Review

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Bt maize and integrated pest management - a European perspective

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Abstract

The European corn borer (*Ostrinia nubilalis*), the Mediterranean corn borer (*Sesamia nonagrioides*) and the western corn rootworm (*Diabrotica virgifera virgifera*) are the main arthropod pests in European maize production. Practised pest control includes chemical control, biological control and cultural control such as ploughing and crop rotation. A pest control option that is available since 1996 is maize varieties that are genetically engineered (GE) to produce insecticidal compounds. GE maize varieties available today express one or several genes from *Bacillus thuringiensis* (*Bt*) that target corn borers or corn rootworms. Incentives to growing *Bt* maize are simplified farm operations, high pest control efficiency, improved grain quality and ecological benefits. Limitations include the risk of resistance evolution in target pest populations, risk of secondary pest outbreaks and increased administration to comply with licence agreements. Growers willing to plant *Bt* maize in the European Union (EU) often face the problem that authorisation is denied. Only one *Bt* maize transformation event (MON810) is currently authorised for commercial cultivation, and some national authorities have banned cultivation. Spain is the only EU member state where *Bt* maize adoption levels are currently delivering farm income gains near full potential levels. In an integrated pest management (IPM) context, *Bt* maize can be regarded as a preventive (host plant resistance) or a responsive pest control measure. In any case, *Bt* maize is a highly specific tool that efficiently controls the main pests and allows combination with other preventive or responsive measures to solve other agricultural problems including those with secondary pests.

Keywords: genetically modified crops; insect pests; integrated production; integrated farming; Cry1Ab; Cry3Bb

1 INTRODUCTION

Genetically engineered (GE) crops are grown on a steadily increasing global area, reaching 148 million hectares in 2010.[1] The area of biotech crops was largest in the United States (67 million hectares), followed by Brazil and Argentina (25 and 23 million hectares respectively), India, Canada, China, Paraguay, Pakistan, South Africa (2–9 million hectares) and 20 more countries. While 89 million hectares were cultivated with crops that carry a gene providing tolerance against a particular herbicidal active substance, crops with resistance to certain insect pests were planted on 26 million hectares. Crops with both properties (so-called stacked events) were grown on 32 million hectares worldwide. In addition, small areas have been planted with virus-resistant crops.[1] In the European Union (EU), insect-resistant maize has been cultivated since 1998, and GE potato with modified starch production (Amflora) has been grown since 2010 on a total of 245 hectares. Herbicide-tolerant crops are currently not grown commercially in the EU. Within the next 5 years, the number of transformation events for herbicide tolerance and insect resistance is predicted to increase, and new traits will be commercialised, such as optimised product composition for biofuel or industrial inputs, improved nutrient profiles and abiotic stress tolerance, e.g. against drought or salt.[2,3]

In most of today's GE crops, insect resistance is achieved by the expression of one or more genes from the bacterium *Bacillus thuringiensis* (*Bt*) that encode insecticidal crystal (Cry) proteins. Cry-protein-producing *Bt* bacteria are fairly abundant in European agricultural fields.[4] Cry proteins are known for their narrow spectrum of activity, and microbial *Bt* products have a long history of safe use.[5] The most important crop transformed with *Bt* genes is maize, with a global area of 39 million hectares, followed by cotton, with 20 million hectares in 2010.[1] In the United States, *Bt* maize varieties producing a combination of six different Cry proteins (SmartStax™) have been approved recently, and maize expressing a vegetative insecticidal protein (Vip3A) from *Bt* has been commercialised.[6]

In the European Union, Spain has been leading commercial production of *Bt* maize since 1998, with 76 575 hectares in 2010. In addition, Portugal, the Czech Republic, Poland, Slovakia and Romania cultivated *Bt* maize on a total of 14 600 hectares (Fig. 1).[1] Compared with the total maize-cropping area of 13 million hectares in the 27 EU member states,[7] the proportion of *Bt* maize so far has remained below 1%. In certain areas of Spain with high corn borer infestations (e.g. Catalonia), however, adoption levels reached 84% in 2010.[1]

The present article addresses the major pests in European maize production, how they are controlled in conventional agriculture, incentives and limitations of growing *Bt* maize and what role *Bt* maize can play in integrated pest management (IPM) systems. Although many new *Bt* maize events that are currently under evaluation in the EU are stacked events that provide resistance to insect pests and tolerance to herbicidal active substances (Table 1),

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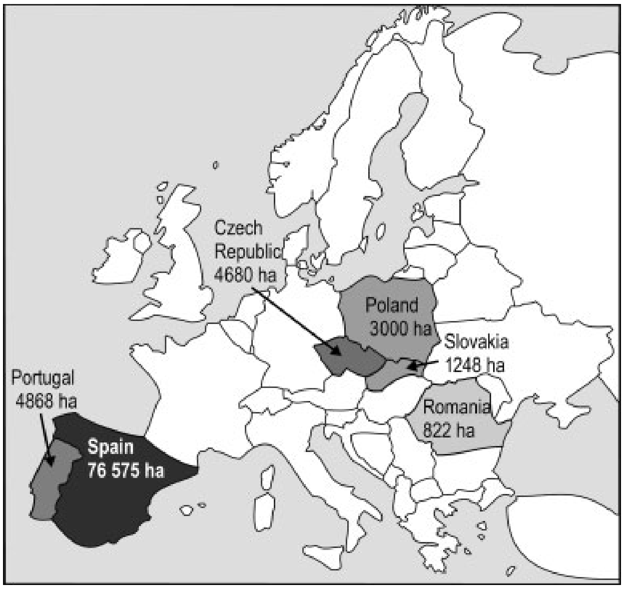

Figure 1. *Bt* maize cultivation 2010 in Europe (in hectares). Data from James.[1] Darker shading reflects larger cultivation area.

this review focuses on the insect resistance trait. Benefits and risks associated with herbicide-tolerant maize are discussed for the European situation by Dewar.[8]

2 PEST PROBLEMS IN EUROPEAN MAIZE PRODUCTION

The currently most important arthropod pest of maize in Europe is the European corn borer, *Ostrinia nubilalis* (Hbn.) (Lepidoptera: Crambidae).[9] The species is widespread throughout Europe (Fig. 2). Another stem-boring Lepidoptera is the Mediterranean corn borer, *Sesamia nonagrioides* Lefèbvre (Lepidoptera: Noctuidae), which is largely restricted to the Mediterranean region (Fig. 2). The larvae of both species are stalk-boring caterpillars that damage the ears as well as the stalks by chewing tunnels. This leads to reduced plant development and nutrient and water transport and can cause the maize stems and ears to break. In the Mediterranean region, both corn-boring species have 2–3 generations, while, in northern countries, *O. nubilalis* has one generation.[10–12] Between 2 and 4 million hectares of maize suffer economic damage due to corn-boring pests in the EU.[13] Since 1965, *O. nubilalis* populations have been expanding in central, northern and eastern Europe, following the increased cultivation of maize. In the future, the distribution of corn borers is expected to increase further, mainly because of warmer climatic conditions.

In the mid-1980s, the western corn rootworm, *Diabrotica virgifera virgifera* LeConte (Coleoptera: Chrysomelidae), was accidentally introduced into Europe. Since 1992 it has been invading the continent at an average rate of 40 km per year (Fig. 2).[14] The larvae of this beetle feed on maize roots, thereby decreasing nutrient and water uptake and plant stability. Adults feeding on silk and grains are particularly damaging in seed and sweet maize production.[15] The pest is considered most destructive for maize production in the United States, and economic damage has been reported from central and eastern European countries as well as Italy.[9] In Europe, populations are expected to expand further.[16]

Other arthropod pests in maize are of more regional or of minor importance and include noctuid lepidopteran pests such as *Sesamia cretica* Led., *Agrotis* spp., *Helicoverpa armigera* (Hbn.) and *Mythimna unipuncta* (Haw.), coleopteran pests such as wireworms (*Agriotes* spp., Elateridae), cereal leaf beetles (*Oulema melanopus* L., Chrysomelidae), sap beetles [*Glischrochilus quadrisignatus* (Say), Nitidulidae], the corn weevil (*Tanymecus dilaticollis* Gyll., Curculionidae) and white grubs (*Melolontha melolontha* L., Scarabaeidae), different species of flies and midges including the frit fly (*Oscinella frit* L., Chloropidae) and other species [*Delia platura* (Meig.), *Geomyza* spp., *Tipula* spp.), as well as spider mites (*Tetranychus* spp.), aphids (Aphididae), leafhoppers (Cicadellidae) and thrips (Thysanoptera).[9,17]

3 PRACTISED PEST CONTROL MEASURES

If damage by pests and estimated yield loss is low, and if current pest control options show little success, no pest control might be the most economic strategy. However, in areas highly infested with the European corn borer, yield losses without control measures range typically between 5 and 30%.[9] In several European countries, corn borers remain untreated in spite of economic losses.[13] For the western corn rootworm, similar values of yield loss across Europe are assumed, and modelling revealed that this pest would cause an estimated damage worth €472 million annually if no particular pest control measures were applied.[18]

In the following, the main measures currently applied to control corn borers and corn rootworm in Europe are discussed. Research into more or improved chemical, biological, biotechnical and cultural methods has been conducted, but commercial application has often not been achieved yet because of constraints in availability, efficacy, knowledge and costs.[9]

3.1 Chemical control

In European maize production, the European corn borer and other arthropod pests are often controlled with broad-spectrum insecticides including pyrethroids and organophosphates.[9] Spraying is effective only when timed shortly after the eggs hatch and before the larvae bore into the maize stem. This requires frequent scouting and often several treatments. The Mediterranean corn borer, however, is even more difficult to reach with foliar insecticides, because the females lay eggs between the sheath and the stem of maize plants, where the larvae are protected. Against adults of the western corn rootworm, insecticide sprays are often applied in central and eastern Europe if infestations are high to prevent silk clipping in seed and sweet maize production and to reduce the number of eggs for the next growing season in continuous maize production.[19] To control the larval stage of this pest, seed treatments and soil insecticides applied at planting are frequently used.[19] In regions where western corn rootworm populations have been detected but are not yet established (e.g. in south-west Germany, France and the United Kingdom), eradication programmes that are mandatory in the EU include the application of chemical insecticides and planting restrictions of maize in buffer zones surrounding new introduction points.[20] In spite of these measures, the success in delaying the spread of the pest appears to be limited.[20]

In general, chemical insecticides are cheap and growers are equipped and experienced in using them. Foliar application of insecticides on high maize stands, however, requires special and expensive spray equipment. The spectrum of activity is usually

Table 1. Genetically modified maize events that have been approved or are awaiting approval for cultivation in the EU according to EU Directive 2001/18 (data adapted from GMO-compass[84] and EFSA[92]). The genes conferring resistance to insect pests (IR genes) and the target insect order, as well as the genes conferring tolerance to herbicidal active substances (HT genes) and the herbicidal active substances, are presented together with the company name, status and date of the application

Transformation event	IR gene(s)	Target insect order	HT gene(s)	Herbicidal substance	Company	Status[a]	Year of application
MON810	*cry1Ab*	Lepidoptera			Monsanto	Renewal report	2007
T25			*pat*	Glufosinate	Bayer CropScience	Renewal submitted	2007
Bt11	*cry1Ab*	Lepidoptera	*pat*	Glufosinate	Syngenta Seeds	Report	1996[b]
1507	*cry1F*	Lepidoptera	*pat*	Glufosinate	Pioneer HiBred	Report	2001
NK603			*cp4 epsps*	Glyphosate	Monsanto	Report	2005
59122	*cry34Ab1, cry35Ab1*	Coleoptera	*pat*	Glufosinate	Pioneer Hi-Bred/Myogen Seeds	Submitted	2005
1507 × 59122	*cry1F, cry34Ab1, cry35Ab1*	Lepidoptera, Coleoptera	*pat*	Glufosinate	Mycogen Seeds (Dow AgroScience)	Submitted	2005
1507 × NK603	*cry1F*	Lepidoptera	*pat, cp4 epsps*	Glufosinate, Glyphosate	Pioneer Hi-Bred/Myogen Seeds	Submitted	2005
NK603 × MON810	*cry1Ab*	Lepidoptera	*cp4 epsps*	Glyphosate	Monsanto	Submitted	2005
59122 × 1507 × NK603	*cry1F, cry34Ab1, cry35Ab1*	Lepidoptera, Coleoptera	*pat, cp4 epsps*	Glufosinate, Glyphosate	Pioneer Hi-Bred	Submitted	2006
MON88017	*cry3Bb1*	Coleoptera	*cp4 epsps*	Glyphosate	Monsanto	Submitted	2008
GA21			*mepsps*	Glyphosate	Syngenta Seeds	Submitted	2008
MON89034 × MON88017	*cry1A.105, cry2Ab2, cry3Bb1*	Lepidoptera, Coleoptera	*cp4 epsps*	Glyphosate	Monsanto	Submitted	2009
MON89034 × NK603	*cry1A.105, cry2Ab2*	Lepidoptera	*cp4 epsps*	Glyphosate	Monsanto	Submitted	2009
MIR604	*mcry3A*	Coleoptera			Syngenta Seeds	Submitted	2010
Bt11 × MIR604 × GA21	*cry1Ab, mcry3A*	Lepidoptera, Coleoptera	*pat, mepsps*	Glufosinate, Glyphosate	Syngenta Seeds	Submitted	2010
MON89034	*cry1A.105, cry2Ab2*	Lepidoptera			Monsanto	Submitted	2011

[a] *Submitted*: application submitted, evaluation of risk assessment in progress by National Competent Authority (NCA) and/or European Food Safety Agency (EFSA); *Report*: risk assessment completed by both NCA and EFSA (GMO Panel), scientific report available (GMO-compass[84]), awaiting decision by European Commission; *Renewal*: notified as existing product (authorised since 22 April 1998), renewal of authorisation (including update of information) in progress.
[b] Application was expanded in 2003 according to EU Directive 2001/18.

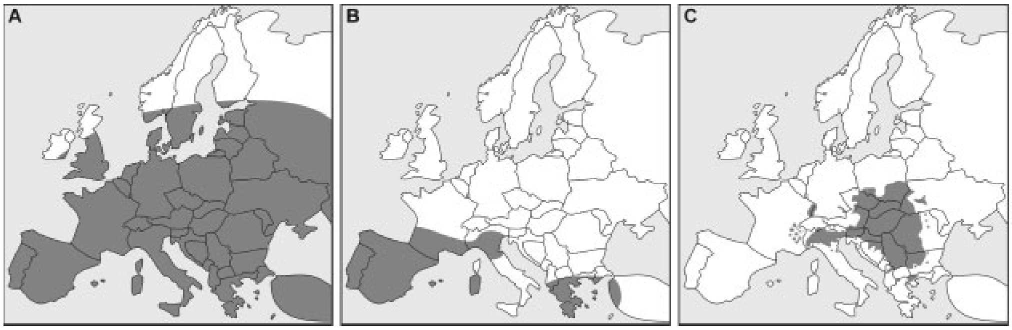

Figure 2. Distribution of the three main maize pests in Europe. A: European corn borer (*Ostrinia nubilalis*); B: Mediterranean corn borer (*Sesamia nonagrioides*); C: western corn rootworm (*Diabrotica virgifera virgifera*). Map for *O. nubilalis* based on CABI[93] (data from 1991) and Hill,[10], for *S. nonagrioides* based on CABI[93] (data from 1979) and Naïbo *et al*.[17] and for *D. v. virgifera* based on Edwards and Kiss[94] (data from 2010). Note that the area where the pest species cause damage to crops is generally smaller than the actual distributions of the species.

broad, which allows the control of several arthropod pests simultaneously. This, however, is also the major drawback, as deleterious effects on valued non-target organisms are frequent. These include species that fulfil important ecosystem services, such as predators, parasitic wasps, pollinators and decomposers. Another drawback of chemical insecticides is the possibility that the pest evolves resistance against the active ingredient, which has happened several times in the United States with corn rootworms.[21] In the EU, different initiatives from scientific organisations and policy makers have the aim of reducing pesticides in modern agriculture,[22] and the recently published EU directive 2009/128/EC requires national action plans for a reduction in pesticides and the implementation of IPM by 2014.[23]

3.2 Biological control

Trichogramma wasp spp. that parasitise eggs of the European corn borer are one alternative to reduce insecticide applications in maize. In Europe, the small wasps are released on about 150 000 hectares per year, with the largest area in France.[9,24,25] Cardboards with parasitised eggs are applied to the plants manually. Under optimal conditions, efficacy can be comparable with chemical insecticides. Appropriate scouting, forecast systems and efficient logistics ensure optimal timing, which is crucial for success. Similarly to chemical insecticides, however, parasitisation of the hidden eggs of the Mediterranean corn borer is low. In the future, below-ground pests, such as larvae of the western corn rootworm, could be controlled with entomopathogenic nematodes or entomopathogenic fungi. While research on entomopathogenic nematodes is particularly promising and has achieved control efficacies comparable with chemical soil insecticides, no commercial product is available yet.[26] Biological control is a preferable option for agricultural systems to become more sustainable, because it is environmentally safe with high specificity to the target pests. Establishment as a more widespread agricultural practice, however, is only possible if growers and consultants are trained and if regional hurdles in logistics, costs and efficacy can be overcome.

3.3 Cultural methods

Against corn borers, cultural measures include cutting and chopping stems close to the ground and ploughing under plant remains in autumn or early spring to reduce the number of emerging adults and thus the number of eggs laid in the new crop. In some areas, however, no-till or reduced-tillage methods are practised, e.g. to prevent soil erosion or improve water availability. Against the western corn rootworm, crop rotation is highly effective, because females lay their eggs mainly in maize fields, and the larvae hatching in the following year are largely restricted to maize roots as food. In the United States, however, simple crop rotations consisting of maize and soybeans in annual alternation have led to the evolution of beetles that oviposit less in maize and more in soybean, which can cause problems in maize in the following year.[14] Furthermore, in some regions, continuous cultivation of maize is most economic,[27] and many farms are not adapted to rotation systems. Crops in continuous cultivation, however, are generally more susceptible to agricultural problems including pests, weeds and diseases. Therefore, crop rotation is a basic cornerstone in IPM systems and important for sustainable agriculture. Diversified and more complex rotation systems are warranted to prevent the evolution of rotation-resistant corn rootworm strains in Europe.

4 INCENTIVES TO GROWING *Bt* MAIZE

While the Cry1Ab-expressing *Bt* maize event MON810 to control corn borers is the only insect-resistant crop approved for cultivation in the EU, applications for other transformation events, expressing Cry1Ab or Cry1F against corn borers and other Lepidoptera pests, Cry3Bb1, mCry3A or Cry34Ab1/Cry35Ab1 against corn rootworms or a combination of these *Bt* proteins, have been submitted (Table 1). *Bt* maize has several advantages over conventional pest control strategies, which has led to the fast adoption of the technology in some world areas.

4.1 High efficiency

Bt maize is highly efficient in controlling its target pests, which frequently results in higher yields compared with chemically protected maize crops.[28,29] In the Mediterranean region, Lepidoptera-specific *Bt* maize has the major advantage that it controls both the European and the Mediterranean corn borer.[30] The latter pest has not been controllable efficiently with other strategies, because larvae remain sheltered from insecticides applied to the plant surface as well as from *Trichogramma* wasp spp. If highly efficient pest control measures are adopted on a regional scale, area-wide suppression of the target pest can be achieved. This has been observed in several US states, where populations of the European corn borer have declined significantly since *Bt* maize has been introduced, and substantial economic benefits have been reported also for non-*Bt* maize growers.[31,32]

4.2 Simple farm operations

When growing *Bt* maize, no critical timing for the application of the plant protection products is necessary, because the insecticidal protein is expressed within the plant tissue and is present over the whole growing season. This is an advantage compared with current European corn borer control with *Trichogramma* spp., which requires scouting, forecast systems and high manpower in a narrow time window. Similarly, insecticide sprays need to be timed precisely to reach the larvae of the European corn borer or the adults of the western corn rootworm.[9,19,24] *Bt* maize does not need additional time investment for control of the target pests after sowing. This is particularly beneficial in southern and central Europe, where several generations of corn borers often require additional applications of *Trichogramma* spp. or insecticides. Both measures are more time consuming and expensive later in the season because a 2–3 times higher number of parasitic wasps need to be released for efficient control and special spray equipment is necessary to enter high maize stands.[9] The latter is also applicable for the chemical control of adult western corn rootworms.

4.3 High grain quality

Fungal diseases, including *Fusarium* spp. causing root, stem and ear rot, often enter the maize plant through feeding wounds caused by arthropod pests, especially second-generation corn borer larvae feeding on maize ears.[33] In addition, arthropods carrying fungal spores can contribute to the spreading of fungal diseases. One major problem with *Fusarium* spp. is the production of mycotoxins, which can lead to acute or chronic toxic effects in humans or livestock.[34,35] Strict maximum levels for certain *Fusarium* mycotoxins in foodstuffs[36] and guidance values for animal feed[37] have been implemented in the EU. The fact that *Bt* maize suffers less damage by corn borers or western corn rootworm adults results in reduced opportunities for *Fusarium* spp. to enter and infect the plants. In a recent study from south-western France, *Bt* maize decreased concentrations of the mycotoxins fumonisin and zearalenone by 90 and 50%, respectively, compared with unsprayed conventional maize.[38] The authors concluded that, according to EU regulation, 93% of the *Bt* maize crops could be sold as food/feed, compared with only 45% for conventional maize. A significant reduction in certain mycotoxins in *Bt* maize compared with conventional maize has also been reported from other experimental studies across European countries and the United States.[13,39] Furthermore, reduced silk clipping and kernel feeding by corn borer larvae and corn rootworm adults is particularly beneficial in seed and sweet maize production, where high grain quality is essential for marketing.[15]

4.4 Ecological benefit

The insecticidal proteins produced in *Bt* maize have a narrow spectrum of activity, and their potential for adverse effects on valued non-target organisms is assessed prior to the commercial release of any novel transformation event.[40,41] Review articles and statistical meta-analyses of numerous laboratory and field studies conducted in Europe and elsewhere revealed generally no detrimental effects of *Bt* maize on non-target species including above-ground predators and parasitoids,[42–45], bees[46,47] and below-ground species.[48] A few studies, however, claimed direct negative effects of *Bt* maize on non-target arthropods[49,50] and resulted in considerable scientific dispute concerning appropriate methodology and data quality and interpretation.[51–55] No such claims, however, have been confirmed.

Non-target species closely related to the targets are likely to be affected by *Bt* crops. This includes Lepidoptera species whose larvae feed on host plants in close vicinity to Cry1Ab-producing *Bt* maize during anthesis.[56,57] In the risk assessment of current Lepidoptera-specific *Bt* maize, the likelihood of adverse impacts on valued butterflies was found to be low because of low toxin doses in pollen and thus low exposure.[58,59] In the case of Chrysomelid-specific, Cry3Bb1-producing *Bt* maize, no valued non-target Chrysomelid species inside maize fields or nearby that require protection could be identified.[60]

On a global scale, *Bt* maize led to a 35% reduction in the use of insecticidal active ingredients, and the environmental impact was estimated to be 29% lower compared with conventional maize.[61] In Spain, conventional maize farmers applied on average 0.86 treatments per year (2002–2004) compared with 0.32 treatments for *Bt* maize farmers, and the percentages of farmers applying no insecticides were 70% for *Bt* maize growers and 42% for conventional maize growers.[28] Therefore, *Bt* maize has a clear ecological benefit if it replaces chemical insecticides, which often cause side effects on non-target species.[42,44,45] In addition, the ecological risk of uncontrollably spreading *Bt* genes is negligible, because there are no wild relatives of maize in Europe and maize hybrids have very little potential to survive outside managed fields.[58,62]

5 LIMITATIONS OF GROWING *Bt* MAIZE

As with any other technology, the application of *Bt* maize varieties carries risks, and different factors limit their use.

5.1 Resistance evolution

The fact that *Bt* maize produces insecticidal proteins in a relatively high dose over the whole season leads to a high selection pressure for the target pests evolving resistance against the *Bt* proteins. To delay resistance evolution, resistance management plans are part of the regulatory authorisation and need to be followed by growers. For MON810 maize in the EU, the European Food Safety Authority (EFSA) requested that 20% conventional maize needs to be planted as a refuge for the maintenance of susceptible corn borer populations if the total *Bt* maize area of a farm or a cluster of fields (irrespective of field and farm size) is larger than five hectares.[58] The aim is that resistant individuals surviving on *Bt* maize mate with susceptible moths emerging in large numbers from the refuge. For this so-called 'high-dose refuge' strategy to be effective, random mating is necessary, resistance has to be recessive and the toxin concentration in plants has to be high enough to kill susceptible and resistant heterozygous insects.[63] In addition to strict refuge requirements, resistance evolution to Cry1Ab-expressing maize (MON810) has been monitored for *S. nonagrioides* and *O. nubilalis*.[30,64,65] In Spain, where *Bt* maize has been cultivated most intensively since 1998, there is no indication of a decrease in susceptibility to the *Bt* protein.[30,65] Evidence of resistance evolution in Cry1Ab-expressing *Bt* maize fields, however, comes from the African stem borer *Busseola fusca* (Fuller) (Lepidoptera: Noctuidae) in South Africa.[66,67] However, in contrast to *O. nubilalis* and *S. nonagrioides*, which are highly sensitive to the Cry1Ab concentrations expressed in *Bt* maize, *B. fusca* is more tolerant to the toxin. In addition, South African farmers did not comply to refuge requirements until recently, or declared non-irrigated conventional maize as refuges for irrigated *Bt* maize, which most likely decreased random mating and egg laying, because the moths prefer high humidity.[66,67] Field resistance was also reported for *Spodoptera frugiperda* (JE Smith) (Lepidoptera: Noctuidae) from Cry1F-expressing *Bt* maize in Puerto Rico.[68] Continuous year-round planting of maize, moderate sensitivity of the pest to Cry1F, limited migration from external ecosystems (island geography) and drought conditions that concentrated pest populations in irrigated fields might have contributed to unprecedented levels of selection pressure on *S. frugiperda* populations.[68]

Glasshouse experiments revealed that *D. v. virgifera* shows only moderate susceptibility to Cry3Bb1 and has therefore a high potential to evolve resistance.[69] Consequently, resistance management plans based on the high-dose refuge concept that are deployed successfully against corn borers may be less effective for the corn rootworm. New *Bt* crops have been developed that produce two or more different *Bt* proteins that target the same pest, but with different modes of action (e.g. SmartStax™). With those so-called pyramided traits, pests need to evolve resistance against several proteins simultaneously, which will reduce the likelihood of resistance evolution (Table 1).[70]

5.2 Secondary pest outbreaks

The narrow spectrum of activity of *Bt* proteins can be a disadvantage if populations of secondary pests are no longer controlled by broad-spectrum insecticides previously applied against the target pests. When populations exceed economic thresholds and insecticides need to be applied against those pests, the ecological benefit of *Bt* crops may be limited. Even more problematic are situations where secondary pests remain uncontrolled in the *Bt* crops and build up high populations, which can spill over to other crops in the agricultural landscape. Such problems have recently been recorded with mirid bugs (Heteroptera: Miridae) in *Bt* cotton in China.[71] Maize, however, has a smaller pest spectrum than cotton, and insecticide input in conventional maize is generally lower than in conventional cotton, which limits the likelihood of such effects. However, one example for a secondary pest problem in *Bt* maize is the western bean cutworm, *Striacosta albicosta* (Smith) (Lepidoptera: Noctuidae), which is not affected by the Cry1Ab protein. A remarkable range expansion across the corn belt in the United States has been observed during the last decade, and problems in maize production have been increasing.[72] One explanation is the lack of competition, which allows the pest to fill the ecological niche of the more susceptible corn earworm, *Helicoverpa zea* (Boddie) (Lepidoptera: Noctuidae), and European corn borer.[73,74] In the EU, however, there are no reports of secondary pest outbreaks associated with the cultivation of *Bt* maize.[75] In most maize-growing regions, the biological control function of natural enemies, which is preserved in *Bt* maize, is sufficient to keep secondary pest populations below economic injury levels.[42,44] The enhancement of natural enemies has to be an important aim in integrated *Bt* maize production.

5.3 Complying to license requirements

Growers that decide on planting *Bt* maize currently face more administrative work than that associated with growing conventional maize. This involves notifications, detailed bookkeeping, specific training and the acceptance that resistance management measures are controlled on-farm. In addition, each *Bt* maize grower needs to ensure that other growers in the region have the ability to make a practical choice between conventional, organic and GM-crop production according to national regulation (coexistence of different agricultural systems).[76] In current legislation, the EU has defined 0.9% as the maximum percentage of GE material that is allowed in food and feed without the need for labelling as GE.[77] Maize is an open pollinated crop, and pollen can be dispersed by wind, even though movement is limited by the large size of the pollen grains. To reduce the likelihood that *Bt* maize pollen fertilises conventional maize growing nearby, obligatory isolation distances are to be determined by national regulations. If existing, these national rules differ greatly between EU member states. The Netherlands, for example, demands a distance of 25 m between conventional and *Bt* maize fields, while Luxemburg asks for as much as 600 m.[78] Based on scientific meta-analysis, isolation distances of 10–50 m would be sufficient to keep GM inputs below the 0.9% threshold in most cases, even though greater distances may be needed for stacked or pyramided transformation events, which contain more introduced genetic material.[76,78] More flexible coexistence measures than the fixed isolation distances that are mandatory today could include strips of conventional maize planted next to *Bt* or next to conventional maize fields that serve as pollen barriers and potentially also as a refuge for resistance management.[76] Furthermore, planting times could be adjusted, particularly in Mediterranean countries, to avoid *Bt* maize flowering at the same time as conventional maize.[76] In addition to measures avoiding cross-pollination, separate production chains (machinery and facilities for sowing, harvesting, drying, transport and storage) for *Bt* maize and conventional maize are recommended to avoid mixing before and after harvest.[76,79] For *Bt* maize growers, this requires a number of discussions and agreements with neighbours, contractors and cooperatives, and may lead to increased production difficulties and costs.[76,80]

6 AUTHORISATION OF *Bt* MAIZE IN THE EU

Growers willing to plant *Bt* maize often face the problem that authorisation is denied by EU or national authorities. Today, only one transformation event (MON810) for insect resistance is authorised for cultivation in the EU, but 200 maize varieties carrying MON810 are currently included in the EU common catalogue of varieties of agricultural plant species.[81,82] In addition, registration applications for the cultivation of 13 other transformation events are in the approval pipeline (Table 1). In the current European regulatory system, diverging political opinions of the EU member states result in a de facto moratorium for new approvals.[83] An example is the case of *Bt*11 maize, a transformation event with the same *cry1Ab* gene as MON810 targeting corn borers. The application was submitted in 1996 and no decision has been reached yet (Table 1).[84] In the case of MON810, Austria, France, Germany, Greece, Luxembourg and Hungary have banned cultivation under the safeguard clause (Articles 16 and 18).[85] While these countries justified the bans with studies claiming potential adverse effects of *Bt* maize on biodiversity, EFSA did not see evidence to change its original evaluation (http://www.efsa.europa.eu/en/gmo/gmoscdocs.htm). For a discussion of the scientific basis for the recent ban in Germany, see Ricroch *et al*.[86] In addition to national bans, some regional initiatives proclaim 'GMO-free regions'.[76,83]

7 ECONOMICS OF ADOPTING *Bt* MAIZE

Seed prices for *Bt* maize are generally higher than for conventional seeds, because industry is charging a premium for the *Bt* technology. Crop protection is thus paid at the beginning of the season and the costs are independent of the actual pest

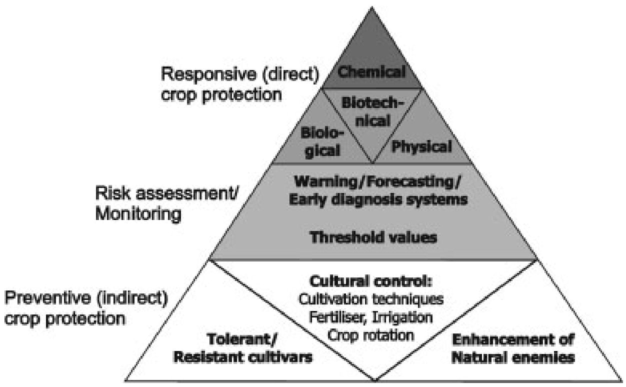

Figure 3. Principles of integrated pest management (IPM), based on Boller *et al.*[88].

pressure in a particular year. In areas with low or sporadic pest pressure, it may not be economically viable for growers to pay higher prices for *Bt* maize seeds. However, industry is adapting prices regionally according to the expected benefit to growers, as evident from Spanish data from 2002–2004.[28] While conventional seeds were less than 7% cheaper than *Bt* maize seeds in Albacete, a province with low corn borer pressure, industry charged 20% more for *Bt* maize seeds in the province of Zaragoza, which suffers high pest pressure. Not surprisingly, adopting *Bt* maize led to only a small increase in grower's gross margin in Albacete, below €10 per hectare. In contrast, *Bt* maize growers in Zaragoza were able to increase their gross margin by €105–135 per hectare, in spite of the higher seed prices, because of higher yields and lower costs for insecticide treatments.[28] Spain is the only EU member state where *Bt* maize adoption levels are currently delivering farm income gains near full potential levels, while across the EU only 8–12% of the total potential benefit and 14–25% of the potential environmental benefit are being realised.[13] Surprisingly, Italy, France, Germany and Austria have banned MON810, in spite of the fact that they are among the countries with the largest estimated economical and environmental benefit from corn-borer-resistant *Bt* maize.[13] Similarly, the non-authorisation of corn-rootworm-resistant *Bt* maize in the EU results in foregone economic benefits for growers. Values of between €10.5 and €62 per hectare were estimated on the basis of a bioeconomic model for countries with high pest pressure, such as Hungary, Austria, Czech Republic, Poland, Romania, Serbia, Slovakia and Ukraine.[27,87]

8 *Bt* MAIZE – ONE TOOL IN INTEGRATED PEST MANAGEMENT

Essential components of integrated farming are the production of high-quality products in a sustainable way by using natural resources and regulating mechanisms to replace polluting inputs, preserving and improving soil fertility, maintaining a diversified environment and observing ethical and social criteria.[88] Within this context, the basic goal of IPM is to achieve effective crop protection in a manner that provides sustainable economic benefits to growers and society, and minimal impact on the environment. Biological, technical and chemical methods are balanced carefully, with an emphasis on methods that are least harmful to the environment and most specific to the particular pest.[88] IPM includes both preventive (indirect) and responsive (curative, direct) pest management tactics (Fig. 3). Preventive tactics include host plant resistance (choice of resistant or tolerant cultivars), cultural controls (adequate cultivation techniques, optimal crop rotations, balanced fertilisation and irrigation) and enhancement of natural enemies (adequate plant protection measures and ecological infrastructures within and outside production areas). Pests are monitored, and appropriate tools determine whether and when preventive plant protection methods are not sufficient to keep levels of pests below an economic injury threshold. When responsive crop protection methods need to be applied, the use of biological control agents, biotechnical methods (e.g. mating disruption, deterrents, sterile insect technique) and physical measures must be preferred to chemical methods.[88]

The insecticidal protein produced in *Bt* maize can be regarded as a responsive measure against the target pest. Insecticidal protein is produced season long in relatively high concentrations and independently of the actual pest pressure, which seems to contradict IPM principles.[89] However, *Bt* maize can also be regarded as a preventive measure, a GE host plant resistance against specific target pests. This built-in host plant resistance and the high specificity allow the flexible use of *Bt* maize and its combination with other control measures against non-target pests in a sustainable way, depending on the situation in a particular field and season, which fits well in the concept of IPM. With the growing number of stacked maize events conferring resistance to several pests (and tolerance to several herbicidal active substances) (Table 1), GE maize traits may also be used in areas where their use in pest management is not justified, i.e. when target pests of some expressed *Bt* proteins are not present or not expected to reach damaging levels. Such conflicts with good IPM practice with the use of *Bt* maize may particularly arise in the future, if only stacked events become commercially available.[89] Exposure for non-target species in *Bt* maize is limited to species feeding on plant tissue (including pollen), or prey that has consumed plant material because the insecticidal protein is produced inside the plant.[90,91] More importantly, however, toxicity to humans, pollinators, soil organisms, natural enemies and also non-target herbivores is negligible, which is desirable in the IPM concept. Furthermore, a positive environmental effect can be achieved if growing *Bt* maize leads to a reduction in synthetic insecticides with a broad spectrum of exposed species and toxic effects for humans and non-target species.[28]

9 CONCLUSIONS

Bt maize is a highly specific and highly efficient pest control measure that allows growers to produce high-quality grain with reduced insecticide inputs and farm operations. In spite of higher seed prices and administrative requirements to fulfil licence agreements, *Bt* maize growers in areas with high pest pressure have generally been able to increase their gross margin considerably. In consequence, the non-authorisation of *Bt* maize results in foregone economic benefits for growers in several European countries. In the case where *Bt* maize replaces broad-spectrum insecticides, ecological benefits are evident because valued non-target organisms remain unharmed. However, increasing populations of secondary pests and resistance evolution in populations of the target pests are potential risks for the sustainability of *Bt* maize that need appropriate management plans (refuges, enhancement of natural enemies) and close monitoring. Because of its high efficacy, *Bt* maize targeting the corn rootworm could also support, or partly replace, large-scale insecticide applications in eradication programmes. In an IPM context, *Bt* maize is a highly specific tool that efficiently solves the main pest problem and can be combined with other preventive or responsive measures to solve problems including those with secondary pests.

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