Robert Horsch

REVIEW ARTICLE

PUTTING PLANT BIOTECHNOLOGY TO WORK FOR FOOD, NUTRITION AND DEVELOPMENT

Rob Fraley[1], Gerard Barry[1], Roy Fuch[1]s, Harvey Glick[1], Robert Horsch*[1], Jill Montgomery[1], Tom Nickson[1], John Purcell[1], Eric Sachs[1], Marcia Vincent[1]

ABSTRACT

Plant biotechnology is safely bringing valuable new benefits to farmers around the world, including those in developing countries where the needs for food, nutrition and overall development may be greatest. From the current base of experience, it is reasonable to expect even greater benefits in the future, provided that progress continues on three fronts: a pipeline of products with human and environmental benefits, implementation of science-based local and global regulations and regulatory capacity, and partnerships to ensure development and attention to the needs of resource-poor farmers. This paper reviews the current impacts of products developed with biotechnology, the regulatory systems that ensure safe use of these products, and gives examples of the technologies that will yield second and third generation products. Of particular importance, partnerships between the private sector and universities, government agencies and non-governmental organizations are tackling some of the most difficult problems in agriculture and nutrition in the developing world.

Key words: plant biotechnology, regulation, development, impact, benefits, agriculture

METTRE LA BIOTECHNOLOGIE VEGETALE AU SERVICE DE L'ALIMENTATION, DE LA NUTRITION ET DU DEVELOPPEMENT

ARTICLE A REVISER

FRENCH

RÉSUMÉ

La biotechnologie végétale présente en toute sécurité de nouveaux avantages inégalables aux agriculteurs du monde entier, y compris ceux des pays en développement où les besoins en matière de nourriture, de nutrition et de développement général pourraient être les plus importants. A partir de l'expérience actuelle, il est raisonnable de s'attendre même à de plus grands avantages à l'avenir, pourvu que le progrès continue sur trois fronts: une pipeline de produits qui présentent des avantages pour les hommes et pour l'environnement, la mise en œuvre de règlements et capacités réglementaires aux niveaux local et mondial en se basant sur les sciences, ainsi que des partenariats en vue d'assurer le développement et l'attention par rapport aux besoins des agriculteurs munis de peu de ressources. Cet exposé évalue les impacts actuels des produits mis au point au moyen de la biotechnologie, des systèmes réglementaires qui garantissent l'utilisation sûre de ces produits ; il donne également des exemples des technologies dont les résultats seront des produits de deuxième et troisième générations. Etant d'une importance particulière, les partenariats entre le secteur privé et les universités, entre les agences gouvernementales et les organisations non-gouvernementales, s'embarquent actuellement sur certains problèmes des plus difficiles qui se posent en agriculture et en nutrition dans le monde en développement.

Les mots clés : Biotechnologie végétale, Règlement, Développement, Impact, Avantages, Agriculture

*Corresponding author Email: robert.b.horsch@monsanto.com
[1]Monsanto Company, 800 North Lindbergh Boulevard, St. Louis, Missouri 63167, USA

INTRODUCTION

Plant breeders have been introgressing genes for a wide range of beneficial traits into crops for millennia. Most of today's major food plants do not closely resemble their original wild ancestors. Modern varieties have been developed to incorporate improved resistance to pests, tolerance of environmental stresses, ability to take up nitrogen and other soil nutrients, color, flavor, yield, content of human nutrients, and other useful features from a wide range of related plants. Using the tools of plant biotechnology, we now have the ability to more broadly introgress useful genes from an even wider range of organisms into crops.

Over the past twenty years of development and use, plant biotechnology has been combined with the best improvements of plant breeding and farming practices to address many challenges in food production, in both developed and developing countries. Numerous regulatory agencies around the world have assessed the food, feed and environmental safety of these products. Furthermore millions of farmers around the world have planted these new biotechnology crop varieties and are confirming the benefits the crops have for both large and small-scale farmers. The tools of plant biotechnology also hold great promise for meeting increasingly important human nutrition and development needs. This paper describes the impacts of plant biotechnology so far, the ways in which its safe use has been assured, and the special opportunities and challenges in putting this powerful technology to work in developing countries.

ASSESSING THE IMPACTS OF PLANT BIOTECHNOLOGY PRODUCTS

Herbicide tolerant (HT) crops and insect protected (*Bt - Bacillus thuringiensis*) crops have been rapidly adopted by farmers in many regions of the world. The rapid adoption of these crop technologies is clear evidence that the benefits greatly exceed the incremental costs of this new technology. These first generation crops produced with biotechnology are providing direct benefits to growers in terms of improved and simplified pest management. Additionally, these crops provide environmental benefits in terms of reducing the overall use of pest control products, increasing biodiversity and facilitating the adoption of sustainable reduced tillage farming systems. Maize that is protected against insect damage through the introduction of *Bt* insect control proteins is less susceptible to contamination with mycotoxigenic fungi. These fungi produce mycotoxins such as fumonisin B1 which is carcinogenic, toxic to the liver and kidneys of farm animals and causes fatal degenerative brain damage in horses. Future developments will include crops with other agronomic characteristics such as high yield, cold tolerance, drought tolerance and the ability to grow in soils that are saline or that contain a high concentration of metals.

Improved Pest Management

Perhaps the single most important benefit of the first generation of biotech crops is that they provide the farmer with better methods of pest control. Pests, either weeds or insects, can significantly reduce crop yields. Therefore, farmers use a variety of programs to protect their crops from these pests.

Insect protected *Bt* crops provide the farmer with season-long protection against several damaging insect pests and reduce or eliminate the need for insecticide sprays. This technology also often overcomes the yield losses that may result even when insecticides are applied. The reduced need for spraying allows the farmer more time for other farm management duties [1]. In some cases, growers are better able to control pests with *Bt* crops than with conventional insecticide sprays and this improved control results in higher yields [2]. In 1999, US cotton growers who planted *Bt* cotton varieties eliminated 15 million insecticide spray applications compared with growers who planted conventional varieties. In 1999, corn growers who planted *Bt* corn reduced one million acre treatments of chemical insecticides [1].

Herbicide tolerant crops also offer the farmer improved weed control options. In some cases, a single herbicide application made to an herbicide tolerant crop can replace several applications of a complicated mixture of two or more herbicides. This greatly simplifies the timing of application and the need for careful mixing calculations to insure the right amount of each product is applied [1].

Often, in the case of Roundup Ready soybeans, cotton or oilseed rape (canola), a grower will use a single application of Roundup herbicide for weed control, instead of a mixture of several herbicides that may be applied in sequence. Roundup controls a broad spectrum of weed species that is unmatched by most other herbicides. Growers in the US who planted Roundup Ready soybean in 1999 eliminated 19 million herbicide applications compared to growers who planted conventional soybeans. This 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 [1].

In a study of Canadian canola, growers in 2000, over 80% reported that weed control was more effective with herbicide tolerant canola varieties compared to conventional [3].

Greater Net Return

Improved weed control with herbicide tolerant and *Bt* crops, and lower input costs, often contribute to a higher net return compared to conventional crops. Weed and insect populations can vary from year to year and will have an impact on overall pest control costs and net returns. Nevertheless, herbicide tolerant and *Bt* crops have resulted in better overall returns for farmers compared to conventional crops. Studies have shown that US farmers who planted biotech crop varieties in 2001 improved their bottom line by $1.5 billion [4]. Biotech soybeans provided the greatest savings ($1 billion), followed by herbicide tolerant cotton ($133 million), insect resistant corn ($125 million), insect resistant cotton ($103 million) and herbicide tolerant corn ($58 million). In Canada, farmers who planted herbicide tolerant canola earned an additional $C 5.80/ acre compared to growers who planted conventional varieties [3]. An analysis of *Bt* Cotton growers in Argentina reported that *Bt* Cotton generated an average incremental benefit of $65.05/ha [5].

Reduction in Pesticide Use

Since 1996, when the first crops from biotechnology were planted, there has been a reduction in the amount of pesticides used in the production of these crops. *Bt* and herbicide tolerant crop varieties have contributed to a reduction in the total use of herbicides and pesticides in many different countries. A study by the United States Department of Agriculture reported that 8.2 million pounds of pesticide active ingredient were eliminated by farmers who planted biotechnology crops in 1998 compared with 1997 [6].

Several studies have shown that US growers who planted *Bt* cotton have eliminated over 2.4 million pounds of insecticide active ingredient in the 1998 growing season [1]. Significant reductions have also been reported in China and in Argentina, where pesticide reductions resulting from the use of *Bt* cotton ranged from 60 - 70% [5]. Recently, a study of small holder farmers in China showed that production costs with *Bt* cotton were US$1.61/kg compared to US$2.23 for conventional cotton, a reduction of almost one third of production costs [7]. Similar results were observed with small holder cotton farmers in the Makhatini flats region of South Africa. Planting *Bt* cotton allowed growers to reduce the overall amount of pesticide used. [8]

In Canada, a study reported that canola growers who planted herbicide tolerant canola eliminated over 12 million pounds of herbicide product in the 2000 growing season [3].

Studies on the impact of Roundup Ready soybeans on pesticide use have been mixed, with some studies reporting no change in overall use and other studies reporting a small reduction in overall pesticide use with Roundup Ready soybean [2]. A thorough analysis by the USDA for the 1997 year reported that small but significant decreases in herbicide use was a result of Roundup Ready soybean planting [2]. Even in cases where the total amount of pesticide active ingredient has remained stable, Roundup Ready soybean farmers have replaced some or all of the herbicides normally used with Roundup applications. A USDA analysis reported that US soybean growers eliminated 7.2 million pounds of synthetic herbicides (eg *imazethapyr, pendimethalin* and *trifluralin*) and replaced them with 5.4 million pounds of Roundup Herbicide [6]. Glyphosate has an average half-life of 47 days, compared with 60 - 90 days for the herbicides it replaces. Additionally, the herbicides that glyphosate replaces are 3.4 to 16.8 more toxic, according to a chronic risk factor based on the EPA (US Environmental Protection Agency) reference dose for humans. Thus the substitution enabled by RR (Roundup Ready) soybeans results in Roundup herbicide replacing other synthetic herbicides that are at least 3 times as toxic and that persist nearly twice as long as glyphosate [6].

Small holders in China also benefited from lower pesticide use [7], and reported that farmers planting *Bt* cotton in China reduced the number of applications from 19.8 to 6.6 , a reduction of 66%. Overall volumes of pesticides were reduced from 60.7 kg/ha to 11.8 kg/ ha with *Bt* cotton, a reduction of 80%.

A recent study by Kline and Company, a New Jersey based consulting firm, has analyzed the future trends in pesticide utilization in the US by the year 2009. Their analyses of the market indicates that by 2009, herbicide tolerant crops will contribute to an annual reduction of 45 million pounds in herbicide active ingredient. Similarly, insect protected *Bt* crops are predicted to contribute to an annual reduction of 13 million pounds of insecticide active ingredient by 2009 [9].

Improved Conditions for Non-target Organisms

Studies in cotton and potatoes have shown that non-target insect populations, including economically important predatory species, are larger in *Bt* crops than in conventional fields treated with broad-spectrum insecticides. Studies of cotton in the United States have shown that populations of predatory bugs (Orius and Geocoris species), spiders and ants are all significantly higher in *Bt* cotton fields than in conventional cotton fields treated with insecticides . In China, lower insecticide use in *Bt* cotton fields is associated with 24% larger generalist predator populations . Similarly, populations of predatory bugs, ladybird beetles and spiders have been shown to be greater in *Bt* potato fields than in fields of conventional potatoes treated with insecticidal sprays [10].

By maintaining significant populations of important arthropod predators, secondary pest species on *Bt* crops can be controlled by their natural enemies, reducing the need to apply pesticides for control of these pests (which, unlike the target pests, are not controlled by the *Bt* expressed in the plant). In the United States, pest aphid populations have been found to be lower in *Bt* cotton fields than in insecticide-treated conventional cotton fields, reflecting the effects of biological control . In a separate study, certain secondary lepidopteran pests (Spodoptera species) were less likely to occur at economic levels in *Bt* cotton than in conventional cotton apparently because of higher numbers of generalist predators in the *Bt* cotton fields [11]. In *Bt* potato fields, beneficial arthropods alone kept aphids below damaging levels [10].

Sustainable Farming Systems

The use of herbicide tolerant crops, and Roundup Ready crops in particular, are very compatible with farming systems that reduce or eliminate the need for tillage or cultivation. These reduced tillage farming systems are very desirable as they greatly reduce soil erosion as well as sediment runoff from fields into watersheds. Tillage is one of the primary means of weed control and so the reduction in the amount of tillage can create weed management problems for the growers. This is often cited as one of the reasons that farmers choose not to adopt reduced tillage farming systems. Herbicide tolerant crops provide an alternative means of controlling weeds in the crop and thus provide a solution to growers who want to adopt this farming system. Recent surveys of soybean and canola farmers have confirmed that farmers are using less ploughing with these crops, and the primary reason is the availability of Roundup Ready technology and Roundup herbicide.

In addition, the use of herbicide tolerant crops and insect protected crops are an important component of Integrated Pest Management (IPM) farming systems that enable farmers to implement long term sustainable systems of crop production.

Less Mycotoxin in Corn

Fungi of the genus Fusarium are commonly associated with corn grown throughout the world. These fungi can produce disease in all parts of the corn plant including the ears (ear rot), but may also infect the plant without causing overt symptoms of disease. Certain Fusarium species, e.g. F. verticillioides and F. proliferatum, infect corn through wounds caused by insects such as the European corn borer (Ostrinia nubilalis). These fungi produce secondary toxic metabolites called fumonisins which are structurally related to sphingoid bases. The toxic mode of action of fumonisins is interfering with the *de novo* synthesis of complex glyco-sphingo-lipids. This results in disturbances of cellular processes such as cell growth, cell differentiation and cell morphology, endothelial cell permeability and apoptosis [12].

Fumonisins have been detected in corn wherever it is grown and the most frequent occurrence is in countries with warm and subtropical conditions [13]. According to Visconti [14], approximately 59% of corn grain samples collected globally were contaminated with fumonisins with the highest incidence of contamination occurring in Oceania (82%) followed by Africa (77%), North and South America (63%), Europe (53%) and Asia (51%). The incidence of contamination of corn kernels and commercially available corn products for human consumption varied from 47% to 82% between different continents. These samples were frequently contaminated with FB11 levels close to 1 mg/kg, although exceptionally high levels have been found in South Africa (up to 117 mg/kg) and China (up to 150 mg/kg) with high incidence of esophageal cancer [14].

Fumonisins can produce fatal brain damage (leukoencephalomalacia) in horses when fed at levels of >10 mg/kg in corn (equivalent to a daily dosage of 0.1 to 0.2 mg/kg body weight[2]. Fumonisins cause pulmonary edema in swine, liver and kidney damage in many species, and liver and kidney cancer in rodents when fed at dietary levels up to 150 mg/kg [15]. In regions of Africa and China where there are high levels of fumonisin contamination in corn, higher rates of esophageal and liver cancer have been reported in subsistence farmers who consume the corn as a major dietary staple [19]. While there are a number of risk factors present in these populations, some epidemiologists have proposed that the high cancer rates may be related to fumonisin exposure [12]. Since fumonisins are found routinely in corn grown around the world, scientific organizations have met and assessed the health risks of humans and farm animals exposed to these toxins in the diet. Switzerland has set a fumonisin limit of 1 mg/kg for imported corn [16]. The US FDA recently proposed limits of 3-4 mg/kg fumonisins in corn used for human food, 5 mg/kg in corn for horses, and higher levels for corn fed to other farm animals [2]. The Joint FAO/WHO Expert Committee on Food additives recently established a provisional maximum tolerable daily intake (PMTDI) of 2 μg/kg/day intake of fumonisins for human consumption . The same TDI was proposed earlier by the EU Scientific Committee on Food [12].

As stated previously, mycotoxigenic fungi that produce fumonisins can enter the corn plants opportunistically through portals and labyrinths created by boring insects. Boring insects are among the most important insect pests of corn worldwide. Corn plants that have been improved with biotechnology to produce the Cry 1Ab insect control protein from *Bt* (*Bacillus thuringiensis*) are protected against damage from corn borers. Gary

Munkvold at Iowa State University was the first to report that corn which expressed the Cry 1Ab protein throughout the plant had significantly reduced ear rot and fumonisin levels (up to 90% reductions) compared to non-protected corn plants [13]. This was demonstrated consistently over several years of field trials. These findings were corroborated by Pat Dowd of USDA in Peoria, Illinois who found a similar significant reduction in fumonisin levels in corn varieties that expressed *Bt* insect control proteins throughout the plant [19]. Recent reports have confirmed similar levels of reductions of fungal contamination and fumonisin levels in biotech corn grown in Italy, France and Spain [20]. Additional trials are underway in other countries to see if similar reductions (3 to 40 fold) in fumonisins are observed in countries where high insect pressure and high fumonisin contamination are common. Protection of corn plants against insect damage and subsequent fungal infection may have important health implications for farmers and farm animals that are routinely exposed to fumonisins on the corn they grow.

Biotechnology offers the potential to reduce the occurrence of other important mycotoxin contaminants such as aflatoxins and ochratoxins in food crops. This could be possible by inserting insect control genes into plants that control a broader spectrum of insect pests that cause damage, allowing toxigenic fungi to invade the plant. Alternatively, other ways may be found to either reduce fungal growth in plants or detoxify mycotoxins produced in plants.

ENSURING THE SAFE USE OF BIOTECHNOLOGY

Over 120 million acres of agricultural biotechnology crops were grown worldwide in 2001 [21]. The food, feed and environmental safety of these products has been assessed by numerous regulatory agencies around the world, based on regulatory safety assessments that are generally consistent with international safety assessment guidelines. However, there are distinct regulations, data requirements and regulatory procedures in various countries globally.

Regulatory Authorities

In the United States, regulatory authority is clearly delineated among three regulatory agencies: the US Department of Agriculture (USDA), the Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA). The USDA assures that biotechnology-derived plants are not plant pest risks and propose no significant risks to the environment or production agriculture. The FDA is responsible for the food and feed safety of products, including those derived from biotechnology. The EPA has authority to assess the safety of biotechnology-derived plants that protect themselves from pests. This authority comes under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). The EPA also has authority over all herbicides, including those used in conjunction with herbicide-tolerant plants.

Regulatory authorities in numerous other countries have also put regulatory processes in place to assess the food, feed and environmental safety of biotechnology crops. In Canada, the Canadian Food Inspection Agency (CFIA) regulates feed and environmental safety while food safety is regulated by Health Canada. Japan also divides regulatory authority by food safety (Ministry of Health and Welfare) and feed and environmental safety (Ministry of Agriculture, Food and Fisheries). In the European Union (EU), environmental assessments are conducted under 90/220 and the new 2001/18 regulations. Food safety is currently handled under the Novel Foods Act, which is untested through approval, and this may also be impacted by the implementation of the European Food Safety Agency. Feed safety for the EU is currently handled through an individual EU country although an EU-wide Novel Feed Act is under consideration.

Safety Assessment

Safety assessment of agricultural biotechnology crops focuses on the properties of the introduced traits, the genes/proteins that confer the introduced traits (typically conferred by one or a few newly expressed proteins) and the resulting crop or grain produced by the crop. Based on the information collected to date, the proteins that confer the expressed traits (for example, insect protection or herbicide tolerance) raise no safety concerns. Information on history of use (such as, prior existence in foods and the environment), function, mode-of-action and similarity of the encoded proteins to proteins currently in the diet is readily available. Food produced from biotechnology crops has been assessed to be as safe and nutritious as conventional foods and crops. Furthermore, biotechnology crops have been shown to pose no greater risks to the environment than conventional crop varieties produced through the current agronomic practices.

In 1996, a joint report from an expert consultation sponsored by the World Health Organization (WHO) and the Food and Agricultural Organization (FAO) of the United Nations concluded that *"biotechnology provides new and powerful tools for research and for accelerating the development of new and better foods"* [23]. The FAO/WHO expert consultation also concluded that it is vitally important to develop and apply appropriate strategies and safety assessment criteria for food biotechnology to ensure the long-term safety and wholesomeness of the food supply. Following these criteria, foods derived from products produced through biotechnology have been extensively evaluated to assure they are as safe and nutritious as foods from conventionally grown crops. All foods, independent of whether they are derived from agricultural biotechnology crops or conventionally bred plants, must meet the same rigorous food safety standard. Numerous national and international organizations have considered the safety of foods from biotech crops [23-26]. They have concluded that food safety considerations are basically of the same nature for food from biotech crops as for those foods from crops grown using other methods like traditional breeding.

Protein Safety

A key component in the evaluation of the safety of a resulting food is a thorough assessment of the inserted DNA/genes and the protein(s) produced. Usually when a gene is chosen for transformation into a crop, the encoded protein has been well characterized in terms of function (mechanism of action, evolutionary heritage, physicochemical properties, and so on.). An important consideration in protein safety is whether or not the protein can be established to have been consumed previously. In other words, has there been a history of safe use?

Protein digestibility studies, *in vitro,* are conducted to assess whether the protein is rapidly degraded like other dietary proteins. Protein toxicity is assessed by evaluating acute oral toxicity, typically in mice [27]. This study is typically a two- week program in which the purified protein is fed to animals at doses which should be 100 to 1,000 times higher than the highest anticipated exposure via consumption of the whole food product containing that protein. The data from several acute oral toxicity studies reported that although these studies were designed to obtain LDs, in fact no lethal dose has been achieved for these proteins [28,38].

A significant hazard that has been assessed for all biotech crops is the possibility of accidental transfer of existing allergens from one crop to another. All proteins/genes introduced into biotech crops have been assessed for allergenic potential early in the development process using internationally accepted experimental and clinical allergy testing methods [23]. Genes obtained from sources known to cause allergy are presumed to encode allergens unless proven otherwise using clinical testing. These procedures are the same tests used by laboratory allergy testing, diagnostic skin prick tests, and clinical food challenges. All proteins undergo a further review of detailed items such as whether the new protein has an amino acid sequence similar to known allergens, is resistant to digestion, is heat stable, and is abundant - all factors which contribute to allergenicity of proteins [29]. Based on the totality of this information, an assessment is made on the safety of the newly introduced proteins.

Substantial Equivalence

The comparative process of substantial equivalence involves comparing the characteristics, including the levels of key nutrients and other components, of the food derived from a biotech crop to the food derived from conventional plant breeding. The principle strategy for the assessment of substantial equivalence of biotech crops has been to evaluate the biochemical composition of resulting whole food or feed. The goal is to assess whether the composition of the new food or feed falls within the generally accepted definition or specification compared to a traditional variety. For example, the composition of insect protected corn has been compared to traditional corn. The evaluation of composition focuses on macronutrients, vitamins and minerals, but may also include an evaluation of relevant anti-nutrients or toxins such as endogenous phytoestrogens, protease inhibitors and lectins. When a novel food is shown to be substantially equivalent to a food with a history of safe use, ***"the food is regarded to be as safe as its conventional counterpart"*** [23]. If the food were substantially equivalent except for the introduced trait, the remaining focus would be on the safety of the introduced trait, for example, the newly expressed protein(s) that confer the trait. A FAO/WHO expert consultation in 1996 concluded, ***"this approach provides equal or greater assurance of the safety of food derived from genetically modified organisms as compared to foods or food components derived by conventional methods"*** [23].

Agronomic Equivalence

In addition to a demonstration of substantially equivalent composition, agronomic evaluation of the biotech crop adds information to assess whether there are any unexpected biological effects of the introduced trait. Compositional assessments provide good assurance that no untoward metabolic, nutritional or anti-nutritional effects have occurred. An additional and very sensitive measure is to compare a wide variety of biological characteristics at the whole plant level. The agronomic and yield characteristics of any crop are very sensitive to untoward perturbations in metabolism and in genetic pleiotropy, serving to as sensitive indicator of unexpected changes that might have occurred. Biotech crops must meet stringent performance criteria.

Animal Feed Performance Studies

Animal feed performance (nutrition) studies have provided supplementary confirmation of the substantial equivalence, nutritional equivalence and safety of biotech crops. Currently there are many options for animal studies, the choice of which depends on the crop being improved and its intended use. Factors evaluated in these studies may include feed intake, body weight, carcass yield, feed conversion, milk yield, milk composition, digestibility and nutrient composition.

A recent report outlines the extensive safety assessment studies that are conducted for individual biotechnology-derived crops [30]. Case-by-case assessments are particularly important for whole food studies for biotech crops. According to a recent U.S. Government Accounting Office (GAO) report, contacted experts generally agreed that long-term monitoring of the human health risks of biotech foods through epidemiological studies is not necessary because there is no scientific evidence suggesting any long-term harm from these foods [31].

Environmental Safety Assessment

The basic principles of assessing the environmental safety of biotech crops were originally outlined in 1989 [32]. Some of the fundamental premises of environmental safety outlined and later reaffirmed by a panel of independent experts convened by the National Research Council [32] are: firstly, the risks present with biotech crops are no different than those present from traditional breeding (for example, the process by which the plant was produced is irrelevant to the risk assessment); secondly, risk should be assessed on a case-by-case basis; thirdly, risk should be assessed in a comparative manner; and fourthly, risk should be assessed using a scientific approach. In addition to the publications from the NRC, others have published guidance and recommended risk assessment approaches that are also founded on these basic principles [33].

Every potential new product is thoroughly evaluated by regulatory authorities for potential environmental safety risks. While the details of the process and the amount of data requested differ between regions, the information required to assess environmental safety is essentially the same. Information concerning the biology of the crop, its ecological relationships, the introduced trait and intended use provide the basis for the risk assessment. Technology providers must produce a detailed characterization of the biotech plant along with information to assess the potential for altered weediness, impact to non-target organisms, altered pathogenicity, and altered interactions with plant pests. The information can be scientific rationale and/or experimental data that is often collected by independent experts. Based on this information and any subsequent data requested by a regulatory authority, new crops are approved for release into the environment. In cases where the regulatory authorities decide that appropriate risk management is needed, release is granted with geographic restrictions or monitoring requirements (see[34] for examples of risk assessments and decisions).

Current Status

At least 50 different agricultural biotechnology crops have completed the regulatory process in one or more countries [21]. A wealth of data is provided to regulatory agencies around the world to support the food, feed and environmental safety of biotechnology-derived crop plants [35]. Biotechnology derived products are widely used and consumed and have an established history of safe use since their introduction seven years ago. A recent U.S. General Accounting Office study concluded that experts agree adequate testing is done to assess the safety of biotechnology-derived foods. The recent announcement of the re-registration of *Bt* cotton and *Bt* corn by the U.S. EPA reaffirmed the safety of these insect-protected crops. This confirmation was based on extensive scientific review and evaluation of all commercialized *Bt*-based biotech crops and consultations with scientific experts on the key issues as well as consideration of public comments. The European Commission also recently published a report on EU biotechnology policies and launched a round table on biotechnology safety research. Publication of the EU-supported research in biotechnology, which included over 80 different studies, shows that the Commission believes in agricultural biotechnology regulated by sound science. The European Commission also stated their belief that crops and foods derived using biotechnology are at least as safe as conventional foods and are subject to greater testing and regulatory oversight than conventional foods [22].

As new products are assessed, similar safety assessment questions should be asked and addressed. A key consideration is the global standardization and harmonization of safety assessment processes to ensure that questions are addressed using similar science-based risk assessment approaches that are accepted by international scientific experts. Continued communication and guidance through focused expert committees with stakeholders from industry, government, food/feed industry, academia and health and scientific organizations will help to ensure that global safety assessment approaches are grounded in sound scientific principles.

OPPORTUNITIES FOR BETTER NUTRITION AND AGRICULTURAL DEVELOPMENT

Plant biotechnology has had positive impacts on food production, particularly through HT and *Bt* crops, and its safety has been carefully scrutinized. Several of these products are already having important food production impacts for small-scale farmers in developing countries, and new applications of plant biotechnology are actively being pursued to meet nutrition and overall development needs with the participation of local public researchers and the endorsement of international bodies. The need is great: one in every five people in the developing world is chronically undernourished, and more than two billion people suffer micronutrient deficiencies . The UN Human Development Report 2001 notes that *"transgenics offer the hope of crops with higher yields, pest- and drought-resistant properties and superior nutritional characteristics - especially for farmers in ecological zones left behind by the green revolution."* The June 2002 official Declaration of the World Food Summit explicitly resolves that 'the introduction of tried and tested new technologies including biotechnology should be accomplished in a safe manner and adapted to local conditions to help improve agricultural productivity in developing countries'. However, there remain some challenges in ensuring that the new products are created and diffused in ways that fully contribute to human nutrition and development goals.

Current Products

While *Bt* cotton is largely thought of for the large cotton growing regions of the world and in particular for the large farmers in these regions, the growing experience of small-scale farmers with these products in China, South Africa, Mexico, Indonesia, and in farm-scale trials in India, have clearly shown that this technology is at least scale-neutral in economic terms for farm size and that it effectively addresses production constraints for farms of all sizes [21]. Plant biotechnology can also contribute to more sustainable farming by reducing or eliminating the need for tillage or cultivation - thus conserving soil moisture, nutrients and structure. The use of herbicide tolerant crops is compatible with farming systems that reduce or eliminate the need for tillage or cultivation. These reduced tillage farming systems are very desirable as they greatly reduce soil erosion, reduce sediment runoff from fields into watersheds, help control weeds that can reduce crop yields, and also directly improve crop yield. The lessons from the use of these first technologies are important for the continued and new development of plant biotechnology solutions in crops and for problems that are sometimes unique to small-scale and resource-poor farmers.

New products for nutrition and development needs

Fueled initially by the promise of the technology, and later bolstered by *ex ante* economic analyses, successes in other crops, and specific technical advances, a growing number of research and development activities are directed to the application of plant biotechnology to provide solutions to crop production constraints and crop quality issues for these same small-scale and resource-poor farmers. Coalitions of local public researchers, public agencies, private foundations, non-governmental organizations, and the private sector have come together to effectively use plant biotechnology to solve problems that have been identified by the local agriculture and research communities.

As illustrated above, plant biotechnology can often provide solutions to heretofore-intractable agriculture-related problems, usually those for which no solution or no cost-effective solution existed. Again, such examples include the introduction of resistance to lepidopteran pests using *Bt* genes, pests for which little or no resistance could be provided by plant breeding alone and against which biological and chemical pesticides offered only limited (and expensive) solutions. Additional examples can be seen in the development of crops tolerant to insect-vectored poty- and luteoviruses, crop products that enhance the often-limited plant genetic tolerances and that effectively controlled the plant disease and spared the use of insecticides (to control the insect vectors). These very same types of problems plague agriculture production and crop and food quality almost everywhere.

Sweet potato

For millions of people in developing countries, sweet potatoes (*Ipomoea batatas*) are an important part of the diet because they are nutritious and easy to grow. Because they can be stored underground for an extended length of time, sweet potatoes can be a reliable source of food, even in dry seasons. However, attacks by pests and disease can reduce yields by as much as 80 percent. Biotechnology research has been put to use since 1991 to develop a sweet potato that protects itself against a devastating plant virus. Field evaluations of virus-resistant sweet potato plants have begun in Kenya, while research and development continues.

Papaya

In the last two decades a pernicious plant virus, the Papaya Ringspot Virus (PRSV), has invaded Southeast Asia, destroying one of the region's most important crops: papaya (Carica papaya). The disease has had a devastating impact on farmers throughout the region, particularly on small-scale subsistence farmers who rely on papaya as an easy-to-grow, highly nutritious, and locally marketable fruit. Both production and yields have dramatically declined. Every country in Southeast Asia is grappling with the same problem, and in response, the Papaya Biotechnology Network of Southeast Asia was formed to develop papaya with PRSV resistance and to enhance the region's capacity to develop and deploy other transgenic crops in the future. Building on technology and training provided by Monsanto, a consortium of national institutes is now developing papaya varieties resistant to the virus. The virus-resistant papaya, which will be grown and marketed primarily by smallholders, will enhance the economics of farming and the availability of food in the region. A similarly improved papaya in Hawaii has been attributed with a 33 percent increase in production from 1999 to 2000 [4].

"Golden" Crops

Agricultural biotechnology has the potential to help address malnutrition in developing countries, when used to produce staple crops with higher levels of important nutrients. A multi-year project is underway to develop "Golden Mustard" *(Brassica spp.)* that will yield cooking oil high in beta-carotene (Pro-Vitamin A). Successful development and adoption of the enhanced oil from "Golden Mustard" has the potential of helping hundreds of thousands of children suffering from vitamin A deficiencies, particularly in northern and eastern India, where mustard oil is commonly used for food preparation and cooking. Recent estimates reveal that more than 18 percent of the children in India suffer some level of vitamin A deficiency, which can lead to vision impairment, inability to absorb proteins and nutrients, and reduced immune function.

Another example of the application of biotechnology to enhance nutrition is "Golden Rice," *(Oryza sativa)* which was developed to combat vitamin A deficiency and to be delivered free-of-charge for humanitarian purposes. It is hoped that technology used to develop golden rice and golden mustard oil might one day be extended to other crops such as maize *(Zea mays)*, a staple food in many African countries where vitamin A deficiency is also prevalent. Collectively, projects such as these can put biotechnology to work to improve the nutritional quality of staple foods grown and consumed by the poorest households.

Potato

In 1991, a cooperative project was initiated to develop, through use of biotechnology, virus resistance in varieties of potato *(Solanum tuberosum)* grown by resource-poor Mexican farmers. The research phases of this project are complete and the partners in Mexico are moving toward regulatory approval and distribution. Once subsistence farmers grow the improved varieties, their yields could increase 10 to 15 percent.

The application of this relatively mature research, driven by the identification of local needs, and built on a cooperative foundation that emphasizes the role of African scientists in developing these new crops, and that integrate all aspects of the crop from research to distribution of clean and reliable planting materials, form the basis of a number of efforts underway on cassava, cowpea, and maize [21,38,39,40].

PUTTING PLANT BIOTECHNOLOGY TO WORK

The rapid adoption of crops improved using biotechnology is indicative of the significant benefits being realized by farmers. Studies have shown that farmers who plant herbicide tolerant and *Bt* crop varieties are more efficient in managing their weed and insect pests. This is expressed in several ways, including 1) more effective control of pests, 2) fewer pesticide applications per season, and 3) greater flexibility in timing of pesticide applications. Improved pest control, lower cost of pesticides and improved yields can all contribute to a greater net return for a grower who has adopted biotech crops. In addition, the adoption of biotech crops has contributed to a reduction in the overall amount of pesticides used in crop production, which has positive environmental effects. The use of insect protected maize varieties has also been shown to reduce the levels of fumonisin mycotoxin in maize grain. The majority of the positive statistics about these benefits have been from experiences in developed countries where the technology has been adopted first. There is growing experience now in developing countries, which is beginning to show similar benefits to those seen in developed countries. A variety of environmental and food safety assessments are in place in many developed countries and increasingly in developing countries to ensure safe use of the technology. The tools of plant biotechnology hold great promise for meeting increasingly important human nutrition and development needs.

However, in order for plant biotechnology to fully contribute to meeting the needs of developing countries, there are a set of needs that must be addressed in both developed and developing countries. Greater public investment in basic plant science and biotechnological applications relevant to subsistence crops would certainly help ensure that the needs of all resource-poor farmers can be adequately met. The lack of functioning biosafety processes in developing countries can also delay access to the technology for these countries. In terms of safety assessments, some current and proposed regulations (national and international) for plant biotechnology crops might require substantially larger resources and capacity to be implemented in many developing countries. International public policy makers should ensure that any and all regulations for plant biotechnology are aimed at providing truly necessary information on health and environmental safety, taking advantage of existing safety information as appropriate, and allowing international market access for all safe agriculture products. There are a number of on-going capacity-building programs for enhancing the capabilities in developing countries. These need to be coordinated, expanded and resourced appropriately.

Another problem in countries on continents such as Africa is the fragmentation of farming and poor rural infrastructure - leading to difficulties in delivering any kind of solutions to the farmers and their communities. Numerous examples of cooperation between public sector, NGO, private sector, and national organizations have developed models where these difficulties may be addressed for the benefit of farmers and their communities. Other processing, storage, and transport needs for plant biotechnology crops are not greatly different than the infrastructure needed to handle conventional crops. It is the case in many developing countries that improving this infrastructure would be extremely beneficial to human health and development. Fortunately, there is significant evidence that these needs are being addressed at national, regional and international levels.

At the national level, many agriculture ministries and national agricultural research institutes are making significant investments in both the science and policy capacity needed to gain the fullest benefit from plant biotechnology. Public sector scientists in Asia, Africa and Latin America are working collaboratively to apply existing technology to crops in their countries, as well as investing in developing their own new technology which they will regulate, market, and license for themselves.

At the regional level, public sector scientists are working together on crop production issues that they may face collectively, and sharing knowledge and strategies to ensure that newly developed products can be used most effectively. The ISAAA-facilitated SE Asian Papaya Biotechnology Network is one such example, with institutions from Indonesia, Malaysia, Philippines, Thailand, and Vietnam working together to develop virus-resistant and delayed-ripening papaya (www.isaaa.org). There are also a number of regional biosafety capacity building efforts.

At the international level, governments, NGOs, foundations and private companies are all working together to ensure that the impacts of plant biotechnology for resource-poor farmers and the food insecure are as beneficial as possible. Some developed countries have international aid programs that are dedicated to building the scientific and policy capacity needed in developing countries. Several foundations and non-governmental organizations (Rockefeller Foundation, ISAAA) have substantial programs to link private sector resources with small farmers' needs.

The positive impacts of plant biotechnology for food, nutrition and development can be significant particularly for developing countries. However, the technology requires innovative partnerships to put it to work.

Acknowledgement

The authors thank the following people for contributions to this manuscript: Bruce Hammond, Graham Head, and Mike McKee.

REFERENCES

1. **Gianessi LP and JE Carpenter** Agricultural Biotechnology: Updated Benefit Estimates. January 2001. National Center for Food and Agricultural Policy. 2001

2. **US FDA**. Guidance for industry (2000). Fumonisin Levels in Human Foods and Animal Feeds: Draft Guidance. Center for Food Safety and Applied Nutrition, Centre for Veterinary Medicine. 2000.

3. **Canola Council of Canada**. An Agronomic and Economic Assessment of Transgenic Canola. January 2001.

4. **Gianessi LP, Silvers CS, Sankula SS and JE Carpenter** Plant Biotechnology: Current and Potential Impact for Improving Pest Management in US Agriculture. An analysis of 40 case studies. National Center for Food and Agriculture Policy. June 2002.

5. **Elena MG** Economic Advantage of Transgenic Cotton in Argentina. In proceedings of the 2001 Beltwide Cotton Conference, Anaheim California. 2001.

6. **Heimlich RE, Fernandez-Cornejo J, McBride W, Klotz-Ingram SJ and N Brooks** Genetically Engineered Crops: Has Adoption Reduced Pesticide Use? USDA Publication AER-786. 2000. **http://www.ers.usda.gov/epubs/pdf/aer786/**

7. **Huang J and C Pray** Plant Biotechnology in China. Science. 2002; 295: 674-677.

8. **Ismael Y, Thirtle C and L Beyers** Efficiency effects of *Bt* Cotton Adoption by Small holders in Makhatini Flats, South Africa. Proceedings of the 5th International Conference on Biotechnology, Science and Modern Agriculture: A new industry at the Dawn of the Century. Ravello, Italy. 2001.

9. **Kline and Company.** Plant Biotech Impact Business Analysis 2009. 2000

10. **Reed GL, Jensen AS, Riebe J, Head G, and JJ Duan** Transgenic *Bt* potato and conventional insecticides for Colorado potato beetle management:

comparative efficacy and non-target impacts. Entom. Exp. Appl. In press. 2001.

11. **Smith RH** An extension entomologist's 1996 observations of Bollgard technology. In Proceedings of the Beltwide Cotton Conference. National Cotton Council, Memphis, TN. 1997: 856-858.

12. **Scientific Committee on Food** (SCF). Opinion of the Scientific committee on Food on Fusarium Toxins Part 3: Fumonisins B1 (FB1) (October 17, 2000) SCF/CS/CNTM/MYC/24. Final. 2000.

13. **Miller JD** Factors Affecting the Occurrence of Fumonisin in Corn. ILSI North America International Conference on the Toxicology of Fumonisin. June 28-30, 1999. 1999.

14. **Visconti A** Fumonisin Levels in Corn and Corn Products - Global Perspectives. FDA Fumonisins Risk Assessment Workshop. January 10-12, 2000. 2000.

15. **NTP.** Technical Report on the Toxicology and Carcinogenesis of Fumonisin B1 in F334/N Rats and B6C3F1 Mice. NTP TR 496. NIH Publication No. 99-3955 (draft). 1999.

16. **FAO.** Food and Nutrition Paper # 64. Worldwide Regulations for Mycotoxins 1995. A Compendium. 1997.

17. **FAO/WHO.** Joint FAO/WHO Expert Committee on Food Additives. Fifty-Sixth Meeting. Geneva 6-15, February 2001. 2001.

18. **Munkvold GP, Hellmich RL and LG Rice** Comparison of Fumonisin Concentrations in Kernals of Transgenic *Bt* Maize hybrids and Nontransgenic hybrids. Plant Disease. 1999; 83(2): 130-138

19. **Dowd P** Indirect Reduction of Era Molds and associated Mycotoxins in *Bt* Corn Under Controlled and Open Field Conditions: Utility and Limitations. Journal of Economic Entomology 2000; 93: 1669-1679.

20. **Cahagnier B and D Melcion** Mycotoxines de Fusarium dans les mais-grains a la recolte; relation entre la presence d'insectes (pyrale, sesamie) et la teneur en mycotoxines. Proceedings of the 6th International Feed Conference, Food Safety: current situation and perspectives in the European Community. Piacenza, Italy. G. Piva, F. Masoero (edits) 27-28 November 2000. 2000: 237-249.

21. **ISAAA.** Virus resistant Sweet potato. 2002. **http://www.isaaa-africenter.org/sweetpotatoes.htm**

22. **European Commission.** EU Commission Report on Biotechnology Policy, 2002. "Towards a Strategic Vision of Life Sciences and Biotechnology: Consultation Document". 2002. **http://europa.eu.int/comm/biotechnology/pdf/doc_en.pdf**

23. **FAO/WHO.** Biotechnology and Food Safety. Report of a Joint Consultation. FAO, Food and Nutrition Paper 61. 1996.

24. **FAO/WHO.** Safety Aspects of Genetically Modified Foods of Plant Origin. Report of a Joint FAO/WHO Consultation, WHO, Geneva, Switzerland. 2000.

25. **International Life Sciences Institute** (ILSI). Allergy and Immunology Institute, and International Food Biotechnology Council (1996). Allergenicity of food produced by genetic modification. [CRC Press Boca Raton]. Crit. Rev. Food Sci. Nutr.1996; 36 (supp): 46-51.

26. **OECD.** Report of the OECD Task Force for the Safety of Novel Foods and Feeds; Okinawa, Japan. 2000. **http://www.oecd.org/subject/biotech/report_taskforce.pdf**

27. **Hammond BG and RL Fuchs** Safety evaluation for new varieties of food crops developed through biotechnology. In: Thomas JA, Taylor ML and PA Philadelphia (eds) Biotechnology and Safety Assessments. 1998: 61-79.

28. **Sanders P, Lee TC, Groth ME, Astwood JD and RL Fuchs** Safety Assessment of Insect-Protected Corn. In: Thomas JA (ed). Biotechnology and Safety Assessment, 2nd Ed. 1998; 241-256.

29. **Kimber I, Kerkvliet NI, Taylor SL, Astwood JD, Sarlo, K and RJ Dearman** Toxicology Of Protein Allergenicity: Prediction And Characterization. Tox. Sci. 1999: 157-162.

30. **Nair RS, Fuchs Rl and SA Schuette** Current Methods for assessing safety of genetically modified crops as exemplified by data on Roundup Ready Soybeans. Tox. Path. 2002; 30(1): 117-125.

31. **United States General Accounting Office** (GAO). Report. "Genetically Modified Foods: Experts View Regimen of Safety Tests as Adequate, but FDA's Evaluation Process could be Enhanced". 2001. **http://www.gao.gov/new.items/d02566.pdf**

32. **NRC.** (National Research Council). Field Testing Genetically Modified Organisms: Framework for Decisions. Committee on Scientific Evaluation of the Introduction of Genetically Modified Microorganisms and Plants into the Environment. National Academy Press, Washington, D.C. 1989.

33. **Kjellsson G** Methods for Risk Assessment of

Transgenic Plants, II.Pollination, Gene-Transfer and Population Impacts. Kjellson G, Simonsen V, and K Ammann (eds). 1997: 221-236.

34. **Office of Science and Technology Policy** (OSTP). Case Study II - *Bt* Maize: 2001: 1-70. **http://www.ostp.gov/html/ceq_ostp_study3.pdf.**

35. **Fuchs RL** Foods derived from genetically modified crop plants. In: Federal R (ed) Nutritional Toxicology. 2002; 104: 22984-3005

36. **FAO.** The spectrum of malnutrition. FAO Food and Nutrition Division. 2001.

37. **United Nations Development Programme.** Human Development Report 2001: Making new technologies work for human development. Oxford University Press. 2001.

38. **Wambugu F** Why Africa needs agricultural biotech. Nature. 1999; 400(6739): 15-16.

39. **CIMMYT.** Insect Resistant Maize for Africa. 2002. **http: // www.cimmyt.cgiar.org/ABC/InvestIn-InsectResist/htm/InvestIn-InsectResist.htm**

40. **Machuka J** Agriculture biotechnology for Africa. African scientists and farmers must feed their own people. Plant Physiol. 2001; 126 (1): 16-19