Rational Risk/Benefit Analysis of Genetically Modified Crops

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Safety concerns over the use of molecular biotechnology in the improvement of crops has generated substantial, heated and confusing debates, often driven by ideology and hysterics. Modification of crops is not new, and biotechnology (in its broadest sense) has been used for over a century to accelerate the development of new crops for food, feed and fibre, so as to meet the demands of a growing global community. The introduction of crops developed via molecular biotechnology [Genetically Modified Crops (GMCs)] represents the latest step in this inexorable innovative progression of technology. However, misinformed concern has led to a broad embrace of the Precautionary Principle as a regulatory paradigm for GMCs, such that research, development and deployment are delayed, hindered or outright halted. Although of possible use in limited applications, the Precautionary Principle is likely impracticable, as it posits an untenable philosophical paradox of proving the negative proposition that GMCs will never be unsafe. If such a position is accepted, then any technological process can be permanently stymied. To date, empirical observations indicate that there have been no documented problems associated with GMCs. On the contrary, all of the documented fiascos have been due to conventional ‘biotechnology’, e.g., mad cow disease, virus contaminated vaccines and the development of toxic crops via conventional plant breeding. Therefore, regulation of GMCs, whether in the United States or in Europe, should move away from a process/method focus and to a product risk/benefit analysis, that is, a case-by-case evaluation of any new organism, regardless of how it was developed, or (as in the case of introduced exotic plants) if it even was the product of biotechnology. A rationally based, risk assessment, risk management paradigm appears to be a far better regulatory approach, especially in the light of empirical determination of actual risks and benefits.

Keywords: Biotechnology, regulation, precautionary principle, risk analysis, genetically modified crops, genetic engineering, plant breeding

The debate over the research, development and deployment of GMCs in agriculture has all too often been characterized by polarizing emotion-laden tirades, rather than reasoned, and reasonable, discussions. Virtually, there are risks and benefits associated with the use of modern methods of molecular biotechnology, e.g. DNA modification, cloning and transformation, in crop improvement. This paper will attempt to sort through the debate, and arrives at a reasonable proposition for how GMCs can be developed, regulated and used, with minimal risk and maximal benefit. For the purposes of this paper, GMCs are defined as crops developed, improved or otherwise modified via application of modern methods of molecular biotechnology, as so defined immediately hereinafter.

Risks and Benefits of GMCs

In order to coherently discuss how to rationally regulate GMCs, it is prudent to establish what the known risks and benefits actually (and not theoretically) are. This can then function as a reference baseline, from which to formulate recommendations for policies that are grounded in reality and not emotional, political or agenda-driven discourse; wishful thinking, conjecture or paranoia should not unduly influence, or possibly even overwhelm, this already complicated process. Therefore, it is hoped that this detailed listing of what is known about the risks and benefits of GMCs, that is to say a comprehensive risk/benefit accounting, can then serve as a point of reference as the thesis of the discussion is developed.

Risks of Using GMCs

The potential risks of GMCs include: Migration of transgenes into non-targeted organisms, increased creation of resistant weeds and pests, potential adulteration of foods, non-target pest impacts, crop plant and biodiversity impacts, GMCs overwhelming an ecosystem, negative impacts on the environment, e.g. soil bacteria, fungi, etc., GMCs and metabolic imbalances and antibiotic resistance.
The migration of transgenes into non-targeted organisms poses dilemma of contamination of non-genetically modified species with pollen from GMCs, provided that the two are, in fact, cross-compatible, i.e. can successfully set seed. One of the potential scenarios suggested is that the errant transgenes will become incorporated into cross-compatible weed species, e.g. sorghum pollen finding its way to the closely related noxious weed, Johnson grass, and thereby increasing its fitness potential as an aggressively invasive weed species. However, viable species-species cross-fertilization is a very rare occurrence, and the likelihood that such gene transfer will confer additional fitness on the part of the weed seems remote.

Regarding the generation of totally new weeds from the incorporation of errant genes (a previously innocuous plant suddenly becoming a ‘super-weed’), it is important to realize that weediness in plants is not simply conferred by one, or two genes. On the contrary, there are over ten phenotypic traits associated with conferring the characteristic of weediness, with multiple genes involved (a polygenic trait). Hence, it seems quite unlikely that a stray gene would cause a complex phenotypic manifestation such as weediness. It is also similarly unlikely that the GMC itself would achieve invasive weedy status due to the incorporation of one, or two, genes. Crops are typically poorly adapted to survival without intensive inputs; over the centuries they have been specifically bred for production. A few ‘volunteer’ plants (e.g. corn seedlings) might still be present in a field for a year or two, but do not long persist, and are incapable of sustained competitive survival against established weeds. Actually the real threat is the introduction of invasive exotic species, often-wild relatives of cultivated species, which can truly wreak havoc. For example, highly noxious and toxic soda apple, an introduced exotic species that has spread throughout the southern United States, is a wild relative of the cultivated potato. It produces green berries similar in appearance to striped watermelons but much smaller, only the size of golf balls. These berries, which cattle love to munch on, contain a toxic alkaloid compound. It is difficult to imagine how one or two genes could transform a cultivated potato into something resembling the truly dreadful soda apple, and it is correspondingly perplexing why regulatory oversight concerns for introduced invasive exotic species is so often not prioritized to the level of that for GMCs.

Nevertheless, for every GMC introduced, the National Research Council has recommended that criteria should include what the related wild relatives are, and what the impact of potential risks might be. Relevant criteria to consider include whether the specific crop is cross pollinating or self-pollinating, the nature of the trait that has been genetically engineered, and the natural occurrence of wild species that could be targets of genetically modified pollen, for example, Johnson grass endemic to a region set for deployment of the genetically modified sorghum. A similar potential scenario has been suggested for genetically modified rice, i.e. gene flow from the transgenic rice to a closely related wild species, thereby conferring a fitness advantage (e.g. herbicide tolerance). This sort of scenario could be a legitimate cause for concern when a GMC is grown in proximity to closely related wild relatives (a crop’s center of origin), for example, genetically modified rice cultivated in regions of South East Asia. However, empirical observations indicate that, after over twenty years of cultivation, herbicide resistance genes from canola, wheat and soybean (incorporated by non-molecular ‘conventional’ plant breeding techniques) have not caused any problems. A more likely possibility for the generation of herbicide resistant weeds may be prolonged application of herbicides to vast populations of weeds creating intense artificial selection, that while unlikely (less than one in a quintillion), nevertheless could occur with both conventional cropping systems and with the cultivation of GMCs.

As with the possibility of creation of herbicide resistant weeds, there may be a potential risk associated with the deployment of GMCs pertaining to the generation of insecticide resistant pests. The possibility of herbicide genes jumping from sorghum to Johnson grass, or from cultivated to wild rice, may be analogized to similar scenarios, i.e. gene migration from GMCs into insect pests and pathogenic microorganisms, e.g. fungal, bacterial, viral, pests. However, as these species become increasingly taxonomically remote from the GMC, so the likelihood of species-to-species genetic transfer also becomes remote.

Adulteration of foods is a potential risk of GMCs that worries many consumers. This worry has been particularly acute in Europe. Two areas of tangible concern are the presence of allergens and toxins. Allergens pose a very real threat, and the engineering
of Brazil nut genes into soybean illustrates just how serious this can become. On the other hand, toxins, such as the anti-lepidopteron Bt toxin widely engineered into maize and cotton, may present risks of only long-term toxicity; however, with this present generation of engineered toxins such risks appear minimal. In spite of that, future advances in genetically engineered toxicants should be monitored for both short and long term toxicity.

Non-target pest impacts, widely popularized by the scientifically challenged report that Bt toxin kills monarch butterflies, is a concern raised by the National Research Council, but with certain caveats. The most compelling caveat is the recommendation that the impact of GMCs, engineered with insect resistance genes, be carefully compared to the impact that wide-spectrum chemical insecticides currently in use have. For example, it is possible, albeit unlikely, that maize pollen containing Bt toxin will kill certain non-target lepidopteron larvae, e.g. monarch butterfly caterpillars. But when balanced against the widespread, species-wide devastation wrought by spraying a field with a broad-spectrum insecticide, analogous to a poison gas attack, the deployment of Bt engineered maize or cotton appears relatively benign.

Crop plants and biodiversity impacts relate to the potential for GMCs to come to dominate commercial agriculture, to the point of marginalizing and even eliminating other varieties, cultivars and related germplasm. Then again, this has been a problem for centuries with modern commercialized agriculture; the rise of GMCs in agricultural production is just another step in the growing consolidation and uniformity of modern crop production. The antiquity of this issue is now legendary: The Irish potato famine was the result of cultivating a single potato clone (notorious ‘lumper’ variety) across the whole of the Emerald Isle. This variety was uniform in its high yield, hence the rapid increase in the Irish population (from 4M-8M between 1750 and 1845), but also quite uniform in its susceptibility to fungal pathogens, hence the subsequent decline in the Irish population (from 8M-4M between 1845 and 1900). Such erstwhile crop failures exemplify the continuing need for careful monitoring of uniform stands of crops, whether they are genetically modified or developed via more conventional technologies.

More generalized environmental and ecosystem risks also exist with GMCs. GMCs may present the risk of overwhelming an ecosystem by affecting non-target organisms in ways that are non-specific and thus difficult to predict. Negative impacts on the environment, e.g. soil bacteria, fungi, and the soil itself might result. This might arise due to interspecific gene transfer or by other biological mechanisms still to be determined.

Genetic modification of crops via molecular cloning could lead to metabolic imbalances with results that are both difficult to predict and far-reaching. Manipulation of plant genomes might cause system-wide disruptions, either at the level of DNA expression or at the complex level of plant secondary metabolism. The intricate regulation of the plant’s biosynthetic apparatus could thereby be thrown out of kilter, with the potential accumulation in the plant of toxins, e.g. various alkaloids, allergens, e.g. various proteins, or even a reduction in the plant’s overall nutritional value. However, this is still in the realm of educated speculation, and hard empirical evidence must be forthcoming in order to substantiate these sorts of concerns.

Antibiotic resistance is the final risk concern as to GMCs. In the generation of molecular clones to be inserted into plant DNA, i.e. genetic engineering, several antibiotic resistance genes are employed as markers. The most commonly used are kanamycin and neomycin resistance genes. The principal risk concern is gene transfer from plant to microbe. However, this is not known to happen in nature. Furthermore, the commonly used antibiotics used, kanamycin and neomycin, have limited clinical value.

Benefits of Using GMCs
The benefits of GMCs include: A general reduction in the use of chemical pesticides needed, the introduction of disease resistance into crops that were previously susceptible to virulent pathogens, an improvement in stewardship of soil resources, an overall increase in yields, a net savings in time and cost to farmers, and finally, no known detrimental environmental impact. As in the preceding section, each of these will be briefly discussed in turn.

Deployment of GMCs has led to a general reduction in the use of chemical pesticides needed and deployed, overall estimated to be in the tens of millions of pounds. Cotton is the most highly sprayed crop in the United States. The introduction of Bt-engineered Bollgard® cotton has contributed to a significant reduction in the application of pesticides in
the United States, an approximate 850,000 gallons between 1996 and 1999. Some of the beneficial results of reduced pesticide usage include cleaner groundwater, less pollution of ecosystems, and decreased accumulation of pesticide runoff in oceanic ecosystems. In Australia, a 30% reduction in pesticide use as been attributed to the successful deployment of GMCs.

The introduction of disease resistance into crops that were previously susceptible to virulent pathogens is another benefit of GMCs. This application of biotechnology can have a significantly positive impact in developing countries. For example, papaya ringspot virus has had a devastating impact on papaya production in Brazil. In the 1990s, Brazil (the world’s leading producer of papaya) deployed genetically engineered papaya lines which are resistant to the papaya ringspot virus, thereby preserving this valuable commodity in the Brazilian economy. Such an application of biotechnology is a cost-effective remedy for a crisis where few, if any, other feasible control measures exist.

Use of GMCs can contribute to an improvement in stewardship of soil resources. Typically, less time is required in the field for either tillage (weed control) or boom-spray applications (insect, disease control). Hence, there is less soil compaction from tractor tires, less soil erosion from wind and water, and less disruption of the soil’s ecosystem. Soil stewardship can also, in an indirect yet tangible way, contribute to conserving biodiversity. Specifically, by improving soil management and increasing agricultural production on existing farmland, the trend towards continuing expansion of agriculture into marginal areas will be lessened, thereby curtailing ongoing aggressive deforestation with the concomitant destruction of possibly irreplaceable biodiversity.

And finally, an overall increase in yields has been attributed to GMCs: Genetically modified rice in South East Asia, with 25% yield increase; genetically modified maize in Mexico, with 40% yield increase; genetically modified potatoes in Peru, with increased yields due to enhanced resistance to potato blight; genetically modified cotton in Argentina, China, India, Mexico and South Africa, all showing increased yields, lower pesticide use, higher net return; genetically modified canola in Canada, with up to 30% higher yield returns when compared to the performance of conventional varieties.

Risks of Not Using GMCs

Professor Drew Kershen has put forward a novel idea as to risk/benefit analysis of GMCs. He has examined the risks of not using GMCs, and seeks to provide balance to the discussion by adding this side of the argument. Several examples from Professor Kershen’s paper are:

First, aflatoxins are potent toxic compounds produced by fungi that infest cereal grains, producing a moldy grain that is highly toxic. Ingestion of these toxins can lead to hepatic or throat cancer and premature death. The primary means by which cereal grains become infested with aflatoxin producing fungi is via insect vectors, much the same way as mosquitoes spread malaria to humans. However, Bt-engineered grain is resistant to these insects, and hence by not deploying this resistance, the risk of aflatoxin contamination of grain, as well as milk produced by cows that consume this tainted grain, increases.

Second, use of toxic pesticides instead of GMCs with Bt based resistance in potatoes can result in the contamination of ground water with environmental and social impacts following. Some of these chemical insecticides are organophosphate nerve toxins, lethal to fish, and highly toxic to humans.

The third example deals with chicken manure accumulation and its negative impact on the environment. Phosphorous in chicken manure is present primarily in the bound form of phytic acid; chickens cannot digest phytic acid because they lack the phytase enzyme. However, this enzyme can be fed to chickens so that they are then able to digest the phytic acid and thereby utilize the liberated free phosphorous. If phytic acid is not digested, it is passed in the manure, and thereupon becomes the principal source of phosphorous pollution in fresh water, often resulting in waterways clogged with swaths of green scummy algae. Therefore, reluctance to use maize engineered with phytase genes (and hence with endogenous phytase) as poultry feed, due to public outcry against GMCs, will only amplify the risk of resulting heavy phosphorous leaching from the uneasy loads of chicken manure that accumulate next to the chicken processing plants, and the inevitable pollution of precious fresh water.

The several examples noted underscore the point that the added risk is societal, and that adoption of a blind precautionary principle approach will cripple science-based risk assessment and management.
Benefits of Not Using GMCs

In addition, there may be benefits of not using GMCs, for example, a reintroduction of biodiversity in crops, that is, reduction of use of highly uniform commercial varieties and cultivars, e.g. the Monsanto soybean varieties, with the concomitant reintroduction of landraces and heirloom varieties; although these may be only of limited marketable applicability at the commodity level, i.e. niche markets, in an economy that demands cheap, high quality food for its enormous urban centres. Another possible benefit of not using GMCs would be a generalized reduction in public paranoia vis-à-vis the makeup of the food supply; although such a benefit might only be dubious, at best.

Risk Assessment, Risk Management and the Precautionary Principle

Externalities analysis is part of an overall risk appraisal in agricultural biotechnology and the deployment of GMCs. ‘Externalities created by spread of certain of these new gene-forms raise issues of both private and public nuisance.’ As per Van Cleve, externalities are:

environmental and social impacts which are not reflected in the price of goods and services. There are many ways that these impacts can be recognized – for example, through strategic environmental assessment or life cycle assessment. Full account should be taken of hidden or neglected environmental and social factors in the decision-making at policy, business and individual levels. They should be identified, quantified, and when possible given a monetary value.18

It is a general principle in the United States, that those who create unwanted externalities bear the brunt of the responsibility that said externalities generate. Similarly, in Europe, the general principle is that polluter pays.1 With regard to GMCs and the concept of externalities, the question raised is whether the risks associated with these new crops are acceptable or unacceptable, that is, whether the externalities are of any legal significance. Examples of externalities include contamination of the food supply with genetically modified food (the StarLink problem), genetically modified pollen drift, the emergence of killer weeds, and the list could go on and on, as per the aforementioned risks of GMCs. The type of analysis requisite to make this determination is the emerging challenge.

Application of the Precautionary Principle is one suggested prophylactic approach to the crop biotechnology externalities dilemma. The Precautionary Principle has been defined and redefined: ‘[The Precautionary Principle seeks] to impose early preventative measures to ward off even those risks for which we have little or no basis on which to predict the future probability of harm.’19 Or, to put it even more opaquely, ‘When there is scientific uncertainty regarding an issue that could have serious, long-term effects, the lack of scientific certainty should not stand in the way of preventing these efforts.’20 Indeed, this is a simply enunciated, yet complicatedly implemented proposition. Or, as Jeremy Leggett of Greenpeace has defined it: ‘The modus operandi is: ‘do not admit a substance unless you have proof that it will do no harm to the environment’. Which presents us with the uncomfortable philosophical dilemma of proving a negative proposition.21 Or, as the US Chamber of Commerce has so defined: ‘The Precautionary Principle says that when the risks of a particular activity are unclear or unknown, assume the worst and avoid activity. It is essentially a policy of risk avoidance.’22 The Precautionary Principle has been incorporated into international agreements, including the Convention on Biological Diversity (CBD) and the Cartagena Protocol (connected to the CBD), and it has also been applied to policy and regulatory issues in many countries.23

According to Applegate, the Precautionary Principle can be broken down into four sub-components:24

1 The trigger: This incorporates an anticipated serious or irreversible harm and minimal scientific information as to the basis of said harm.
2 Timing: This sets regulatory actions in motion even before solid proof of a relationship is shown between the action and the projected harm, hence timing is anticipatory, addressing not only known, but also unknown risks.
3 Response: This defines what type of regulatory response follows, e.g. outright bans on the GMC, process controls such as isolation of fields, additional testing, alternative technologies, further research.
4 Iteration: As additional information becomes available as to a specific GMC, the response step should be periodically reviewed and appropriate changes made as to the regulatory provisions.
GMCs could fit into this scheme of the Precautionary Principle. There is a trigger mechanism, that is, the proffered list of risks, some of which could be viewed as potentially serious. As for timing, the plethora of potential interactions between GMCs and the environment, as exemplified by their complexity and novelty, suggests that the potential magnitude of risks requires timely action. By setting a regulatory scheme appropriate to the perceived risk, the response prong can be directly applied to GMCs. Finally as for iteration, as new information becomes available, the regulatory mechanisms can be more accurately tailored to fit the GMC under review.24

However, the Precautionary Principle may have serious limitations as to practicable implementation, e.g. in at least one recent case the Precautionary Principle has arguably run amok. The governmental rejection of genetically modified maize in Zambia and Zimbabwe, as too hazardous to feed even starving people, was a stunningly catastrophic application of the Precautionary Principle.25 Calling the UN-donated maize ‘poison’, the governments rejected the maize, in the face of looming famine.26 However, this ultra cautious …bordering on paranoid, application of the Precautionary Principle was at least partially driven by the warranted fear that the European export markets would close their doors to any Zimbabwean or Zambian produced maize that might be tainted with genetically modified kernels, i.e. the imports doors would be slammed shut because the corn could not be proven ‘safe’.27 In this case, the precautionary ‘cure’ creates a human calamity.

Europe’s embrace of the precautionary principle, which amounts to hyper-caution, could lead to long-term non-use of GMCs with long-term consequences that are difficult to predict. As illustrated too well with the Zimbabwean/Zambian rejection of possible GMCs (‘contaminated’ corn), the realities of globalization and world food market integration can drive agendas far from where they arise.28 GMCs have the potential of providing the poor of developing countries with affordable, high quality food, feed and fibre; yet, this potential may be truncated due to strict regulatory systems thousands of miles to the north.29 The loving embrace of the Precautionary Principle in its purer form by the Europeans has had a disquieting impact on the poor of Sub-Saharan Africa, and is disturbingly reminiscent of previous European interactions with the African continent, i.e. a twisted politically correct neocolonialism. As aptly stated by Professor Paarlberg, ‘Instead of helping Africa’s hungry grow more food, European donors are helping them grow more regulations’.30 Of course, it is ironic to note that a healthy diet of non-GMC food can lead to obesity as readily as that from GMC derived ingredients, and the resultant obesity-driven epidemic in developed countries31 has created sustained demand for high quality insulin, which, amazingly, is nearly entirely produced using recombinant human insulin (industrial biotechnology at its finest).32 No one seems to complain about this particular genetically modified product.

As already alluded to hereinabove, the Precautionary Principle may be grounded in a philosophical proposition that is unworkable: Proving a negative proposition.21 Furthermore, the Precautionary Principle may be based on a series of propositions of suspect rationality. As such, the Precautionary Principle may be inadequate, based on misapplication of fundamental human cognition. Sunstein has listed five such propositions, and suggested that each is problematic:33

**Loss Aversion**, that is, people dislike loss, and, in a deep psychological way, view the status quo as safe, without adequately considering possible benefits of new technology. However, taken to the extreme, humans would still be squabbling with hyenas over the rotten scraps of a lioness’s kill. **Myth of a Benevolent Nature** (the ‘Mother Nature’ syndrome), informs that nature is safe, healthy and that new technologies are risky human interventions with the ‘balance’ of nature, hence proceeding from the paradigm that nature exists in a stasis and is not dynamic. **Availability Heuristic**, holds out some risks as far greater than they actually are, simply because they are available, that is, brought to the fore of the argument, whereas other risks, i.e. Kershen’s risks of not using GMCs remain in the shadows. **Probability Neglect**, is similar to the availability heuristic, in that there is a disproportionate consideration of which risks are more probable, such that focusing on negligible risks precludes consideration of other, possibly greater, countervailing risks. **System Neglect**, is the summation of the four factors, which as a group, impact the regulatory system such that externalities are improperly evaluated and decisions are made without a proper risk/benefit analysis.
Susstein further points out that the anxiety of understanding, and accepting, the inevitability of risk might be at the heart of the embrace of the Precautionary Principle as a ‘safe’, albeit delusional, alternative. Ironically, in certain circumstances, GMCs might be safer than traditionally bred or even organically grown crops, as will be discussed hereinbelow.

Possibly one of the greatest limitations of the Precautionary Principle is that it fails to take into account that any decision carries an attendant burden of risk. Risk management is about identifying and controlling risk. However, when institutionalized, the Precautionary Principle essentially abrogates this option, and thereby plunges head first into an abyss of unknown risk. Any decision, even a decision to not use biotechnology, involves risk. Decision-making is inherently a risk associated process, and a balancing of risks and benefits, based on empirical evaluation, is a realistic, and rational, approach. Unfortunately, the Precautionary Principle, as comforting as it can be, will not remove us from this fundamental dilemma. Hence, the Precautionary Principle when applied to regulations often generates a lopsided decision-making process. It is based on the flawed assumption that hindering, or even blocking, the entry of advanced technology into the marketplace carries little attendant risk, i.e. the decision not to decide is harmless. In so amplifying the dangers, and minimizing the benefits, of a new technology, the longer-term potential of innovative advances, e.g. agricultural biotechnology, for addressing pressing societal and humanitarian needs is extinguished. If such a version of the Precautionary Principle had been firmly established in 1750, this would indeed be a very different world, with, for example, rampant infectious disease, chronic malnutrition and many other types of human misery that no rational human would wish for.

A balanced, logical and rational approach, in order to temper the Precautionary Principle’s skewness, will permit externalities to be sensibly analysed via a system of Risk Assessment and Risk Management. Risk Assessment ‘describes a precise probabilistic estimate of the potentially harmful effect of the intake of or exposure to a substance, determined in accordance with scientifically accepted methodology.’ Risk Management ‘is a political and value-based decision, which considers the result of risk assessment and subsequently determines how high a level of risk society is willing to tolerate and which measures to take to control the risk in question.’ As it currently stands, an over-extended version of the Precautionary Principle weakens science since it advocates the use of non-scientific criteria. However, depending on how one interprets the extent of the Precautionary Principle, whether over-extended or rationally balanced, it may not necessarily be inconsistent with risk assessment and management tenets. Based on sound scientific principles, there should be a way to evaluate and regulate the potential externalities attendant to GMCs.

Comparative Risks of GMCs: A Scientist’s Perspective

An important question to address is how the ongoing discussions as to GMCs and their safety relate to the precedent scientific paradigm. In other words, how do the known risks and documented hazards as to GMCs that have already been developed compare to other types of biotechnologically generated plants, animals or pharmaceuticals? Note that for the purposes of this discussion, the term ‘biotechnologically’ is used in the broadest sense of the word, that is, the official USDA definition of ‘the use of living organisms to solve problems or make useful products.’ Only when such a comparison is rationally made, can the potential risks of GMCs be put into perspective.

From a historical perspective, past advances in biotechnology were also viewed with fear, anxiety and suspicion, e.g. modern genetics, cross-species breeding and radiation induced mutational breeding all had critics. A notable example was the great plant breeder Luther Burbank, who in 1906, perhaps overcautiously, uttered the now famous warning: ‘[w]e recently advanced our knowledge of genetics to the point where we can manipulate life in a way never intended by nature. We must proceed with utmost caution in the application of this new found knowledge.’ However, the 100-year long record of crop improvements made via genetics techniques has generated a cornucopia of benefits and a handful of known risks.

As of 2001, no harmful, toxic effects on mammals have been found by feeding them the products derived from GMCs. This was reiterated more recently by the FAO in 2004: ‘To date, no verifiable untoward toxic or nutritionally deleterious effects resulting from the consumption of foods derived from genetically modified foods have been discovered anywhere in the
world.’ (citing the UN FAO 2003-2004 report on the State of Food and Agriculture). Similarly, although potential threats of allergenicity have been identified, e.g. the brazil nut protein expressed in genetically engineered soybean, there have not been any verifiable allergic reactions clearly attributable to proteins expressed in GMCs. This should not, however, lull us into disregarding the arising of potential allergens; appropriate testing should be available to adequately ascertain the potential for allergenicity of any novel proteins expressed in GMCs. The brazil nut protein example can serve as a useful guide for this specific purpose.

Where have the most notorious of biotechnologically produced organism fiascos occurred (hint: not with GMCs)? Six of the most famous are worth noting:

The polio vaccine and SV-40 contamination (SV = simian virus) stands as one of the single most arresting fiascos. In the early 1960s, the polio vaccine had been enthusiastically administered to 100 million Americans. However, around the same time it was discovered that approximately 20% of the administered vaccine had been contaminated with live SV-40, a troubling discovery since compelling empirical evidence had demonstrated that SV-40 was a causative cancer agent in humans.

The recently notorious bovine Spongiform Encephalopathy, i.e. ‘mad-cow disease’ which has been shown to be the causative agent of Creutzfeldt-Jakob disease in humans, has been attributed to extraordinarily poor animal husbandry practices: cattle-feed formulations were supplemented with contaminated ruminant-derived proteins, in other words, cannibalism in cattle, which then led to a drastic multiplier effect of the causative factors, likely to be prions.

Dioxin-tainted chicken presented a food scare, similar to that caused by mad-cow disease. The fourth and fifth examples are arguably more relevant to the scope of this paper, in that they deal with the ‘old’ biotechnology of plant breeding, and what can go wrong with this traditional method of crop improvement.

The Lenape Potato Variety was developed via conventional plant breeding, by crossing the domesticated potato (Solanum tuberosum) with a wild relative (Solanum chacoense). The resulting variety had marvelous insect resistance, produced beautifully white potato chips (albeit slightly bitter to the taste), and contained toxic levels of alkaloids that can cause significant gastrointestinal distress. Similar to the Lenape saga, a celery variety, conventionally bred, was found to accumulate toxic levels of linear furanocoumarins, known to cause phyto-photo-dermatitis. Verily, but perhaps not surprisingly, ‘new varieties developed by traditional crossing appear somewhat more likely to show human toxicity than transgenic varieties.’

The needs and problems of developing countries, where, in Africa, cassava, a basic food source for millions, contains toxic cyanogenic glycosides; in Latin America, kidney beans, an extremely important source of protein, contain toxic phytohemagglutinin; and in India, the vetch pea, a popular legume known for hardiness and popular with poor farmers, contains dangerous neurotoxins.

In other words, ‘natural and traditional’ crops and technologies are not always safe either. And, to complete the circle of this discussion (and illustrate the inherent danger of the Precautionary Principle), molecular biotechnology might offer solutions to these problems, e.g. development of genetically engineered non-cyanogenic glycosidal cassava for subsistence level agriculture in Africa.

The picture that emerges from the foregoing observations of either anticipated nonevents or actual events is that in regulating biotechnologically produced organisms or technologies, whether developed via conventional methods (e.g. plant breeding) or via new technologies (e.g. genetic engineering), a rational assessment of danger must be at the heart of risk analysis. Human manipulation of nature is nothing new, and neither is the attendant risk.

The hereinafore discussion underscores the fundamental proposition that the process should not be the subject of regulation. Instead, the product should be evaluated, on a case-by-case basis. In agriculture, the process of ‘traditional’ crop breeding has not been proven to be inherently safer than genetic engineering. Indeed, as illustrated so clearly above, the use of conventional breeding has re-introduced deleterious genes back into cultivated crops from wild relatives (e.g. the Lenape Potato Variety). The notion that traditional crop breeding is natural and that genetic engineering is unnatural simply ignores the facts. Crop scientists have
employed advanced technologies for years, including tissue culture, embryo-rescue, radiation breeding and chemically-induced chromosome doubling, to produce entirely novel crops, such as triticale, an artificial hybrid of wheat and rye, a new species that is not found in nature. Molecular techniques have not yet achieved a similar result, that is, generation of an entirely new crop species. Hence, it is better to shift the paradigm: the risk is posed by the organism itself, regardless of how (e.g. conventional or molecular crop improvement), or even whether (e.g. the tropical soda apple cited hereinabove), it has been modified.

The Regulation of GMCs: The Law as it Stands

The various laws and regulations that deal with GMCs are structured such that they regulate the levels of perceived risk, of course depending on the jurisdiction the law or regulation is from. Hence, the American and European paradigms and corresponding laws and regulations vary accordingly. This section, therefore, seeks to present a broad overview of these laws and regulations, and briefly examine some of them from the perspective of the foregoing discussion. These laws include both national law and treaties. After reviewing these laws, the question accordingly inevitably arises: How can rationally drafted and implemented rules and regulations maximize benefits, minimize risks and serve as a guide for developing, accessing and utilizing these emerging technologies so as to exploit their full potential?

Laws governing US regulation of GMCs are administered via the federal governmental agencies and their respective regulatory responsibilities. These include the Food and Drug Administration (FDA), the United States Department of Agriculture (USDA) and the Environmental Protection Agency (EPA). Each of these is briefly discussed in turn.

The FDA regulates feed, food, food additives and veterinary drugs. The review for safety is as to whether the product is safe to eat. As for GMCs, the FDA has a voluntary review process, since it deems GMC derived food products as a priori safe. Still and all, the FDA has reviewed all such products that are currently on the market. The FDA review seeks to determine whether the food product is biologically or nutritionally different from a corresponding food product that is derived from the non-GMC source. The approach to review does not seem to conform to the strictures of the Precautionary Principle.

The products regulated by the USDA include plant pests, plants and veterinary biologics. The review for safety is whether the plant is safe to grow. The USDA seeks to make its regulatory activities as transparent as possible, as per the statement of the Clinton Administration’s Secretary of Agriculture Dan Glickman: ‘fostering open, public, and arm’s length regulatory processes.’ The USDA’s Animal Plant Health Inspection Service (APHIS), pursuant to the Plant Protection Act (PPA) functions as the primary regulator of GMCs.

The products regulated by the EPA include microbial/pest-pesticides, new uses of existing pesticides and novel microorganisms. Hence, with GMCs, the EPA’s regulatory mandate focuses on ‘biopesticides’, e.g. Bt genetically engineered maize, cotton, and the potential impact these will have on the environment. EPA’s authority to regulate is pursuant to the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA); environmental use permits are required if test plots exceed 10 acres. The EPA’s review for safety is whether the GMCs are safe for the environment as well as whether there is a safe new use of a companion herbicide. The EPA’s approach to regulation is more systematic than the FDA, as it sets precise limits on biopesticides:

Such limits are based on product characterization (how different is this product from its non-GMO counterpart?), toxicology (how long does it take to break down in the body once consumed?), allergenicity (will the protein possibly create an allergic reaction and therefore require a consumer label?), non-target organisms (will it affect organisms or animals that were not intended to be affected?), environmental fate (how fast will the protein break down in the soil?), and potential pest resistance.

It is important to note that, in addition to federal regulations, there are also state laws that permit states to monitor field tests of GMCs. The regulatory apparatus in the European Union (EU) appears to be more stringent than that of the USA, embracing the fundamentals of the Precautionary Principle. The EU approach to regulation of GMCs is based, at least partly on, the Principle 15 of the Rio Declaration, which states that ‘lack of full scientific certainty shall not be used as a reason for postponing cost effective measures to prevent environmental degradation.’
Directive 90/220, adopted in 1990, formed the framework by which GMCs regulation is approached; these include pre-market notification, approval decision and the labeling requirement. In light of the articulated known risks of biotechnologically modified organisms (as discussed hereinabove), the specific language of 90/220’s applicability appears peculiar: ‘[90/220] applies not only to novel plants, but to all GMOs, which are defined as organisms ‘in which the genetic material has been altered in a way that does not occur naturally by mating and/or recombination’. Ergo, the Lenape potato variety would apparently not be subject to 90/220. Miller and Conko address this peculiar paradigmatic dichotomy directly:

[B]road scientific consensus holds that agbiotech is merely an extension, or refinement, of less precise and less predictable technologies that have long been used for similar purposes, and the product of which are generally exempt from case-by-case review. … Many of these ‘classical’ techniques for crop improvement, such as wide cross hybridization and mutation breeding, entail gross and uncharacterized modifications of the genomes of established crop plants and commonly introduce entirely new genes, proteins, secondary metabolites, and other compounds into the food supply.

The EU Directive of March 2001, 2001/18/FC addresses the release and marketing of GMC products. This is a case-by-case analysis of each product released with assessment of the potential long-term effects: risk to human health, risk to the environment, whether risk is direct, indirect, immediate or delayed, and possible cumulative long-term effects. As with many international environmental treaties, the Precautionary Principle is widely applicable.

However, a recent development might eventually be an impetus towards modification of Europe’s regulatory stringencies. The World Trade Organization (WTO), paradoxically a European-based organization, ruled that the six-year European ban on genetically engineered crops violates international trade rules. The WTO ruling, in favour of the United States, Canada and Argentina, challenged the bans on specific GMCs put in place by Austria, France, Germany, Greece, Italy and Luxemburg. This issue, nevertheless, still appears far from resolution, as the parties differ significantly on how world trade rules for biotechnology products should be structured, and how they can be reconciled with national laws regulating GMCs. Regulation, however, driven by the uncompromising strictures of a rigorously applied Precautionary Principle, could result in over-regulation, with collateral risks not readily anticipated:

Overly burdensome regulatory requirements could negatively impact the crops and traits that are inherently non-commercial, e.g. subsistence level agriculture for developing countries. Hence, ironically, the crops and traits that survive the regulatory apparatus will be those suited for industrialized agriculture, while those with value-added for poor farmers in developing regions will fall by the wayside.

Conclusion

The Precautionary Principle as applied in the EU is likely an overreaction, based, at least in part, on the public perception and distrust of science and government regulations. However, a balanced approach to regulation, based on ‘a clear set of standards based on science’ might be at least a step towards harmonization of the US and EU in terms of the regulation of GMCs. As a specific example, a set of proposed principles, put forth by a group of respected US scientists, for assessing and managing the risk of allergenicity include:

- Avoid the transfer of known allergens,
- Assume genes from allergenic sources encode for an allergen unless proven otherwise,
- Assess the allergenic potential of all introduced proteins,
- Where allergens are identified, consider alternative sources, and
- Apply the Brazil nut case experience to this proposed series of guidelines.

Hence, GMCs should not be specifically segregated out of an overall regulatory mechanism and placed into some ‘special’ category. As pointed out above, the greatest fiascos thus far have only involved non-genetically engineered ‘biotechnologies’, and GMCs themselves have yet to be implicated in creating any unwanted externalities of similar magnitude. There is simply no empirical support for the oft-advanced proposition that GMCs are inherently more dangerous than other crops/plants because of the process that is employed to develop them (i.e. molecular
biotechnology). Quite the contrary, as illustrated in this paper non-molecular biotechnologies have generated the greatest documented mishaps.

Therefore, instead of being viewed as a totally novel, and hence totally dangerous, method of biotechnology, technologies to develop GMCs should be viewed as part of the total package of biotechnological approaches, all subject to rationally-based, comparative risk assessment and risk management regulation.\(^\text{54}\) Integral to this approach is the regulation of products and not processes, i.e. organisms and phenotypes themselves and not regulation based on the methods of research and development. Hence, regulatory oversight should be driven by the nature of the organism, regardless of whether it has been developed with conventional or molecular methodology, if at all, i.e. noxious/invasive exotic pests such as the tropical soda apple are products of nature.\(^\text{55}\)

Molecular techniques are analogous to, and just another step in, a long history of increasing sophisticated innovations to improve crops and advance agriculture for the good of mankind.\(^\text{56}\) Over caution, over regulation, and over paranoia will not serve the increasing humanitarian needs of a growing global community.

References


51 Victor M, Precaution or protectionism? The precautionary principle, genetically modified organisms, and allowing unfounded fear to undermine free trade, _Transnational Lawyer_, 14(Spring 2001) 295-321.


