment was to prevent personnel from being exposed to a genetically modified organism by building physical barriers in the laboratory (special hoods, proper decontamination). The second leg of risk management involved the use of biologically disabled organisms that could not survive beyond the laboratory bench. Much emphasis in the risk management scheme was placed on the so-called crippled strain of *Escherichia coli* that required a number of not easily available chemicals for the organisms to survive. Finally, the third leg of the strategy for managing risks was controlling behaviour. Scientists were restricted from eating in their labs or from mouth pipetting. They were accountable to an institutional biological safety officer who was responsible for overseeing that safety protocols were obeyed.

A set of safety levels was also established based on some assumptions about the infectivity of organisms across different species. Mammalian virus DNA was considered more potentially dangerous to humans than bacterial viruses because the latter were not known to infect humans. Another assumption was that physical and biological safety could be substituted for one another without compromising safety. The Asilomar II organizers, based on what they believed were the *a priori* probabilities of the new r-DNA constructed organisms, developed these risk assumptions. The Asilomar II experience brought to the scientific community a higher awareness of laboratory safety, while the investigators' autonomy was limited in small but meaningful ways. Some violators were cut off from NIH grants and/or embarrassed by the media.

It is generally understood that the Asilomar II scientists guessed at the risks. A few planned and executed risk assessment experiments sponsored by NIH did not resolve some of the core questions of creating new hazards (Krimsky, 1982, pp. 244–263). There were no laboratory surveillance programmes to determine whether the agents they worked with infected scientists and lab workers. Asilomar II gave the appearance of offering a technical response to problems of risk, but most commentators recognize that uncertainties in science are too great to avoid the intrusion of values and self-interest. As for the legacy of Asilomar II, historian Susan Wright summed it up as follows (Wright, 1994, p. 159):

The proceedings of the Asilomar conference show that a reductionist discourse bearing within it the seeds of a technical solution expressed personal and economic interests in developing the field without external intervention, and at the same time contributed powerfully to defining and reinforcing the central role of the biomedical research community in policymaking.

The NIH director followed the recommendations of Asilomar II and convened a committee that drafted guidelines on recombinant-DNA molecule experiments. While the ink was still wet, though, new efforts were underway to downgrade the risk level for proposed experiments. In fact, decisions to downgrade *a priori* risk levels were based, not on new empirical information, but on the presumption that because there were no illnesses or

adverse events in the laboratories where the r-DNA experiments were undertaken, the initial risk estimates were viewed as probably too high.

But the prospect of intentional releases of r-DNA organisms into the environment in the early 1980s brought a new set of risk concerns. The Asilomar II risk management process focused exclusively on human health hazards from laboratory-modified organisms. Large scale field-testing was initially prohibited under the 1976 NIH guidelines. At the outset, there were no ecologists on NIH's risk assessment committee. Ecologists had a less reductionist way of understanding the risks of r-DNA than molecular geneticists, who emphasized the higher predictability of the techniques over conventional hybridization (Krimsky, 1991, pp. 133–151). Several papers in *Science*, among them a report by plant biologist Winston Brill (1985) and another by ecologist Robert Colwell *et al.* (1985), took up the question of ecological risk assessment, but the dominant position was carried by the National Academies of Science (NAS).

National Academies of Science

The NAS issued several reports on the risks of r-DNA technology focused on the release of GMOs into the environment. The first report came in the form of a pamphlet and was published in 1987. A special group of scientists called the Committee on the Introduction of Genetically Engineered Organisms into the Environment wrote the report, which was then vetted through the NAS Council. The report stated, 'There is no evidence that unique hazards exist either in the use of r-DNA techniques or the movement of genes between unrelated organisms. The risks associated with the introduction of r-DNA-engineered organisms are the same in kind as those associated with the introduction of unmodified organisms and organisms modified by other methods' (NAS, 1987, p. 22). When the report was criticized for its sparseness (24 pages), the NAS issued another study two years later in which it provided an extensive review of the scientific literature and reached a similar conclusion, 'Crops modified by molecular methods in the foreseeable future pose no risks significantly different from those that have been accepted for decades in conventional breeding' (NAS, 1989, p. 64).

Three propositions were central to the NAS position on r-DNA techniques (NAS, 1987, p. 22). Proposition 1: 'There is no evidence that unique hazards exist either in the use of r-DNA techniques or in the movement of genes between unrelated organisms'; Proposition 2: 'The risks associated with the introduction of r-DNA-engineered organisms are the same in kind as those associated with the introduction of unmodified organisms and organisms modified by other methods'; and, Proposition 3: 'Assessment of the risks of introducing r-DNA-engineered organisms into the environment should be based on the nature of the organisms and the environment into which it is introduced, not on the method by which it was produced'. The NAS study affirmed that the new power to alter organisms was unique, but the risks were not. This is how the report described the new technology: 'Powerful new molecular methods for DNA manipulation provide a means for constructing microorganisms with novel genotypes that cannot be duplicated by classical methods and would be highly unlikely to occur naturally' (NAS, 1989, p. 86).

The concept of unique risks was never fully analyzed in either report. What constitutes a unique risk? Logic alone tells us that for there to be a unique risk, there must be a risk and that said risk must be unique. How would one falsify the statement, 'There are no unique risks?' One would have to find a risk and then determine whether it is unique. There is no

disagreement among the scientists that it was possible to create risks with genetic engineering. The question is, is that risk unique? There are certainly genetic exchanges accomplished by r-DNA that do not occur in nature (that is, botulism toxin gene in *E. coli*). What would count as unique? Could a non-r-DNA process create the same genetic construct? If so, then it is not unique; but there are clearly some genetic constructs whose natural probability of occurrence is so low, we might as well say it is unique to r-DNA. Under this definition, a ‘unique risk’ from gene splicing is a phenotype of an organism whose occurrence by other means is so improbable (not impossible) as to make the organism and its associated risks the sole outcome of r-DNA techniques.

Perhaps what the NAS meant by a ‘unique risk’ is a unique class of risks. For example, a unique risk would be the creation of a new variety of pathogens. Clearly, there are many ways that pathogens get created, so in that sense r-DNA is not unique. Because the NAS did not define or explain what it meant by a ‘unique risk’ it was not possible to validate its claim about r-DNA and unique risks.

Geneticization of Environmental Risks

Large-scale releases of GM crops brought into focus two ways of understanding the effects on the phenotype of organisms modified with foreign gene inserts. I refer to these as the *Lego System* versus the *Ecosystem* models of the genome.² The *Lego* system refers to a highly mechanistic and reductionist model that frames the possibilities resulting from reorganizing the genome of highly evolved organisms (Krimsky, 2000). Functional genes added or deleted from the plant or animal genome either contribute a new protein to the phenotype of the organism or are quiescent. Risk assessment is reduced to: (1) understanding how the gene functioned in the parent organism (what protein it coded for); (2) whether the foreign gene expresses the protein in the new organism; (3) how much expression of the protein there is; (4) what vector is used to transport the gene; and, (5) what other genes (for example, antibiotic resistance genes) are carried by the vector.

The *Ecosystem* model of transgenics is guided by a non-reductionist view of genomics. It looks at multiple pathways of gene expression and is informed by the knowledge that the introduction of foreign genes may affect the expression of other genes in the host plant. The *Ecosystem* model (in contrast with the analogy of a child’s game of Lego—a system of blocks whereby the individual components are not affected by the addition of another block) asserts that adding a gene to a living cell can affect other genes in the system. This model takes into account the ‘position effect’ of foreign genes, gene–gene interactions, and the fact that the initial belief in ‘one-gene–one protein’ has been proven false. The location of the gene introduced into the host organisms can be important to its mode of expression and can affect whether other genes are up regulated (greater expression) or down regulated (lower expression). One scientist commented, ‘These positioning effects are not simple to predict. Think of William Tell shooting an arrow at a target. Now put a blindfold on the man doing the shooting and that’s the reality of the genetic engineer when he is doing a gene insertion’.³ According to biologist Mae-Wan Ho (1998, p. 131), ‘because no gene ever functions in isolation, there will almost always be unexpected and unintended side-effects from the gene or genes transferred into an organism’.

The structure of the NIH and its relative isolation from the ecological community kept geneticists in control of the risk assessment. Winston Brill’s published article in *Science*

titled 'Safety Concerns and Genetic Engineering in Agriculture' turned the old vitalist debate on its head, when he argued that biology was more predictable than chemistry. He wrote

Even if a new chemical is only a slightly modified analog of a known safe chemical, the degree of safety cannot be extrapolated from the safe chemical. In fact, analogs of normal metabolites can be most dangerous. By comparison, minor modifications obtained by breeding safe plants or mutating safe microbes do not yield progeny that become serious problems . . . A program that aims to utilize, in agriculture, a plant, bacterium or fungus considered to be safe but with several foreign genes will have essentially no chance of accidentally producing an organism that would create an out-of-control problem (Brill, 1985, p. 383).

By way of contrast, the Ecological Society of America (ESA) took an ecosystem view of transgenics. Its members placed their faith in field tests over genetic analysis of GMOs. In his 1986 congressional testimony, Elliott Norse, representing the ESA, highlighted the difference in perspective:

Molecular biologists work in laboratories to penetrate the mystery of the invisibly tiny world within cells. In contrast, for the most part, ecologists work in the fields and wetlands and forests to unravel the mysteries of nature at a vastly larger scale . . . our work examines the interactions of living things in the fascinatingly complex world that we can see (Norse, 1986, pp. 171–177).

Ecologist Martin Alexander explained the limits of ecology in predicting or explaining how genetically altered organisms would behave in the environment: 'Ecologists are unable to predict which introduced species will become established and which will not, and it is often not possible to explain successes or failure after the fact' (Alexander, 1985, p. 60). The schism between geneticists and ecologists persisted throughout the 1980s. By 2000, more nuanced viewpoints from cell biologists and a greater recognition of the *ecosystem model* of the genome began to emerge.

David Schubert, a cell biologist at the Salk Institute, broke a long silence within the cell biology community in a commentary he published in *Nature Biotechnology* in responding to the notion that genetic engineering is just like traditional plant breeding. Schubert (2002, p. 969) cited three conclusions from genetics research relevant to risk assessment: (1) 'Introduction of the same gene into two different types of cells can produce two very distinct protein molecules'; (2) 'Introduction of any gene, whether from different or the same species, usually significantly changes overall gene expression and therefore the phenotype of the recipient cell'; and (3) 'Enzymatic pathways introduced to synthesize small molecules, such as vitamins, could interact with endogenous pathways to produce novel molecules'. From these scientific results, Schubert (2002, p. 969) concluded, 'The potential consequence of all these perturbations could be the biosynthesis of molecules that are toxic, allergenic, or carcinogenic. And there is no *a priori* way of predicting the outcome'.

US Federal Oversight over Biotechnology

By 1978, the NIH had issued revised guidelines for scientific research using r-DNA techniques that eased safety requirements. The guidelines, however, applied exclusively to those institutions that received federal funding. The concerns over laboratory risks had diminished and the relaxation of the guidelines was on a steady course. When industrial biotechnology came of age in 1980, a number of companies, which were not legally bound by the NIH guidelines, still looked for the imprimatur of the NIH for their field tests of genetically modified plants and microorganisms. To meet the needs of an emerging industry concerned about public anxiety over the safety of GMOs, the NIH established a 'Voluntary Compliance Program' for companies who sought the RAC approval for their proposed field experiments (Krimsky, 1991, pp. 102–104). The types of risks associated with field studies, involving open ecological systems, were not part of the expertise that NIH had concentrated on the RAC. Thus, after Congress jettisoned any hope that the private biotechnology sector would be regulated by new legislation, the responsibility to assess the ecological risks of field releases was passed on to the EPA by its authority under existing legislation.

Beginning in the 1980s, the US regulatory response to biotechnology moved toward guidelines, which documents a departure from the command control regulations of the 1970s. This was a response to a pro-market, anti-regulatory shift in the political culture of government. As part of this shift, a new ideology of 'junk science' created a false dichotomy between 'good science' and 'bad science' to derail any attempts to use the weight of circumstantial evidence and precautionary approaches to regulate biotechnology. No new laws were passed in the United States for genetically modified organisms. Instead, laws passed to regulate chemicals were stretched to apply to GMOs. This resulted in some unusual adaptations of language, such as designating a ubiquitous non-GM soil organism (*Pseudomonas*) a pesticide. This microbe, which resides on the leaf surfaces of plants, possesses a protein that can act as an ice-nucleating particle for super-cooled water when the temperature reaches a few degrees below freezing. When the gene that codes for this protein is excised ('ice minus'), it no longer can serve as a nucleating site for frost formation. If the natural organism ('ice plus') facilitates ice formation below freezing temperatures thereby causing damage to the plant then it can be designated a pest; its GM variant ('ice minus') can then be thought of as a pesticide since it protects the plant from frost damage.

As the risk assessment moved from the NIH to the Environmental Protection Agency (EPA), greater emphasis was placed on pleiotropy (unanticipated effects) and epistasis (gene–gene interactions). The EPA's regulatory culture was more comfortable than NIH with the language of ecology. At its inception, the EPA had ecologists on its staff, whereas it had to recruit geneticists when the first field trial releases were placed under its regulatory authority.

The US Office of Science and Technology Policy (OSTP) also issued its 'product versus process' distinction for the regulation of GMOs. According to OSTP, r-DNA techniques (a process for making genetic alterations in organisms) should not be selected out for regulation. Rather, agencies should regulate on the basis of the product (whether it showed any characteristics of producing hazards to people or the environment). The EPA had difficulty towing the line in grounding its regulation without special consideration given to r-DNA techniques. In 2001, the EPA decided not to deregulate genetically modified

plant-incorporated pesticides (PIPs) derived from sexually compatible plants, whereas conventionally bred PIPs from sexually compatible plants were deregulated. The agency chose as a hypothesis that the GM PIPs might pose a greater risk than conventionally bred PIPs. This was a departure from the product (not process)-based regulation advanced by the OSTP (Murphy and Krimsky, 2003, pp. 102–104).

The US Food and Drug Administration (FDA) is largely a toxicology-driven agency, one highly receptive to reductionist genomics through being comfortable with the reductionism of biochemistry. During the 1980s, FDA officials vigorously supported a product-based approach. When OSTP's Coordinated Framework for Regulation of Biotechnology was released in 1986, federal regulatory agencies interpreted the framework for their own regulations (OSTP, 1986). The FDA had a choice of whether or not to consider foreign genes added to plants by genetic engineering techniques as food additives. Such a decision would require mandatory testing under the US Food, Drug and Cosmetic Act. In its 1992 policy of GM foods, the FDA instead chose to exempt foreign genes from being classified as food additives and designated them GRAS, a regulatory term meaning 'generally regarded as safe' (Kessler *et al.*, 1992).

The US agro-biotechnology companies were also given a guidance document that gave them options for how to deal with GM products. GM food producers were asked to contact the FDA if they believed their GM food product was likely to introduce allergens or raise its microtoxin levels. Companies were not required to notify the agency before they introduced a genetically modified food product into the marketplace. The FDA left to the producers the responsibility for pre-market testing and providing the agency with any information supporting the conclusion that the GM product was as safe as its conventional counterpart.

Meanwhile, new knowledge from the science of genetics was becoming increasingly at odds with the Lego conception of the plant genome. Studies confirmed that adding foreign genes to a plant genome could affect the expression of other functional genes. The FDA began to acknowledge the new findings and modified its regulatory requirements. For example, in 2001, the FDA issued a draft policy that saw a slight shift from its pure 'product-based' regulation by requiring pre-market notification before any GM products were introduced into the marketplace. The policy emphasized the uncertainties of transferring foreign genes into an organism. The FDA stated that the phenotypes of transgenic crops might be completely different than their parental strains and that unanticipated effects might be more prevalent with bioengineered products (FDA, 2001). To illustrate how the agencies incorporated the new anti-reductionist science into their regulatory discourse, even while remaining true to the reductionist regulations, consider the following passage from an FDA document that discusses pre-market information to be submitted to the agency (FDA, 2001, p. 4733).

Characterization of the introduced genetic material, including the number of insertion sites, the number of gene copies inserted at each site, information on the deoxyribonucleic acid (DNA) organization within the inserts and information on the potential reading frames that could express unintended proteins in the transformed plants.

In providing reasons why companies should avail themselves of the consultation opportunities under the FDA, the agency described the ways that biotechnology could introduce new and unique risks (FDA, 2001, p. 4728).

[B]ecause bioengineering enables developers to introduce genetic material from a wider range of sources than has traditionally been possible, there is a greater likelihood that a developer using bioengineering to modify a food plant may introduce genetic material whose expression results in a substance that is significantly different from substances historically consumed in food . . . it is also possible with bioengineering that the newly introduced genetic material may be inserted into the chromosome of a food plant in a location that causes the food derived from the plant to have higher levels of toxins than normal, or lower levels of a significant nutrient. In the former case the food may not be safe to eat, or may require special preparation to reduce or eliminate the toxic substance. In the latter case, the food may require special labeling, so that consumers would know that they were not receiving the level of nutrients they would ordinarily expect from consuming comparable food.

The reductionist programme in regulatory biotechnology was applied opportunistically by the commercial sector. When laboratory-scale studies suggested that there might be ecological risks, industry's reaction turned against reductionism arguing that the laboratory was not a good model for what actually occurs in nature. The Monarch butterfly study is a case in point. Losey *et al.* (1999) found that Bt pollen sprinkled on milkweed fed to Monarch caterpillars killed the caterpillars. The tests were criticized by industry for making an error of extrapolating from laboratory studies to natural field conditions.

Conclusion

As previously noted, the risk analysis of laboratory GMOs and the legal doctrine of life patents were both rooted in forms of genetic reductionism. The risk assessment framework developed at Asilomar II played a critical role in shaping the regulation of GM products released into the environment or the food supply. The legal doctrine of life patents was an important stimulus for jump-starting the nascent biotechnology industry. This was all occurring during a neo-conservative shift in the American political culture.

The regulatory path from Asilomar II to industrial biotechnology shared a common thread that included: a reductionist approach to risk; the use of flexible guidelines established by and for scientists; the transformation of the university scientific culture into academic enterprise zones with the dual purpose of creating and commercializing knowledge, and the strategic concordance between the universalism of science; and, the globalism of economic policy and intellectual property.

I have argued in this paper that scientific reductionism, beginning with Asilomar and continuing onto the assessment of the first generation of biotechnology products, was synergistic with the growth of economic reductionism in the form of a global biotechnology industry. This latter reductionism meant there would be a monolithic genetically modified seed variety used in many countries and throughout varied ecosystems. Both forms of reductionism marginalized non-technical and normative discourse pertaining to genetic engineering risks in research and product development. I also argued that some of the reductionist discourse on risks was dogmatic and not open to critical evaluation. US Federal regulatory bodies sought ways to build their regulatory response on reductionist principles of molecular genetics by declaring that there is nothing unique about recombinant DNA methods, which some claimed were more predictive of unexpected properties

than traditional breeding. I showed that the contested discourse often relied on two models of the plant genome—the Lego Model and the Ecosystem Model.

Another sector where reductionist genomics and the market system met was in the courts. The United States has exercised its hegemony in the science and development of biotechnology to create a new set of global rules on patents, and product safety. Nations like Canada, Germany and India that opposed US patent provisions were placed under economic pressure to conform to US intellectual property standards. A legal decision reduced all intellectual property to a single idea—bringing discovery, invention, the living and inert, organism, cell and gene under a uniform patent system based on the notion that for the US patent law ‘all is chemical’. Monopoly control over a modified seed was reduced to a patented foreign gene introduced into the plant genome.

In June 1980, a US Supreme Court decision (*Diamond vs. Chakrabarty* 1980) on a contested patent claim afforded the nascent biotechnology industry and academic research institutes involved in gene sequencing new opportunities for acquiring wealth from genetically modified organisms and research-derived intellectual property. By overturning the US Patent and Trademark Offices’ denial of a patent for a microorganism, *sui generis*, in a five–four vote, the US Supreme Court cleared the way for the use of the patent system for all varieties of living organisms and their parts, including animals, cells, human genes and even sub-genomic segments (expressed sequence tags).

The Court ruled that a microorganism altered by humans could be classified as a product of manufacture and thus fall under patent protection [see Krinsky (1999) for a more in-depth discussion of the Supreme Court’s decision]. The reduction of all genetically altered life forms to products of manufacture or patentable discoveries was a boon to the commercial investment in biotechnology and to the growth of university–industry partnerships. In addition, a single genetic alteration could transform an organism from being non-patentable to becoming patentable subject matter. Molecular biology departments became private enterprise zones practically overnight.

At the time the Court ruled on the *Chakrabarty* case there was a backlog of 114 applications on patents for living organisms with applications mounting to 50 per year. The Court was quite aware of the commercial pressures and the stakes of its decision. It viewed as its task to determine whether living organisms fitted under the patent code. In interpreting the law, the Court characteristically sought to ascertain the intention of the US Congress in examining the language and intent of historical documents such as congressional reports, revisions of the patent laws and the like; but, in its passage of the various patent acts, did Congress intend to include living organisms as patentable material? The Court did find a 1952 recodification of the patent statutes, which included a congressional report submitted by the Senate Judiciary Committee stating that patentable subject matter could ‘include anything under the sun that is made by man’ (US Senate, 1952). It was this phrase that convinced the court’s majority that there was congressional intent to include living things under patentable subject matter. The Court also stated that other branches of government, not the judiciary, should address arguments against patentability based on potential hazards that may arise from genetic research. Congress, though, has never taken a vote on the patenting of living things, although bills have been introduced.

By extending the radius of intellectual property ownership to organisms in-and-of-themselves, and by its liberal interpretation of patentable entities, the US Supreme Court gave the patent office its rationale for extending patent rights over genes, sub-genomic elements, animals and cell lines independent of the process in which they

are used. In this way, an organism modified by a single genetic change can be claimed as intellectual property.

Another arena where reductionism enters biotechnology is in global food security. Transnational agro-biotechnology companies argue that genetically modified food varieties can address complex problems of food scarcity and nutritional deficits. Likewise, the Europeans are under siege by the United States through the World Trade Organization to conform to the latter's export standards for GM products. Trade is the basic irreducible commodity of globalization. As Vandana Shiva notes, 'Under the new free trade arrangements of the WTO, the privatization of life and the reduction of living diversity and its parts and processes to tradable commodities have been made legal obligations' (Shiva, 2005). Thus, rather than seeing the problem of vitamin A deficiency in terms of loss of crop biodiversity, poor access to seeds, water resources, farming machinery, and arable land, it is seen as one of nature's failings, namely that its rice lacks beta carotene—something that can be easily fixed through biotechnology and provided through a global seed cartel.

Reductionism of missions—that is the creation of a unifying mission connecting industry, government and the universities, made it possible to justify the creation of permeable boundaries between these sectors. US policy established financial incentives for universities to form partnerships with companies. Universities were willing to compromise traditional academic values to conform to government initiatives promoting technology transfer. Scientists in government were also allowed to engage in entrepreneurial ventures with companies under the Cooperative Research and Development Program (CRADA). Congress provided a windfall for universities in the Bayh-Dole Act of 1980, which transferred all intellectual property rights for any federally funded discoveries to the investigators, their institution, and a corporate partner. Great numbers of university faculty in molecular genetics subsequently became part of the emergent biotechnology industry. In sum, the US policy style of regulating the risks of, and developing biotechnology, has embraced reductionism, an initial scientific legacy of Asilomar that became expanded economically, legally and geo-politically.

Notes

¹Risks ... come into existence through complex multiple processes of inscription, interpretation, and boundary work carried out by a variety of actors and informed by scientific and political discourses' (Gottweis, 1998, p. 77).

²I have also referred to these as the Simple versus the Complex models of genetically modified organisms.

³Remarks made by Arpad Pusztai on 7 May 1999 at the Polish Hearth Club in South Kensington, UK. See <http://www.i-sis.uk/arpad.php>.

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