2018

Risks and opportunities of GM crops: Bt maize example

Andrea K. Carzoli
Iowa State University

Siddique I. Aboobucker
Iowa State University

Leah L. Sandall
University of Nebraska-Lincoln, lsandall5@unl.edu

Thomas T. Lubberstedt
Iowa State University

Walter P. Suza
Iowa State University, wpsuza@iastate.edu

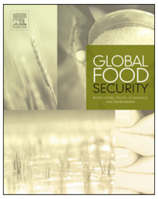
Carzoli, Andrea K.; Aboobucker, Siddique I.; Sandall, Leah L.; Lubberstedt, Thomas T.; and Suza, Walter P., "Risks and opportunities of GM crops: Bt maize example" (2018). *Agronomy & Horticulture -- Faculty Publications*. 1176.
http://digitalcommons.unl.edu/agronomyfacpub/1176

Global Food Security 19 (2018) 84–91

Contents lists available at ScienceDirect

Global Food Security

journal homepage: www.elsevier.com/locate/gfs



Risks and opportunities of GM crops: Bt maize example

Andrea K. Carzoli[a,b], Siddique I. Aboobucker[a], Leah L. Sandall[c], Thomas T. Lübberstedt[a], Walter P. Suza[a,*]

[a] Department of Agronomy, Iowa State University, Ames, IA 50011, USA
[b] Corteva Agriscience™, Agriculture Division of DowDuPont™, Johnston, IA 50131, USA
[c] Department of Agronomy & Horticulture, University of Nebraska-Lincoln, Lincoln, NE 68583, USA

ARTICLE INFO

Keywords:
Bt crops
Risk assessment
Environmental risk
Yield gain
Low input cost
GM crops

ABSTRACT

The anticipated world population growth emphasizes a need to produce more food on less land. Cutting-edge technologies, including genetic engineering, can help to develop improved crop varieties and protect natural resources. In spite of the potential for genetically-modified (GM) crops to make crop production more efficient, they remain a polarizing issue due to safety concerns. This paper provides an overview of the risk assessment process. The safety of *Bacillus thuringiensis* (Bt) proteins is used as an example for how risk assessment is applied to GM crops. Risks associated with GM crops have proven to be low to non-existent. Developing countries would benefit from GM technologies as one tool to improve crop yields and reduce production challenges.

1. Introduction

The first commercialized GM crops were planted in 1996 in the United States, with a total area of 1.7 million hectares (ISAAA, 2017). Since then, there has been a steady increase in the use of GM crops for 22 straight years. By the end of 2017, that number had increased to about 190 million hectares globally, with developing countries growing 53% of the GM crop hectares (ISAAA, 2017). With the rate of adoption and increase in amount of land area dedicated to growing GM crops, it has been claimed that this technology has been the fastest adopted agricultural technique in modern history (Khush, 2012). Such rapid adoption is driven by substantial incentive for farmers to implement the GM technology into their farming practices (Brookes and Barfoot, 2017; Smyth, 2017). Even with substantial deployment of the technology, concerns exist about potential hazards and disadvantages associated with long-term use of GM crops. In addition, there is fear that consumers in developed countries may boycott produce imported from countries that have adopted GM crops (Paarlberg, 2002). The fear of GM crops has led to substantial opposition from non-governmental organizations and politically-motivated groups, who have the ability to influence policies around the establishment of biosafety frameworks in developing countries (Paarlberg, 2010; Smyth, 2017).

In several developed nations of the European Union and Japan, GM crops face strong opposition (Smyth, 2017). In Africa, heated debates continue regarding whether GM crops will help alleviate food insecurity, or whether adoption of this technology could result in negative impacts (Falck-Zepeda et al., 2013). Consequently, African policymakers are hesitant to move forward with establishing biosafety laws and commercializing GM crops, largely due to risk perceptions and fears spread by anti-biotech lobbying groups (Paarlberg, 2010).

The objective of this paper is to review the scientific approach of risk assessment for GM crops, using a few concrete risks of Bt maize (*Zea mays.* L) as illustrative examples. Beyond risk analysis, the paper also reviews some potential benefits of Bt crops, emphasizing examples that may help improve food security in areas where this is a challenge. The information might reassure policy makers, farmers, and consumers of the thorough and methodical approach applied in risk assessment for GM technology so they can make informed decisions about use of GM traits in agriculture. The intention of this paper is not to duplicate the risk assessment process of GM crops, which has already been conducted by experts (Romeis et al., 2008; Wolt et al., 2003, 2010). Instead, the focus is to demonstrate how risk assessment of GM technology is done with scientific rigor as in other disciplines, such as engineering and medicine, by using Bt maize as an example.

2. Application of genetic engineering to protect crops from insect pests

In the decades of use, GM technology has been broadly applied to different crops with varying degrees of success. One of the more successful and widely used applications of GM technology is the integration of genes from the soil bacterium, *Bacillus thuringiensis* (Bt), for

---

[*] Corresponding author.
E-mail address: wpsuza@iastate.edu (W.P. Suza).

https://doi.org/10.1016/j.gfs.2018.10.004
Received 1 August 2018; Received in revised form 4 October 2018; Accepted 31 October 2018

protection against damaging insect pests (Roh et al., 2007). Plants that are genetically-modified to express Bt crystalline (Cry) protein are resistant to insect infestation, and actively control pest populations due to their toxicity to certain insects (Roh et al., 2007). In total, over 70 primary subgroups of Cry proteins have been identified (Adang et al., 2014). However, only a small subset of the Cry proteins has been engineered into Bt crops. By 2017, it was estimated that over 100 million hectares of crops contained Bt genes (ISAAA, 2017).

The major classes of Cry proteins affect different insects which damage crops worldwide (Adang et al., 2014). Insects in the orders Lepidoptera, Diptera and Coleoptera are susceptible to Cry proteins. Susceptible insects with potential to cause significant crop loss include the fall armyworm (*Spodoptera frugiperda*), European corn borer (*Ostrinia nubilalis*), corn earworm (*Helicoverpa zea*), cotton bollworm (*Helicoverpa armigera*), tobacco budworm (*Heliothis virescens*), pink bollworm (*Pectinophora gossypiella*), western corn rootworm (*Diabrotica virgifera virgifera*), and Colorado potato beetle (*Leptinotarsa decemlineata*) (Roh et al., 2007). Other insect pests, which are also susceptible to Cry proteins, include stem borer species *Busseola fusca*, *Chilo partellus*, and *Sesamia calamistis*, have been known to cause an average yield loss of 13.5% (De Groote, 2002). Fall armyworm (FAW) is contributing to significant crop loss in Africa where conventional breeding of tolerant crop varieties and integrated pest management approaches have proven too slow to halt the spread of the emerging threat (Fig. 1).

3. Risk assessment: A valuable tool across many disciplines

Evaluation of the potential hazards and disadvantages of any new technology is an important part of the approval process. Hazards can be weighed by determining risk, which is a product of the probability of and the consequences of a hazard. This concept broadly applies to almost any discipline, and as a result, risk assessment has been utilized as a tool by a variety of technical fields, including the area of crop genetic engineering (Betz et al., 2000; Romeis et al., 2008; USEPA, 2001). Risk assessment as an iterative process includes the following steps: hazard identification, dose-response assessment, exposure characterization, and risk conclusion (Fig. 2).

In engineering, risk assessment can be applied to various structures, including building foundations, pipelines, dams and levees (Stewart et al., 2001). Proper identification of risk prevents overspending of financial and labor resources on improvements or upgrades of structures (Imhof, 2004). Furthermore, risk assessment is recognized as a critical tool in engineering due to the unique nature of most buildings or structures, as compared to other fields where creation of a product is based on extensive product testing and feedback (Imhof, 2004). The results of a risk assessment are often a driver for decisions on design, materials, and maintenance schedules. For example, the maintenance of bridges is one area that is subjected to risk assessment studies (Imhof, 2004; Stewart et al., 2001). Potential causes of bridge failure can include natural hazards (weather conditions); design errors; overloading; impact of ships, trains, or vehicles; human workmanship error; vandalism; deterioration; or other unknown phenomena (Imhof, 2004). Since all existing bridges are subject to a risk of collapse due to the variety of natural and human-induced stressors, regular risk assessments can help to minimize failure events (Imhof, 2004).

In the medical field, risk assessment is used to help quantify the risk of adverse health reaction or disease from a number of factors ranging from human behavior, medical or pharmaceutical treatments, or environmental exposure (National Research Council, 2003). In many cases, the outcome of the risk assessment process from the medical standpoint is the likelihood of disease to occur as a result of a specific hazard.

In one example, risk assessment has analyzed the impact of exposure to radon, a known carcinogen and significant health hazard

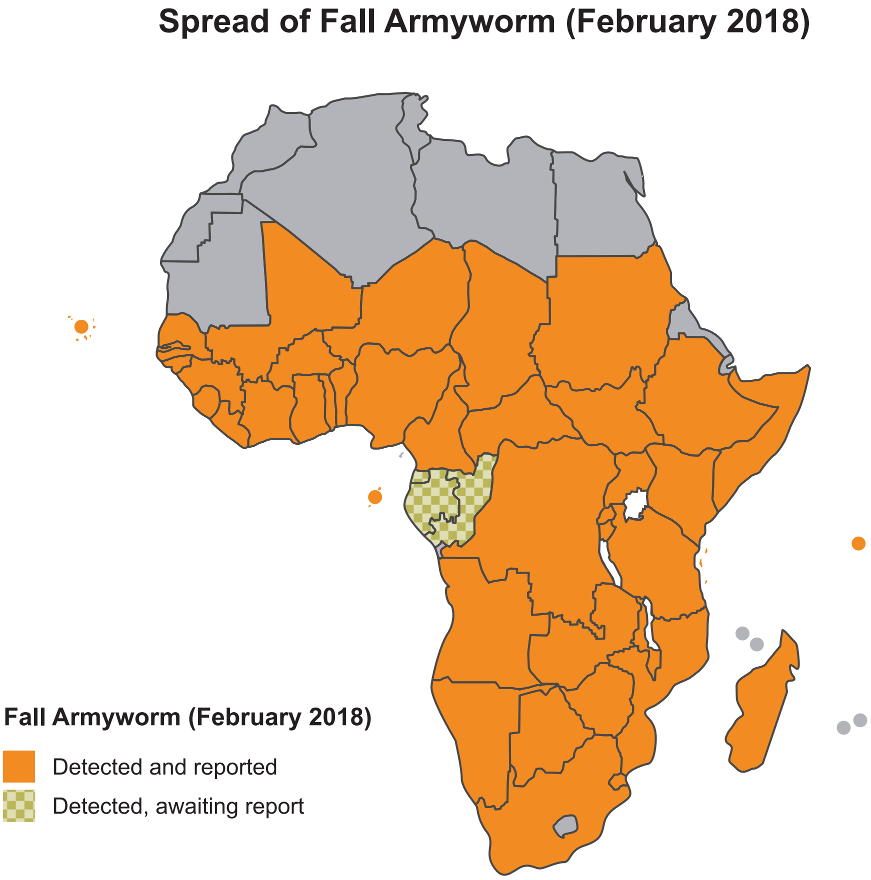


Fig. 1. Distribution of fall armyworm across the continent of Africa (Adapted from FAO, 2018).

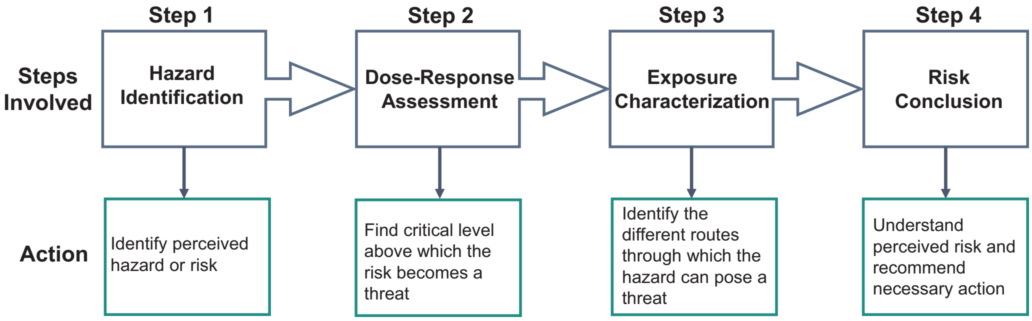


Fig. 2. An overview of risk assessment steps and the actions provided by each step.

recognized by many international agencies (USEPA, 2003). Radon, a clear and odorless gas, is naturally present in homes as a result of radioactive decay of uranium found in soil (National Research Council, 1999; USEPA, 2003). Risk assessment studies have used a combination of lung cancer incidence statistics and radon exposure measurements to create realistic estimates of the likelihood of lung cancer due to radon (Lubin and Boice, 1997; National Research Council, 1999). Eliminating exposure to radon is not feasible, however risk assessment studies have determined an action level of 4 picocuries per liter (pCi/L) of radon inside homes, above which radon mitigation efforts are recommended (National Research Council, 1999). Chronic exposure above this threshold could result in a significant risk of lung cancer (National Research Council, 1999).

4. Risk assessment of Bt maize

As with any new technology, consideration of potential harm is a critical step before large scale deployment (National Research Council, 1983). Evaluation of GM crops is no different. Genetically modified Bt crops have been a subject of significant scientific evaluation using risk assessment principles (Betz et al., 2000; Romeis et al., 2008; USEPA, 2001). Thus, the following discussion will focus on risk assessment of two of the top concerns regarding Bt maize, (a) dietary exposure to Cry proteins in humans and animals and (b) environmental impact of Cry proteins on non-target organisms. While this list does not reflect the full scope of potential risks, it will provide examples that demonstrate the process of risk assessment (Fig. 2) as applied to GM crop technologies (Table 1).

4.1. Dietary risk assessment: Cry protein example in Bt maize

4.1.1. Hazard identification

Hazard identification in dietary risk assessments begins with finding evidence of toxicity resulting from consumption. Typically, animal models are used to inform human health risks for a potential toxin. While the target pests are exposed to the toxins primarily through leaf and stalk material, Cry proteins are also expressed in other parts of the plant, including trace amounts in maize kernels which are ultimately consumed by both humans and animals (Koch et al., 2015).

4.1.2. Dose-response assessment

Repeated dose-response studies are conducted to generate a conservative value at which no adverse reactions are likely to occur (Delaney, 2007). This value is known as the “no observed adverse effect level” (NOAEL), which is expressed as milligrams of the compound per kilograms of body weight per day (mg/kg/day) and becomes the regulatory endpoint of concern to which exposure doses are compared (Delaney, 2007). Many dietary risk assessments use the following mathematical model for exposure to a given compound when determining the NOAEL (Betz et al., 2000):

$$Exposuredose(ED) = \Sigma(Residueconcentration \times Foodconsumption) / Bodyweight \tag{1}$$

To maintain conservative risk estimates, results from toxicological animal studies incorporate three, 10-fold multipliers into their NOAEL values to reflect the uncertainty of potential differences between and within species, and for sensitive members of a subpopulation (Wolt, 1999). Based on the NOAEL value obtained through toxicological evaluation of animal models, potential risk can be calculated in human populations consuming products containing the Bt Cry proteins (Delaney, 2007).

4.1.3. Exposure characterization

Based on studies conducted in multiple animal models, no sign of toxicity was observed from any class of Cry proteins, even at the maximum dose in acute oral feeding studies (Betz et al., 2000). The US Environmental Protection Agency recognizes oral toxicity animal studies that included treatment with values greater than 5000 mg of Cry protein/kg body weight (USEPA, 2001). Using 5000 mg of Cry protein/kg body weight as a hypothetical NOAEL, and applying the 1000-fold uncertainty factor to account for variation between and within species and sensitive subpopulations, would result in the human reference dose being 5 mg of Cry protein/kg body weight. Assuming the concentration of Cry protein in maize grain to be one part per million (Betz et al., 2000), and an average human body weight of 70 kg, it would require consumption of 350 kg of maize per day to attain the dosage of 5 mg of Cry protein /kg body weight. As the consumption of 350 kg of Bt maize/day is unlikely, the results of hazard identification studies suggest that exposure to Cry proteins from consumption of Bt maize by human or animal poses no risk (Betz et al., 2000; USEPA, 2001). Moreover, research on other known toxic proteins suggests that proteins are usually toxic at low doses. Therefore, further increasing the amount of potential Cry protein consumed is not likely to result in an adverse effect that was not previously observed in the described studies (Sjoblad et al., 1992).

4.1.4. Risk conclusion

Acute studies involving Cry protein consumption showed no adverse effects, therefore chronic studies were not considered necessary as the proteins were shown to be digested in the stomach, making acute exposure the main concern (USEPA, 2001). In addition, since Bt has been used as a foliar insecticide for several decades with no adverse effects to humans, the weight of evidence suggests that there is no adverse risk in human or animal consumption of Cry proteins from Bt crops (Betz et al., 2000; USEPA, 2001).

4.2. Ecological risk assessment: Impact of Bt maize on non-target species

4.2.1. Hazard identification

The monarch butterfly (*Danaus plexippus*) is a common insect in North America. Monarch adults feed on nectar from many forb species, but their caterpillars feed exclusively on non-crop milkweed species (*Asclepias* spp.), especially common milkweed (*Asclepias syriaca*), making them no threat to crop yields (Sears et al., 2001). As a member of the order Lepidoptera, it is conceivable that monarchs consuming Bt maize pollen might be sensitive to Cry proteins and this has been the focus of ecological risk assessment of Bt crops (Hellmich et al., 2001; Oberhauser et al., 2001; Pleasants et al., 2001; Sears et al., 2001). While monarchs are unlikely to emerge as larvae on Bt crop plants, the potential for pollen to disperse and land on milkweed has become a concern as a possible unintended negative ecological impact of Bt maize (Losey et al., 1999).

4.2.2. *Dose-response assessment*

In insect feeding studies using multiple classes of Cry proteins, Hellmich and coworkers reported no toxic effects due to larval consumption of Cry9C or Cry1F, but did observe sensitivity to Cry1Ac and Cry1Ab (Hellmich et al., 2001). Furthermore, dose-response testing was conducted to demonstrate toxic effects from different amounts of toxin consumed and at different larval life stages (called instars). First instars were more susceptible and displayed weight loss or death from consuming purified Cry protein compared to later stages, where second to third instars showed 12- to 23-fold greater tolerance throughout the feeding studies (Hellmich et al., 2001). Additionally, pollen consumption studies indicate that larval feeding on leaves dusted with pollen from Bt maize does not result in weight loss or death (Hellmich et al., 2001). Similar pollen feeding studies using maize hybrids containing transgenic events Bt11 and Mon810 showed that pollen concentrations of greater than 1000 pollen grains/cm^2 are needed to observe toxic effects on first instars (Hellmich et al., 2001). However, maize hybrids containing event 176, which produces significantly higher levels of Cry protein in the pollen than other hybrids tested, showed toxic effects at much lower exposure concentrations of 7–30 pollen grains/cm^2 (Hellmich et al., 2001). It should be noted the reported highly toxic event 176 did not contribute to more than 2% of the total area cultivated with maize and has since been phased out of production (Hellmich et al., 2001; Sears et al., 2001).

4.2.3. *Exposure characterization*

The exposure of monarch larvae to the Cry protein in pollen is dependent on a number of factors. Monarch larvae must be present during pollen shed, the pollen must travel to the host milkweed plants at high enough concentrations, and a large enough percentage of the monarch population must be feeding within range of Bt maize fields (Hellmich et al., 2001; Oberhauser et al., 2001; Pleasants et al., 2001; Sears et al., 2001).

Oberhauser and colleagues screened multiple sites throughout North America to measure monarch larvae density and pollen shed in surrounding maize fields (Oberhauser et al., 2001). Findings indicate that a significant overlap exists between the timing of larval emergence and pollen shedding, averaging between 15% and 40% of the time, depending on the location (Oberhauser et al., 2001). These data indicate that exposure of monarch larvae to Bt pollen in their feeding environments is possible.

Further characterization of exposure is still needed to determine the amount of pollen present on each milkweed leaf. Studies evaluating the pollen concentrations on milkweed plants in and near maize fields determined that amount of pollen present depends on proximity to maize fields, amount of rain falling during pollen shedding, and the progression of pollen release (Pleasants et al., 2001). The results indicate that 99% of leaf samples tested showed pollen counts with fewer than 900 grains/cm^2, a value below the observed toxicity level of 1000 grains/cm^2 described previously (Hellmich et al., 2001; Pleasants et al., 2001). Additionally, pollen counts dropped significantly on milkweed plants at distances of 4–5 m from the edge of maize fields, where 99.6% of samples recorded pollen counts less than 100 grains/cm^2 (Pleasants et al., 2001).

Table 1
Comparison of four steps of risk assessment as applied to different disciplines.

Steps	Engineering: Bridge maintenance	Medicine: Cancer risk	Ecology: GM Cry proteins in non-target species, e.g., Monarch butterfly	Agriculture: GM Cry proteins in human and animal diets
Hazard identification	Improperly maintained bridges can be hazardous to humans.	Radon, a known carcinogen, is present in the environment and can reach high concentrations when contained in homes.	Pollen from Bt plants contains Cry protein.	Cry proteins are present in maize grain.
Dose-response assessment	Natural and human-made stressors are known to cause deterioration over time.	Increasing exposure to radon increases risk of lung cancer.	Threshold concentration of pollen consumption was found above which toxicity occurs.	Consumption of Cry protein above a conservative value can cause toxicity.
Exposure characterization	The bridge has 300,000 vehicles pass /year and is exposed to climate changes seen in the Midwestern US.	Radon cannot permeate skin but can pass through lung membranes. Radon concentration in homes can be measured.	Pollen does not travel far enough or reach significant numbers of larvae to cause damage.	Humans consume low levels of Cry protein relative to their body weight.
Risk conclusion	Bridge is safe and not likely to have a hazardous impact in the next 5 years.	Household exposure below 4 pCi/L does not result in significant health risks.	Monarch butterfly populations are not likely to suffer from the use of Bt maize.	It is safe for humans to consume grain produced from Bt maize plants.

4.2.4. Risk conclusion

When a cross-comparison of the results of hazard identification, dose-response studies, and exposure characterization is done, the overall risk posed to the monarch population appears negligible (Sears et al., 2001; Wolt et al., 2003). Importantly, the toxic conditions created in laboratory studies do not accurately reflect what is found in the typical monarch breeding environment. The small likelihood of toxic conditions manifesting in any given area suggests that the impact on the total population of the species is negligible (Hellmich et al., 2001). Furthermore, additional exposure-limiting considerations were not discussed here; including overall percentage of maize fields that do not contain Bt traits and total amount of milkweed plants that are not located in agricultural areas. This further lowers the monarch population's exposure to Cry proteins, decreasing the potential for risk (Sears et al., 2001; Wolt et al., 2003).

Assessment of the impact of Bt crops on non-target Lepidopterans such as the monarch butterfly is just one example of an ecological risk assessment. However, it does illustrate the importance of following the iterative process of risk assessment to be able to make informed decisions regarding safety (Fig. 2). Many other examples of ecological risk assessment of Bt crops have been successfully conducted by following a similar framework, including those with focus on concerns such as impact on aquatic organisms (Wolt and Peterson, 2010) and impact on other non-target species (Shu et al., 2018).

5. Potential opportunities resulting from adoption of Bt crops

After nearly two decades of commercialization, GM crop use is continuing to rise globally (ISAAA, 2017). The upward trend suggests that adopting one or more GM traits confers tangible benefit to the farmers to overcome higher seed cost (Carpenter, 2010). Numerous studies have reported the results of converting to GM crop varieties regarding yields, costs, and labor (Brookes and Barfoot, 2017; Smyth, 2017). Specifically, plant-incorporated protection using Cry protein genes has been proven to be effective at controlling damaging pest populations, including many of those that threaten crops of economic importance in developing countries such as maize and cotton (Mugo, 2011). However, adoption of GM crops would be delayed in countries that do not have biosafety frameworks to enable commercialization of GM crops to address effects of climate change and population pressures (FAO, 2015).

5.1. Plant protection against insect pests

Bt maize varieties provide protection against Lepidopteran and Coleopteran insect pests (Mugo et al., 2011; Siebert et al., 2012), including FAW (Box 1). This is important for regions such as Africa (Fig. 1) where locally adapted maize varieties lack resistance to the FAW and where Bt maize is only commercially available in South Africa (Prasanna et al., 2018; Box 1). As previously stated, death of targeted insect pests is not only highly effective, but also rapid, resulting in little to no observable damage to Bt maize plants. Additionally, due to the specificity of the mode of action of Cry proteins, beneficial non-target arthropods are preserved and can aid in control of other crop pests, such as aphids (Betz et al., 2000).

While the use of Bt maize will provide additional pest management options for farmers, there is a need for education on the development of insect resistance to Bt maize. Development of insect resistance to Bt maize is a reality if measures are not taken to fully implement insect resistance management strategies (Box 1). Using insect resistance management methods, such as planting a non-Bt maize refuge, will promote longevity of the Bt maize technology. In locations where FAW resistance to Cry proteins has already developed, insecticides are being used in combination with Bt maize to assist with the control (Burtet et al., 2017). In places where GM crops have not been widely used, however, the effectiveness of Bt maize against FAW can be important for farmers with limited control options against this pest (Paini et al., 2016). Due to the documented ability of FAW to rapidly evolve resistance to certain Cry proteins (Box 1), it will be imperative that insect resistance management strategies are used simultaneously with Bt maize.

5.2. Reduced fungal infection and mycotoxin

An additional benefit of Bt crops is reduced fungal infection. Damage caused by organisms feeding on plants, such as maize borers, promotes growth of mycotoxin-producing fungi in damaged plants (Betz et al., 2000). Two of the most significant sources of hazardous fungal mycotoxins are fumonisin-producing *Fusarium verticilloides* and *F. proliferatum* and aflatoxin-producing *Aspergillus flavus* and *A. parasiticus* (Bakan et al., 2002; Barrett, 2005). Chronic aflatoxin exposure has been linked to development of liver cancer, and acute exposure to high doses, while rare, can result in fatal liver damage (Barrett, 2005). Aflatoxin contamination can be problematic in certain parts of Africa, as illustrated by the 2004 outbreak in Kenya where contaminated maize caused 317 cases of acute aflatoxin-related illness, including 125 deaths (Barrett, 2005; Lewis et al., 2005). In addition, fumonisins have been associated with increased rates of esophageal and liver cancer (Braun and Wink, 2018). The use of Bt traits to control pests that contribute to the spread of fungal pathogens has been shown to reduce levels of mycotoxins from both aflatoxins and fumonisins in multiple studies, both in controlled environments and in field trials (Bakan et al., 2002; Hammond et al., 2004; Munkvold et al., 1999). While Bt varieties of maize will not completely eliminate mycotoxins and fumonisins, it is an effective way to reduce their impact, especially in developing countries (Randall, 2016).

5.3. Increase in yield and decrease in agricultural inputs

Bt crops impact yield by decreasing the amount of produce lost due to infestation, making gains from adoption of the technology variable, and dependent upon pest pressure for a given season (Betz et al., 2000; Gómez-Barbero et al., 2008). During early stages of adoption in the United States, Bt maize resulted in an increase in yield between 0.27 and 0.75 t per hectare over comparable non-transgenic lines in 1998–1999 (Gianessi and Carpenter, 1999). In addition, multi-state trials in the United States revealed that Bt maize is more effective in controlling *H. zea* than non-Bt maize sprayed with insecticides (Shelton et al., 2013). An analysis on the global economic impact of GM technology from 1996 to 2015 showed a benefit of $167.8 billion to farm income, with 49% and 51% of farmers in developed and developing countries, respectively, sharing these economic benefits. These benefits are gained from about 72% in yield and production gains and 28% from cost savings (Brookes and Barfoot, 2017). Cumulatively, the increased yields and decreased costs of pesticides result in profits that exceed the increased seed cost (Betz et al., 2000; Klumper and Qaim, 2014). In a comprehensive literature-based analysis of the adoption of GM crops relative to their traditionally-bred counterparts, Klümper and Qaim observed an average decrease of 37% in pesticide use and a 39% reduction in pesticide costs for farmers (Klumper and Qaim, 2014). Similarly, Betz and coworkers reported comparable reductions across multiple regions, including the United States, Australia, and China (Betz et al., 2000).

5.4. Opportunities for developing countries

Bt crops have the potential to add to the income of smallholder farm households, thus reducing poverty and improving food security in the small farm sector. The most pronounced yield and farmer profit gains would be expected in developing countries over developed countries (Klumper and Qaim, 2014). In India, use of Bt cotton increased farmers' profit by 50% and reduced food insecurity by 15–20% (Kathage and

Box 1

Impact of FAW across Africa.

Fall armyworm (FAW) can decimate a maize crop and has now been reported in all Sub-Saharan Africa except for Djibouti, Eritrea and Lesotho (Fig. 1) (FAO, 2018). Research conducted on the FAW in Brazil has shown the ability of the insect to evolve resistance to Bt in as few as three years (Fatoretto et al., 2017). FAW resistance can be attributed to many factors including the biology and genetics of FAW, environmental conditions, crop production management practices and lack of insect resistance management.

Given the current distribution of FAW in Africa and the documented speed of insect resistance evolution in Brazil, what can be done to reduce the impact of FAW on maize crops in Africa?

Two main strategies could expand management options for farmers in Africa:

- Adoption of GM Bt maize hybrids throughout Sub-Saharan Africa (ISAAA, 2018)
- Education and training on proper insect resistance management following approval of GM maize crops; especially training on proper implementation of refuge (Fatoretto et al., 2017; FAO, 2018).

The reality of a refuge means that FAW will destroy the maize in this portion of the field, equaling little or no harvestable yield. Education and training for farmers will be important especially when it comes to using refuge as part of a long-term insect resistance management plan. However, implementing and monitoring non-Bt refuges will likely be a challenge in the smallholder farm context as seen in India and China (Tabashnik et al., 2013). Mixing non-Bt seeds into Bt seed bags ("refuge in a bag") may be a more suitable option, at least when seeds are purchased in the formal seed market. Adoption of Bt maize hybrids requires change in policy. Research, data and education are important components to policy change. Currently, 13 countries in Africa are engaged in research and testing of GM crops (ISAAA, 2017).

Qaim, 2012; Qaim and Kouser, 2013). Similar gains from adoption of Bt traits to control damaging new pests (Fig. 1) would be expected to result in yield protection, increased wages for those working in agriculture and potentially a more stable food supply for the entire region (Prasanna et al., 2018).

Currently there are only two countries in Africa, South Africa and Sudan, growing commercialized GM crops. Eleven additional countries in Sub-Saharan Africa are engaged in GM research trials (ISAAA, 2017). Given the increasing food demand and the threats of emerging insect pests to crop production (Fig. 1), there is a need to expedite the approval and commercialization of GM crops, such as Bt maize, to benefit farmers and consumers (Box 1). There has been significant scrutiny of GM technology with no substantial evidence of risk to humans. Making GM technology available provides farmers with another option to protect crops from pests and increase crop yields.

6. Challenges and benefits of alternative approaches to GM crops

Continued utilization of traditionally-bred crops is the expected alternative to the adoption of GM varieties. However, this decision is not without challenge – specifically surrounding the Bt insect control example being discussed (Table 2). Although there are some benefits of continuing to plant traditionally bred crops, such as lower seed cost or no export restrictions, the risks outweigh the benefits. In fact, some of these benefits may become negligible once performance of the non-GM seeds is considered. For example, reducing seed cost by turning to traditionally bred crops might result in yield losses due to lack of resistance against insects. Additionally, in the case of traditionally-bred crops having no export restrictions, the entire harvested lot can be rejected if fungal contamination is detected.

If farmers in developing countries, for example in Africa, continue to utilize non-GM crop technologies pesticide use may increase to protect crop losses. However, GM crops cannot necessarily prevent periodic outbreaks of new pests and diseases, which is therefore a risk not exclusive to non-GM crop scenarios. Nonetheless, increased use of pesticides and pest outbreaks will be more concerning as the population in regions such as Africa increases in the coming decades (UN DESA, 2015), and if pest pressure increases (Fig. 1, Box 1). Since adoption of Bt crops can reduce the use of pesticides (Qiao et al., 2017), there is a need to establish proper biosafety frameworks in developing nations that could benefit from GM crop traits including but not limited to Bt insect control traits.

7. Conclusions

The rapidly changing climate and expanding human population are a threat to global food security. One of the solutions to increasing food security is to enhance agricultural productivity. This requires cutting-edge technologies, including GM technologies, which can be utilized to develop stress-tolerant and more nutritious crop varieties, and to protect natural resources and human health. The development of GM crops has been subjected to careful examination and study. Even with approval of expert scientists and medical personnel, the application of GM technology has moved forward carefully and conservatively concerning potential unintended consequences. As a result, various food and health products that improve quality of life have been created. Specifically, agriculture has seen unprecedented gains worldwide from GM technologies concerning insect resistance. While each new GM product is evaluated on a case-by-case basis, approved commercial products, such as those containing Bt genes, have been subjected to rigorous scientific scrutiny through a risk assessment process that relies upon expertise from a variety of different fields. Risks associated with GM crops have

Table 2

Comparison of advantages and disadvantages of GM vs. traditionally-bred crops with regards to insect resistance (Betz et al., 2000; Falck-Zepeda et al., 2013).

	Benefit	Risk
Traditionally-bred varieties	• Lower cost of seed • Fit the current biosafety frameworks • No restriction of export of product	• Susceptible to yield loss due to lack of effective resistance against insects • Insect damage results in fungal infection • Seed lots risk being rejected due to fungal contamination
GM varieties	• Plant-incorporated insect protection • Decreased pesticide costs and labor • Lower risk of fungal infection • Increased yields	• Increased seed cost • Requires established biosafety framework • GM status may limit export opportunities • Rejection due to negative public perception

proven to be low to non-existent. The opportunities for developing countries, where large proportions of the land area and population are dedicated to farming, to improve agricultural output by adopting GM technologies is significant. GM traits, including but not limited to plant-incorporated Bt protection, should be considered as a tool for improving crop yields, food safety, and income for food-insecure farmers.

However, adoption of GM technologies will not succeed if imposed on farmers. There must be public discourse regarding the science and risk procedures guiding development of GM crops. Biosafety regulatory systems and extension education networks are needed to ensure the information about risks and benefits of GM technologies is widely shared. The production of GM crops alone will not solve the challenges of increasing populations and the changing climate, but when combined with other production practices this technology is an important tool to help address these global concerns. Risk assessment can prove to be an important component of the GM technology evaluation process and a way to communicate to the public any associated hazards or disadvantages of GM technology.

Acknowledgements

We apologize to those colleagues whose important contributions may have been omitted owing to space constraints.

Conflict of interest

None

Declarations of Interest

None

Funding

This work did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

Adang, M.J., Crickmore, N., Jurat-Fuentes, J.L., 2014. Diversity of *Bacillus thuringiensis* crystal toxins and mechanism of action. In: Dhadialla, T.S., Gill, S.S. (Eds.), Adv. Insect Physiol. 47. Elsevier Academic Press, Waltham, MA, pp. 39–87.

Bakan, B., Melcion, D., Richard-Molard, D., Cahagnier, B., 2002. Fungal growth and fusarium mycotoxin content in isogenic traditional maize and genetically modified maize grown in France and Spain. J. Agric. Food Chem. 50, 728–731.

Barrett, J.R., 2005. Liver cancer and aflatoxin: new information from the Kenyan outbreak. Environ. Health Perspect. 113, A837–A838.

Betz, F.S., Hammond, B.G., Fuchs, R.L., 2000. Safety and advantages of *Bacillus thuringiensis*-protected plants to control insect pests. Regul. Toxicol. Pharmacol. 32, 156–173.

Braun, M.S., Wink, M., 2018. Exposure, occurrence, and chemistry of fumonisins and their cryptic derivatives. Compr. Rev. Food Sci. Food Saf. 17, 769–791.

Brookes, G., Barfoot, P., 2017. Farm income and production impacts of using GM crop technology 1996–2015. GM Crops Food 8, 156–193.

Burtet, L.M., Bernardi, O., Melo, A.A., Pes, M.P., Strahl, T.T., Guedes, J.V.C., 2017. Managing fall armyworm, *Spodoptera frugiperda* (Lepidoptera: noctuidae), with Bt maize and insecticides in southern Brazil. Pest Manag. Sci. 73, 2569–2577.

Carpenter, J.E., 2010. Peer-reviewed surveys indicate positive impact of commercialized GM crops. Nat. Biotechnol. 28, 319–321.

De Groote, H., 2002. Maize yield losses from stemborers in Kenya. Int. J. Trop. Insect Sci. 22, 89–96.

Delaney, B., 2007. Strategies to evaluate the safety of bioengineered foods. Int. J. Toxicol. 26, 389–399.

Falck-Zepeda, J., Gruère, G., Sithole-Niang, I., 2013. Genetically Modified Crops in Africa: Economic and Policy Lessons From Countries South of the Sahara. International Food Policy Research Institute, Washington, DC.

FAO, 2015. Regional Overview of Food Insecurity: African Food Security Prospects Brighter Than Ever. Food and Agriculture Organization of the United Nations, Accra (FAO).

FAO, 2018. Sustainable management of the fall armyworm in Africa: A framework for partnership. 〈http://www.fao.org/3/I9160EN/i9160en.pdf〉 (accessed 30 July 2018).

Fatoretto, J.C., Michel, A.P., Silva Filho, M.C., Silva, N., 2017. Adaptive potential of fall armyworm (Lepidoptera: noctuidae) limits Bt trait durability in Brazil. J. Integr. Pest Manag. 8, 17.

Gianessi, L.P., Carpenter, J.E., 1999. Agricultural Biotechnology: Insect Control Benefits. National Center for Food and Agricultural Policy, Washington, DC.

Gómez-Barbero, M., Berbel, J., Rodríguez-Cerezo, E., 2008. Bt corn in Spain–the performance of the EU's first GM crop. Nat. Biotechnol. 26, 384–386.

Hammond, B.G., Campbell, K.W., Pilcher, C.D., Degooyer, T.A., Robinson, A.E., McMillen, B.L., Spangler, S.M., Riordan, S.G., Rice, L.G., Richard, J.L., 2004. Lower fumonisin mycotoxin levels in the grain of Bt Corn grown in the United States in 2000–2002. J. Agric. Food Chem. 52, 1390–1397.

Hellmich, R.L., Siegfried, B.D., Sears, M.K., Stanley-Horn, D.E., Daniels, M.J., Mattila, H.R., Spencer, T., Bidne, K.G., Lewis, L.C., 2001. Monarch larvae sensitivity to *Bacillus thuringiensis*-purified proteins and pollen. Proc. Natl. Acad. Sci. 98, 11925–11930.

Imhof, D., 2004. Risk Assessment of Existing Bridge Structures (Ph. D. Dissertation). Kings College, University of Cambridge.

ISAAA, 2017. Global Status of Commercialized Biotech/GM Crops in 2017: Biotech Crop Adoption Surges as Economic Benefits Accumulate in 22 years (ISAAA Brief No. 53). ISAAA, Ithaca, NY.

ISAAA, 2018. Scientists recommend Bt maize as solution to fall armyworm infestation in Kenya. 〈http://www.isaaa.org/kc/cropbiotechupdate/article/default.asp?ID=16136〉 (accessed 30 July 2018).

Kathage, J., Qaim, M., 2012. Economic impacts and impact dynamics of Bt (*Bacillus thuringiensis*) cotton in India. Proc. Natl. Acad. Sci. 109, 11652–11656.

Khush, G.S., 2012. Genetically modified crops: the fastest adopted crop technology in the history of modern agriculture. Agric. Food Secur. 1, 12.

Klumper, W., Qaim, M., 2014. A meta-analysis of the impacts of genetically modified crops. PLoS One. 9, e111629.

Koch, M.S., Ward, J.M., Levine, S.L., Baum, J.A., Vicini, J.L., Hammond, B.G., 2015. The food and environmental safety of Bt crops. Front. Plant Sci. 6, 283.

Lewis, L., Onsongo, M., Njapau, H., Schurz-Rogers, H., Luber, G., Kieszak, S., Nyamongo, J., Backer, L., Dahiye, A.M., Misore, A., Decock, K., Rubin, C., Group, T.K.A.I., 2005. Aflatoxin contamination of commercial maize products during an outbreak of acute aflatoxicosis in Eastern and Central Kenya. Environ. Health Perspect. 113, 1763–1767.

Losey, J.E., Rayor, L.S., Carter, M.E., 1999. Transgenic pollen harms monarch larvae. Nature 399, 214.

Lubin, J.H., Boice, J.D., 1997. Lung cancer risk from residential radon: meta-analysis of eight epidemiologic studies. J. Natl. Cancer Inst. 89, 49–57.

Mugo, S., Murenga, M.G., Karaya, H., Tende, R., Taracha, C., Gichuki, S., Ininda, J., M'Bijjewe, K., Chavangi, A., 2011. Control of Busseola fusca and chilo partellus stem borers by *bacillus thuringiensis* (Bt)-δ-endotoxins from Cry1Ab gene event MON810in greenhouse containment trials. Afr. J. Biotechnol. 10, 4719–4724.

Munkvold, G.P., Hellmich, R.L., Rice, L.G., 1999. Comparison of fumonisin concentrations in kernels of transgenic Bt maize hybrids and nontransgenic hybrids. Plant Dis. 83, 130–138.

National Research Council, 1983. Risk Assessment in the Federal Government: Managing the Process. The National Academies Press, Washington, DC.

National Research Council, 1999. Health Effects of Exposure to Radon: BEIR VI. The National Academies Press, Washington, DC.

National Research Council, 2003. Risk Assessment: Evaluation Risks to Human Health and Safety. In: Occupational Health and Safety in the Care and Use of Nonhuman Primates. The National Academies Press, Washington, DC, pp. 68–82.

Oberhauser, K.S., Prysby, M.D., Mattila, H.R., Stanley-Horn, D.E., Sears, M.K., Dively, G., Olson, E., Pleasants, J.M., Lam, W.-K.F., Hellmich, R.L., 2001. Temporal and spatial overlap between monarch larvae and corn pollen. Proc. Natl. Acad. Sci. 98, 11913–11918.

Paarlberg, R.L., 2002. The real threat to GM crops in poor countries: consumer and policy resistance to GM foods in rich countries. Food Policy 27, 247–250.

Paarlberg, R.L., 2010. GMO foods and crops: Africa's choice. New Biotechnol. 27, 609–613.

D.R. Paini, A.W. Sheppard, D.C. Cook, P.J. De Barro, S.P. Worner, M.B. Thomas (2016). Global Threat to Agriculture From Invasive Species. Proceedings of the National Academy of Sciences, 7575–7579.

Pleasants, J.M., Hellmich, R.L., Dively, G.P., Sears, M.K., Stanley-Horn, D.E., Mattila, H.R., Foster, J.E., Clark, P., Jones, G.D., 2001. Corn pollen deposition on milkweeds in and near cornfields. Proc. Natl. Acad. Sci. 98, 11919–11924.

Prasanna, B.M., Huesing, J.E., Eddy, R., Peschke, V.M., 2018. Fall Armyworm in Africa: A Guide for Integrated Pest Management, First edition. CDMX, CIMMYT, Mexico.

Qaim, M., Kouser, S., 2013. Genetically modified crops and food security. PLoS One. 8, e64879.

Qiao, F.-B., Huang, J.-K., Wang, S.-K., Li, Q., 2017. The impact of Bt cotton adoption on the stability of pesticide use. J. Integr. Agric. 16, 2346–2356.

Randall, R., 2016. GMO Bt corn's underrated ability to reduce mycotoxins benefits health and economy. 〈https://geneticliteracyproject.org/2016/09/23/gmo-bt-corns-underrated-ability-to-reduce-mycotoxins-benefits-health-and-economy/〉 (accessed Jul 9, 2018).

Roh, J.Y., Choi, J.Y., Li, M.S., Jin, B.R., Je, Y.H., 2007. *Bacillus thuringiensis* as a specific, safe, and effective tool for insect pest control. J. Microbiol. Biotechnol. 17, 547–559.

Romeis, J., Bartsch, D., Bigler, F., Candolfi, M.P., Gielkens, M.M.C., Hartley, S.E., Hellmich, R.L., Huesing, J.E., Jepson, P.C., Layton, R., Quemada, H., Raybould, A., Rose, R.I., Schiemann, J., Sears, M.K., Shelton, A.M., Sweet, J., Vaituzis, Z., Wolt, J.D., 2008. Assessment of risk of insect-resistant transgenic crops to nontarget arthropods. Nat. Biotechnol. 26, 203–208.

Sears, M.K., Hellmich, R.L., Stanley-Horn, D.E., Oberhauser, K.S., Pleasants, J.M., Mattila, H.R., Siegfried, B.D., Dively, G.P., 2001. Impact of Bt corn pollen on monarch butterfly populations: a risk assessment. Proc. Natl. Acad. Sci. 98, 11937–11942.

Shelton, A.M., Olmstead, D.L., Burkness, E.C., Hutchison, W.D., Dively, G., Welty, C., Sparks, A.N., 2013. Multi-state trials of Bt sweet corn varieties for control of the corn earworm (Lepidoptera: noctuidae). J. Econ. Entomol. 106, 2151–2159.

Shu, Y., Romeis, J., Meissle, M., 2018. No interactions of stacked Bt maize with the non-target aphid *Rhopalosiphum padi* and the spider mite *Tetranychus urticae*. Front. Plant Sci. 9, 39.

Siebert, M.W., Nolting, S.P., Hendrix, W., Dhavala, S., Craig, C., Leonard, B.R., Stewart, S.D., All, J., Musser, F.R., Buntin, G.D., Samuel, L., 2012. Evaluation of corn hybrids expressing Cry1F, cry1A.105, Cry2Ab2, Cry34Ab1/Cry35Ab1, and Cry3Bb1 against southern United States insect pests. J. Econ. Entomol. 105, 1825–1834.

Sjoblad, R.D., McClintock, J.T., Engler, R., 1992. Toxicological considerations for protein components of biological pesticide products. Regul. Toxicol. Pharmacol. 15, 3–9.

Smyth, S.J., 2017. Genetically modified crops, regulatory delays, and international trade. Food Energy Secur. 6, 78–86.

Stewart, M.G., Rosowsky, D.V., Val, D.V., 2001. Reliability-based bridge assessment using risk-ranking decision analysis. Struct. Saf. 23, 397–405.

Tabashnik, B.E., Brévault, T., Carrière, Y., 2013. Insect resistance to Bt crops: lessons from the first billion acres. Nat. Biotechnol. 31, 510–521.

United Nations, Department of Economic and Social Affairs, Population Division (UN DESA), 2015. World population prospects: The 2015 revision, key findings and advance tables. Working paper no. ESA/P/WP.241.

USEPA, 2001. Bt plant-incorporated protectants: Biopesticides registration action document. 〈https://www3.epa.gov/pesticides/chem_search/reg_actions/pip/bt_brad2/2-id_health.pdf〉 (accessed Jul 9, 2018).

USEPA, 2003. EPA Assessment of Risks From Radon in Homes. Office of Radiation and Indoor Air, Washington, DC.

Wolt, J., Keese, P., Raybould, A., Fitzpatrick, J., Burachik, M., Gray, A., Olin, S., Schiemann, J., Sears, M., Wu, F., 2010. Problem formulation in the environmental risk assessment for genetically modified plants. Transgenic Res. 19, 425–436.

Wolt, J.D., 1999. Exposure endpoint selection in acute dietary risk assessment. Regul. Toxicol. Pharmacol. 29, 279–286.

Wolt, J.D., Peterson, R.K., 2010. Prospective formulation of environmental risk assessments: probabilistic screening for Cry1A(b) maize risk to aquatic insects. Ecotoxicol. Environ. Saf. 73, 1182–1188.

Wolt, J.D., Peterson, R.K.D., Bystrak, P., Meade, T., 2003. A screening level approach for nontarget insect risk assessment: transgenic Bt corn pollen and the monarch butterfly (Lepidoptera: danaidae). Environ. Entomol. 32, 237–246.