

19 Case Study in Benefits and Risks of Agricultural Biotechnology: Roundup Ready Soybeans

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Introduction

The development of crops tolerant to the herbicide glyphosate (Roundup) began in the early 1980s. The first generation of glyphosate tolerant soybeans was grown in a greenhouse during the winter of 1990–1991, the seeds of which were then planted in field tests during the summer of 1991 (Padgett *et al.*, 1996a). Approvals for commercialization of glyphosate tolerant soybeans were granted by FDA and USDA in 1994 and by EPA in 1995. Glyphosate tolerant soybeans, commonly known as 'Roundup Ready' soybeans, were first made available for planting by US farmers in 1996.

Glyphosate tolerant soybean varieties have been widely adopted by US growers. Figure 19.1 shows adoption of glyphosate tolerant soybeans since 1996 in the USA. By 2000, growers planted 54% of US soybean acreage to glyphosate tolerant soybeans (USDA NASS, 2000a).

Glyphosate controls weeds by inhibiting the enzyme 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS), which catalyses the synthesis of amino acids essential for survival of plants and bacteria. EPSPS is present in plants, bacteria and fungi, but not animals, as animals do not make their own aromatic amino acids but rather receive them from plant, microbial or animal-derived foods.

Several bacteria exhibit tolerance to glyphosate. A glyphosate tolerant EPSPS from the soil bacterium

Agrobacterium sp. strain CP4 was isolated and introduced into the genome of a soybean cultivar using the particle acceleration method. DNA is coated on to microscopic gold particles, which are then accelerated and penetrate target plant cells. Resulting cells are then incubated to produce shoots, which will eventually grow into mature plants. Successfully transformed plants are selected that exhibit unaltered agronomic traits from the parent line.

Soybean is the second largest crop in the USA after maize, planted on 30 million hectares in 2000 (USDA NASS, 2000a). Area planted to soybean has expanded in recent years owing to several factors. Improved yields through variety improvements, adoption of moisture-saving no-till practices, strong soybean prices relative to other crops, and elimination of acreage reduction programmes are all factors that have contributed to expanded plantings. Total soybean crop value in 1999 was US\$13,000 million (USDA ERS, 1999).

Soybean acreage is centred on the Midwestern states, though 30 states have significant acreage planted to soybeans each year. Illinois and Iowa each plant over 4 million hectares of soybeans. Other major soybean states include Minnesota, Indiana, Missouri and Ohio.

The USA is the largest producer of soybeans in the world, growing nearly half of the total world soybean crop. Other major producing countries include Brazil, China and Argentina. The USA

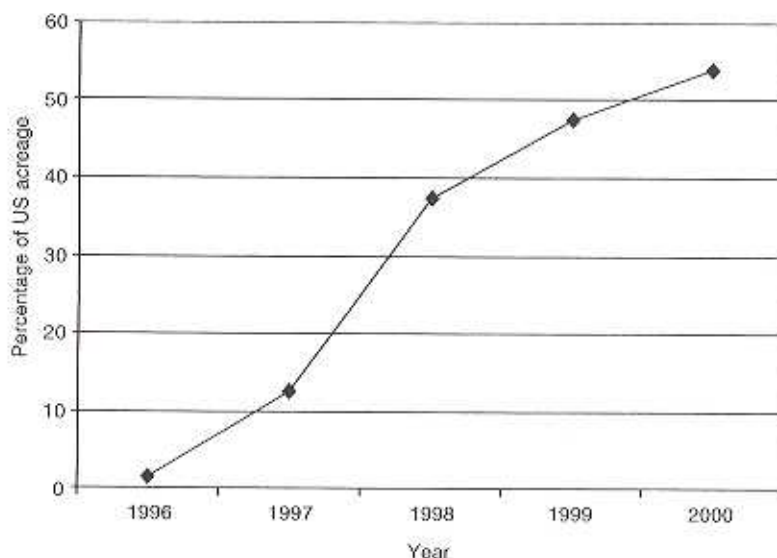


Fig. 19.1. Glyphosate tolerant soybean adoption. (Sources: K. Marshall, 2000, Monsanto, personal communication; USDA NASS, 2000a.)

exports approximately one-third of its soybean production, primarily to Asia and Europe, which together account for over 70% of total exports. Competition in export markets comes from Brazil and Argentina, as China is a net importer of soybeans (USDA NASS, 2000b).

Risks

Concern has been raised about the risks associated with GM crop varieties. Potential human health risks include allergenicity, toxicity and development of resistance to orally administered antibiotics. Environmental risks include potential for increased weediness of the crop plant, out-crossing of GM plants with closely related wild plant species, non-target effects and the development of pesticide resistance. In response to these concerns, US regulatory agencies routinely assess the risks involved with the introductions of GM plant varieties. The approval of crop varieties developed through biotechnology falls under the jurisdiction of three agencies: the US Department of Agriculture (USDA), the Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA). The risks of agricultural biotechnology are examined in the context of the regulatory framework that governs the introduction of GM crops in the USA. The majority of risk studies that have been conducted on these new crop vari-

eties has been conducted by the developers of the technology in order to meet the requirements of the regulatory agencies.

US regulatory framework

The US regulatory framework for agricultural biotechnology has evolved over time as new technologies emerged that allowed the manipulation of genetic material, beginning in the early 1970s. Over the past 25 years, policy has developed to address potential risks in a process open to public review and comment.

Initially, responsibility for oversight of the technology rested with the National Institutes of Health (NIH), but as applications of the technology changed, involvement of other agencies was deemed appropriate. As diverse products were presented for field-testing and commercialization (e.g. human insulin, ice minus bacterium, insect resistant tobacco, chymosin, rbST) involvement of the various agencies was required, and the system developed accordingly. Following is a brief overview of the development of regulations for agricultural biotechnology in the USA.

Concerns about the potential dangers arising from new recombinant DNA (rDNA) techniques first arose in the early 1970s. In 1973, scientists gathered at an annual conference on nucleic acids, known

as the Gordon Conference, heard descriptions of experiments where DNA molecules from diverse sources were joined. By the end of the conference, many attendees had voiced reservations about the ethical and moral problems as well as the safety issues that might arise from the technology. The conference attendees voted that a letter should be sent to the National Academy of Sciences pointing out that a problem had been raised meriting investigation (Goodfield, 1977). It was also decided to go public with the issue, by publishing their letter in *Science* on 21 September 1973 (Singer and Soll, 1973). The letter noted that although no hazards had yet been established, 'prudence suggests that the potential hazards be seriously considered', and suggested that the Academies establish a study committee on the subject to recommend specific actions or guidelines as appropriate.

The National Academy of Sciences quickly convened a committee in 1974, publishing the recommendations in *Science* in July of that year (Berg *et al.*, 1974). The committee recommended that three types of experiments be deferred until the potential hazards were better evaluated or until adequate methods were developed for preventing the spread of biologically active recombinant DNA molecules: constructing replicating plasmids that would introduce either antibiotic resistance or bacterial poisons into bacterial strains; linking DNA from likely cancer-causing viruses to bacterial plasmids; and the linking of fragments of animal DNA to bacterial plasmid DNA or bacteriophage DNA. The committee also suggested that the director of NIH establish an advisory committee to develop an experimental programme to evaluate the hazards, develop procedures that would minimize the spread of such molecules within populations and devise guidelines to be followed by investigators. They also called for an international meeting of scientists to further discuss appropriate ways to deal with the potential biohazards of recombinant DNA molecules.

The Asilomar Conference was held in 1975, convening nearly 140 international scientists to 'review scientific progress in research on recombinant DNA molecules and to discuss appropriate ways to deal with the potential biohazards involved' (Berg *et al.*, 1975). The recommendations of the conference consolidated and extended those of the National Academy of Sciences Committee.

The Recombinant Molecules Advisory Committee (RAC) of the NIH began meeting as soon as the Asilomar Conference ended, working on

research safety issues of experimental facilities and personnel, as well as of the proposed experiments themselves. In February 1976, the director of NIH called a public hearing in response to increased public interest in the subject. Four months later, in June 1976, NIH published its final guidelines for laboratories conducting recombinant experiments under federal grants (Goodfield, 1977).

As a standing committee, the RAC meets periodically to address and incorporate emerging scientific understanding of the potential risks involved with rDNA technologies. By 1983, experience with rDNA had allayed many fears, and NIH guidelines had been successively weakened to allow experiments that had been delayed awaiting better understanding of the associated risks. NIH had become comfortable with the vast majority of ongoing basic and biomedical research (Thompson, 1987). Risk assessment work helped to assure the scientific community and the public that many rDNA experiments were not as hazardous as originally believed (Korwek, 1997).

Although the NIH Guidelines govern only federally funded research, private industry and trade associations generally abide by the Guidelines as well. Through institutional biosafety committees, private industry reviews risk and ethical concerns of prospective research areas, referring any questions to the RAC for advice and consultation. It is believed that individuals and institutions that are not required to follow the NIH Guidelines do so for legal liability concerns. A 1987 General Accounting Office report found that private companies appeared to follow the Guidelines more closely than public sector organizations (Korwek, 1997).

The landscape of risk issues changed in the early 1980s as genetic engineering was to move out of the laboratory and into agricultural fields with the development of 'ice minus', a genetically altered bacterium intended for use on a variety of crops to reduce the risk of freezing. The regulation of a product that was to be purposely introduced into the environment presented quite a different set of issues from those involved with laboratory experimentation, the risks of which were controlled primarily by containing engineered materials and insuring against introduction into the environment.

Originally proposed in 1983, field testing of 'ice minus' was delayed through a series of legal challenges for 4 years. During this time, the authority of NIH over field tests was questioned, and EPA, USDA and FDA were proposed as the appropriate bodies for regulating in this area. The lack of coordi-

nation and uncertainty about oversight of biotechnology led to the formation of an interagency working group under the White House Cabinet Council on Natural Resources and the Environment. The working group was composed of approximately 13 member agencies, as an interagency effort to review regulatory requirements for conventional technologies, to clarify regulatory requirements for new products and to determine whether current regulatory requirements were adequate. Initial results of the working group were published for public comment in the Federal Register in 1984 (OSTP, 1984). The Office of Science and Technology Policy (OSTP) published its final notice of how each agency would regulate biotechnology applications in 1986, in the policy that would become commonly known as the 'Coordinated Framework' (OSTP, 1986). In this notice, existing laws were deemed adequate to oversee modern biotechnology applications. The notice also set forth which regulatory bodies were designated as the lead agency where the possibility of duplication of oversight existed (Korwek, 1997). USDA is the lead agency for plants grown to produce food or feed crops, while the food or feed itself is subject to regulation by FDA. EPA would primarily handle pesticide microorganisms. Notably, the initial policy of EPA addressed microbial pesticides, but did not address the regulation of pesticidal plants, which had not yet been developed at that point.

EPA, USDA and FDA each issued statements outlining their regulatory policy, which were incorporated into the Coordinated Framework. A common theme in the policies of all three agencies is the concept of product- not process-based risk assessment, based on the conclusion that the risks associated with the introduction of rDNA-engineered organisms are the same as those associated with introductions of unmodified organisms and those modified by other methods. This concept was supported by three reports, issued by the National Academy of Sciences and the National Research Council.

The first report was published in 1987, entitled *Introduction of Recombinant DNA-engineered Organisms into the Environment: Key Issues*, which concluded that the risks associated with the introduction of genetically engineered organisms were the same as those associated with introductions of unmodified organisms and those modified by other methods. In 1989, the National Research Council (NRC) issued *Field Testing Genetically Modified Organisms: Framework for Decisions*, which more specifically addressed the scientific foundation for

regulatory decisions governing the release of genetically engineered microorganisms and plants into the environment. The 1989 report further supported the concept of the product not process-based standard for oversight put forth in the 1987 study. In 2000, the NRC released a report entitled *Genetically Modified Pest-protected Plants: Science and Regulation*, the purpose of which was primarily to evaluate the EPA's regulatory system for pesticidal plants. In the 2000 report, the committee was critical of EPA's policy of exemptions for plant varieties produced using particular methods.

The scope of regulation was the subject of a review prepared by the White House Council on Competitiveness, published in 1990 for public comment in the Federal Register. This document excluded from regulation organisms developed by traditional techniques, though the document did not propose any rules. The Council later published four principles of regulatory review for biotechnology and a report on national biotechnology policy. These publications, along with the final scope document, published in 1992, articulated a risk-based approach to regulation.

USDA

The USDA Animal and Plant Health Inspection Service (APHIS) is responsible for protecting US agriculture from pests and diseases. Under the Federal Plant Pest Act, USDA retains the authority to regulate plant pests and other articles to prevent direct or indirect injury, disease, or damage to plants, plant products and crops. In 1987, USDA published regulations that finalized the rule that was proposed under the Coordinated Framework (USDA APHIS, 1987). The requirements extended regulations imposed by APHIS for non-genetically engineered organisms or products which are plant pests or could harbour plant pests. APHIS promulgated these new regulations because it deemed that the existing regulations did not provide any way to determine whether or not a genetically engineered organism or product would fall under existing regulations of plant pests. The rule specifically notes that APHIS is not treating genetically engineered organisms and products differently from non-genetically engineered organisms. These regulations were amended in 1993 and 1997 (USDA APHIS, 1993a, 1997).

The regulations provide the rationale for determining whether a genetically engineered organism or

product would be considered a 'regulated article', that is one with plant pest characteristics, and also calls for additional data for making a determination on the plant pest status of certain genetically engineered organisms or products. A genetically engineered organism is deemed a regulated article either if the donor organism, recipient organism or vector agent used in engineering the organism is listed in the regulation and is also a plant pest, is unclassified, or if APHIS has reason to believe that the genetically engineered organism presents a plant pest risk. This criterion for determining whether a particular modified plant is subject to regulation by APHIS was criticized in the recent National Research Council report, which noted that some pest-protected plant varieties did not fall under its scope given the definition of regulated article (NRC, 2000).

APHIS is responsible for approving introductions of GM crops at two stages: for field trials and for full market release. Prior to conducting field trials, it is necessary to either obtain a permit or notify APHIS. The notification option was established in 1993 for certain regulated articles with which the department is familiar, provided that the introduction is conducted in accordance with established requirements and standards (USDA APHIS, 1993a).

APHIS regulations also provide for a petition process for the determination of non-regulated status, which allows the unregulated movement and release of the product. In the petition for non-regulated status, applicants must 'describe known and potential differences from the unmodified recipient organism that would substantiate that the regulated article is unlikely to pose a greater plant pest risk than the unmodified organism from which it was derived' (USDA APHIS, 1993a).

Environmental assessments are prepared for field tests, and for petitions for non-regulated status. These assessments detail the nature of the genetic modification and assess the potential for environmental impacts from the introduction of the crop varieties into the environment. When a product is approved for full release, a Determination of Non-regulated Status is published in the Federal Register.

Lack of plant pest risk may be concluded when there is evidence that the plant under consideration: (i) exhibits no plant pathogenic properties; (ii) is no more likely to become a weed than its non-engineered parental varieties; (iii) is unlikely to increase the weediness potential for any other cultivated plant or native wild species with which the organism can

interbreed; (iv) does not cause damage to processed agricultural commodities; and (v) is unlikely to harm other organisms, such as bees, that are beneficial to agriculture.

APHIS received a petition from Monsanto on 15 September 1993, seeking a determination from APHIS that glyphosate-tolerant soybean (GTS) line 40-3-2 and its progeny do not present a plant pest risk and are therefore not regulated articles (Re *et al.*, 1993). On 6 December 1993, APHIS announced receipt of the Monsanto petition in the Federal Register, stating that the petition was available for public review (USDA APHIS, 1993b).

APHIS received 33 comments on the Monsanto petition. With one exception, the comments were favourable to the petition. The one unfavourable comment stated that USDA should not approve the Monsanto petition or any other petition until the federal government has revised its oversight programme for transgenic crops at the commercialization stage, including establishment of standardized assessment and data collection schemes for consideration of risks of transgenic crops to ecosystems in the USA and worldwide, with particular attention to centres of diversity for food and fibre crops. The commenter also expressed the view that development of herbicide-tolerant crops should not be encouraged because they increase farmers' dependence on chemical herbicides (USDA APHIS, 1994b).

The Roundup Ready gene contained in GTS line 40-3-2 is a single insert of DNA comprising the enhanced 35S promoter derived from cauliflower mosaic virus, the chloroplast transit peptide coding sequence from *Petunia hybrida* fused to the 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS) gene derived from *Agrobacterium* sp. strain CP4, and the nopaline synthase 3' terminator from *Agrobacterium tumefaciens*.

GTS line 40-3-2 has been considered a 'regulated article' because it contains components from organisms that are known plant pathogens: the bacterium *A. tumefaciens* and cauliflower mosaic virus. Field testing of GTS line 40-3-2 had been conducted with APHIS approval since 1991. Monsanto submitted its petition after the completion of field tests of GTS line 40-3-2 under nine APHIS permits. These permitted field tests took place at approximately 54 sites in 19 states and Puerto Rico. Additional trials were conducted in the USA and Puerto Rico under permit and notification during the 1993 growing season. All field trials were per-

formed under conditions of physical and reproductive confinement.

The Monsanto petition describes the genetically engineered soybean plants and provides information relevant to determining whether glyphosate tolerant soybean plants are more likely than conventional varieties to become a plant pest. The petition addresses potential environmental consequences of unregulated release of glyphosate tolerant soybean varieties, including the development of glyphosate tolerant weeds, enhanced weediness, effects on non-target organisms, impacts of human and animal exposure, indirect effects on other agricultural products and the potential for outcrossing. Reports from field trials are included with observations of yields, plant growth, outcrossing, survival and gene expression gathered during field tests of glyphosate tolerant varieties compared with conventional varieties. Examples of the monitoring forms used by investigators who conducted the experiments are also included in the petition. In addition, letters from six land grant university weed scientists are included addressing the potential for development of weed resistance to glyphosate, weed population shifts and the overwintering of glyphosate tolerant soybeans, which were issues of concern to USDA.

APHIS granted the petition in May 1994, issuing a Finding of No Significant Impact. This conclusion was based on the nature of the genetic modification, the fact that soybean has no weedy relatives with which it can interbreed in the USA and its territories and the fact that this modification will not increase the weediness of the soybeans or negatively affect any non-target organisms, including beneficials (USDA APHIS, 1994b).

Weediness

Soybean (*Glycine max*) possesses few of the characteristics of plants that are notably successful weeds. *G. max* cv. 5403, the cultivar which was GM, is not considered to be a weed, and glyphosate tolerance is not expected to confer any additional weedy characteristics. Standard texts and lists of weeds give no indication that cultivated soybean is regarded as a weed anywhere (USDA APHIS, 1994a). Overwintering of soybeans is rare due a lack of innate dormancy. A lack of dormancy is selected for in commercial soybean seeds, so soybean seeds germinate quickly. Any seed that might remain in a field

after harvest is likely to germinate, emerge and be killed by frost or field preparation for the following crop. Very few volunteers were observed in field testing. The number of seeds produced, germination characteristics, final stands, overwintering capability and disease or insect susceptibility were all found to be similar for the tested glyphosate tolerant line compared with conventional varieties. These findings were based on yield data and observations of germination, stand counts and disease or insect susceptibility. Further, increased weediness of the glyphosate tolerant soybean plant compared with conventional varieties would have to be due to selection pressure in association with glyphosate use. This was judged not to be an issue since glyphosate is not applied to the soybean for control of the soybean itself, but rather for controlling weeds in the field (USDA APHIS, 1994a).

Outcrossing

The genus *Glycine* is divided into two subgenera, *Glycine* and *Soja*. The first consists of 12 wild perennial species that are primarily distributed in Australia, South Pacific Islands, Philippines and Taiwan. The subgenus *Soja* consists of three annual species from Asia, *Glycine max*, *Glycine soja* and *Glycine gracilis*. The first species is the cultivated soybean, the second species is the wild form of the soybean and the third species is referred to as the 'weedy' form of the soybean.

Cultivated soybean is sexually compatible only with members of the genus *Glycine*. Cultivated soybean is the only member of the genus *Glycine* that grows in the USA and its territories and is sexually compatible with cultivated soybean, with the exception of specialized research collections. However, some members of the wild perennial species of subgenus *Glycine* may be found in US territories in the Pacific. There are no known reports of successful natural hybridization between the cultivated soybean and the wild perennial species.

The wild annual species, *G. soja*, is found in China, Taiwan, Japan, Korea and the former USSR. Natural hybridizations between *G. soja* and cultivated soybean occurs. *G. soja* is not native to North America and occurs only in research plots. There are no reports of its escape or dispersal from research plots. *G. soja* has never been found as a weed or naturalized in the USA. Thus, the possibility of gene transfer is very low within the USA.

Even if non-agricultural land containing any wild *Glycine* populations were near sites of commercial soybean production, it is highly unlikely that pollen from GTS line 40-3-2 would fertilize the wild relative, because soybeans are almost completely self-pollinated. The anthers mature in the bud and shed their pollen directly on to the stigma of the same flower, thus ensuring a high degree of self-pollination. Cross-pollination is generally very low and various studies have shown it to be from 0.03 to 3.62%. Honeybees are responsible for the occasional cross-pollination.

The limited potential for cross-pollination is evident in certified seed regulations for Foundation seeds, the most stringent category in the Certified Seed Regulations, which permit zero distance between different soybean cultivars in the field.

Non-target effects

Glyphosate tolerant soybeans were judged to have no detrimental effects on non-target organisms. EPSPS enzymes are present in plants and microorganisms and are therefore normally found in food and feed. No effects on non-target organisms were expected. The glyphosate tolerant EPSPS that was introduced into soybeans is not known to have any toxic properties. Field observations revealed no negative effects on non-target organisms including insects, birds or other species that frequent soybean fields (USDA APHIS, 1994a).

Weed resistance

Although the development of herbicide resistant weeds is not specifically considered by USDA in the approval process, Monsanto's petition to USDA provided information addressing this possibility. Glyphosate is considered to be a herbicide with a low risk for the development of weed resistance. Major factors which can contribute to the development of resistant weeds include: a single target site and a specific mode of action, broad spectrum of activity, long residual activity, and frequent applications without rotation to other herbicides or cultural control practices. Glyphosate essentially has no residual activity in the soil and is relatively quickly broken down by microorganisms in the soil. Also, there is no other herbicide on the market today that has the same mode of action as glyphosate. Glyphosate has been widely used for over 20 years, as a pre-plant burn-

down, directed, spot or postharvest treatments. However, some have questioned the impression of 'invincibility' of glyphosate to the development of resistance (Gressel, 1996). Resistant weed populations have been reported in Malaysia and Australia (Sindel, 1996; Doll, 1999).

Plant pest risk

APHIS also assessed the possibility that glyphosate tolerant soybeans would pose a plant pest risk due to the presence of pathogen-derived sequences. Neither of the gene sequences from *A. tumefaciens* or the cauliflower mosaic virus cause any plant or animal disease, is the source of pathogenicity in its host or encodes any polypeptide. No crown gall, the disease caused by *A. tumefaciens*, or cauliflower mosaic virus disease were observed in any glyphosate tolerant soybean plants during greenhouse or field studies.

Yields

Further information was submitted by Monsanto on 19 November 1993, to address a slight yield reduction observed at three of seven sites in initial yield trials.

EPA

The EPA assesses the safety of pesticides, both chemical and those that are produced biologically. Under the authority of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), EPA regulates the distribution, sale, use and testing of plants and microbes producing pesticidal substances. Under the Federal Food, Drug and Cosmetics Act (FFDCA), EPA sets tolerance limits, maximum allowable residue concentrations, for substances used as pesticides on and in food and feed, or establishes an exemption from the requirement of a tolerance. The EPA also establishes tolerances for residues of herbicides used on novel herbicide-tolerant crops.

The goal of FIFRA is to register pesticides that do not have unreasonable adverse effects on human health or the environment and have benefits outweighing risks. Unreasonable adverse effects on the environment are defined as any unreasonable risk to 'man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide' (Korwek, 1997).

Any substance that is considered a pesticide under FIFRA is automatically subject to regulation under FFDCA if used on a food or feed crop (Nelson and Abramson, 1999). Until recently, EPA's decision making under FFDCA also involved a balancing of risks and benefits; however, only dietary risks to humans and other animals were considered, as opposed to FIFRA which also takes into account environmental risks (US EPA, 1994). Since passage of the Food Quality Protection Act in 1996, Congress has required EPA to apply a safety-only standard when examining the potential dietary risks associated with pesticide residues that may be found in food (Nelson and Abramson, 1999).

Early policy statements of EPA were focused on the regulation of GM microbial pesticides. A 1984 statement of interim policy required notification prior to small-scale field tests involving certain microbial pesticides, including those that had been genetically altered, in order to determine whether an experimental use permit (EUP) would be required for testing (US EPA, 1984). In 1986, as part of the Coordinated Framework, EPA published its statement of policy pertaining to regulating microbial pesticides under FIFRA, which sought to define which microbial products would be subject to review under FIFRA as well as the nature of the review (OSTP, 1986). In a 1989 Notice, EPA requested comments on the regulatory approach to microbial pesticides articulated in the 1986 policy statement (US EPA, 1989). A proposed rule was published by EPA in 1993, based on the 1984 interim policy and the 1986 proposed policy, addressing the requirements for small-scale field testing of microbial pesticides, as regards notification and EUPs (US EPA, 1993).

It was not until 1994 that the agency began to publish policy applicable to GM organisms other than microbial pesticides and products. That year, EPA published a proposed policy for 'plant pesticides' to be regulated under FIFRA and FFDCA. The 1994 proposed policy announced the agency's intent to regulate the pesticidal substances in plants, but not the plants themselves, leaving the regulation of the plants to USDA. This stance followed from an earlier policy by EPA to exempt from regulation under FIFRA all biological control agents, except for certain microorganisms, which has been interpreted to include plants (US EPA, 1994).

Several exemptions were proposed in the 1994 statement. First, plant pesticides derived through conventional breeding methods were granted a

generic exemption from registration under FIFRA. Further, EPA proposed to exempt from regulation under FIFRA plant pesticides that are derived from sexually compatible plants. Viral coat proteins were also proposed to be exempt under FIFRA. Three categories of exemptions from tolerance setting under FFDCA were also proposed: plant pesticides that would not result in new dietary exposures, nucleic acids in plants and coat proteins from plant viruses. With these exemptions, the agency intended to regulate those plant pesticides that have the greatest potential for adverse effects, on the environment or on health (US EPA, 1994).

A recent report by the National Academy of Sciences addressed the issue of the exemptions proposed by EPA. Though the committee agreed that conventionally bred plants should be exempt for practical reasons based on historical safe use and benefits of these crops, the committee questioned the scientific basis used by EPA for this exemption. Regarding the exemption for plant pesticides derived from sexually compatible plants, the committee questioned the categorical nature of the exemption, while noting that exemptions for certain sexually compatible transgenic plant pesticides would be appropriate. The committee agreed that viral coat proteins should be exempt from regulation under FFDCA, but questioned the exemption under FIFRA due to concerns about potential outcrossing with weedy relatives (NRC, 2000).

The 1994 proposed policy also describes the risk issues with which the regulations are concerned. The following environmental risk issues are considered for both field testing and sale or distribution of a plant pesticide: increasing the ability of the modified plant to survive outside cultivation through the introduction of a specific trait; gene capture and expression of the introduced trait by a wild or weedy relative; potential for a trait conferring a selective advantage to a plant in a natural plant community with the result of increasing the 'weediness' of that species; environmental fate of the pesticidal substance, the dosage to soils after plant senescence and incorporation into the soil, rate of degradation or dissipation and transport in the environment. A further issue is whether or not the pesticidal substance is either exuded or volatilized from the plant during the growing season, resulting in a continuous application to the environment (US EPA, 1994).

Under FFDCA, EPA maintains jurisdiction over food safety issues related to the plant pesticide. Food safety issues related to compositional changes

Table 19.1. Glyphosate mammalian toxicology test results submitted to support revised glyphosate tolerances.

Subject animal	Type of study	Dosages	Results
Dogs	1-year feeding	0, 20, 100 and 500 mg kg ⁻¹ day ⁻¹	NOEL 500 mg kg ⁻¹ day ⁻¹
Mice	2-year carcinogenicity	0, 150, 750, 4500 mg kg ⁻¹ day ⁻¹	No carcinogenic effects at 4500 mg kg ⁻¹ day ⁻¹
Rats	Chronic feeding/ carcinogenicity	0, 3, 10 and 31 mg kg ⁻¹ day ⁻¹ (males) 0, 3, 11 and 34 mg kg ⁻¹ day ⁻¹ (females)	No carcinogenic effects at any dose level; Systemic NOEL of 31 mg kg ⁻¹ day ⁻¹ (males); Systemic NOEL of 34 mg kg ⁻¹ day ⁻¹ (females)
Rats	Chronic feeding/ carcinogenicity	0, 89, 362 and 940 mg kg ⁻¹ day ⁻¹ (males) 0, 113, 457 and 1183 mg kg ⁻¹ day ⁻¹ (females)	No carcinogenic effects at any dose level; Systemic NOEL of 362 mg kg ⁻¹ day ⁻¹ (males) based on increased incidence of cataracts and lens abnormalities, decreased urinary pH, increased liver weight and increased liver weight/brain ratio at 940 mg kg ⁻¹ day ⁻¹ (males); Systemic NOEL of 457 mg kg ⁻¹ day ⁻¹ (females) based on decreased body weight gain at 1183 mg kg ⁻¹ day ⁻¹
Rats	Developmental	0, 300, 1000 and 3500 mg kg ⁻¹ day ⁻¹	Developmental NOEL of 1000 mg kg ⁻¹ day ⁻¹ based on an increase in number of litters and fetuses with unossified sternbrae, and decrease in fetal body weight at 3500 mg kg ⁻¹ day ⁻¹ ; Maternal NOEL of 1000 mg kg ⁻¹ day ⁻¹ based on decrease in body weight gain, diarrhoea, soft stools, breathing rattles, inactivity, red matter in the region of nose, mouth, forelimbs, or dorsal head and deaths at 3500 mg kg ⁻¹ day ⁻¹
Rabbits	Developmental	0, 75, 175 and 350 mg kg ⁻¹ day ⁻¹	Developmental NOEL of 350 mg kg ⁻¹ day ⁻¹ ; Maternal NOEL of 175 mg kg ⁻¹ day ⁻¹ based on increased incidence of soft stool, diarrhoea, nasal discharge and deaths at 350 mg kg ⁻¹ day ⁻¹
Rats	Multigenerational reproduction	0, 3, 10 and 30 mg kg ⁻¹ day ⁻¹	Developmental NOEL of 10 mg kg ⁻¹ day ⁻¹ based on increased incidence of focal tubular dilation of the kidney of F3b pups
Rats	Two generation reproduction	0, 100, 500 and 1500 mg kg ⁻¹ day ⁻¹	Developmental NOEL of 500 mg kg ⁻¹ day ⁻¹ based on decreased pup body weight and body weight gain on lactation days 14 and 21 at 1500 mg kg ⁻¹ day ⁻¹ ; Systemic NOEL of 500 mg kg ⁻¹ day ⁻¹ based on soft stools in F0 and F1 males and females at 1500 mg kg ⁻¹ day ⁻¹ ; Reproductive NOEL of 1500 mg kg ⁻¹ day ⁻¹

NOEL, no observable effects level.

in the plant itself are under FDA jurisdiction. Environmental issues related to the plant itself are regulated by USDA APHIS, as mentioned above.

Crops that have been genetically modified to be herbicide tolerant do not face regulation under FIFRA, as the plants contain no pesticidal substance. EPA must grant any changes in tolerances for residues that might be needed to accommodate altered use patterns for in-season applications of the herbicide. Further, EPA must approve the modification of the label for the herbicide to allow for in-season use of the herbicide over the growing crops, which would not have been allowed previously.

In April 1996, EPA established new tolerances and food additive regulations for the residues of glyphosate on several commodities for several end uses, in response to a number of petitions submitted by Monsanto. The revised tolerances were based on data submitted from several toxicological studies, as summarized in Table 19.1. In addition to those studies listed in Table 19.1, several acute toxicology studies were submitted that placed technical grade glyphosate in Toxicity Categories III and IV. All mutagenicity tests were negative. The carcinogenic potential of glyphosate has been judged to belong in Group E, evidence of non-carcinogenicity for humans, based on the lack of convincing carcinogenicity evidence in adequate studies in two animal species (US EPA, 1996). Revised tolerances for glyphosate are provided in Table 19.2. EPA approved a change in the label for Roundup to allow use of Roundup over the top of growing soybean plants in 1995. Since this change did not affect the registration of Roundup, this approval was not published in the Federal Register (Korwek, 1997).

Table 19.2. Glyphosate tolerances in soybeans (p.p.m.). (Source: EPA, 1996.)

	Revised tolerance
Soybeans	20
Soybeans, grain	20
Soybeans, aspirated grain fractions	50
Soybeans, forage	100
Soybeans, hay	200

FDA

FDA regulates foods and food ingredients, including animal feed and feed additives, under the FFDCA. The agency's authority to regulate the safety of food

is generally exercised under two sections of the Act. Section 402(a)(1) applies to unintended occurrences of unsafe levels of toxicants in food. This section is the agency's primary legal tool for regulating the safety of whole foods, placing liability for food safety on the producer of a new food, and it is under this section that new plant varieties, including those produced using conventional techniques, have historically been regulated. Under this section, the agency retains the authority to remove a food from commercialization if it is found to be unsafe. However, under this section, there is no requirement for safety testing prior to commercialization. Section 409 of the Act applies to food additives, or intentional changes in the composition of foods. Under this section, premarket approval is required unless the food additive is generally recognized as safe (GRAS), or is a pesticide and therefore regulated by the EPA. The GRAS exception allows many ingredients derived from natural sources (e.g. salt, pepper, spices) and some chemical additives (some sweeteners, preservatives, artificial flavours) to be marketed without having been formally reviewed by FDA (US FDA, 1992).

In its 1986 statement, as part of the Coordinated Framework, FDA announced its intention to apply the existing regulatory framework to genetically engineered plant varieties. In that statement, FDA clearly states its intention to base its regulation of food on rational and scientific evaluation of the product, not on the process used to develop the product (US OSTP, 1986).

Further refinements to FDA policy were made in 1992 as the agency issued its policy statement establishing the regulatory framework under which FDA currently operates with regard to foods developed using biotechnology (US FDA, 1992). Under the 1992 policy, regulation of genetically engineered varieties under the food additive provisions of FFDCA which would require premarket review are interpreted to apply to the transferred genetic material and the intended expression product. The introduced genetic material itself is considered to be GRAS, as nucleic acids are present in the cells of every living organism. Expression products, such as proteins, carbohydrates, fat or oil, would only require premarket review if they differ significantly in structure, function or composition from a substance found currently in food, or sufficient safety issues are raised.

Several scientific issues are highlighted in the 1992 statement, including unintended effects,

known toxicants, nutrients, new substances, allergenicity and antibiotic resistance selectable markers. These issues are the focus of FDA regulation of new plant varieties.

FDA has been particularly attuned to the potential of new plant varieties to cause allergies. The agency's principal concern is the possibility that an allergy-causing protein would be transferred from one food plant to another, making the recipient plant cause an allergic response in those allergic to the donor plant. In the case where a protein is derived from a commonly allergenic source, it is possible to test the new variety for allergenic responses in individuals known to be sensitive to the donor plant. For proteins that are derived from non-food sources, testing for potential allergenicity is less straightforward.

In April 1994, FDA, EPA and USDA hosted a scientific conference on allergenicity in transgenic food crops. Attendees concluded that methods are available to assess allergenic potential for proteins that are derived from sources to which consumers have reacted and for which serum is available, but it may be useful to establish a serum bank. There are no direct methods to assess potential allergenicity of proteins from sources that are not known to produce food allergy. Some assurance can be provided to minimize the possibility that a new protein will cause an allergic reaction by evaluating its similarity with characteristics of known food allergens. However, this is an area where more research has been called for. The National Academy of Sciences recommended that priority be given to developing improved methods for identifying potential allergens (NRC, 2000).

FDA is also concerned with the use of antibiotic resistance marker genes in transgenic plants and the risk of reducing the effectiveness of antibiotics in humans and animals (FDA, 1998). The kanamycin resistance marker gene is commonly used in transgenic plants. Calgene, the developer of the FlavrSavr® tomato, the first transgenic crop to be approved by FDA, requested that FDA subject the kanamycin resistance gene to evaluation under food additive regulations. At the time, FDA convened a Food Advisory Committee to consider Calgene's petition. The committee considered both direct risks of allergenicity and toxicity and the effects on the efficacy of antibiotics.

The 1992 policy statement includes a section on guidance to the industry for foods derived from new plant varieties, which describes scientific considerations for the evaluation of the safety and nutritional aspects of new plant varieties. The guidance

section of the statement includes decision trees to assist developers in determining whether their product would be subject to regulation as a food additive or if consultation with FDA is necessary to determine the regulatory status of the product. Informal consultation with the agency has been standard practice for the food industry, and FDA expects that developers of genetically engineered varieties would continue this practice (US FDA, 1992).

One controversial aspect of the FDA policy is that no premarket review has been required for these crops. Consultations have been technically voluntary, though the agency knows of no product that has been commercialized without prior consultation with the agency. However, in 2000, consultations with the agency became mandatory (US FDA, 2000).

The most controversial aspect of FDA's policy has been the decision that foods developed using rDNA technology would not require labelling (FDA, 1993). This decision was based on the judgement that these products do not differ in any significant way from their conventional counterparts solely due to the process through which they were developed. It should be noted that labelling is required for genetically engineered foods that contain genetic material from foods that are commonly allergenic, unless it can be demonstrated that the allergenic property has not been transferred to the new plant variety. Further, plant varieties that have altered nutritional characteristics, such as modified oil content, would also require labelling.

Monsanto began the consultation process with FDA in June 1993. In accordance with the consultation guidelines, data describing the crop that was being transformed, the introduced genetic material, the identity and function of the expression product, comparison of composition of GM and conventional soybeans was included, as well as data and information addressing potential allergenicity and toxicity issues.

The safety evaluation can be broken down into two categories, unintended effects and intended effects, in accordance with the statutory structure, which regulates these effects differently, requiring premarket review only for intended effects under section 409.

Unintended effects

In order to address the possibility of the genetic modification having unintended effects on the crop,

Table 19.3. Animal studies submitted to FDA on glyphosate tolerant soybeans.

Animal	Feed	Duration of study	Parameters measured
Rats	Processed soybean meal	4 weeks	Mortality; body weight; cumulative body weight gain; organ weight; food consumption
Rats	Unprocessed soybean meal	4 weeks	Mortality; body weight; cumulative body weight gain; organ weight; food consumption
Broiler chickens	Processed soybean meal	6 weeks	Body weight; body weight gain; feed intake; feed/gain; liveability
Dairy cows	Raw soybeans	4 weeks	Milk production; fat-corrected milk*; milk composition; dry matter; net energy intakes; body weight changes; dry matter digestibility; nitrogen balance; volatile fatty acids in rumen; rumen nitrogen
Catfish	Processed soybeans	10 weeks	Feed efficiency; percentage weight gain; survival; food consumption*; body composition; moisture, protein, fat and ash in filets
Bobwhite quail	Raw soybean meal	5 days	Mortality; body weight gain; food consumption

* Statistical differences found between animals fed conventional soybean product and GM soybean product.

studies were performed to assess the composition of the GM soybeans compared with conventional soybeans. In addition, wholesomeness studies were performed to evaluate any differences in feeding characteristics of GM soybean feed and conventional feed.

In the compositional analysis, evaluations were performed on seed, toasted meal, defatted meal (flour), protein isolate, protein concentrate, crude lecithin and refined, bleached, deodorized oil. Differences in seed composition were seen to be an indication that differences in other products would be found. Other products were chosen as they represent the various uses of soybeans. Toasted meal is widely used in animal feed. Defatted meal, protein isolate and protein concentrate are commonly used in food, as are lecithin and soybean oil. For seeds, the parameters compared were: protein, fat, fibre, ash, carbohydrate, amino acids, fatty acids, soybean seed proteins, trypsin inhibitor, lectin and isoflavones. Significant differences in fat, ash and carbohydrate were observed in one study, while no significant differences in these parameters were observed in similar studies conducted the next year. Protein, fat, fibre, ash and carbohydrate content were measured for defatted toasted meal, defatted non-toasted meal, protein isolate and protein concentrate, and no significant differences were found for these values between GM soybeans and conventional soybeans. Antinutrient content (trypsin inhibitor and urease,

phytate, stachyose, raffinose, lectins, isoflavones) was measured in toasted meal and, apart from lectin concentrations which were below detection limits, no significant differences were found. Fatty acid composition was measured for soybean oil and no significant differences were found. The composition of crude lecithin was also compared, with no significant differences found.

Animal feeding studies were performed using rats, broiler chickens, dairy cattle, catfish and bobwhite quail. Two separate rat studies were performed, using processed and unprocessed meal. The study using processed meal was intended to address mammalian health issues, while the unprocessed meal was intended to address risks to wild animals that might feed on unharvested beans in the field. Broilers were included due to the prevalent use of processed soybeans in broiler operations. Similarly, dairy cattle were fed raw soybeans to reflect the widespread use of soybeans in cattle feed. Catfish were fed processed meal as this composes a great portion of feed used in aquaculture. Finally, bobwhite quail were fed unprocessed soybeans in order to address potential risks to birds that might feed on soybeans in the field. These studies were not designed as toxicology tests, but rather were undertaken to determine whether there were any differences in wholesomeness, or the ability to support growth and well-being. Table 19.3 summarizes the setup of the animal studies that were

performed by Monsanto. It was concluded that no material differences were found in the wholesomeness of soybean products in any of the animal studies.

Intended effects

In the evaluation of intended effects, several aspects of the GM crop are considered: expression level of introduced protein, similarity of introduced protein to those already common in food and feed, allergenic potential, toxicity, prevalence of protein in food and feed, and changes in carbohydrate, fat or oil composition, structure or levels.

The expression level of CP4 EPSPS in soybean seed and processed soybean products was evaluated. In whole seed, the concentration of CP4 EPSPS was found to be 0.3 $\mu\text{g mg}^{-1}$ fresh weight. Concentrations in toasted meal, defatted meal, protein isolate and protein concentrate were measured and found to be less than 0.1% of total protein. No enzymatic activity was found in any of the processing fractions.

The introduced protein, CP4 EPSPS was found to be similar to EPSPS already commonly present in food due to similarity in the reaction catalysed, amino acid sequence, homology of active site residues and three-dimensional structure.

Soybeans are known to cause allergies to some sensitive individuals. The allergenicity of GM soybeans was assessed in relation to conventional varieties. Known allergenic proteins of soybeans were found to be unchanged, based on an evaluation of protein extracts from non-toasted, defatted soy flour. Assessing the allergenicity of proteins that are not derived from allergenic sources is more problematic, as discussed above. CP4 EPSPS fits one of the criteria common to allergenic proteins, that of molecular

weight, but does not share any of the other characteristics. Table 19.4 shows the characteristics common to allergenic proteins.

Potential toxicity was assessed by considering the similarity of CP4 EPSPS to known protein toxins, an acute mouse gavage study and the study of the stability of CP4 EPSPS to digestion. First, CP4 EPSPS was not found to show any meaningful amino acid sequence homology when compared with known protein toxins in available databases. Next an acute mouse gavage study was performed, which resulted in no adverse effects (body weight, cumulative body weight and food consumption) at a dose representative of a 1300-fold safety margin relative to the highest potential human consumption of the protein in a diet including GM soybeans, maize, tomatoes and potatoes (assuming no loss in processing). An acute study was judged to be adequate in the toxicity assessment as proteins act as toxins by acute mechanisms. Finally, CP4 EPSPS was found to have a short half-life in simulated digestive fluids. The half-life was measured as less than 15 s in gastric fluids and less than 10 min in intestinal fluids. The relatively short digestion time of the protein indicates a reduced likelihood that the protein would be toxic.

Finally, the prevalence of CP4 EPSPS in the diet was considered. As CP4 EPSPS was found to represent 0.025% of the extractable protein in soybean seed tissue, it was not expected to become a macroconstituent of the human or animal diet. The addition of the CP4 EPSPS gene was also not found to alter the carbohydrate, fat or oil composition, structure or levels of the soybean compared with conventional varieties, as described in the compositional analysis above.

Monsanto has published the research results that were submitted to FDA on the composition of glyphosate tolerant soybeans, toxicity and feeding studies in a series of peer-reviewed articles in the *Journal of Nutrition* (Hammond *et al.*, 1996; Harrison *et al.*, 1996; Padgett *et al.*, 1996b). In addition, research results on the composition of glyphosate-tolerant soybeans treated with glyphosate, which were not submitted to FDA, were published in the *Journal of Agriculture and Food Chemistry* (Taylor *et al.*, 1999).

Benefits

The primary reason why growers have adopted Roundup Ready weed control programmes is the

Table 19.4. Characteristics of known allergenic proteins (source: Monsanto, data submitted to FDA, obtained by FOIA request from FDA).

Characteristic	Allergens	CP4 EPSPS
Molecular weight 10–70 kDa	yes	yes
Glycosylated	yes ^a	no
Stable to digestion	yes	no
Stable to processing	yes	no
Similar to known allergens	— ^b	no
Similar to soybean proteins	—	yes
Prevalent protein in food	yes	no

^a Typically but not absolutely.

^b Implicit for allergenic proteins from soybeans. FOIA, Freedom of Information Act.

simplicity of a weed control programme that relies on one herbicide to control a broad spectrum of weeds without crop injury or crop rotation restrictions. Before the introduction of Roundup Ready soybean varieties, growers would choose between many herbicides, often applying three or more active ingredients, some of which would cause damage to the growing soybean plants, or cause harm to maize crops that commonly follow soybeans (Gianessi and Carpenter, 2000).

Roundup is a highly effective broad spectrum herbicide that controls both broadleaf and grass weeds. Each year, state extension services release weed control guides for field crops including soybeans. The guides provide information on the efficacy of available herbicide treatments on specific weed species, as well as ratings of crop safety. In the Michigan State University weed control guide, in which 182 treatments are rated on 24 different weed species, Roundup used over Roundup Ready soybeans received 23 good or excellent ratings. In addition, the Roundup treatment is rated with a minimal risk of crop injury. The next best available treatment with similar crop safety received 16 good or excellent ratings (Kells and Renner, 1999).

Growers also have more flexibility in timing herbicide treatments with the Roundup Ready system. Maximum weed heights at which Roundup is effective on most weed species are higher than other available herbicides. This allows growers to treat later if needed and still get effective weed control. Further, some commonly used soybean herbicides may cause injury to rotation crops. Because of this potential for injury to crops following soybeans, rotation restrictions are specified on the labels of these herbicides. For instance, sugarbeets may not be planted for 40 months after a field is treated with imazethapyr, a commonly used soybean herbicide.

Potential impacts of adopting Roundup Ready weed control programmes include changes in costs, yields and pesticide use. Roundup Ready programmes were introduced to be price competitive

with existing conventional programmes. The introduction of competitively priced Roundup Ready programmes resulted in manufacturers of other products dropping their prices, in some cases by 40%. This resulted in an estimated US\$216 million cost savings for soybean growers in 1999 compared with 1995, the year before Roundup Ready varieties were introduced, including the technology fee paid by growers who planted Roundup Ready varieties. Table 19.5 shows estimated soybean weed control programme costs for 1995, 1998 and 1999.

The impact on yields is less clear (Carpenter and Gianessi, 1999). Survey data on which to base a comparison of yields from Roundup Ready fields with conventional fields are scarce. Two areas of research assist in understanding the consequences of the adoption of Roundup Ready varieties on yield. The first is weed control research, comparing weed control strategies. The second type of research is variety trials, where the yield potential of conventional and Roundup Ready varieties have been compared.

In weed control trials, weed control programmes are compared in terms of efficacy against particular weed species and resulting yields. The purpose of these types of studies is to determine optimal herbicide application rates and timing to achieve control of various weeds. In general, these tests are conducted using a single variety. Recently, researchers have chosen to use Roundup Ready varieties in order to include Roundup treatments in their studies. Yield differences in these studies are due to more effective weed control and from avoiding crop injury. However, since only one variety is used in each study, the yield potential of the variety is not directly considered. It is difficult to generalize about the results from the weed control studies, although there seems to be no resounding yield advantage or disadvantage in the Roundup Ready systems compared with conventional programmes (Breitenbach and Hoverstad, 1998).

Variety trials are conducted by state universities to assess the characteristics of the varieties that will be available to growers the following year. The trials assess yield, maturity, lodging, protein and oil content, and resistance to pathogens and soybean cyst nematode and are generally maintained weed free, in order to eliminate competition from weeds as a factor influencing yield. Based on a compilation of variety trials from several states, it appears that available Roundup Ready varieties generally yield lower than conventional varieties (Minor, 1998; Oplinger *et al.*, 2000).

Table 19.5. Soybean weed control costs (US\$ millions).

	1995	1998	1999
Herbicide expenditures	1865	1482	1441
Technology fee	0	160	208
Net weed control costs	1865	1642	1649

Calculated assuming herbicide expenditures in 13 states represent 80% of US total.

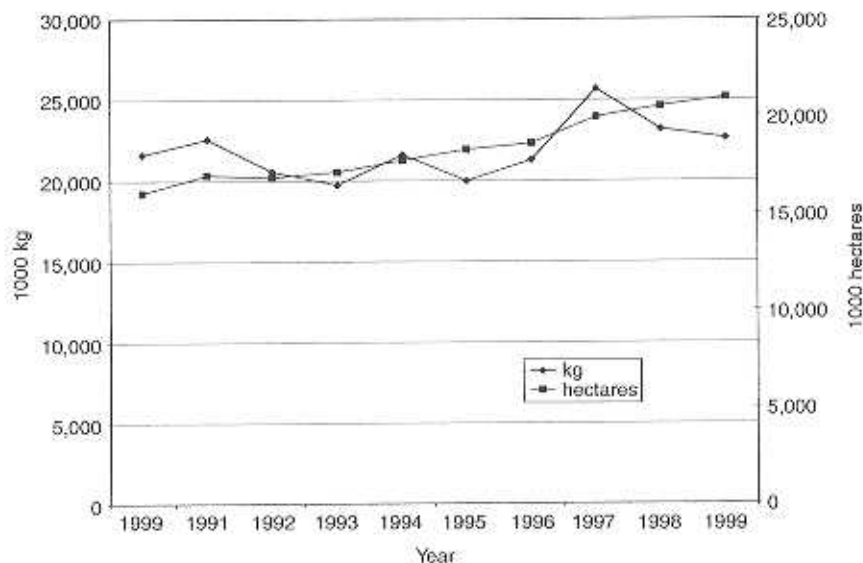


Fig. 19.2. Herbicide use in soybeans (AR, IA, IL, IN, MN, MO, NE, OH). (Source: USDA NASS, 1991–2000.)

Based on weed control and variety trials, it appears that Roundup Ready varieties do not have a yield advantage over conventional varieties.

Herbicide use in soybeans has been affected dramatically by the introduction of Roundup Ready soybean varieties. The USDA estimates the total number of acres treated and number of treatments by herbicide each year. The total number of pounds of herbicides used per soybean acre has remained unchanged since the introduction of Roundup Ready soybeans. The mix of herbicides being used in soybeans has changed. As one would expect, the use of glyphosate has increased, from being used on 20% of acreage in 1995 as a burndown or spot treatment, to being used on 62% of acres in 1999. The use of other herbicides has decreased. Imazethapyr, the most widely used soybean herbicide in 1995, was used on 44% of soybean acres in 1995, compared with 16% in 1999. Figure 19.2 shows trends in herbicide use and land area for 1990–1999 for eight states. Growers have also reduced the number of herbicide applications. Comparing 1995, the year before Roundup Ready varieties were introduced, and 1999, the last year for which data are available,

the number of herbicide application-acres has decreased by 19 million, or 12%.¹ These changes in herbicide use occurred even though the total number of soybean acres increased by 18% between 1995 and 1999. The decrease in herbicide applications demonstrates that growers are using fewer active ingredients and making fewer trips over the field, which translates into ease of management.

Summary

Roundup Ready soybeans have been rapidly adopted by US farmers, yet their approval for commercialization is under scrutiny. This case study provides a description of the regulatory process governing agricultural biotechnology and traces the approval of Roundup Ready soybeans, summarizing the information that was submitted to US regulatory agencies by Monsanto. Estimates of the impact that the adoption of Roundup Ready soybeans has had on US agriculture are also provided.

The regulatory structure for agricultural biotechnology has evolved over the past 25 years, as

¹ An application-acre is the number of different active ingredients applied per acre multiplied by the number of repeat applications, and differs from the number of trips over the field, as one trip across the field to apply two active ingredients is treated as two applications, as is two treatments each containing a single ingredient.

technology allowing for genetic modification developed. The system continues to evolve as new and different applications of the technology emerge. Indeed, the most recent report of the National Research Council recommended that any new rules for regulating GM plants be flexible to reflect improvements in scientific understanding (NRC, 2000).

In reviewing the studies that were conducted on the safety of Roundup Ready soybeans, no indication of greater health or environmental risks were found compared with conventional varieties. The benefits of the introduction of Roundup Ready soybeans include a cost savings of US\$216 million in annual weed control and 19 million fewer soybean herbicide applications per year.

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