Food and Energy Security
Open Access

REVIEW

# Crop biotechnology: a pivotal moment for global acceptance

Eric Hallerman[1] & Elizabeth Grabau[2]

[1]Department of Fish and Wildlife Conservation, Virginia Polytechnic Institute and State University, Blacksburg, Virginia 24061
[2]Department of Plant Pathology, Physiology and Weed Science, Virginia Polytechnic Institute and State University, Blacksburg, Virginia 24061

**Keywords**
Bioregulation, genetically engineered crops, public perception of biotechnology.

**Correspondence**
Elizabeth Grabau, Department of Plant Pathology, Physiology and Weed Science, Virginia Polytechnic Institute and State University, Blacksburg, VA 24061.
Tel: +001 540 231 3197;
Fax: +001 540 231 7477;
E-mail: egrabau@vt.edu

**Funding Information**
USDA Foreign Agricultural Service. Virginia Agricultural Experiment Station

Received: 4 August 2015; Revised: 29 October 2015; Accepted: 2 December 2015

***Food and Energy Security* 2016; 5(1): 3–17**

doi: 10.1002/fes3.76

## Abstract

The development and judicious use of agricultural biotechnology offers important contributions to food security and sustainability. Key contributions include improved yield, heightened pathogen and herbivore resistance, enhanced nutrient content, improved product quality, reduced spoilage, as well as entirely new traits. While a first wave of genetically engineered (GE) crop products has been commercialized and contributed to yield, other products – some posing significant benefits to target populations in the developing world – have become mired in controversy. Public misconception about nutritional and ecological risks, fears about multinational corporate dominance, as well as regulatory inaction have delayed the approval and use of GE crops. With new GE lines ready to pass through regulatory oversight, many of which originate from developing countries, we regard this as a pivotal moment for global acceptance of agricultural biotechnology. However, we note that some countries, international regulators, and even biotechnology companies seem willing to forego useful applications of GE crops. We conclude that educating and informing the public to combat misperception, and implementing review of regulatory guidelines based on decades of experience can help to realize the benefits of GE for food security, human well-being, and ecological sustainability.

## Introduction

A major challenge facing mankind is how to increase world access to adequate food without depleting nonrenewable natural resources and causing environmental damage. The concept of food security has been defined (WHO 2015) as including both physical and economic access to food that meets people's dietary needs as well as their food preferences. Dramatic advances in food production, distribution, and access will be required if we are to meet future needs (National Academies 2000, National Research Council 2015). Since the first plant cell transformation successes over 30 years ago (Herrera-Estrella et al. 1983), transformation using *Agrobacterium tumefaciens* and other systems has been developed and extended to a widening variety of agricultural crops. This journal has previously reviewed successes, failures, and potential applications of plant biotechnology to agriculture (Halford 2012). In addition to support for basic science to advance plant biotechnology, there is also a critical need for translating plant science discoveries to the benefit of the poor in developing regions of the world (Delmer 2005).

Application of biotechnology approaches to crop improvement has resulted in increased yields, enhanced agronomic traits, better product quality and novel uses of crop products. After the first genetically engineered (GE) line – a Roundup-Ready soybean produced by Monsanto – was approved for commercial use in the United States in 1996, other lines followed and the percentage of GE crop production increased rapidly. However, commercial production is dominated by a few herbicide-resistant and insect-resistant crops, environmental benefits are disputed, and food safety is debated. Negative attitudes toward GE crops in some sectors of the developed world complicate their adoption in the developing world, where they are potentially most valuable for addressing the issue of food security (Whitty et al. 2013). Although these negative attitudes are generally at odds with scientific evidence, they persist in both the developed and developing worlds (Blancke et al. 2015).

In a landmark study, a working group representing several national and international academies of science (National Academies 2000) concluded that GE technology, coupled with important developments in other areas, should be used to increase the production of main food staples, improve the efficiency of production, reduce the environmental impact of production, and provide access to food for small-scale farmers. However, the potential utility of GE crop plants has been only partially realized in countries where food security is at issue. Success is partial because of different attitudes and because of the impacts of the respective regulatory oversight policies. In our review and synthesis, against the background of GE crops currently in production, we note examples of new products in the pipeline, some posing important implications for promoting food security and sustainability. Yet, we also note that regulatory and public acceptance issues complicate the adoption of GE plants for production agriculture. We regard this as a pivotal moment for regulatory action and practical adoption of agricultural biotechnology, a moment when decisions made within the next few years will have major bearing on the realization – or failure – of its potential for improving global food security. We focus on issues pertinent to GE crops; similar issues regarding genetically modified animals have been discussed elsewhere (Van Eenennaam et al. 2011, 2013). We call for thoughtful application of all agronomic and plant breeding technologies, including genetic engineering, to increase crop production and effectively address food security.

## Adoption of Crop Biotechnology

Since they were first commercialized in 1996, GE crops have gained a rising share of agricultural production; 181.5 million ha of GM crops were planted in 2014 in 28 countries (ISAAA 2015), with most production in the United States (73.1 million ha), Brazil (42.2), Argentina (24.3), Canada (11.6), and India (11.6). A total of 18 million farmers planted GE crops, 16.9 million of whom were small farmers in developing countries. Most of the production was accounted for by four crops, soybean (82% of which was GE), cotton (68%), corn (30%), and canola (25%). Among 30 traits that have been engineered into crop plants (Nature 2013d), the most popular are herbicide tolerance, insect resistance, or both as stacked traits. Adoption of these GE crop lines has increased yields. Producing glyphosate-resistant corn and soybeans, farmers control most weeds with one herbicide rather than several and are better placed to adopt no-till soil conservation practices. However, many weed species recently have evolved resistance to glyphosate and other overused herbicides that are required by these GE crops, such that the long-term sustainability of facilitating low- and no-till agriculture is not certain (Mortensen et al. 2012). Production of *Bt* cotton and rice increases yield (9% in the case of cotton – Huang et al. 2003; 9–29% for rice – reviewed by Chen et al. 2011), whereas less pesticide is sprayed on the field, decreasing impacts on nontarget organisms (Huang et al. 2003; Li et al. 2015; Qiao 2015), including the farmers themselves (Huang et al. 2015a, 2015b). GE crops have been adopted faster than any other agricultural advance in the history of humanity (Alberts et al. 2013). The global value of GE seed in 2012 was US$15 billion (Nature 2013d).

Not all GE plants currently in production are row crops. One of the key early successes for GE agricultural plants – and one that is not widely recognized by the public – is disease-resistant papaya. Papaya is cultivated worldwide in the tropics and subtropics (GMO Compass 2013); the main producing countries are Brazil, Mexico, Nigeria, and India. In 2005, approximately 6.75 million tons were produced worldwide. Papaya ringspot virus (PRSV) is a major production problem, and can lead to dramatic losses of yield. GE papayas engineered for resistance to PRSV (Gonsalves 1998) have been produced commercially in Hawaii since 1998, and are credited with having saved the industry there. They have been approved by government regulators and sold commercially in the United States. These papayas are an important export product, mainly to Japan. After the success in Hawaii, other GE papaya lines are being developed in other regions for the viruses prevalent in those areas. In 2006, a GE virus-resistant papaya was approved and now is in commercial production in China. A cooperative project involving international companies and organizations from India, Indonesia, Thailand, Malaysia, the Philippines, and Vietnam is aimed at development of a GE virus-resistant papaya for Southeast Asia. However, despite the agricultural and commercial success of GE papaya, it remains controversial. Anti-GE activists destroyed papaya trees at least three times in Hawaii, and bills that would impose restrictions on agricultural biotechnology have been debated in Hawaii's legislature (Huffington Post 2013, Harmon 2014). Import of GE papayas into the European Union is not allowed (GMO Compass 2013). Despite virus-resistant papaya being a "pro-poor" GE crop, Greenpeace activists destroyed a test plot of transgenic papaya in Thailand in 2004, leading to a countrywide moratorium on all field testing of transgenic crops (Davidson 2008).

Adoption of GE crops varies widely among countries, with 32 now having approved lines for production or import for use as food and feed (Table 1). Not

 

**Table 1.** Numbers of GE crop events approved by given countries for commercialization, planting, or import for food and feed use.[1]

| Country | Corn | Soybean | Canola | Rice | Potato | Other crops |
|---|---|---|---|---|---|---|
| Argentina | 30 | 6 | – | | | – |
| Australia | 21 | 16 | 14 | 1 | 10 | 3 alfalfa, 2 sugar beet, 1 wheat |
| Bangladesh | – | – | – | – | | 1 eggplant[2] |
| Bolivia | – | 1 | – | – | | – |
| Brazil | 21 | 6 | – | – | | 1 bean[3] |
| Canada | 59 | 20 | 22 | 1 | 20 | 3 alfalfa, 1 papaya, 1 squash, 2 sugar beet, 4 tomato |
| Chile | 1 | 1 | 1 | – | – | 1 tomato |
| China | 16 | 8 | 12 | 2[4] | – | 1 papaya, 1 sugar beet, 1 sweet pepper[5], 3 tomato[6] |
| Colombia | 39 | 10 | – | 2 | – | 1 sugar beet, 1 wheat |
| Costa Rica | – | 2 | – | – | – | – |
| Egypt | 1 | – | – | – | – | – |
| European Union | 39 | 8 | 11 | – | 1 | 1 sugar beet |
| Honduras | 7 | – | – | 1 | – | – |
| Indonesia | 7 | 2 | – | – | – | 3 sugar cane[7] |
| Iran | – | – | – | 1[8] | – | – |
| Japan | 111 | 19 | 17 | 1[9] | 8 | 3 alfalfa, 1 papaya, 3 sugar beet |
| Malaysia | 6 | 6 | – | – | – | – |
| Mexico | 65 | 18 | 11 | 1 | 13 | 3 alfalfa, 1 sugar beet, 5 tomato |
| New Zealand | 21 | 16 | 14 | 1 | 10 | 3 alfalfa, 2 sugar beet, 1 wheat |
| Panama | 1 | – | – | – | – | – |
| Paraguay | 8 | 3 | – | – | – | – |
| Philippines | 46 | 9 | 1 | 1 | 8 | 2 alfalfa, 1 sugar beet |
| Russian Federation | 12 | 7 | – | 1 | 2[10] | 1 sugar beet |
| South Africa | 33 | 9 | 4 | 1 | – | – |
| South Korea | 60 | 19 | 11 | – | 8 | 3 alfalfa, 1 sugar beet |
| Switzerland | 3 | 1 | – | – | – | – |
| Taiwan | 63 | 18 | – | – | – | – |
| Thailand | 12 | 3 | – | – | – | – |
| Turkey | 16 | 3 | – | – | – | – |
| United States of America | 38 | 24 | 20 | 3 | 38 | 3 alfalfa, 3 chicory, 2 melon[11], 3 papaya[12,13], 1 plum[14], 2 squash, 3 sugar beet, 8 tomato, 1 wheat |
| Uruguay | 11 | 7 | – | – | – | |
| Vietnam | 5 | | | | | |

[1]Data from ISAAA (2015) http://www.isaaa.org, accessed 7 January 2015.
[2]*Bt*-transgenic eggplant developed by Maharashtra Hybrid Seed Company.
[3]Antisense RNA viral disease resistance bean, Brazilian Ministry of Agriculture – Brazilian Agricultural Research Corporation (EMBRAPA).
[4]Two *Bt* rice lines, Huazhong Agricultural University.
[5]Pathogen-derived viral disease-resistant sweet pepper, Beijing University.
[6]Modified product quality tomato, Chinese Academy of Science; delayed-ripening tomato, Huazhong Agricultural University; pathogen-derived viral disease-resistant tomato, Beijing University.
[7]Drought-resistant sugar cane, PT Perkebunan Nusantara Xi (Persero).
[8]*Bt* rice, Agricultural Biotechnology Research Institute.
[9]Hypoallergenic rice, National Institute of Agrobiological Sciences.
[10]Two *Bt* potato lines protected from coleopteran insects, Centre Bioengineering, Russian Academy of Sciences.
[11]Delayed ripening melon, Agritope, Inc.
[12]Two pathogen-derived virus-resistant papaya lines, Cornell University and University of Hawaii.
[13]Pathogen-derived virus-resistant papaya line, University of Florida.
[14]Pathogen-derived virus-resistant plum line, U.S. Department of Agriculture – Agricultural Research Service.

surprisingly, adoption of GE crops is further advanced in developed countries than in developing ones. One crop in particular, insect-resistant *Bt* cotton, has been widely planted in many countries, developed and developing alike. For example, most cotton in India is GE and has provided economic benefit to many small producers. This is in stark contrast to sentiment against production of GE food crops in India (see below). While most GE crop lines currently in use were developed by multinational corporations, a growing number of GE lines developed by universities, government agencies, small companies, and nongovernmental organizations are now proceeding through regulatory approval for possible agricultural production (see footnotes for Table 1). These GE lines include *Bt* eggplant in India, rice in China and Iran, potato in Russia, disease-resistant pepper and tomato in China, and drought-resistant sugar cane in Indonesia.

## Nonadoption of Crop Biotechnology

Despite their record of improved yield, improved profitability, heightened nutrition, and potential for addressing food security, GE plants remain controversial. Some countries or international unions, notably ones *not* facing food security issues, have chosen not to adopt GE crops. We explore selected cases.

## European Union

Approvals of GE crops in Europe have proven highly controversial within countries and between member countries and the European Union itself. For GE crops to be approved in Europe, they must be deemed safe by the European Food Safety Authority (EFSA). The European Commission then must produce a draft decision within 3 months, to be voted upon by representatives of EU member states before approval can be finalized (Cressy 2013b). The EFSA has found eight crops safe, some as long ago as 2005. Only two GE crops have been approved by the European Union science advisory committees as safe for agricultural production, MON810 (a *Bt*-expressing, insect-resistant corn) and Amflora (a potato for use by the paper industry). However, eight EU nations have imposed a ban on cultivation of MON810 corn, and Poland has also banned Amflora (Nature 2013a, Science 2013a). These moves come despite EU legislation that requires all member states to permit cultivation of approved crops; European courts have already ruled against bans in two countries (Nature 2013c). France's highest court overturned the national ban on the GE corn, ruling that the government must prove that the crop causes health or environmental risks (Nature 2011c) and its State Council found the ban invalid for procedural reasons, but the agriculture minister said he would work to uphold the ban. The European Court of Justice ruled in 2011 that honey containing trace amounts of pollen from GM plants could no longer be sold in the European Union without a safety review (Nature 2011b), which could affect imports of honey from countries such as Argentina, where GE crops are produced at a large scale. Against this background, Germany-based BASF Corporation shifted its transgenic plant operations to the Americas in 2012 (Nature 2012a). Monsanto announced in mid-2013 that it would withdraw pending applications for GE crops including several lines of corn, a line of soybean, and a line of sugar beet (Science 2013a) and that it would focus on sales of conventionally bred seed in Europe. European GE plant researchers expressed regret, but not surprise (Cressy 2013b); many European GE plant researchers now do their work in more agbiotech-friendly countries outside the EU.

## Developing Countries

Although food security is not perceived as a pressing issue within the European Union, it is important in many regions of the developing world. Yet, many developing countries have not adopted production of GE crops. Among sub-Saharan African countries, only South Africa has approved production of GE lines. For example, in Kenya, where more than one-quarter of the population is malnourished, the government banned the import of GE foods in 2012, although it did not ban research on GE crops (Owino 2012; Whitty et al. 2013). In Asia and Latin America, some countries have approved GE lines and others have not. Notable holdouts for production of GE food crops include India (Science 2013b), which is considering a 10-year moratorium on all field trials. We note that India also fought the adoption of Borlaug's selectively bred wheat lines that were the leading edge of the Green Revolution (Vietmeyer 2012). In South America, Ecuador banned GE crops in 2008 (Science 2011). Groups representing Peru's indigenous people campaigned for a ban on cultivation of GE crops, arguing that GE plants could damage native agriculture and threaten the country's flora, including over 2000 species of potato. Seeking more study, Peru's Congress passed a 10-year moratorium on the cultivation of GE crops (Science 2011); the legislation will not, however, stop research on GE crops. Meanwhile, Bolivian President Evo Morales opened the door to cultivation of GE lines there (Science 2011).

## Case Studies of GE Plants Targeting Food Security and Sustainability

The first GE crops to be commercialized on a large scale offer herbicide tolerance and pest resistance traits, especially targeting developed-world farmers using high-input production methods and buying their seed each generation. While such production has indirect bearing on issues of food security, there also is a new wave of GE lines aimed at both staple and minor crops for production in the developing world. Another line of research aims to develop food products that are less prone to bruising or spoilage, thereby minimizing postharvest loss and promoting sustainability. Here, we present selected case studies of GE lines, noting their state of development and adoption. We note that many of these GE crops are at a pivotal stage of development or adoption, with some lines not being utilized because they are misunderstood by the public or delayed in regulatory review.

## Golden Rice

The leading example of ongoing controversy and politicization of a GE plant intended for addressing food security and nutrition is the development of golden rice. Rice is the major staple grain for almost half of humanity. However, rice is usually milled to remove the oil-rich aleurone layer, and the remaining endosperm lacks several essential nutrients including provitamin A, or β-carotene. Heavy rice consumption promotes vitamin A deficiency, which is a serious health problem in at least 26 countries in Asia, Africa, and Latin America (WHO 2005) and is responsible for 1.9–2.8 million preventable deaths per year (Mayo-Wilson et al. 2011). In a technical tour de force, Ingo Potrykus and Peter Beyer and their research groups introduced multiple genes into rice to complete the β-carotene biosynthetic pathway. Heralding the original report in *Science*, Guerinot (2000) wrote of hope that this application of plant genetic engineering would ameliorate human misery and restore gene transfer technology to political acceptability.

Golden rice, however, proved the focus of intense controversy. Greenpeace (2002) claimed that an adult would have to consume at least 12 times the normal intake of 300 grams of rice in order to take in the daily recommended amount of provitamin A, calling claims that golden rice would provide nutritional benefits an "intentional deception". Since the first scientific publication reporting 1.6 μg of vitamin A precursor per gram of edible rice (Ye et al. 2000), collaborative work between the developers and the International Rice Research Institute has increased the level of β-carotene to 35 μg (Potrykus 2010), a sufficient quantity that a few ounces of cooked rice can provide enough β-carotene to eliminate the morbidity and mortality of vitamin A deficiency (Alberts et al. 2013). The inventors intend to make golden rice technology a public good without cost or license fees to public-sector rice-breeding institutions or smallholder farmers (Dubock 2013). No individual or organization involved in its development will benefit financially from its adoption. Using the empirical GTAP model of the world economy, Anderson et al. (2004) estimated that adoption of golden rice in Asia would lead to benefits of $15.2 billion per year through enhanced productivity of unskilled labor, exclusive of any gains due to welfare gains from reduced vitamin A deficiency.

The putative nutritional benefit arguably has been the focal controversy regarding golden rice. Golden rice was shown to be an effective source of vitamin A to adults in the United States (Tang et al. 2009). To prove most relevant to resolving the issue, however, a study would have to be conducted in a rice-consuming population and in children, who are most vulnerable to vitamin A deficiency. Against this background, Tang et al. (2012) fed 732 Chinese children golden rice, spinach, or capsules with β-carotene in oil and found that golden rice was as good a source of vitamin A as the capsules and better than spinach. However, upon publication of the study, Greenpeace China released a hostile message to the press, leading several of the Chinese collaborators on the study to distance themselves from the work; one was suspended from his position (Hvistendahl and Enserink 2012). While the study's results were not disputed, the investigator was cited for not documenting reviews and approvals in China and for having made changes to the study without approval of the Tufts University Institutional Review Board for research on human subjects (Science 2013b). Participants were found to have not been adequately informed about the GE nature of the rice, and Tang was banned from conducting human research for 2 years by the university (Nature 2013e). The Tang et al. (2012) article was retracted by the American Society for Nutrition (2015) because the authors were unable to demonstrate that the study had been approved by a local ethics committee in China or that parents of the children involved in the study had provided full consent.

Escalating requirements for testing have stalled the release of golden rice for more than a decade (Alberts et al. 2013). Golden rice is being evaluated in the Philippines; however, protestors from two anti-GE groups vandalized a field of golden rice there (Dubock 2013, Nature 2013e, Science 2013c). The destruction was condemned by over 6000 people in the scientific community (Chassy et al. 2013). Golden rice has not yet been approved for general production in any country. It could clear regulatory hurdles and reach farmers soon (Cressy 2013a), likely first in the Philippines and in Bangladesh (Nature 2011a, Dubock 2013), countries where food security is an issue. Despite media reports that golden rice had been approved for production in the Philippines, the International Rice Research Institute (2013) reported that data from 2 years of field trials had yet to be submitted to government regulators for evaluation as part of the biosafety approval process; golden rice will become broadly available to farmers and consumers if it is approved and shown to reduce vitamin A deficiency under community conditions, a process that was expected to take 2 years or more.

Golden rice is only one example of a crop that is GE to address a micronutrient deficiency (Mayer et al. 2008). The folate content of tomato (Diaz de la Garza et al. 2007) and rice (Storozhenko et al. 2007), as well as the iron content of rice (Goto et al. 1999; Lucca et al. 2001) have been increased dramatically. The Grand Challenges in Global Health initiative of the Bill and Melinda Gates Foundation has funded biofortification projects on banana, cassava, and sorghum in Africa (Mayer et al. 2008).

## *Bt* Eggplant

Eggplant is an important vegetable in India, where it is valued for being a good source of fiber, calcium, phosphorus, folate, and vitamins B and C (ISAAA 2013b). Eggplant is grown on nearly 550,000 ha in India, an important cash crop for more than 1.4 million small farmers. Eggplant is prone to attack from insect pests and diseases, including the fruit and shoot borer (FSB) *Leucinodes orbonalis*; cultivation is often input intensive, especially regarding insecticide applications (George et al. 2002; ISAAA 2013b). However, since the larvae are concealed within shoots and fruits, they normally escape insecticide sprays; hence, farmers tend to overspray, contributing to cost, negative effects on the environment, high pesticide residues in vegetables, and risk to producers and consumers. Although several attempts have been made to develop resistant cultivars through traditional plant breeding, little or no success was achieved. Scientists at the Maharashtra Hybrid Seeds Company (Mahyco) have developed an eggplant line that can resist FSB attack and donated the technology to the Tamil Nadu Agricultural University and the University of Agricultural Sciences in Dharwad. Since its development in 2000, the crop has undergone eight assessments of food safety, environmental safety, human and animal health safety and biodiversity (Mahyco 2009). At a production level, the GE line yielded an average increase of 116% in marketable fruits over conventional hybrids, and a 166% increase over popular open-pollinated varieties. The significant decrease in insecticide usage reduced farmers' exposure to insecticides and resulted in a substantial decline in pesticide residues in the fruits. Scientists estimated that *Bt* eggplant would deliver farmers a net economic benefit ranging from US$330–397 per acre (Tamil Nadu Agricultural University 2008). *Bt* eggplant is the first food crop under evaluation for commercial release in India. The Genetic Engineering Approval Committee in 2009 recommended the commercial release of *Bt* eggplant event EE-1, the penultimate step before commercializing *Bt* eggplant hybrids and varieties in India. However, in 2010, the Ministry of Environment and Forest announced a moratorium on approval of *Bt* eggplant (USDA-FAS 2013), thereby preventing dissemination of this line to farmers and sales to consumers.

Mahyco donated the transgenic eggplant technology to public research institutions in the Philippines (Science 2012a) and Bangladesh (ISAAA 2014). However, Greenpeace vandalized field plots in the Philippines in 2011 and petitioned the Supreme Court, claiming that the crops are dangerous to humans and the environment and that the approval procedures were flawed. The Philippine National Academy of Science and Technology criticized Greenpeace actions (Science 2012a), with its president saying that scientists conducting the trials and government departments will file briefs explaining the biosecurity precautions.

Eggplant is also an important vegetable in Bangladesh, where it is grown by about 150,000 small farmers on about 50,000 ha (ISAAA 2014). In 2013, Bangladesh approved the release of four GE varieties of *Bt* eggplant for seed production and initial commercialization. In 2014, seedlings of four *Bt* eggplant varieties were distributed to 20 small eggplant farmers in four regions. The Bangladesh Agricultural Development Corporation undertook seed multiplication of four *Bt* eggplant varieties to be distributed to farmers in 2014. In 2015, *Bt* genes will be introduced in five other popular eggplant varieties. Over the next 5 years, the government of Bangladesh plans to introduce nine *Bt* eggplant varieties into cultivation on 20,000 ha across 20 districts (ISAAA 2014). Field-trial data indicate that *Bt* eggplant can improve yield by at least 30% and reduce the number of insecticide applications by 70–90%, resulting in a net economic benefit of US$1868/ha. At the national level, *Bt* eggplant is estimated to have the capacity to generate a net additional economic benefit of US$200 million per year for around 150,000 eggplant growers in Bangladesh (ISAAA 2014). Consumers will benefit from a blemish-free, more affordable food product.

## GE Plums

Sharka or plum pox, caused by plum pox virus (PPV), is the most serious disease of *Prunus* sp. stone-fruit trees. Most cultivated *Prunus* species are highly susceptible, and conventional breeding has not produced highly resistant, commercially acceptable varieties. Transformation of plum (*Prunus domestica*) using DNA from the PPV coat protein gene led to production of transgenic plum lines resistant to the PPV (Ravelonandro et al. 2000). Field tests of GE transgenic lines in Poland, Romania, and Spain demonstrated that trees inoculated by bud-grafts allowed low-level PPV multiplication, from which they rapidly recovered. GE plants exposed to natural infection for 3 years did not become infected, whereas control trees were infected in the first year. Hybrid plums with the transgene inherited from the GE line were virus-resistant, demonstrating the usefulness of this line as a parent in developing new PPV-resistant plum varieties.

Outcrossing is expected in *P. domestica* because of high levels of self-incompatibility (CERA 2007). The risk of gene flow from transgenic to nontransgenic plums was evaluated in an 11-year study. Gene flow was detected in only four of the 11 years and then in only 0.31% of over 12,000 seeds tested. The results of the study suggested that a 400-m distance from non-GE plums would allow for coexistence (Scorza et al. 2013b). Bees were considered the most likely vector for pollen movement.

The GE plum line proceeded slowly through the regulatory process in the United States. Following application for nonregulated status (Scorza 2007), the U.S. Department of Agriculture reached a finding that its cultivation posed no significant impact (USDA-APHIS 2007a) and published notice in the Federal Register (USDA-APHIS 2007b). The U.S. Food and Drug Administration (2009a, 2009b) subsequently stated that it regarded the regulatory consultation process as complete. The Environmental Protection Agency registered the "HoneySweet" line in 2011; hence, cultivation of the product is approved within the United States (Scorza et al. 2013a). To our knowledge, the line is not yet in commercial production – this is a pivotal moment for its adoption. The Organic Consumers Association and other organic organizations opposed deregulation of the product because of concern for genetic "contamination" of conventional and organic stone-fruit varieties (Novak 2013). We note that outbreaks of plum pox pose an international problem to plum production, and that the GE plum project was the product of an international public institutional collaboration supported in part by the European Union. Yet, the EU, a major plum-producing region, seems unlikely to approve production of the product.

## Simplot Potato

A new wave of GE food crops aims to provide benefits to consumers in terms of improved product quality and to sustainability through reduced loss to bruising or spoilage. The degree to which these benefits increase acceptability of GE food products is, however, yet to be seen. One example of a crop with improved product quality is Simplot's low acrylamide "Innate" potato, named to convey to the public that the modified product contains only potato DNA (Simplot Plant Sciences 2015).

Asparagine is the compound in starchy foods that is converted to acrylamide when products are baked, roasted or fried at high temperatures. The consumption of processed potato products contributes to approximately one-third of the average dietary intake of acrylamide (Boettcher et al. 2005). Concerns about potential health issues associated with dietary intake of acrylamide led Rommens et al. (2008) of Simplot Plant Sciences to reduce the accumulation of the asparagine in tubers of potato. A 20-fold reduction in asparagine yielded a similar decrease in the amount of acrylamide accumulated during heat processing and did not affect tuber yield or French fry quality. Rommens et al. (2008) estimated that replacement of existing potato lines by low-asparagine varieties would lower the ingestion of acrylamide by approximately 30%.

The U.S. Department of Agriculture approved commercial planting of Innate potatoes in late 2014 (Waltz 2015a). Simplot submitted the potato for a voluntary food safety review by the U.S. Food and Drug Administration, which it received in 2015 (Simplot Plant Sciences 2015). Growers will pay a premium for potato seed, but the crop will have fewer blemishes, and hence a higher percentage of the crops can be sold at a high price (Waltz 2015a). Three Innate varieties were expected to be available in limited quantities in 2015 in the fresh and fresh-cut markets. Fresh-cut potatoes are widely sold to institutional food service providers; in addition to decreased acrylamide production upon cooking, the Innate potato is advantageous because it does not require preservatives or additives to prevent browning.

Simplot is a major producer of potatoes for French fries, which raises questions as to whether fast-food chains will find the Innate potato an acceptable product. In the 1990s, previous lines of GE potatoes with virus and insect resistance traits were spurned by McDonalds and Frito-Lay, leading Monsanto to withdraw the line from the market (Waltz 2015a). Simplot is hoping that lack of foreign DNA in the Innate potato will address anti-GE sentiment. However, a company spokesman for the fast-food giant was widely quoted as saying that "McDonald's USA does not source GMO potatoes nor do we have current plans to change our sourcing practice." (Perkowski 2014). Simplot has secured commitments from farmers across multiple states for multiple years of production of Innate potatoes (Philpott 2014). The company's strategy is to market the potato directly to the consumer, and will introduce the product in test markets as early as summer 2015.

Concern for potato growers is not limited to consumer acceptance, however, and includes concerns about product segregation from export markets (Perkowski 2014). Monsanto previously received U.S. Department of Agriculture approval for five lines of GM potatoes offering resistance to disease and insects, but they did not succeed commercially. Monsanto's potatoes caused a trade disruption with Japan, which stopped importing U.S. potatoes when some were found in an imported shipment. A speaker for Simplot said that growers would have to keep GE potatoes separate from conventional potatoes and out of export channels (Pollack 2014). The University of Idaho recommended isolation distances for Innate fields and use of dedicated machinery for processing the potatoes

 

(Perkowski 2014). Simplot plans to apply for regulatory approval of the potatoes in major markets, including Canada, Mexico, Japan, and other parts of Asia (Pollack 2014). Lines of a second generation of Innate potatoes offering increased resistance to late blight disease and better storability are currently under review by the U.S. Department of Agriculture and the U.S. Environmental Protection Agency.

## Arctic Apple

Okanagan Specialty Fruits of Canada has applied RNA interference technology in the Granny Smith and Golden Delicious varieties of apples to silence the expression of at least four genes involved in browning, yielding the Arctic apple (Waltz 2015b). Browning of cut or bruised fruits is caused by the enzyme polyphenol oxidase naturally present in the fruit. The enzyme catalyzes the oxidation of polyphenols to quinones, causing oxidative browning. While the damage is superficial, it affects appearance, taste, and texture of the fruit. Apples that do not brown could prove more appealing to consumers and reduce waste by minimizing disposal of bruised apples. Food service companies could cut and package apple products without using browning inhibitors such as calcium ascorbate.

The U.S. Department of Agriculture approved the Arctic apple in February 2015 (Waltz 2015b). About 22,000 trees will be planted in the United States during spring 2015, with the resulting fruit available in fall 2016. Okanagan has applied for regulatory approval of its apple in Canada. Whether the Arctic apple will become popular within the apple-production industry or will get caught up in anti-GE or labeling controversies is yet to be seen. Growers associations in the United States argued against regulatory approval for fear of disruption of export markets. Okanagan pledged to identify their product in marketing and packaging, to some degree addressing such concerns.

## Other Examples in the Pipeline

While we have elaborated on a few selected case studies, in Table 2, we note other examples of GE plants whose approval and production would contribute to food security.

## New GE Technologies – Highly Promising, but are Regulatory Oversight Authorities Ready?

We have cited a number of cases where GE plants produced through now-traditional transformation techniques have been approved – or not – by regulatory bodies. We have made the case that lack of timely passage through regulation has stymied the development and adoption of GE crops, especially those targeting food security in developing nations. Regulators will soon need to examine current guidelines and policies as new crops are developed using more recent approaches such CRISPR-Cas9 technology (Belhaj et al. 2013; Xie and Yang 2013; Doudna and Charpentier 2014; Hsu et al. 2014; Lozano-Juste and Cutler 2014; Bortesi and Fischer 2015). Using this RNA-guided genome editing approach, the resulting plants contain no genes from another species and leave no residual vector sequences that triggered regulatory oversight in first-generation GE crops. For example, regulatory oversight in the United States is triggered by the use of sequences from plant pathogens such as the *A. tumefaciens* Ti plasmid or the constitutive promoter from the cauliflower mosaic virus, both of which are widely used. These sequences subject transgenic crops to the authority of the U.S. Department of Agriculture's Animal and Plant Health Inspection Services (APHIS) Biotechnology Services (BRS) under the Plant Pest Act. Plants lacking pathogen or any vector-derived DNA sequences and showing additional no signs of genetic modification, may be treated differently in the regulatory process (Cressy 2013a). Since 2010, the

**Table 2.** Examples of GE crops in development whose production could enhance food security.

| Crop | Trait | Comments |
|---|---|---|
| Pinto bean | Virus resistance | Bonfim et al. (2007), Tollefson (2011) |
| Corn | Drought resistance | Castiglioni et al. (2008) |
| Sugarcane | Drought tolerance | ISAAA (2013c) |
| Banana | Wilt resistance | Juma (2011a) |
| Cowpea | Insect resistance | ISAAA (2013a), Whitty et al. (2013) |
| Cassava | Virus resistance | Cressy (2013a), Whitty et al. (2013) |
| Banana | Increased β-carotene, iron, and other micronutrients, fungal wilt resistance | Cressy (2013a) |
| Sweet potato | Increased provitamin A | Hotz et al. (2012), Whitty et al. (2013) |
| Cassava | Increased vitamin A, iron, and protein | Nature (2011a) |
| Eggplant | Insect resistance | ISAAA (2013b) |
| Potato | Virus resistance | Mansoor et al. (2006), Qu et al. (2007) |
| Various crops | Insect and nematode resistance | Huang et al. (2006), Mao et al. (2007), Baum et al. (2007) |
| Tobacco, tomato | Male sterility | Rehman et al. (2007), Sandhu et al. (2007) |
| Tobacco, corn | Herbicide resistance | Townsend et al. (2009), Shukla et al. (2009) |
| Rice | Disease resistance | Li et al. (2012) |

 

U.S. Department of Agriculture has told at least 10 groups that their products would not require regulation (Ledford 2013), removing a substantial financial barrier and speeding development; this has encouraged academic laboratories and small companies to pursue specialty crops that have been ignored by multinational seed companies, a development with implications for promoting food security in developing countries. Similar changes to regulatory philosophy in the developing world could improve prospects for GE crops to address food security.

## A Pivotal Moment for Oversight and Adoption

Despite the clear benefits posed by cultivation of particular GE crops to increasing food security in the developing world, a number of issues have precluded widespread adoption. Key among these are: (1) regulatory issues including costs and delays and (2) public perception, corporate mistrust and misinformation. Against this background, we pose the question, "What must be realized for GE crops to contribute to food security?" We note that many of the complicating issues do not pertain to the products themselves.

## Regulatory Issues and Cost

Current review of GE crops in the United States is governed by the Coordinated Framework for the Regulation of Biotechnology, which is based on extending the scope of existing legislation to the products of biotechnolgy. Tenets for review include an assessment of whether a crop poses a plant pest risk to agriculture (through the U.S. Department of Agriculture's Animal and Plant Health Inspection Service), whether a product is considered a pesticide with the potential to pose a risk to health and the environment (through the U.S. Environmental Protection Agency), and whether plant-derived food and feed products are safe for consumption (through the U.S. Food and Drug Administration). The original intent was that the safety of the product, rather than the method of generating the product, should be the guiding principle for regulatory oversight. It has been argued that the way forward in realizing benefits to global food security is to revise the regulatory framework based on biosafety record of GE crops for the past 25 years (Federoff and Beachy 2012). Rather than testing for the presence of DNA sequences that have been safely used for over 30 years as a trigger for regulatory oversight, issues that should guide review include health and environmental issues. Current regulatory protocols have delayed or prohibited potentially transformative crops from reaching human populations that would benefit from their cultivation. Revision of the regulatory protocols could guide wise adoption of public-domain varieties where they are most needed. Policy makers in developing countries should resist being affected by the politicized debate in Europe, instead starting with consideration of the food security problem before them and reaching their own judgment of the balance of pros and cons for their own context, guided by biosafety legislation (Whitty et al. 2013). We note that a recent action by the White House Office of Science and Technology Policy (OSTP) has called for a review of the Coordinated Framework for the Regulation of Biotechnology (OSTP 2015).

Another way in which current regulatory policy impacts global development and adoption of GE crops is the expense required to pass regulatory review. A recent review of the process of developing GE crops cited estimates of US $136 million and 13 years from concept to launch of a new product (Prado et al. 2014). This enormous investment excludes most public research institutions from the process and gives multinational companies a de facto monopoly on the technology. Governments should recognize the need for public-interest research in plant genomics, selective breeding, and biotechnology (National Academies 2000). Public-private collaboration is needed for the benefits of GE technology to be brought to all of the world's people (Nature 2013b). Incentives are needed to encourage the private sector to share with the public sector more of their capacity for innovation. Care should be taken so that research and development are not inhibited by overly protective intellectual property regimes. To enhance food security in the developing world, there will be instances where farmers are allowed to save seed for future use (National Academies 2000). Because broad intellectual property claims can stifle research, development and use of GE plants, agreements must be reached so that the benefits of GE crop research can reach field use in the developing world.

National governments must ensure that they have the capacity to implement biosafety guidelines and regulations (National Academies 2000). At present, only a few African countries have permitted cultivation of GE crops, only one for food purposes, partly because of restrictive national biosafety policies that impose regulatory barriers to the adoption of agricultural biotechnology (Juma 2011b).

## Perception

Regulatory language also contributes to the perception that there is something unnatural or sinister about GE crops, and today we face a major public perception problem (Nature 2013b). A number of issues such as the scientific complexity, fast transition to utilization, and ethical, legal, and social issues all contribute to politicizing GE crops (NRC 2015). Blancke et al. (2015) applied ideas from the cognitive sciences, psychology, and culture to understand the appeal of opposition to GE crops, and proposed ways to address the situation. Education can, to some extent, abate the appeal of negative representations of GE crops. Although GE crops are at a disadvantage because they have been associated with unnaturalness by opponents, emphasis on benefits would trigger empathy. For example, it would be useful to inform the public that Bt corn contains less mycotoxin than conventional corn, that herbicide resistance crops improve soil quality by reducing tilling, that Bt crops enhance insect biodiversity, and that GE crops can reduce poverty. One recently published study should change the paradigm of what is considered "natural". The genomes of traditionally derived sweet potatoes have been found to contain the *A. tumefaciens* T-DNA as a result of the natural domestication process (Kyndt et al. 2015). Against this background, we recommend that scientists from both the public and private sectors reach out to the general public and to decision-makers to communicate the potential benefits and risks of GE crop production, and to advocate that we adopt well-targeted applications for GE crops. We support regulation based on the characteristics of the added trait rather than continuing our current protocols where common transformation vector sequences trigger a review even when decades of experience have yielded no concerns.

Well-conceived research and development, combined with well-chosen adoption of GE crop lines, will result in increased food security, human well-being, and ecological sustainability, whereas flawed research adds to the public concerns and misperceptions. For example, Séralini et al. (2012) investigated the health effects of Roundup herbicide and a Roundup-tolerant GE corn through the lifetime of rats, reporting altered sex hormone profiles and increased histological disruptions, tumor frequency, and mortality. The paper was promoted to the press, coinciding with release of a book and film (Nature 2012b). Predictably, the public response, especially in Europe, was hostile to GE food products. However, many scientists criticized the methodology and inferences drawn in the study, noting small sample sizes and use of a rat strain known to develop tumors spontaneously. After letters to the editor of the journal where the study was published, response by the authors, and critical reappraisal of the data, the journal retracted the publication as "inconclusive" (Food and Chemical Toxicology 2014). Similar findings had been reached by the EFSA and six European member states (Nature 2012c). While this case study shows the value of scientific debate and regulatory review, the public likely will remember only the breaking story (Nature 2012b), which serves only to extend the myth of the unnaturalness and potential safety issues of GE foods. A recent review of several key advances in GE crop improvement describes the fearmongering and fraud often perpetrated by GE opposition groups such as Greenpeace (Saletan 2015). The public – at least in Europe – perceives GE plant-derived foods differently from experts (Savadori et al. 2004), perceiving less benefit and greater harm to both humans and the environment. Such perceptions affect the adoption of GE crop technology not only in Europe, but also in the developing world where food security is at issue.

The potential environmental effects, both positive and negative, of GE plant technologies should be assessed within the context of specific applications, with effects assessed relative to those of conventional agricultural practices currently in use in places for which the GE crop was developed (National Academies 2000). Critics of GE crops often presume that most ecological consequences of their cultivation – for example, gene flow into wild relatives – are likely to prove negative. However, a review of 130 research projects by the European Commission (2010) showed the GE crops are not inherently more risky than conventionally bred plants. The application of crop biotechnology has had a number of ecological benefits (Juma 2011a). Production of *Bt* crops has reduced the manufacture of pesticides and farmers' exposure to them. Use of herbicide-tolerant plants has allowed farmers to reduce tilling and weeding, freeing their time for other activities, while reducing erosion and carbon release from the soil. For 2009, it was estimated that GE crops resulted in 7.6 billion kg of carbon dioxide sequestration, the equivalent of removing over 7 million cars from the road (Juma 2011a).

The first GE crops to be commercialized on a large scale have targeted herbicide tolerance and pest resistance traits as opposed to consumer benefits. Hence, the rewards of the first generation of GE crops mostly accrued to multinational corporations and large farmers, and were largely irrelevant to addressing world hunger (Nature 2010). This mismatch of interests has led to mistrust of multinational chemical and seed companies. Combined experience of over 50 years by the authors in discussing biotechnology in the classroom, with agricultural producers, regulators and the public has revealed a blending of issues in the minds of nonscientific audiences. Public mistrust of corporations that develop and market GE crops often is equated with the product itself. Traits with clear benefits to the end user, such as those developed in the pharmaceutical industry (e.g., recombinant insulin), might have been viewed more favorably as first-generation candidates in agriculture. Issues such as health, nutrition, environmental sustainability, and food security are much more compelling to the average consumer.

## Conclusion

To ensure food security for all people, agriculture must evolve to meets the needs of a growing population while minimizing global environmental impacts. Above, we note many examples of how research and development on GE plants has resulted in lines that can improve the stability and yield of food production, provide nutritional benefits to the consumer, and reduce the environmental impacts of intensive and extensive agriculture. An agricultural model that combines the best features of traditionally bred and GE crops can make major contributions to global food security. We argue that revising regulations guided by experience of many thorough biosafety studies from the past 25 years will make it feasible to apply these technologies to crop improvement of minor crops and crops important to the nourishment and economic well-being of a greater segment of the world's population. Improving public communication and education are also critical to realizing the benefits of GE crops. A recent cover article in Newsweek magazine declared that "You are totally wrong about genetically altered food", which represents a change from past treatment of GE crops by the popular press. The article highlighted new technological breakthroughs that should help reduce unease the part of biotechnology skeptics. It revealed many examples of misinformation spread by polarizing opponents of new technology. In short, GE crops provide a valuable technical alternative among the variety of approaches that can and should be responsibly marshaled to feed a growing population. We close by repeating a quotation from John F. Kennedy, which although offered in another context, is fitting here: "The great enemy of truth is very often not the lie – deliberate, contrived and dishonest – but the myth – persistent, persuasive, and unrealistic. Too often we hold fast to the cliches of our forebears. We subject all facts to a prefabricated set of interpretations. We enjoy the comfort of opinion without the discomfort of thought".

## Acknowledgments

The authors were supported in part by a grant from the U.S. Department of Agriculture-Foreign Agriculture Service. Funding for this work was provided in part by the Virginia Agricultural Experiment Station and the Hatch Program of the National Institute of Food and Agriculture, U.S. Department of Agriculture.

## Conflicts of Interest

None declared.

### References

Alberts, B., R. Beachy, D. Baulcombe, G. Blobel, S. Datta, N. Fedoroff, et al. 2013. Standing up for GMOs. Science 341:1320.

American Society for Nutrition. 2015. Retraction of Tang G, Hu Y, Yin S-A, Wang Y, Dallal GE, Grusak MA, and Russell RM. ß-carotene in Golden Rice is as good as ß-carotene in oil at providing vitamin A to children. Am J Clin Nutr 2012;96:658–64. Am. J. Clin. Nutr. 102:715.

Anderson, K., L. A. Jackson, and C. Pohl Nielsen. 2004. Genetically modified rice adoption: implications for welfare and poverty alleviation. Discussion Paper 0413, Center for International Economic Studies, Discussion Paper 0413. http://www.goldenrice.org/PDFs/Anderson_CIES_2004.pdf. Also available as World Bank Policy Research Working Paper 3380, August 2004 Available at http://elibrary.worldbank.org/doi/pdf/10.1596/1813-9450-3380 (accessed 16 June 2014).

Baum, J. A., T. Bogaert, W. Clinton, G. R. Heck, P. Feldmann, O. Ilagan, et al. 2007. Control of coleopteran insect pests through RNA interference. Nat. Biotechnol. 2511:1322–1326.

Belhaj, K., A. Chaparro-Garcia, S. Kamoun, and V. Nekrasov. 2013. Plant genome editing made easy: targeted mutagenesis in model and crop plants using the CRISPR/Cas system. Plant Methods 9:39.

Blancke, S., F. Van Breusegem, G. De Jaeger, J. Braeckman, and M. Van Montagu. 2015. Fatal attraction: the intuitive appeal of GMO opposition. Trends Plant Sci. 20:414–418.

Boettcher, M. I., T. Schettgen, B. Kütting, M. Pischetsrieder, and J. Angerer. 2005. Mercapturic acids of acrylamide and glycidamide as biomarkers of the internal exposure to acrylamide in the general population. Mutat. Res. 580:167–176.

Bonfim, K., J. C. Faria, E. O. P. L. Nogueira, É. A. Mendes, and F. J. L. Aragão. 2007. RNAi-mediated resistance to bean golden mosaic virus in genetically engineered common bean (*Phaseolus vulgaris*). Mol. Plant Microbe Interact. 20:717–726.

Bortesi, L., and R. Fischer. 2015. The CRISPR/Cas9 system for plant genomic editing and beyond. Biotechnol. Adv. 33:41–52.

Castiglioni, P., D. Warner, R. J. Bensen, D. C. Anstrom, J. Harrison, M. Stoecker, et al. 2008. Bacterial RNA chaperones confer abiotic stress tolerance in plants and improved grain yield in maize under water-limited conditions. Plant Physiol. 147:446–455.

CERA (Center for Environmental Risk Assessment). 2007. GM Crop Database: ARS-PLMC5-6 (C5). Available at http://cera-gmc.org/index.php?evidcode%5B%5D=C5&auDate1=&auDate2=&action=gm_crop_database&mode=Submit.

Chassy, B., N. Fedoroff, D. Kershen, M. McGloughlin, W. Parrott, and C. S. Prakash. 2013. Global scientific community condemns the recent destruction of field trials of Golden Rice in the Philippines. Change.org Available at http://chn.ge/143PyHo (accessed 12 January 2016).

Chen, M., A. Shelton, and G. Y. Ye. 2011. Insect-resistant genetically modified rice in China: from research to commercialization. Annu. Rev. Entomol. 56:81–101.

Cressy, D. 2013a. A new breed: the next wave of genetically modified crops is making its way to market – and might just ease concerns over 'Frankenfoods'. Nature 497:27–29.

Cressy, D. 2013b. Monsanto drops GM in Europe: region abandoned owing to stalled approval process. Nature 499:387.

Davidson, S. N. 2008. Forbidden fruit: transgenic papaya in Thailand. Plant Physiol. 147:487–493.

Delmer, D. P. 2005. Agriculture in the developing world: connecting innovations in plant research to downstream applications. Proc. Natl Acad. Sci. USA 102:15739–15746.

Diaz de la Garza, R. I., J. F. III Gregory, and A. D. Hanson. 2007. Folate biofortification of tomato fruit. Proc. Natl Acad. Sci. USA 104:4218–4222.

Doudna, J. A., and E. Charpentier. 2014. The new frontier of genome engineering with CRISPR-Cas9. Science 346:1077 DOI: 10.1126/science.1258096.

Dubock, A. 2013. Golden Rice: a long-running story at the watershed of the GM debate. Golden Rice Humanitarian Board. Available at http://b4fa.org/golden-rice-long-running-story-watershed-gm-debate/.

European Commission. 2010. A decade of EU-funded GMO research (2001–2010). Available at https://ec.europa.eu/research/biosociety/pdf/a_decade_of_eu-funded_gmo_research.pdf (accessed 15 January 2015).

Federoff, N. V., and R. Beachy. 2013. Facilitating market access for GE crops developed through public sector research. Pp. 377–390 *in* C. A. Wozniak, A. McHughen, eds. Regulation of agricultural biotechnology: the United State and Canada. Springer, Dordrecht, Netherlands.

Food and Chemical Toxicology. 2014. Retraction notice to "Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize" [Food Chem. Toxicol. 50:4221-4231]. Food Chem. Toxicol. 63:244.

George, S., H. S. Singh, and G. Naik. 2002. Brinjal shoot and fruit borer (*Leucinodes orbonalis*) status in coastal districts of Orissa. Pp. 121–123 *in* B. S. Babu, K. S. Varaprasad, K. Anitha, R. D. V. J. Prasada Rao, S. K. Chakrabarty, P. S. Chandurkar, eds. Resources management in plant protection during 21st century, volume II. Plant Protection Society of India, Hyderabad.

GMO Compass. 2013. Papaya. Available at http://www.gmo-compass.org/eng/database/plants/59.papaya.html (accessed 6 December 2013).

Gonsalves, D. 1998. Control of papaya ringspot virus in papaya: a case study. Annu. Rev. Phytopathol. 36:415–437.

Goto, F., T. Yoshihara, N. Shigemoto, S. Toki, and F. Takaiwa. 1999. Iron fortification of rice seed by the soybean ferritin gene. Nat. Biotechnol. 17:282–286.

Greenpeace. 2002. Genetically engineered "golden rice" is fool's gold. Pp. 52–54 *in* M. Ruse, D. Castle, eds. Genetically modified foods: debating biotechnology. Prometheus Books, Amherst, NY.

Guerinot, M. L. 2000. The green revolution strikes gold. Science 287:241–243.

Halford, N. G. 2012. Toward two decades of plant biotechnology: successes, failures and prospects. Food Energy Secur. 1:9–28.

Harmon, A. 2014. A lonely quest for facts on genetically modified crops. New York Times, January 4, 2014, A1.

Herrera-Estrella, L., A. Depicker, M. van Montagu, and J. Schell. 1983. Expression of chimaeric genes transferred into plant cells using Ti-plasmid-derived vector. Nature 303:209–213.

Hotz, C., C. Loechl, A. de Brauw, P. Eozenou, D. Gilligan, M. Moursi, et al. 2012. A large-scale intervention to introduce orange sweet potato in rural Mozambique increases vitamin A intakes among children and women. Br. J. Nutr. 108:163–176.

Hsu, P. D., E. S. Lander, and F. Zhang. 2014. Development and applications of CRISPR-Cas9 for genome engineering. Cell 157:1262–1278.

Huang, J., R. Hu, C. Pray, F. Qiao, and S. Rozelle. 2003. Biotechnology as an alternative to chemical pesticides: a case study of Bt cotton in China. Agric. Econ. 29:55–67.

Huang, G., R. Allen, E. L. Davis, T. J. Baum, and R. S. Hussey. 2006. Engineering broad root-knot resistance in transgenic plants by RNAi silencing of a conserved and essential root-knot nematode parasitism gene. Proc. Natl Acad. Sci. USA 103:14302–14306.

Huang, J., R. Chen, F. Qiao, and K. Wu. 2015a. Biosafety management and pesticide use in China's Bt cotton production. China Econ. Rev. 33:67–75.

Huang, J. K., R. F. Hu, F. B. Qiao, Y. H. Yin, H. J. Liu, and Z. R. Huang. 2015b. Impact of insect-resistant GM rice on pesticide use and farmers' health in China. Sci. China Life Sci. 58:466–471.

Huffington Post. 2013. Possible eco-terrorists attack genetically modified papayas on the Big Island. Available at http://www.huffingtonpost.com/2013/09/29/ecoterrorism-papayas-hawaii_n_4013292.html?view=print&comm_ref=false (accessed 6 December 2013).

Hvistendahl, M., and M. Enserink. 2012. Charges fly, confusion remains of golden rice study in Chinese children. Science 337:1281.

 

International Rice Research Institute. 2013. Clarifying recent news about Golden Rice. Available at http://irri.org/blogs/golden-rice-blog/clarifying-recent-news-about-golden-rice.

ISAAA (International Service for the Acquisition of Agri-biotech Applications). 2013a. Nigeria develops *Maruca*-resistant cowpea to reduce farm loss. Crop Biotech Update, April 3, 2013. Available at http://www.isaaa.org/kc/cropbiotechupdate/article/default.asp?ID=10799 (accessed 24 December 2013).

ISAAA (International Service for the Acquisition of Agri-biotech Applications). 2013b. Pocket K No. 35: *Bt* brinjal in India. Available at http://www.isaaa.org/resources/publications/pocketk/35/(accessed 24 December 2013).

ISAAA (International Service for the Acquisition of Agri-biotech Applications). 2013c. Sugarcane - *Saccharum* sp: 3 events. Available at: http://www.isaaa.org/gmapprovaldatabase/advsearch/default.asp?CropID=27&TraitTypeID=6&DeveloperID=Any&CountryID=Any&ApprovalTypeID=Any (accessed 24 December 2013).

ISAAA (International Service for the Acquisition of Agri-biotech Applications). 2014. Top ten facts about Bt brinjal in Bangladesh. ISAAA Brief 47-2014: Executive summary. Available at https://www.isaaa.org/resources/publications/briefs/47/executivesummary/default.asp. (accessed 26 May 2015).

ISAAA (International Service for the Acquisition of Agri-biotech Applications). 2015. Pocket K No. 16: global status of commercialized biotech/GM crops in 2014. Available at http://www.isaaa.org/resources/publications/pocketk/16/(accessed 29 May 2015).

Juma, C. 2011a. Preventing hunger: biotechnology is key. Nature 479:471–472.

Juma, C. 2011b. Science meets farming in Africa. Science 334:1323.

Kyndt, T., D. Quispe, H. Zhai, R. Jarret, M. Ghislain, Q. Liu, et al. 2015. The genome of cultivated sweet potato contains *Agrobacterium* T-DNAs with expressed genes: an example of a naturally transgenic food crop. Proc. Natl Acad. Sci. USA, 112:5844–5849.

Ledford, H.. 2013. US regulation misses some GM crops. Nature 500:389–390.

Li, T., B. Liu, M. H. Spalding, D. P. Weeks, and B. Yang. 2012. High-efficiency TALEN-based gene editing produces disease-resistant rice. Nat. Biotechnol. 30:390–392.

Li, Y., E. Hallerman, Q.S. Liu, Y. Peng, and K. Wu. 2015. Risk analysis and governance issues regarding development of Bt rice lines in China. Plant Biotechnol. J., in press, doi: 10.1111/pbi.12464.

Lozano-Juste, J., and S.R. Cutler. 2014. Plant genome engineering in full bloom. Trends Plant Sci. 19:284–287.

Lucca, P., R. F. Hurrell, and I. Potrykus. 2001. Genetic engineering approaches to improve the bioavailability and the level of iron in rice grains. Theor. Appl. Genet. 102:392–397.

Mahyco. 2009. Biosafety data of Bt brinjal containing cry1Ac (EE1) event developed by M/s Maharastra Hybrid Seeds Company Limited. Available through Government of India Ministry of Environment, Forest, and Climate Change at http://www.envfor.nic.in/divisions/csurv/geac/bt_brinjal.html (accessed 7 October 2015).

Mansoor, S., I. Amin, M. Hussain, Y. Zafar, and R. W. Briddon. 2006. Engineering novel traits in plants through RNA interference. Trends Plant Sci. 11:559–565.

Mao, Y.-B., W.-J. Cai, J.-W. Wang, G.-J. Hong, X.-Y. Tao, L.-J. Wang, et al. 2007. Silencing a cotton bollworm P450 monooxygenase gene by plant-mediated RNAi impairs larval tolerance of gossypol. Nat. Biotechnol. 25:1307–1313.

Mayer, J. E., W. H. Pfeiffer, and P. Beyer. 2008. Biofortified crops to alleviate micronutrient malnutrition. Curr. Opin. Plant Biol. 11:166–170.

Mayo-Wilson, E., A. Imdad, K. Herzer, M. Y. Yakoob, and Z. A. Bhutta. 2011. Vitamin A supplements for preventing mortality, illness, and blindness in children aged under 5: systematic review and meta-analysis. Br. Med. J. 343:d5094.

Mortensen, D. A., J. F. Egan, B. D. Maxwell, M. R. Ryan, and R. G. Smith. 2012. Navigating a critical juncture for sustainable weed management. Bioscience 62:75–84.

National Academies (Royal Society of London, U.S. National Academy of Sciences, Brazilian Academy of Sciences, Chinese Academy of Sciences, Indian National Science Academy, Mexican Academy of Sciences, and Third World Academy of Sciences). 2000. Transgenic plants and world agriculture. National Academy Press, Washington, DC. Available at www.nap.edu.

National Research Council. 2015. Public engagement on genetically modified organisms: when science and citizens connect. Workshop Summary. National Academy Press, Washington, DC. Available at www.nap.edu.

Nature. 2010. How to feed a hungry world. Nature 466:531–532.

Nature. 2011a. Golden rice funds. Nature 472:265.

Nature. 2011b. GM honey concern. Nature 477:254.

Nature. 2011c. No to French GM ban. Nature 480:10.

Nature. 2012a. Transgenic flight. Nature 481:243.

Nature. 2012b. Poison postures: researchers working on controversial topics must take care how they promote their results. Nature 489:474.

Nature. 2012c. GM study rebutted. Nature 492:12.

Nature. 2013a. Poland GM ban. Nature 493:138.

Nature. 2013b. Fields of gold: research on transgenic crops must be done outside industry if it is to fulfil its early promise. Nature 497:5–6.

Nature. 2013c. Tarnished promise: genetically modified crops generate hype and hatred. Nature 497:21.

 

Nature. 2013d. GM crops: a story in numbers. Nature 497:22–23.

Nature. 2013e. GM-rice fallout. Nature 501:467.

Novak, S. 2013. USDA moving to deregulate genetically modified plums. Available at http://recipes.howstuffworks.com/usda-moving-to-deregulate-genetically-modified-plums.htm (accessed 9 December 2013).

Office of Science and Technology Policy. 2015. Improving transparency and ensuring continued safety in biotechnology. Available at https://www.whitehouse.gov/blog/2015/07/02/improving-transparency-and-ensuring-continued-safety-biotechnology (accessed 30 July 2015).

Owino, O. 2012. Scientists torn over Kenya's recent GM food ban. Nature. Available at http://dx.doi.org/10.1038/nature.2012.11929.

Perkowski, M. 2014. McDonald's not interested in GMO potatoes. Capital Press, November 19, 2014.

Philpott, T. 2014. Will this new GMO potato take off: McDonald's has spoken. Mother Jones, Friday November 14, 2014.

Pollack, A. 2014. U.S.D.A. approves modified potato. Next up: French fry fans. New York Times, November 7, 2014:B1.

Potrykus, I. 2010. Regulation must be revolutionized. Nature 466:561.

Prado, J. R., G. Segers, T. Voelker, D. Carson, R. Dobert, J. Phillips, et al. 2014. Genetically engineered crops: from idea to product. Annu. Rev. Plant Biol. 65:769–790.

Qiao, F. 2015. Fifteen years of Bt cotton in China: the economic impact and its dynamics. World Dev. 70:177–185.

Qu, J., J. Ye, and R. Fang. 2007. Artificial microRNA-mediated virus resistance in plants. J. Virol. 81:6690–6699.

Ravelonandro, M., R. Scorza, A. Callahan, L. Levy, C. Jacquet, M. Monsion, et al. 2000. The use of transgenic fruit trees as a resistance strategy for virus epidemics: the plum pox (sharka) model. Virus Res. 71:63–69.

Rehman, N., M. Shah, S. Mansoor, A. A. Khan, Y. Zafar, and R. W. Briddon. 2007. RNAi-mediated male sterility of tobacco by silencing *TA29*. Mol. Biotechnol. 36:159–165.

Rommens, C. M., H. Yan, K. Swords, C. Richael, and J. Ye. 2008. Low-acrylamide French fries and potato chips. Plant Biotechnol. J. 6:843–853.

Saletan, W. 2015. Unhealthy fixation: the war against genetically modified organisms is full of fearmongering, errors and fraud. Labeling them will not make you safer. Slate, July 15, 2015. Available at http://www.slate.com/articles/health_and_science/science/2015/07/are_gmos_safe_yes_the_case_against_them_is_full_of_fraud_lies_and_errors.html. (accessed 30 July 2015).

Sandhu, A. P. S., R. V. Abdelnoor, and S. A. Mackenzie. 2007. Transgenic induction of mitochondrial rearrangements for cytoplasmic male sterility in crop plants. Proc. Natl Acad. Sci. USA 104:1766–1770.

Savadori, L., S. Savio, E. Nicotra, R. Rumiati, M. Finucane, and P. Slovic. 2004. Expert and public opinion of risk from biotechnology. Risk Anal. 24:1289–1299.

Science. 2011. Peru set to forbid GM crops. Science 332:1365.

Science. 2012a. Philippine scientists defend transgenic crops. Science 336:654.

Science. 2013a. Monsanto withdraws E.U. patent applications. Science 341:324.

Science. 2013b. Scientists: freeze GM trials. Science 341:324–325.

Science. 2013c. Activists destroy 'golden rice' field trial. Science 341:699.

Scorza, R. 2007. Application for determination of non-regulatory status of C5 ('HoneySweet') plum (*Prunus domestica* L.) resistant to plum pox virus. Identifier ARS-PLMC5-6, USDA-ARS Appalachian Fruit Tree Research Station, Kearneysville, WV. 93 pp. Available at http://cera-gmc.org/docs/decdocs/07-313-003.pdf (accessed 18 December 2013).

Scorza, R., A. Callahan, C. Dardick, M. Ravelonandro, J. Polak, T. Malinowski, et al. 2013a. Genetic engineering of plum pox virus resistance: 'HoneySweet' plum – from concept to product. Plant Cell Tissue Organ Cult. 115:1–12.

Scorza, R., A. B. Kriss, A. M. Callahan, K. Webb, M. Demuth, and T. Gottwald. 2013b. Spatial and temporal assessment of pollen- and seed-mediated gene flow from genetically engineered plum *Prunus domestica*. PLoS One 8:e75291.

Séralini, G.-E., E. Clair, R. Mesnage, S. Gress, N. Defarge, M. Malatesta, et al. 2012. Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. Food Chem. Toxicol. 50:4221–4231.

Shukla, V. K., Y. Doyon, J. C. Miller, R. C. DeKelver, E. A. Moehle, S. E. Worden, et al. 2009. Precise genome modification in the crop species *Zea mays* using zinc-finger nucleases. Nature 459:437–441.

Simplot Plant Sciences. 2015. Innate™ potato receives FDA safety clearance. Available at http://www.simplot.com/news/innate_potato_receives_fda_safety_clearance (accessed 24 April 2015).

Storozhenko, S., V. De Brouwer, M. Volckaert, O. Navarrete, D. Blancquaert, G. F. Zhang, et al. 2007. Folate fortification of rice by metabolic engineering. Nat. Biotechnol. 25:1277–1279

Tamil Nadu Agricultural University – Department of Plant Molecular Biology and Biotechnology. 2008. Report of the multilocation research trial on Bt brinjal open-pollinated varieties conducted at Coimbatore and

 

Madurai 2007–2008. 57 pp. Available at http://www.moef.gov.in/divisions/csurv/geac/Bt_Brinjal/TNAU-Bt%20brinajl_MLR_report.pdf (accessed 7 October 2015).

Tang, G., J. Qin, G. G. Dolnikovski, R. M. Russell, and M. A. Grusak. 2009. Golden rice is an effective source of vitamin A. Am. J. Clin. Nutr. 89:1776–1783.

Tang, G., Y. Hu, S. Yin, Y. Wang, G. E. Dallal, M. A. Grusak, et al. 2012. β-carotene in golden rice is as good as β-carotene in oil at providing vitamin A to children. Am. J. Clin. Nutr. 96:658–664.

Tollefson, J. 2011. Brazil cooks up transgenic bean. Nature 478:168.

Townsend, J. A., D. A. Wright, R. J. Winfrey, F. Fu, M. L. Maeder, J. K. Joung, et al. 2009. High-frequency modification of plant genes using engineered zinc-finger nucleases. Nature 459:442–445.

USDA-FAS (U.S. Department of Agriculture – Foreign Agriculture Service). 2013. India agricultural biotechnology annual 2013. GAIN Report #IN3083. Available at http://gain.fas.usda.gov/Recent%20GAIN%20Publications/Agricultural%20Biotechnology%20Annual_New%20Delhi_India_7-15-2013.pdf (accessed 28 May 2015).

U.S. Food and Drug Administration – Center for Food Safety and Nutrition, Office of Food Additive Safety. 2009a. Biotechnology consultation: note to the file BNF No. 000101. Available at http://cera-gmc.org/docs/decdocs/09-055-002.pdf (accessed 18 December 2013).

U.S. Food and Drug Administration – Center for Food Safety and Nutrition, Office of Food Additive Safety. 2009b. Biotechnology consultation: agency response letter BNF No. 000101. Available at http://cera-gmc.org/docs/decdocs/09-055-001.pdf (accessed 18 December 2013).

USDA-APHIS (U.S. Department of Agriculture - Animal and Plant Health Inspection Service). 2007a. Approval of USDA-ARS request (04-264-01P) seeking a determination of nonregulated status for C5 plum resistant to plum pox virus.

USDA-APHIS (U.S. Department of Agriculture - Animal, Plant Health Inspection Service). 2007b. Determination of nonregulated status for plum genetically engineered for resistance to plum pox virus. Fed. Reg. 72:38556–38557, Friday, July 13, 2007.

Van Eenennaam, A. L., E. M. Hallerman, and W. M. Muir 2011. The science and regulation of food from genetically engineered animals. CAST Commentary QTA2011-2, Council on Agricultural Science and Technology, Ames, IA.

Van Eenennaam, A. L., W. M. Muir, and E. M. Hallerman. 2013. Are unaccountable regulatory delay and political interference undermining the FDA and hurting American competitiveness? Food Drug Policy Forum 3:1–20.

Vietmeyer, N. 2012. Our daily bread: the essential Norman Borlaug. 284 pp. Bracing Books, Lorton, VA.

Waltz, E. 2015a. USDA approves next-generation GM potato. Nat. Biotechnol. 33:12–13.

Waltz, E. 2015b. Nonbrowning GM apple cleared for market. Nat. Biotechnol. 33:326–327.

Whitty, C. J. M., M. Jones, A. Tollervey, and T. Wheeler. 2013. Africa and Asia need a rational debate on GM crops. Nature 497:31–33.

WHO (World Health Organization). 2005. Global prevalence of vitamin A deficiency in populations at risk 1995–2005. WHO Global Database on Vitamin A deficiency. Available at http://www.who.int/vmnis/vitamina/prevalence/report/en/ (accessed 7 January 2015).

WHO (World Health Organization). 2015. Trade, foreign policy, diplomacy and health: food security. Available at http://www.who.int/trade/glossary/story028/en (accessed 6 October 2015).

Xie, K., and Y. Yang. 2013. RNA-guided genome editing in plants using a CRISPR-Cas system. Mol. Plant 6:1975–1983.

Ye, X., S. Al-Babili, A. Kloti, J. Zhang, P. Lucca, P. Beyer, et al. 2000. Engineering the provitamin A (β-carotene) biosynthetic pathway into (carotenoid-free) rice endosperm. Science 287:303–305.

 