SCIENTIFIC OPINION

Scientific Opinion updating the risk assessment conclusions and risk management recommendations on the genetically modified insect resistant maize 1507[1]

EFSA Panel on Genetically Modified Organisms (GMOs)[2, 3]

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This Scientific Opinion, published on 9 November 2012, replaces the earlier version published on 25 October 2012.[4]

ABSTRACT

Following a request from the European Commission, the Panel on Genetically Modified Organisms of the European Food Safety Authority (EFSA GMO Panel) compiled its previous risk assessment conclusions and risk management recommendations on the genetically modified insect resistant maize 1507, and considered their validity in the light of new relevant scientific publications published from 2005 onwards. The EFSA GMO Panel performed a search of the scientific literature published between 2005 and September 2012, and identified 61 peer-reviewed publications containing evidence specific to the risk assessment and/or management of maize 1507, of which two were relevant for the food and feed safety assessment, and 34 for the environmental risk assessment and/or risk management. None of these publications reported new information that would invalidate the previous conclusions on the safety of maize 1507 made by the EFSA GMO Panel. Therefore, the EFSA GMO Panel considers that its previous risk assessment conclusions on maize 1507, as well as its previous recommendations on risk mitigation measures and monitoring, remain valid and applicable.

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KEY WORDS

GMO, maize (*Zea mays*), 1507, insect resistance, Cry1F, risk assessment, food and feed safety, environment, food and feed uses, import and processing, cultivation

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SUMMARY

Following a request from the European Commission, the Panel on Genetically Modified Organisms of the European Food Safety Authority (EFSA GMO Panel) compiled its previous risk assessment conclusions and risk management recommendations on the genetically modified insect resistant maize 1507, and considered their validity in the light of new relevant scientific publications published from 2005 onwards.

The EFSA GMO Panel performed a search of the scientific literature to identify new scientific publications specific to maize 1507 that may report new information relevant for the risk assessment and/or management of maize 1507. Subsequently, the EFSA GMO Panel evaluated whether the information reported in recent publications, identified by the literature search, would invalidate its previous risk assessment conclusions on maize 1507, as well as its previous recommendations on risk mitigation measures and monitoring.

Following a search of the scientific literature published between 2005 and September 2012, the EFSA GMO Panel identified 61 peer-reviewed publications containing evidence specific to the risk assessment and/or management of maize 1507, of which 25 publications were discussed and cited in previous EFSA GMO Panel scientific outputs. From the remaining 36 publications, two were relevant for the food and feed safety assessment of maize 1507, and 34 for the environmental risk assessment and/or risk management of maize 1507.

The EFSA GMO Panel did not identify new peer-reviewed scientific publications reporting new information that would invalidate its previous conclusions on the safety of maize 1507. Therefore, the EFSA GMO Panel considers that its previous risk assessment conclusions on maize 1507, as well as its previous recommendations for risk mitigation measures and monitoring, remain valid and applicable.

When defining measures to delay resistance evolution to the Cry1F protein from maize 1507 in target insect pests, risk managers should consider that Cry1Ab-expressing maize events (such as MON 810) are approved for cultivation in the EU. The EFSA GMO Panel recommends that, in regions where maize 1507 and Cry1Ab-expressing maize events would be cultivated together, refuge areas equivalent to 20% of the total Lepidoptera-active *Bt*-maize area are established due to the potential for cross-resistance between Cry1Ab and Cry1F.

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BACKGROUND AS PROVIDED BY EFSA

On 24 September 2004, the Scientific Panel on Genetically Modified Organisms of the European Food Safety Authority (EFSA GMO Panel) issued a Scientific Opinion on the notification (reference C/NL/00/10) for the placing on the market of the genetically modified (GM) insect resistant maize 1507 for import and processing under Part C of Directive 2001/18/EC (EFSA, 2004). On 19 January 2005, the EFSA GMO Panel issued a Scientific Opinion (EFSA, 2005a) on the application (reference EFSA-GMO-NL-2004-02) for the placing on the market of maize 1507, for food use, under Regulation (EC) No 1829/2003 and on the notification (reference C/ES/01/01) for the placing on the market of maize 1507 for import, feed and industrial uses and cultivation, under Part C of Directive 2001/18/EC (EFSA, 2005b). In EFSA (2005b), the EFSA GMO Panel recommended that management measures be put in place to delay the possible evolution of resistance to the Cry1F protein in target Lepidoptera. The EFSA GMO Panel was also of the opinion that such measures would reduce the exposure of non-target Lepidoptera to maize 1507 pollen (EFSA, 2005b). Based on the evaluation of the environmental risk assessment (ERA), the EFSA GMO Panel concluded that if its recommended management measures were to be put in place, the cultivation of maize 1507 would not pose a significant risk to the environment.

In both 2006 and 2008, the European Commission requested the EFSA GMO Panel to consider whether new evidence published in the scientific literature required a revision of the conclusions of its 2005 Scientific Opinion on maize 1507 (EFSA, 2005b). Following these requests, the EFSA GMO Panel evaluated the available new scientific information, and found no new evidence for adverse effects caused by the cultivation of maize 1507 (EFSA, 2006, 2008). Therefore, the EFSA GMO Panel concluded that no new scientific information had been made available that would invalidate its previous risk assessment conclusions.

In 2009, the EFSA GMO Panel delivered a Scientific Opinion for the continued marketing of existing products produced from maize 1507 for feed uses, i.e., feed materials and feed additives (EFSA, 2009).

On 14 June 2010, the European Commission requested the EFSA GMO Panel to consider whether new scientific elements might require a revision of the conclusions of its previous Scientific Opinion on maize 1507. On 4 November 2010, the EFSA GMO Panel confirmed[5] that, considering recent studies and advances in methodology, there was a need to further analyse the potential adverse effects of maize 1507 pollen on non-target Lepidoptera, as well as to clarify its recommendations to risk managers. On 16 December 2010, EFSA endorsed a self-task mandate of the EFSA GMO Panel to review its previous safety assessment of maize 1507 in the light of recent advances in methodology and knowledge.

On 20 December 2010, the EFSA GMO Panel requested the applicant to update its application with relevant studies on non-target organisms performed with maize 1507 that became available after the adoption of its 2005 Scientific Opinion (EFSA, 2005b). Following this request, the applicant provided new data to support the assessment of direct effects of the Cry1F protein on European species of non-target Lepidoptera on 22 March 2011.

Given the available data on maize 1507 and recent advances in methodology[6] (i.e., the mathematical model developed by Perry et al. (2010) and further clarified and extended by Perry (2011a,b) and Perry et al. (2011, 2012)), the EFSA GMO Panel decided to supplement its previous conclusions on the safety of maize 1507, and to clarify its previous recommendations to risk managers. To achieve

[5] See minutes of the 61st plenary meeting of the Scientific Panel on Genetically Modified Organisms held on 20-21 October 2010 at http://www.efsa.europa.eu/en/events/event/gmo101020.htm

[6] I.e., the mathematical model developed by Perry et al. (2010) to simulate and assess potential adverse effects on the larvae of non-target Lepidoptera after ingestion of harmful amounts of *Bt*-maize pollen containing Cry1F deposited on the host-plants of the larvae

this goal, the EFSA GMO Panel considered the most recent relevant data published in the scientific literature, along with the new data submitted by the applicant.

On 5 July 2011, the European Commission asked the EFSA GMO Panel, to consider the plan for post-market environmental monitoring (PMEM) of maize 1507 in the light of the 2011 Scientific Opinion providing guidance on PMEM of GM plants (EFSA, 2011b).

On 19 October 2011, the EFSA GMO Panel concluded from its self-task that risk management measures may be needed under specific conditions (e.g., susceptibility and occurrence of non-target Lepidoptera, acreage of *Bt*-maize, host-plant density) in order to reduce the exposure of sensitive non-target Lepidoptera to maize 1507 pollen (EFSA, 2011d). In that Scientific Opinion, the EFSA GMO Panel also considered that the plan previously submitted by the applicant for PMEM, and in particular the methodology, needed further elaboration, according to the requirements of its 2011 Scientific Opinion delivering guidance on PMEM of GM plants, as well as its Scientific Opinions on the annual PMEM reports on maize MON 810 (EFSA, 2011d, 2012a). In 2011, the EFSA GMO Panel concluded that: "*subject to appropriate management measures, maize 1507 cultivation is unlikely to raise safety concerns for the environment*" (EFSA, 2011d). Recently, the EFSA GMO Panel further supplemented its previous recommendations for risk mitigation measures and monitoring by reapplying the mathematical model developed by Perry et al. (2010, 2011, 2012), in order to consider additional hypothetical agricultural conditions, and to provide additional information on the factors affecting the insect resistance management plan (EFSA, 2012b).

On 20 June 2012, the EFSA GMO Panel was requested by the European Commission to deliver a Scientific Opinion updating the risk assessment and/or management of maize 1507 in the light of recent scientific publications.

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

The European Commission requested EFSA: "*to adopt an opinion gathering its previously adopted conclusions on maize 1507 for each area of risk and taking into account recent relevant scientific publications, in accordance with Article 29 of Regulation (EC) No 178/2002*".

ASSESSMENT

1. INTRODUCTION

Maize 1507 has been developed to provide protection against certain lepidopteran target pests, such as the European corn borer (ECB, *Ostrinia nubilalis*), and species belonging to the genus *Sesamia* (in particular the Mediterranean corn borer (MCB, *Sesamia nonagrioides*), by the introduction of a part of a *Bacillus thuringiensis* (*Bt*) gene encoding the insecticidal Cry1F protein. Maize 1507 also expresses the phosphinothricin-N-acetyltransferase (PAT) protein from *Streptomyces viridochromogenes*, which confers tolerance to the herbicidal active substance glufosinate-ammonium. The PAT protein expressed in maize 1507 has been used as selectable marker to facilitate the selection process of transformed plant cells, and is not intended for weed management purposes.

This EFSA GMO Panel Scientific Opinion addresses all intended uses of maize 1507, covering the import, processing, and food and feed uses, as well as cultivation. Since the scope of the notification C/ES/01/01 did not cover the use of glufosinate-ammonium-based herbicides on maize 1507, potential effects due to the use of such herbicides on maize 1507 are not considered in this Scientific Opinion. This is consistent with the recent updated evaluation by the EFSA GMO Panel of the ERA of maize 1507 (EFSA, 2011d).

In accordance with the terms of reference laid down by the European Commission, this Scientific Opinion is based on existing scientific outputs on maize 1507 by the EFSA GMO Panel (i.e., EFSA, 2004, 2005a,b, 2006, 2008, 2009), focusing in particular on the most recent ones (e.g., EFSA, 2010b,c, 2011d,e,f,g, 2012b). To comply with the current mandate of the European Commission, the EFSA GMO Panel performed a search of the scientific literature to identify new scientific publications specific to maize 1507 that may report new information relevant for the risk assessment and/or management of maize 1507 (EFSA, 2010d). The EFSA GMO Panel scrutinised the new scientific publications identified during the literature search, and subsequently assessed whether the information found in these new publications would invalidate its previous conclusions on the safety of maize 1507.

2. LITERATURE SEARCH

In response to the present request of the European Commission and in addition to the continuous screening of relevant scientific literature by the EFSA GMO Panel, an additional search of the scientific literature was performed. The aim of this search was to identify new scientific publications specific to maize 1507 that may report new information relevant to the risk assessment and/or management of maize 1507.

The scientific literature database ISI Web of Knowledge[7] (Thompson Reuters, New York, USA) was used for the literature search. Literature was searched and filtered in a stepwise manner. As a first step, the following combination of generic keywords being both event- and trait-specific was used to retrieve all references for further consideration: "*TOPIC FIELD = 1507* OR *TC1507* OR *Cry*1F* OR *Herculex* AND *maize*". The search by keywords using the topic field, enabled to retrieve publications that contain these keywords, either in the publication's title, list of keywords, or abstract. The asterisk (wildcards) was used to cover all the possible writing forms of the keyword Cry1F (e.g., Cry1F, Cry 1F, Cry_1F). In the second step, search results were sorted by the area of scientific discipline (e.g., molecular characterisation, comparative analysis, food and feed safety assessment, ERA and PMEM) and subsequently considered by the EFSA GMO Panel (see sections below). The search for scientific publications targeted publications published between 2005 – the year during which the EFSA GMO Panel issued its first Scientific Opinions on maize 1507 for all uses, including cultivation (see EFSA, 2005a,b) – and September 2012. The EFSA GMO Panel also performed targeted searches of relevant peer-reviewed journals, in order to identify the most recent publications appearing ahead of print, and which may not have been included in the ISI Web of Knowledge yet. Publications on: the coexistence of maize cropping systems; the detection, quantification, labelling and traceability of

[7] This database includes: Web of Science, CABI, FSTA, MedLine and Current Contents Connect databases

GMOs; socio-economics; and public perception were excluded, as these topics are not in the remit of the EFSA GMO Panel. After having accounted for the scientific literature previously discussed and cited in relevant maize 1507-related applications[8] and/or the numerous EFSA GMO Panel scientific outputs (EFSA, 2005a,b, 2006, 2008, 2009, 2010b,c, 2011d,e,f,g, 2012b)[9], the EFSA GMO Panel found 36 relevant peer-reviewed publications written in English that it had not previously discussed (see sections below; Appendix A – rows highlighted in grey).

The EFSA GMO Panel identified a total number of 61 peer-reviewed publications containing evidence specific to the risk assessment and/or management of maize 1507, of which 25 publications were discussed and cited in previous EFSA GMO Panel scientific outputs. From the remaining 36 publications, two were relevant for the food and feed safety assessment of maize 1507, and 34 for the environmental risk assessment and/or risk management of maize 1507.

Even though no systematic review of the literature is carried out in this Scientific Opinion, the EFSA GMO Panel adhered to some general principles for performing systematic review, in order to ensure methodological rigour and coherence in the retrieval and selection of publications, transparency, and reproducibility of the performed literature search (EFSA, 2010d).

3. MOLECULAR CHARACTERISATION

3.1. Introduction

The summary of the previous assessments of maize 1507, presented below, covers the following key areas of molecular characterisation: (1) description of the methods used for the genetic modification; (2) source and characterisation of nucleic acid used for transformation; (3) description of the traits and characteristics which have been introduced; (4) information on the sequences actually inserted; (5) information on the expression of the inserted sequence; and (6) genetic stability of the inserted sequence and phenotypic stability of the GM plant.

3.2. Molecular characterisation

3.2.1. Summary of previous conclusions by the EFSA GMO Panel

Maize 1507 was generated by particle bombardment. Molecular analyses showed that maize 1507 contains one copy of the DNA fragment used for the transformation (containing the *cry1F* gene and the *pat* gene, encoding PAT) and additional partial fragments of the *cry1F* and *pat* genes. These fragments are present at a single locus in the nuclear genome (EFSA, 2004, 2005a,b, 2009). The structure of the insert in maize 1507 was determined by Southern analyses and DNA sequencing. Morisset et al. (2009) showed that the 35S promoter of event 1507 contains a single nucleotide difference compared to the reported sequence of the DNA fragment used for transformation. Following a request from the EFSA GMO Panel, the applicant has clarified that this difference was present in plants at early stages of product development and is present in all maize 1507 lines and stacks that have been evaluated by the EFSA GMO Panel. Updated bioinformatic analyses confirmed that, in addition to the intact genes, the insert in maize 1507 includes DNA sequences originating from the fragment used for transformation as well as maize chloroplast DNA sequences (EFSA, 2004). Analyses of DNA sequences flanking both ends of the insert showed that they are maize genomic DNA. Updated bioinformatic analyses of these flanking sequences suggest that the insert in maize 1507 is flanked by a putative RIRE2 retrotransposon (downstream) and a Huck1 retrotransposable element (upstream). Transcript and bioinformatic analyses of ORFs spanning all junction regions between genomic and insert DNA, as well as junction regions between partial fragments of *cry1F* and *pat* genes were performed and no novel putative proteins with sequence similarity to known toxins or allergens were identified. The mean level of the newly expressed Cry1F protein was the highest in

[8] GM plant market registration applications with reference EFSA-GMO-NL-2005-15 and EFSA-GMO-2008-CZ-62

[9] Including the minutes of the 61st plenary meeting of the Scientific Panel on Genetically Modified Organisms held on 20-21 October 2010 at http://www.efsa.europa.eu/en/events/event/gmo101020.htm

pollen (20.0 µg/g dry weight [dw])[10]. The Cry1F protein levels ranged between 1.0 and 6.9 µg/g dw for whole plant extract and between 1.2 to 3.1 µg/g dw for kernels. Measurable levels of the PAT protein were only found in leaves (<LOD – 136.8 µg/g total extractable protein [TEP]) and in whole plant extracts (<LOD – 38.0 µg/g TEP). Southern analyses of maize 1507 and maintenance of the phenotype indicated genetic and phenotypic stability of the event over multiple generations.

All previous assessments of maize 1507 by the EFSA GMO Panel (EFSA, 2004, 2005a,b, 2009) led to the conclusion that the molecular characterisation of maize 1507 does not raise a safety issue.

3.2.2. Results from the literature search

From the literature search, no new peer-reviewed scientific publications containing evidence specific to maize 1507 for this specific area of risk were identified.

3.2.3. Conclusion

In the absence of new scientific evidence specific to maize 1507 for this specific area of risk, the EFSA GMO Panel considers that its previous conclusions on the molecular characterisation of maize 1507 remain valid and applicable.

4. COMPARATIVE ANALYSIS

4.1. Introduction

The summary of the previous assessments of maize 1507, presented below, covers the following key areas of the comparative analysis: (1) choice of comparator and production of material for the compositional assessment; (2) compositional analysis; and (3) agronomic traits and GM phenotype.

4.1.1. Summary of the previous conclusions by the EFSA GMO Panel

Whole crops and grain of maize 1507 and its conventional counterpart were collected for compositional analysis from field trials. These field trials were performed during three seasons and at different locations (six locations in Chile (1998-1999), three locations in France and Italy (1999), and six locations in France, Italy and Bulgaria (2000)). GM maize plants in the Chilean field trials were all treated with glufosinate-ammonium-based herbicides, while those in the European field trials were split into treated and untreated groups. Aside from minor modifications, the selection of compounds analysed followed the recommendations of OECD (OECD, 2002). On the basis of the results of compositional analysis of samples from these field trials, the EFSA GMO Panel concluded that forage and grain of maize 1507 were compositionally equivalent to those of conventional maize, except for the presence of Cry1F and PAT proteins in maize 1507.

In addition, field trials carried out over several seasons and at different locations (USA in 1999, France, Italy, and Bulgaria in 2000, Spain in 2002) did not indicate any unexpected changes of agronomic characteristics and performance (EFSA, 2004, 2005a,b).

The data obtained from the same field trials were provided in the renewal application of maize 1507 in 2007 (EFSA-GMO-RX-1507), and in two applications for the placing on the market of maize MON 89034 × 1507 × MON 88017 × 59122 (EFSA-GMO-CZ-2008-62) and maize MON 89034 × 1507 × NK603 (EFSA-GMO-NL-2009-65) for import, processing, and food and feed uses under Regulation (EC) No 1829/2003.

Based on these data the EFSA GMO Panel confirmed the previous conclusions (EFSA, 2004, 2005a,b, 2009) in the Scientific Opinions for these two stacked maize MON 89034 × 1507 × MON 88017 × 59122 (EFSA, 2010b, 2011e) and MON 89034 × 1507 × NK603 (EFSA, 2010c, 2011f) that: "*maize*

[10] The EFSA GMO Panel used a more conservative value of 32 µg/g dw in the ERA of maize 1507 pollen (EFSA, 2011d) based on US EPA data (US EPA, 2001, 2005) for which the applicant used an improved protein extraction and quantification system

1507 does not differ from its conventional counterpart with regard to compositional, phenotypic and agronomic characteristics and is equivalent to commercial maize varieties, except for the newly expressed Cry1F and PAT proteins".

4.1.2. Results from the literature search

From the literature search, no new peer-reviewed scientific publications containing evidence specific to maize 1507 for this specific area of risk were identified.

4.1.3. Conclusion

In the absence of new scientific evidence specific to maize 1507 for this specific area of risk, the EFSA GMO Panel considers that its previous conclusions on the comparative analysis of maize 1507 remain valid and applicable.

5. FOOD AND FEED SAFETY ASSESSMENT

5.1. Introduction

The summary of the previous assessments of maize 1507, presented below, covers the following key areas of the food and feed safety assessment: (1) product description and intended use; (2) effect of processing; (3) toxicology; (4) allergenicity; (5) nutritional assessment of GM food and feed; and (6) post-market monitoring of GM food and feed.

5.1.1. Summary of previous conclusions by the EFSA GMO Panel

Maize 1507 expresses the Cry1F and PAT proteins. A trypsinised *Pseudomonas fluorescens*-produced Cry1F protein, identical to the truncated Cry1F protein expressed in maize 1507, except for a phenylalanine instead of a leucine at position 604 and a C-terminal extension with seven amino acid residues (606-612: Ala-Glu-Tyr-Asp-Leu-Glu-Arg), was used for the safety testing after it had been demonstrated experimentally that it was equivalent to the truncated Cry1F protein present in maize 1507. Similarly, a microbially-produced PAT protein was used for safety studies after it had been demonstrated experimentally that it was equivalent to the enzyme present in maize 1507. No toxicity of the Cry1F and PAT proteins was observed in acute oral toxicity studies in mice. No oral toxicity of maize 1507 was observed in a 90-day rat study where the experimental animals were fed *ad libitum* a diet containing up to 33% maize 1507. In addition, nutritional data comprising target animal feeding studies with maize grain on chickens and dairy cows indicated that maize 1507 is nutritionally equivalent to conventional maize cultivars. The allergenicity risk assessment of the Cry1F and PAT proteins indicated a low probability of potential allergenicity. The allergenicity of the whole crop did not appear relevant to the EFSA GMO Panel since maize is not considered a common allergenic food.

Bioinformatics-supported comparisons of the amino acids sequences of PAT and Cry1F proteins with updated databases of known toxins and allergens, and a study by Ladics et al. (2006) were added in the 2007 renewal application of maize 1507. Ladics et al. (2006) assessed the potential cross-reactivity of the Cry1F proteins from maize 1507 and Der p7 from dust mite with human sera positive for Der p7-IgE. Based on these data, the EFSA GMO Panel concluded that the new information provided, and new information from the scientific literature does not require changes of the previous Scientific Opinions on maize 1507 (EFSA, 2004, 2005a, 2005b). Maize 1507 was considered *"unlikely to have an adverse effect on human and animal health and the environment in the context of its proposed uses"* (EFSA, 2009).

The bioinformatics studies were further updated in two applications for the placing on the market of maize MON 89034 × 1507 × MON 88017 × 59122 (EFSA-GMO-CZ-2008-62) and maize MON 89034 × 1507 × NK603 (EFSA-GMO-NL-2009-65) for import and processing, and food and feed uses, under Regulation (EC) No 1829/2003. Based on the data provided, the EFSA GMO Panel confirmed the previous opinions (EFSA, 2004, 2005a, 2005b, 2009) in the Scientific Opinions for these two stacked maize MON 89034 × 1507 × MON 88017 × 59122 (EFSA, 2010b, 2011e) and maize MON 89034 × 1507 × NK603 (EFSA, 2010c, 2011f) that: "*maize 1507 is as safe as its conventional counterpart and commercial maize varieties and considered it unlikely that the overall allergenicity of the whole plant is changed. Maize 1507 and derived products are unlikely to have adverse effects on human and animal health in the context of the intended uses*".

With regard to the safety of pollen from maize 1507 as compared to that from non-GM maize, the EFSA GMO Panel refers to its Statement on the safety of maize MON 810 pollen occurring in, or as food (EFSA, 2011c). The same rationale that the EFSA GMO Panel used in this Statement is applicable for evaluating the safety of maize 1507 pollen occurring in or as food. Therefore, while the EFSA GMO Panel is not in a position to conclude on the safety of maize pollen in or as food in general, it concludes that the genetic modification in maize 1507 does not constitute an additional health risk if maize 1507 pollen were to replace maize pollen from non-GM maize in or as food.

5.1.2. Results from the literature search

From the literature search, the following two new peer-reviewed scientific publications containing evidence specific to maize 1507 were identified and scrutinised for their possible relevance for the food and feed safety assessment of maize 1507:

- Sindt et al. (2007) reported the growth performance and carcass quality of beef heifers fed finishing diets that were based on steam-flaked grain from maize 1507, its conventional counterpart, or two non-GM maize commercial varieties. These four maize lines were grown in the same field but in physically isolated plots. Maize 1507 received two sequential applications of glufosinate-ammonium-based herbicides. Nutrient composition was determined for the whole and flaked maize grain. Diets were formulated to meet nutrient requirements (NRC, 2000) and the nutrient composition of each diet was determined. Most nutrient values were found to be similar for these four types of grain. Among the test diets, starch content differed statistically ranging from approximately 52% to 56%. It is not clear whether the presence of the Cry1F protein in the maize 1507 diet was determined. Each diet was fed to twenty heifers that were randomly assigned from four body weight groups (average body weight 360 kg). The study ran for 118 days. With regard to growth performance, there were no statistically significant differences in body weight, body weight gains or gain/feed ratio between treatment groups. Carcass traits, yield and quality grades were not different between treatment groups. Thus it was concluded by the authors that beef heifers fed diets containing grain from maize 1507 had similar growth performance and carcass traits compared with heifers fed diets containing grain from the conventional counterpart and two non-GM maize commercial varieties.

- Stein et al. (2009) reported the growth performance and carcass composition of growing and finishing pigs under four dietary treatments with three pigs per pen and eight pen replicates per treatment group (four pens with gilts and four pens with barrows). These four dietary treatments refer to the use of "commercial" maize, "standard" maize, maize 1507 and a "near-isoline" maize hybrid. A three-phase feeding program was used to meet the nutritional needs of pigs during the growing period. Diets were formulated by mixing maize, soybean meal, soybean oil, vitamins and minerals. The inclusion rate of maize was approximately 65%, 73% and 81% in the grower, early finisher and late finisher diets, respectively. Biochemical analysis and gross energy determination of the diets confirmed that they met the nutrient requirements (NRC, 2000). Animals were fed *ad libitum* until their body weight reached approximately 120 kg. Average daily gain, average daily feed intake, and gain/feed ratio were calculated throughout the entire experiment to measure growth performance. Live weights at slaughter were determined, standard carcass measurements (hot carcass weight, 10^{th}-rib backfat thickness, loin eye area, and loin eye depth) were done, and dressing percentage and lean meat percentage calculated. The results of the experiment showed that pig performance was not affected by dietary treatments in any of the three phases and for the overall experimental period. No effects of dietary treatment on any carcass parameter were seen.

5.1.3. Conclusion

Results reported by Sindt et al. (2007) and Stein et al (2009) do not contain new information that would invalidate the previous conclusions on the food and feed safety of maize 1507 made by the EFSA GMO Panel. Therefore, the EFSA GMO Panel considers that its previous conclusions on maize 1507 remain valid and applicable.

6. ENVIRONMENTAL RISK ASSESSMENT AND RISK MANAGEMENT STRATEGIES

6.1. Environmental risk assessment

The outline of this EFSA GMO Panel Scientific Opinion follows the key areas of environmental risk as defined in Directive 2001/18/EC and EFSA (2010a): (1) changes in plant fitness due to the genetic modification; (2) potential for gene transfer and its environmental consequences; (3) interactions between the GM plant and target organisms; (4) interactions between the GM plant and non-target organisms; (5) effects on animal and human health; (6) interactions with biogeochemical processes and the abiotic environment; (7) impacts of the specific cultivation, management and harvesting techniques; and (8) risk management strategies (including PMEM).

The EFSA GMO Panel previously concluded that: "*the cultivation of maize 1507 could have the following adverse effects on the environment in the context of its intended uses: (1) the adoption of altered pest control practices with higher environmental load due to potential evolution of resistance to the Cry1F protein in populations of exposed lepidopteran target pests; and (2) reductions in populations of certain highly sensitive non-target lepidopteran species where high proportions of their populations are exposed over successive years to high levels of maize 1507 pollen deposited on their host-plants*" (EFSA, 2011d).

6.1.1. Changes in plant fitness due to the genetic modification

The EFSA GMO Panel previously evaluated the altered potential of maize 1507 in terms of fitness, persistence and invasiveness (EFSA, 2004, 2005a,b).

6.1.1.1. Summary of previous conclusions by the EFSA GMO Panel

The EFSA GMO Panel indicated that "*there are no indications for an altered ecological fitness of the GM maize in comparison to conventionally bred hybrids with similar genetic background*" (EFSA, 2005b).

6.1.1.2. Results from the literature search

From the literature search, no new peer-reviewed scientific publications containing evidence specific to maize 1507 for this specific area of risk were identified.

6.1.1.3. Conclusion

In the absence of new scientific evidence specific to maize 1507 for this specific area of risk, the EFSA GMO Panel considers that its previous conclusions on changes in plant fitness due to the genetic modification remain valid and applicable.

6.1.2. Potential for gene transfer

The EFSA GMO Panel previously evaluated the potential for horizontal and vertical gene flow of maize 1507, as well as the potential environmental consequences of such gene transfer (EFSA, 2004, 2005a,b).

6.1.2.1. Summary of previous conclusions by the EFSA GMO Panel

Concerning the potential for horizontal gene transfer, the EFSA GMO Panel indicated that: "*owing to the natural occurrence of* cry1F *and* pat *genes in the environment, a low-level gene transfer to*

B. thuringiensis *(for* cry1F*) and to* S. viridochromogenes *(for* pat*) is thought not to confer a new trait and selective advantage*". Considering the intended uses of maize 1507, the EFSA GMO Panel had therefore not identified a concern associated with the horizontal gene transfer from maize 1507 to bacteria (EFSA, 2005b).

For the possible plant-to-plant gene transfer, the EFSA GMO Panel indicated that: "*maize 1507 has no altered survival, multiplication or dissemination characteristics*", and that: "*the likelihood of unintended environmental effects due to the establishment and spread of maize 1507 will be no different to that of traditionally bred maize*". As for any other maize cultivars, it was considered very unlikely that volunteers could survive until subsequent seasons, or would establish feral populations outside agricultural fields under European environmental conditions (EFSA, 2005b).

6.1.2.2. Results from the literature search

From the literature search, no new peer-reviewed scientific publications containing evidence specific to maize 1507 for this specific area of risk were identified.

6.1.2.3. Conclusion

In the absence of new scientific evidence specific to maize 1507 for this specific area of risk, the EFSA GMO Panel considers that its previous conclusions on potential gene transfer from maize 1507 and its potential environmental consequences remain valid and applicable.

6.1.3. Interactions of the GM plant with target organisms

The potential for maize 1507 to cause adverse effects through direct or indirect interactions between the GM plant and target organisms was previously evaluated by the EFSA GMO Panel (EFSA, 2005b, 2006, 2008, 2010a), and the outcome of these evaluations has been updated recently in the light of new relevant scientific publications (EFSA, 2011d).

6.1.3.1. Summary of previous conclusions by the EFSA GMO Panel

The EFSA GMO Panel considered: "*the possible evolution of resistance to the Cry1F protein in lepidopteran target pests as a relevant environmental and agronomic concern associated with the cultivation of maize 1507, as the consequences of resistance evolution may lead to altered pest control practices that may cause adverse environmental effects*" (EFSA, 2011d).

6.1.3.2. Results from the literature search

From the literature search, the following 23 new peer-reviewed scientific publications containing evidence specific to maize 1507 for this specific area of risk were identified and scrutinised for their possible relevance for the ERA of maize 1507:

- Schaafsma et al. (2007) investigated the performance of Cry1F-expressing maize event 1507 and Cry1Ab-expressing maize events MON 810 and Bt176 against the pest species true armyworm (TAW, *Pseudaletia unipuncta*) under greenhouse and field conditions. Greenhouse studies with maize 1507, MON 810 and Bt176 were performed in 2002 and 2004, and a field study with maize 1507 and MON 810 was conducted in 2003. Overall, *Bt*-maize suffered less damage in all three years and had higher fresh masses in 2002 and 2003 than non-*Bt*-maize. In 2002 and 2003, maize 1507 had more damage than maize MON 810 and Bt176.

- Buntin (2008) investigated the performance of the Cry1F-expressing maize event 1507 and Cry1Ab-expressing maize event MON 810 against the pest species fall armyworm (FAW, *Spodoptera frugiperda*) and corn earworm (CEW, *Helicoverpa zea*) under field conditions in the southeastern USA. The field study was performed at four locations during the seasons 2006-2007. A randomised complete block design with four replications was used at all locations. Buntin (2008) reported reduced whorl infestation and damage by FAW for both *Bt*-maize events; maize 1507 provided greater protection from whorl injury than maize MON 810 under severe FAW infestation levels. Maize 1507 usually did not reduce ear infestations by CEW, while maize MON 810 usually had less ear infestation than non-*Bt*-maize. The *Bt*-toxins did not affect grain yield in either year during the first planting when FAW infestation levels were low. Both *Bt*-maize events prevented significant yield loss during the second planting in 2006 when whorl infestation levels exceeded 50% in non-*Bt*-maize. Because of the greater activity in preventing whorl damage by FAW, Buntin (2008) considered that maize 1507 would be useful in mitigating the risk of severe lepidopteran damage to later plantings of maize for grain production. However, CEW and FAW are not present in Europe (Meissle et al., 2012).

- Siebert et al. (2008a,b) investigated the performance of maize 1507 against FAW under laboratory and field conditions. Siebert et al. (2008a) reported significantly less leaf-feeding injury to maize 1507 plants and significantly greater plant height for Cry1F-expressing maize plants compared with non-*Bt*-maize when exposed to natural or artificial FAW infestation levels under field conditions. The authors performed a field study at three southern US locations during the season 2005, using a randomised complete block design with four replications at all locations. In the fresh tissue bioassays, mortality of FAW larvae exposed to maize 1507 leaf tissue was shown to be significantly greater compared with that of larvae fed non-*Bt*-maize leaf tissue. The percent of larvae surviving to pupation was 0.5% and 36.2% for the *Bt*- and non-*Bt*-treatment, respectively (Siebert et al., 2008a). Siebert et al. (2008b) compared FAW injury to vegetative (whorl) stage of maize 1507 and non-*Bt*-maize in a field study conducted at three locations in the USA during the seasons from 2002-2006, and in three locations in Brazil during 2007. A randomised complete block design with four replications was used at all locations. Maize 1507 and non-*Bt*-maize plants were exposed to either natural or artificial FAW infestations of eggs, as well as to various larval stages. The average leaf-feeding injury for maize 1507 was 1.3 as compared to 7.9 for non-*Bt*-maize in the US locations. These results demonstrate that maize 1507 offers high and consistent levels of control against FAW. FAW is not present in Europe (Meissle et al., 2012).

- Virla et al. (2008) identified the occurrence of two FAW strains (a rice and maize strain) in Argentina (similar data were previously reported for Brazil and the USA), and demonstrated through fresh tissue bioassays that these strains displayed different levels of susceptibility to Cry1F. The rice strain was less susceptible to Cry1F than the maize strain. Virla et al. (2008) also reported lower mortality values for FAW larvae exposed to Cry1Ab-expressing maize leaf tissue (68.8%) than Cry1F-expressing maize leaf tissue (83.5%).

- Reavy-Jones et al. (2009) evaluated the performance of various *Bt*-maize events including 1507 on target insect pests in maize in South Carolina. Target insect pressure was low at seedling stages of maize during all three years of the study. In addition, no cornstalk borers (CSB, *Elasmopalpus lignosellus*) were observed and whorl-stage injury by FAW was sporadic. The only consistent insect injury observed was ear feeding by CEW. Maize 1507 had significantly reduced CEW-induced injury compared with non-*Bt*-maize in field trials in 2008 by an average of 51%. Maize MON 810 was shown to be more effective than maize 1507 in reducing CEW-induced ear injury based on both percentage of injured ears and number of injured kernels.

- Schmidt et al. (2009) reported that larvae of the pest species black cutworm (BCW, *Agrotis ipsilon*) were more susceptible to infection by *A. ipsilon* multiple nucleopolyhedrovirus (AgipMNPV: Baculoviridae) after feeding on maize 1507 compared with larvae fed non-*Bt*-maize. Analysis of soluble and membrane-associated gut proteinase activities from larvae fed maize 1507 or non-*Bt*-maize diets indicated that membrane-associated aminopeptidase activity and soluble chymotrypsin-like proteinase activity were significantly lower in larvae fed maize 1507 compared to those fed non-*Bt*-maize. The number and relative molecular masses of soluble chymotrypsin-like proteinases did not differ. Baculoviruses were not susceptible to *in vitro* degradation by bovine chymotrypsin, suggesting that chymotrypsin degradation of baculovirus occlusion-derived virus did not result in reduced infection of larvae fed non-*Bt*-maize. Scanning electron micrographs of the peritrophic matrices of larvae indicated that maize 1507 did not result in damage to the peritrophic matrix that could facilitate subsequent baculovirus infection. The authors concluded that further research is required to delineate the physiological basis for enhanced baculovirus infection following exposure to sublethal doses of Cry1F.

- Hutchison et al. (2010) found that areawide suppression of ECB is associated with the cultivation of *Bt*-maize in the USA. Cumulative benefits over fourteen years were estimated to be 3.2 billion USD for maize growers in Illinois, Minnesota, and Wisconsin, with more than 2.4 billion USD of this total accruing to non-*Bt*-maize growers, and 3.6 billion USD for maize growers in Iowa and Nebraska, with 1.9 billion USD for non-*Bt*-maize growers. According to the authors these results affirm theoretical predictions of pest population suppression, and highlight economic incentives for growers to maintain non-*Bt*-maize *refugia* for sustainable insect resistance management.

- Oppert et al. (2010) investigated the efficacy of the Cry1F protoxin on four stored-product pests, comprising the two lepidopteran species angoumois grain moth (AGM, *Sitotroga cerealella*) and Indianmeal moth (IMM, *Plodia interpunctella*), and the two coleopteran species flat grain beetles (FGB, *Cryptolestes pusillus*) and red flour beetle (RFB, *Tribolium castaneum*). For AGM no conclusion can be drawn, as significant problems were encountered in the bioassays; no method or diet was judged satisfactory for routine screening of compounds with this insect species. The Cry1F protoxin had adverse effects on IMM, as measured by the LC_{50}, but not on the two coleopteran species tested (FGB and RFB), as measured by development period, larval weight or mortality. These data confirm that the insecticidal activity of Cry1F is limited to species belonging to Lepidoptera. The Cry1F protoxin was shown to be less active than Cry1Ab toxin or Cry1Ac protoxin against *Bt*-susceptible IMM in most cases. The authors also suggested the potential for cross-resistance between maize Cry1Ab and Cry1F, as IMM colonies resistant to Cry1Ab were less susceptible to Cry1F than non-resistant colonies. Therefore, the authors suggested that the Cry1F protoxin may be unsuitable for use against Cry1Ab-resistant IMM.

- Pereira et al. (2010) investigated the biochemical mechanism of resistance in a laboratory-selected Cry1F-resistant ECB colony with high resistance levels (> 3,000-fold) to Cry1F and limited cross-resistance to Cry1Ab and Cry1Ac (Pereira et al., 2008b). Analyses of Cry1F binding to brush border membrane vesicles of midgut epithelia from susceptible and resistant larvae using ligand immunoblotting and surface plasmon resonance suggested that reduced binding of Cry1F to insect receptors was not associated with resistance. Additionally, no differences in activity of luminal gut proteases or altered proteolytic processing of the toxin were observed in the resistant ECB colony. Considering these results along with previous evidence of relatively narrow spectrum of cross-resistance and monogenic inheritance, the authors concluded the resistance mechanism in this laboratory-selected Cry1F-resistant ECB colony appears to be specific and may be distinct from previously identified resistance mechanisms reported in other Lepidoptera.

- Thompson et al. (2010) investigated the efficacy of maize 1507 against the Asian corn borer (ACB, *Ostrinia furnacalis*) under field conditions in the Philippines. The field study was performed at seven locations during the season 2006 and across the seasons 2006-2007. A randomised complete block design with four replications was used at all locations. The authors reported that maize 1507 had reduced number of borer tunnels, foliar injury and total tunnel length per plant, and averaged more yield per hectare than the near-isogenic line across twelve test locations in the Philippines covering locations planted during a wet and dry season. Based on these results, the authors concluded that maize 1507 offers an additional effective means of control against ACB. However, ACB is a pest that is not present in Europe (Meissle et al., 2012).

- Xu et al. (2010) and Crespo et al. (2011) investigated the potential for cross-resistance between Cry1Ab and Cry1F. Laboratory-selected Cry1Ab-resistant ACB and MCB colonies were shown to exhibit low levels of cross-resistance (ranging between < 4- and 6-fold) to Cry1F, respectively.

- Ghimire et al. (2011) demonstrated that larvae of a laboratory-selected Cry1Ab-resistant sugarcane borer (SCB, *Diatraea saccharalis*) colony are also resistant to Cry1F in leaf tissue bioassays and intact plant tests conducted under greenhouse conditions, pointing to the potential for cross-resistance between maize events MON 810 and 1507. Results from this study suggest that the mode of action of Cry1Ab and Cry1F (i.e., the binding sites for these proteins in the insect midgut) could overlap. Even though other studies suggested only very low levels or lack of cross-resistance between Cry1Ab and Cry1F (Siqueira et al., 2004; Pereira et al., 2008a; Xu et al., 2010; Crespo et al., 2011), it is prudent to infer the potential for cross-resistance, and to account for this when developing insect resistance management (IRM) strategies for maize 1507 (section 6.2). Further, caution is recommended in deploying pyramided *Bt*-crops[11] that express both Cry1Ab and Cry1F proteins, as their efficacy will be diminished or offset, if cross-resistance occurs (see Storer et al., 2012b, below). SCB is a stalk-boring pest species of sugarcane, maize and other crops, which only occurs in South, Central and North America, but not in Europe (Meissle et al., 2012).

- Hardke et al. (2011) compared the foliar injury and the survival of FAW on Cry1F- and Cry1Ab-expressing maize. Cry1F-expressing maize plants had significantly lower feeding injury ratings than non-*Bt*-maize plants under field conditions, while Cry1Ab-expressing plants did not. In a no-choice leaf tissue bioassay, the growth, development and survival of FAW fed Cry1F-expressing maize was reduced significantly compared with the control (non-*Bt*-maize), despite the use of older instars that are inherently less susceptible than neonates. However, 25-76% of third instars offered Cry1Ab-expressing maize leaf tissues successfully pupated and emerged as adults. These results suggest Cry1Ab has limited effect on this target pest, whereas Cry1F demonstrated significant reductions in foliar injury and lower survival. Hardke et al. (2011) indicated that these levels of survival could affect the efficiency of the IRM strategies in delaying resistance evolution to Cry1Ab in FAW.

- Reavy-Jones and Wiatrak (2011) evaluated the performance of the *Bt*-maize events 1507 and MON 89034 in field trials conducted in South Carolina. The authors reported reduced CEW-induced injury on maize 1507 by 53% across both years and locations of the study, as compared with non-*Bt*-maize.

- Tan et al. (2011) performed insect bioassays with various Cry1 proteins (including Cry1F) to assess the pattern of susceptibility between ECB, ACB and SCB. Of these three lepidopteran maize pests, only ECB is present in Europe. The authors found that: ACB and ECB exhibited similar patterns of susceptibility to Cry1F; ACB was highly susceptible to Cry1F; and that SCB was more tolerant to Cry1F than the two *Ostrinia* species. The lower susceptibility of SCB suggests a need to verify whether the high dose condition for effective IRM strategy is met for maize 1507 and SCB. However, SCB does not occur in Europe (Meissle et al., 2012).

- Leaf tissue and plant seedling feeding bioassays performed by Farinós et al. (2012) indicated that neonate MCB are efficiently controlled by maize 1507.

- Gryspeirt and Grégoire (2012) investigated the impact of diets containing different concentrations of grains from the Cry1Ab-expressing maize event MON 810 and Cry1F-expressing maize event 1507 on IMM. Survival, development time, weight, and larval preference between diets containing *Bt*-maize and non-*Bt*-maize were measured. Adults fed the Cry1F diet as larvae had decreased weight. Cry1F increased the development time from egg to adult, regardless of sex and had no impact on the male adult lifespan. A time lag was reported between metamorphosis from the *Bt*- and non-*Bt*-diets, which increased proportionally with the Cry concentration in the *Bt*-diet. These data confirm that IMM is susceptible to Cry1F. The authors also suggested a repellent factor in Cry1F-containing diets, as more larvae were found in the non-*Bt*-maize zone than the Cry1F zone, compared with the control. However, further investigation is required to confirm this hypothesis. The authors described the relevance of their work in the context of IRM relying on the high dose/refuge (HDR) strategy (section 6.2), but IMM is not considered to be a pest of field crops. IMM is primarily associated with stored foods, and considered a world-wide lepidopteran pest of stored products and processed food commodities (Mohandass et al., 2007).

[11] A pyramided *Bt*-crop combines related traits such as insect resistance against target insect pest species of the same Order

- Siegfried and Hellmich (2012) reviewed all available resistance data in ECB to plant-produced *Bt*-toxins (including Cry1F) obtained under laboratory, greenhouse and field conditions, and concluded that the potential risk of resistance necessitates IRM measures to delay resistance evolution.

- Siebert et al. (2012) compared the efficacy of a several *Bt*-maize events (stacked and single events versus non-*Bt*-maize) against several target lepidopteran and coleopteran maize pests across the southern US. Cry1F in maize 1507 and Cry1A.105 + Cry2Ab2 in maize MON 89034 were evaluated against pests infesting maize on foliage, stalks and ears. Cry34Ab1/Cry35Ab1 in maize DAS-59122-7, and Cry3Bb1 in maize MON 88017 were evaluated against the larvae of Mexican corn rootworm (MCR, *Diabrotica virgifera zeae*). *Bt*-maize expressing Cry1F, Cry1A.105 + Cry2Ab2, Cry34Ab1/Cry35Ab1, and Cry3Bb1 (SmartStax) consistently demonstrated reductions in plant injury and/or reduced larval survivorship as compared with a non-*Bt*-maize. Efficacy provided by *Bt*-maize expressing multiple *Bt*-toxins was statistically equal to or significantly better than *Bt*-maize expressing a single *Bt*-toxin. *Bt*-maize expressing a single *Bt*-toxin provided very high levels of control of southwestern corn borer (SCR, *Diatraea grandiosella*), lesser control of CSB and FAW, and were not significantly different than *Bt*-maize expressing multiple *Bt*-toxins. Significant increases in efficacy were observed for a *Bt*-maize expressing multiple *Bt*-toxins for SCB, beet armyworm (BAW, *Spodoptera exigua*), CEW and MCR. The authors concluded that the cultivation of *Bt*-maize expressing multiple *Bt*-toxins provides a means for managing resistance evolution to *Bt*-toxins and may reduce non-*Bt*-maize refuge requirements.

- Storer et al. (2012a) provided an update on the status of the previously reported instance of field-evolved resistance to Cry1F-expressing maize in FAW in Puerto Rico (Matten et al., 2008; Moar et al., 2008; Tabashnik, 2008; Tabashnik et al., 2008a,b, 2009; Storer et al., 2010). Resistant populations in Puerto Rico and susceptible ones in the southern USA were further monitored, showing high levels of Cry1F resistance and full susceptibility, respectively. The authors concluded that the resistant populations have not spread to any measurable extent from Puerto Rico to mainland USA, and that local selection from Cry1F-expressing maize in the southern USA has caused no measurable change in population susceptibility. However, these data indicate that resistance may persist in a population, and that slowing the spread of resistance genes is more practical than eradicating resistance. Therefore, the authors advocated the deployment IRM measures to delay the evolution of resistance, and to manage the sustainable use of *Bt*-crops.

- Storer et al. (2012b) discussed the potential to delay resistance evolution through the deployment of pyramided *Bt*-crops. They concluded that pyramiding in the same plant of two or multiple *Bt*-toxins, acting independently on target insect pest midgut receptors, is expected to delay the evolution of resistance to either *Bt*-toxin effectively when most individuals that are resistant to one *Bt*-toxin are killed by the other, and when selection for resistance to one of the *Bt*-toxins does not cause cross-resistance to the other.

6.1.3.3. Conclusion

Results reported by Schaafsma et al. (2007), Buntin (2008), Siebert et al. (2008a,b, 2012), Virla et al. (2008), Reavy-Jones et al. (2009) , Schmidt et al. (2009), Hutchison et al. (2010), Thompson et al. (2010), Oppert et al. (2010), Pereira et al. (2010), Xu et al. (2010), Crespo et al. (2011), Hardke et al. (2011), Reavy-Jones and Wiatrak (2011), Tan et al. (2011), Farinós et al. (2012), Gryspeirt and Grégoire (2012), Siegfried and Hellmich (2012) and Storer et al. (2012a,b) do not contain new information that would invalidate the previous conclusions on interactions of maize 1507 with target organisms made by the EFSA GMO Panel. Therefore, the EFSA GMO Panel considers that its previous conclusions on maize 1507 remain valid and applicable.

Findings reported by Ghimire et al. (2011) suggest that the mode of action of Cry1Ab and Cry1F could overlap, and therefore should be accounted for when developing IRM strategies for maize 1507. Even though other studies suggested only very low levels or lack of cross-resistance between Cry1Ab and Cry1F (Siqueira et al., 2004; Pereira et al., 2008a; Xu et al., 2010; Crespo et al., 2011), it is prudent to infer the potential for cross-resistance, and to account for this when developing IRM strategies for maize 1507 (see section 6.2, below).

6.1.4. *Interactions of the GM plant with non-target organisms*

The potential of maize 1507 to have direct or indirect adverse effects on non-target organisms and the ecosystem services they provide in agro-ecosystems was previously evaluated by the EFSA GMO Panel (EFSA, 2005b, 2006, 2008, 2010a) and the outcome of these evaluations has been recently updated in the light of new relevant scientific publications (EFSA, 2011d, 2012b).

6.1.4.1. Summary of previous conclusions by the EFSA GMO Panel

The EFSA GMO Panel indicated that: "*there is no evidence to indicate that the cultivation of maize 1507 is likely to cause adverse effects on non-target soil and aquatic arthropods and to cause reductions to natural enemies or pollinating insects that are significantly greater from those caused by conventional farming where pesticides are used to control corn borers*" (EFSA, 2011d). The EFSA GMO Panel concluded that: "*the studies provided by the applicant confirmed that the target specificity of the insecticidal Cry1F protein is limited to arthropod species of the order of Lepidoptera, as no adverse effects on non-target organisms tested have been reported*" (EFSA, 2011d).

Using a mathematical model of exposure to assess potential adverse effects resulting from exposure of non-target lepidopteran species to Cry1F-containing maize pollen deposited on their host-plants under representative cultivation conditions (Perry, 2011a; Perry et al., 2010, 2011, 2012 referred to in EFSA, 2011d), the EFSA GMO Panel concluded that: "*there is a risk to certain highly*[12] *sensitive non-target lepidopteran species where high proportions of their populations are exposed over successive years to high levels of maize 1507 pollen deposited on their host-plants*" (EFSA, 2011d, 2012b).

6.1.4.2. Results from the literature search

From the literature search, the following four new peer-reviewed scientific publications containing evidence specific to maize 1507 for this specific area of risk were identified and scrutinised for their possible relevance for the ERA of maize 1507:

- Mason et al. (2008) studied whether pollen from Cry1F-expressing maize event 1507 and Cry1Ab-expressing maize events MON 810 and Bt176 causes adverse effects to adult *Chrysoperla plorabunda*. Adult lacewings are not predacious, but are prevalent pollen consumers in maize fields (Meissle et al., 2012), so they could be exposed to the Cry1F protein contained in the pollen when feeding on pollen. Males fed pollen from maize 1507 showed a trend for living longer than males fed non-*Bt*-maize pollen. Such a trend was not observed for females fed pollen from maize 1507 or non-*Bt*-maize. The mean number of eggs produced per female per day was similar for those fed maize 1507 pollen compared with females fed pollen from non-*Bt*-maize. No difference in total egg production was observed between females fed pollen from maize 1507 or non-*Bt*-maize. These results confirm that Cry1F and pollen of maize 1507 are not toxic to *C. plorabunda*.

- Cheeke et al. (2012) investigated the impact of several *Bt*-maize events (including Cry1F-expressing maize) on symbiotic arbuscular mycorrhizal fungi (AMF) under greenhouse potting conditions. The authors observed lower levels of AMF colonisation in the roots of *Bt*-maize, as compared with the non-*Bt*-maize (parental) lines. The reduced mycorrhization was not related to the expression of a specific *Bt*-toxin, but may be the result of other factors such as unintended changes in *Bt*-maize due the genetic modification process. The authors themselves state that scientific uncertainty remains on how the reported observations translate to the field situation, as low levels of fertilisation had to be applied during the experiment to favour mycorrhization (Verbruggen et al., 2012). With the example of Cry1Ab-expressing maize event Bt11, the authors

[12] Here, a "highly sensitive species" means a species in one of the three highest sensitivity categories ('high', 'very high' and 'extremely high') as defined in EFSA (2012b). To place this into context, note that a species at the lower end of the 'high' sensitivity category would be somewhat less sensitive than the moth pest *Plutella xylostella* and close to the 8th percentile of the species sensitivity distribution (see EFSA, 2011d)

demonstrated in a previous study that differences between the *Bt*-maize and non-*Bt*-maize in fact disappeared when fertilisers were added to soil (Cheeke et al., 2011). For the cultivation of maize, in which normally larger amounts of organic or inorganic fertilisers are added to improve maize yield, the effects as observed by Cheeke et al. (2011) are therefore most likely insignificant. Furthermore, under common agricultural practices, the contribution of AMF to improve health or increase yield of maize appears to be negligible or not existent (e.g., as reviewed by Ryan and Kirkegaard, 2012).

- Kim et al. (2012) reported that Cry1F-expressing maize did not adversely affect the aphid species, *Rhopalosiphum padi*. No difference in survival rate, alata vivipara production, or host preference was observed between *R. padi* fed *Bt*-maize or non-*Bt*-maize under laboratory conditions. These data confirm that *Bt*-maize had no sub-chronic adverse effects on *R. padi*, and that Cry1F is not toxic to aphids. ELISA measurements indicated that Cry1F increased gradually in the body of *R. padi* when they were fed *Bt*-maize leaves, but that all ingested Cry1F was excreted within 10 days after aphids reared on *Bt*-maize leaves for 50 days were transferred to non-*Bt*-maize. The Cry1F protein concentrations in aphids were not quantified, but were presented as ratio to a positive control. No information is provided on standard curve (relationship between optical density and Cry1F concentration), limit of detection, sample size, stage of sampled aphids, and Cry1F expression in plants. Therefore, the study by Kim et al. (2012) suggests that *R. padi* might take up Cry1F from *Bt*-maize plants, but the quantity relative to plant tissue remains unknown. Previously published evidence shows that aphids do not ingest significant amounts of Cry proteins when feeding on *Bt*-maize (Head et al., 2001; Raps et al., 2001; Romeis and Meissle, 2011), though recent evidence suggests that aphids feeding on other *Bt*-crops such as oilseed rape can be exposed to Cry proteins (Burgio et al., 2011). Because the study by Kim et al. (2012) does not provide a detailed description of the sampling and measurement procedure, no conclusion on the likelihood and relevance of Cry1F uptake by aphids can be drawn.

- Tian et al. (2012) evaluated the potential impact of Cry1F-expressing maize on some life-history parameters (development time, weight) and reproductive parameters (fecundity, fertility) of the predatory ladybird beetle *Coleomegilla maculata* in a tri-trophic study. *C. maculata* larvae were fed Cry1F-resistant FAW larvae reared on leaves of maize 1507 or its near-isogenic line. Cry1F-resistant fall armyworms were used to overcome prey-mediated effects. The authors found no difference in life-history and reproductive parameters of *C. maculata*. ELISA analyses confirmed the uptake of Cry1F by the ladybird beetle larvae, as larvae contained 20-32 ng Cry1F/g by fresh weight. The authors concluded that Cry1F protein did not accumulate but was strongly diluted when transferred through trophic interactions. These results confirm that Cry1F is not toxic to C. *maculata*.

6.1.4.3. Conclusion

Results reported by Mason et al., (2008), Cheeke et al. (2012), Kim et al. (2012) and Tian et al. (2012) do not contain new information that would invalidate the previous conclusions on interactions of maize 1507 with non-target organisms made by the EFSA GMO Panel. Therefore, the EFSA GMO Panel considers that its previous conclusions on maize 1507 remain valid and applicable.

6.1.5. Effects on human and animal health

The potential of maize 1507 to have adverse effects on human and animal health was previously evaluated by the EFSA GMO Panel (EFSA, 2004, 2005a,b, 2009, 2010b,c, 2011e,f).

6.1.5.1. Summary of previous conclusions by the EFSA GMO Panel

The molecular analysis, comparative analysis and the food and feed safety assessment of maize 1507 did not raise safety concerns for human and animal health. Therefore, in its previous Scientific Opinions on maize 1507 (EFSA, 2004, 2005a,b, 2009, 2010b,c, 2011e,f), the EFSA GMO Panel concluded that: "*maize 1507 is as safe as conventional maize*", and that: "*maize 1507 and derived* *products are unlikely to have any adverse effect on human and animal health in the context of the intended uses*".

6.1.5.2. Results from the literature search

See sections 3, 4 and 5 for further details.

6.1.5.3. Conclusion

See sections 3, 4 and 5 for further details.

6.1.6. Interactions with biogeochemical processes and the abiotic environment

The EFSA GMO Panel previously considered the possible environmental exposure to the Cry1F protein introduced into the soil via physical damage to plant tissues, via decomposition of shed root cells during plant growth, via decomposing plant residues remaining in fields after harvest and that might be incorporated into the soil during tillage operations, and possibly via root exudates (EFSA, 2005b). The outcome of these evaluations has been recently updated in the light of new relevant scientific publications (EFSA, 2011d).

6.1.6.1. Summary of previous conclusions by the EFSA GMO Panel

The EFSA GMO Panel indicated that: "*though the data on the fate of the Cry1F protein and its potential interactions in soil are limited, the relevant scientific publications analysing the Cry1F protein, together with the relatively broad knowledge about the environmental fate of other Cry1 proteins, do not indicate any novel risks that would change its previous conclusion that there are no significant direct effects on the soil environment*" (EFSA, 2011d).

6.1.6.2. Results from the literature search

From the literature search, the following new peer-reviewed scientific publication containing evidence specific to maize 1507 for this specific area of risk was identified and scrutinised for its possible relevance for the ERA of maize 1507:

- Liu et al. (2010) investigated the potential impact of Cry1F-expressing maize event 1507 and CP4 EPSPS-expressing maize event NK603 on the status of soil nutrients in a field experiment. Comparisons were made between the GM maize events and their conventional (near-isogenic) counterparts. Under field conditions, based on four replicates, the authors analysed the soils after harvesting, and found 7% lower values for phosphorous and 14% higher ammonium values in soils where maize NK603 was cultivated, but there was no alteration of soil parameters for maize 1507. Considering the temporal and spatial dynamics of phosphorous and ammonium in agricultural field soils receiving fertilisers, the differences detected are within an expected background variability and, considering the low number of replicates, probably stochastic. In the same publication, the authors also reported data-derived from greenhouse pot experiments. In these pot experiments, the effect of Cry1Ab-expressing maize event Bt176 on soil chemical parameters was analysed in three different soils. Comparisons were made based on eight replicates and minor differences, inconsistent between soils were reported. In one soil, phosphate was 20% lower in phosphate compared to a (not described) control, in another the pH of the soil declined and in the third, soil organic matter and total nitrogen were both approximately 3% higher. These differences are in the normal range of variation which would be expected between soil and/or technical replicates, and they give no indication for an event-specific effect of maize Bt176. The authors themselves stated that the effects were small and inconsistent and do not allow general conclusions of the analysed GM maize events.

6.1.6.3. Conclusion

Results reported by Liu et al. (2010) do not contain new information that would invalidate the previous conclusions on interactions of maize 1507 with biogeochemical processes and the abiotic environment made by the EFSA GMO Panel. Therefore, the EFSA GMO Panel considers that its previous conclusions on maize 1507 remain valid and applicable.

6.1.7. Impacts of the specific cultivation, management and harvesting techniques

The consequences of changes in crop management practices associated with maize 1507 were previously evaluated by the EFSA GMO Panel (EFSA, 2005b). Recently, the outcome of this evaluation has been reviewed to account for clarifications supplied on the scope of the notification (reference C/ES/01/01) for maize 1507 cultivation (EFSA, 2011d).

6.1.7.1. Summary of previous conclusions by the EFSA GMO Panel

The EFSA GMO Panel indicated that: "*apart from changes in insecticide regimes, there are no anticipated changes in management that will occur with the cultivation of maize 1507*". The EFSA GMO Panel noted that: "*the incidence of secondary pests and the environmental consequences of changes in management measures is highly dependent upon farming systems and regional environmental factors, and is therefore difficult to predict. Risk managers should be aware that, whenever pest management measures change, species assemblages will change accordingly and the environmental consequences should be considered in the framework of IPM in National Action Plans according to Directive 2009/128/EC*" (EFSA, 2011d).

6.1.7.2. Results from the literature search

From the literature search, no new scientific publications containing evidence specific to maize 1507 for this specific area of risk were identified.

6.1.7.3. Conclusion

In the absence of new scientific evidence specific to maize 1507 for this area of risk, the EFSA GMO Panel considers that its previous conclusions on impacts of the specific cultivation, management and harvesting techniques associated with the cultivation of maize 1507 remain valid and applicable.

6.2. Risk management strategies (including post-market environmental monitoring)

6.2.1. Risk mitigation measures

The EFSA GMO Panel previously considered that the potential risk of resistance evolution in target insect pests and that the risk of reductions in populations of certain highly sensitive to extremely highly sensitive non-target lepidopteran species require management, and recommended the implementation of risk mitigation measures under certain conditions (EFSA, 2005b, 2011d, 2012b).

6.2.1.1. Summary of previous conclusions by the EFSA GMO Panel

For target insect pests, the EFSA GMO Panel indicated that: "*appropriate Insect Resistance Management (IRM) strategies (i.e., 'high dose/refuge' strategy) should be employed, in order to delay the potential evolution of resistance to the Cry1F protein in target pests*". It also made specific recommendations (in terms of sampling and target insect pest species to be considered) to the applicant to improve the proposed IRM plan (EFSA, 2011d).

For non-target Lepidoptera, the EFSA GMO Panel proposed to risk managers the implementation of risk mitigation measures to reduce pollen exposure of highly to extremely highly sensitive non-target lepidopteran species found in maize 1507 fields, field margins and in nearby protected habitats (EFSA, 2011d). These could include: (1) placing non-*Bt*-maize strips between maize 1507 plants and field margins; (2) isolation distances to habitats where protected Lepidoptera are present (according to Directive 2004/35/EC); or (3) providing refuge areas where host-plants for Lepidoptera are not exposed to pollen from maize 1507 or other Lepidoptera-active maize events (EFSA, 2011d).

The EFSA GMO Panel indicated that: "*if maize 1507 cultivation remains below 5% of the Utilized Agricultural Area*[13]*, the global mortality is predicted to remain below 1%, even for extremely highly sensitive species, and then risk mitigation measures are not required. Whenever mitigation measures are needed, the implementation of non-Bt-maize border rows will reduce the mortality of non-target lepidopteran species for both within fields and in field margins*" (EFSA, 2011d).

Recently, the EFSA GMO Panel further supplemented its previous recommendations for risk mitigation measures and monitoring by reapplying the mathematical model developed by Perry et al. (2010, 2011, 2012) to consider additional hypothetical agricultural conditions and to provide additional information on the factors affecting the insect resistance management plan (EFSA, 2012b).

The EFSA GMO Panel concluded that risk mitigation measures can appropriately delay resistance evolution in target Lepidoptera, and reduce the identified risks of maize 1507 cultivation to a level of no concern for non-target Lepidoptera.

6.2.1.2. Results from the literature search

From the literature search, the following ten new peer-reviewed scientific publications containing evidence specific to maize 1507 for this specific area were identified and scrutinised for their possible relevance for the risk management of maize 1507:

- Alyokhin (2011) recommended a larger refuge size for pyramided *Bt*-crops (20% instead of 5% for pyramided *Bt*-maize) due to the potential for cross-resistance between structurally different *Bt*-toxins.

- Burkness et al. (2011) reported that ears of non-*Bt*-maize plants from refuge areas, when cross-pollinated by nearby planted *Bt*-maize plants, can result in sublethal exposure of ECB larvae to the *Bt*-toxin (see also Burkness and Hutchison, 2012). According to the authors, this sublethal exposure may reduce the efficacy of IRM relying on the HDR strategy, implemented to delay resistance evolution. However, the recent model predictions by Glaum et al. (2012) and Kang et al. (2012) estimated that pollen-mediated gene flow from *Bt*-maize to refuge plants has little impact on the evolution of resistance of the target insect pests.

- Coates et al. (2011) revealed that a single locus is responsible for resistance in a Cry1F resistant colony exhibiting: (1) high levels of resistance; and (2) the ability to survive on Cry1F-expressing plants under greenhouse conditions (Pereira et al., 2008a). Whether this resistance is caused by a loss of *Bt*-toxin binding to midgut receptors has yet to be confirmed (Pereira et al., 2010; Siegfried and Hellmich, 2012). The authors also reported that the Cry1F resistance is autosomal and recessive. Simulation models predict the longest delays in resistance evolution for resistance traits that are completely recessive. If resistance is completely recessive, then heterozygous offspring resulting from crosses between resistant and susceptible individuals are expected to be susceptible to the *Bt*-toxin, thus preventing or slowing resistance evolution (Bates et al., 2005).

- Ghimire et al. (2011) demonstrated that larvae of a laboratory-selected Cry1Ab-resistant SCB colony are also resistant to Cry1F in leaf tissue bioassays and intact plant tests conducted under greenhouse conditions, pointing to the potential for cross-resistance between maize MON 810 and 1507. Results from this study suggest that the mode of action of Cry1Ab and Cry1F (i.e., the binding sites for these proteins in the insect midgut) could overlap. Even though other studies suggested only very low levels or lack of cross-resistance between Cry1Ab and Cry1F (Siqueira et al., 2004; Pereira et al., 2008a; Xu et al., 2010; Crespo et al., 2011), it is prudent to infer the potential for cross-resistance, and to account for this when developing IRM strategies for maize 1507.

[13] For example, an uptake of 20% of maize 1507 in a region where maize represents 25% of the arable land; i.e., zv = 0.05, and with conservative assumptions for the other parameters y=a=x=0.5, yielding R = 0.00625 (EFSA, 2011d)

- Model predictions by Buschman and Ramaswamy (2012) indicated that the HDR strategy could be optimised by cultivating *Bt*-crops that are truly high dose and that express traits that deter oviposition of the target insect pest (termed by the authors as toxin-oviposition deterrance-pyramided plants). Both traits were postulated to reinforce each other ecologically, and were shown to delay resistance evolution more under certain conditions, as compared with a pyramided *Bt*-crop expressing two *Bt*-toxins. According to the authors, the use of toxin-oviposition deterrance-pyramided plants would substantially delay, or even prevent resistance evolution, and may also allow reducing refuge size. The authors recognised there are several challenges to identify highly effective oviposition deterrents against ECB and subsequently to use those to create toxin-oviposition deterrance-pyramided plants. Further, the authors noted that *Bt*-toxins are active against several different maize target insect pest species, and that finding oviposition deterrance that will be effective on exactly the same spectrum of pest insects will be challenging.

- In their review, Head and Greenplate (2012) summarised: the current adoption status of *Bt*-cotton and *Bt*-maize globally; the principles of IRM for *Bt*-crops and what they mean for the design of IRM plans; how these IRM plans have been implemented; key factors affecting successful implementation of IRM plants; and how IRM plans are evolving to properly steward *Bt*-crops in different geographies around the world. The lack of resistance in some major insect pests targeted by *Bt*-crops attests that the HDR strategy is capable to prevent or at least delay resistance under field conditions, despite 15 years of intensive use of some *Bt*-crops. In contrast, where resistance issues have been observed, they have been associated with first generation technologies and incomplete or compromised IRM plans (i.e., insufficient planting of refuges, inadequately structured refuges, non-recessive inheritance of resistance, specific agronomic/environmental factors, non-compliance) (see also Andow 2008; Tabashnik et al. 2008a,b 2009; Huang et al. 2011; Siegfried and Hellmich 2012). Head and Greenplate (2012) argued that the deployment of pyramided *Bt*-crops together with the implementation of IRM plans that are more dependent upon manufacturing and less dependent upon grower behaviour (e.g., seed blends) will optimise IRM plans for the next generation of *Bt*-crops further.

- Razze and Mason (2012) assessed the movement and dispersal behaviour of neonate ECB on *Bt*-maize. Results indicated that neonate dispersal may be significantly greater in *Bt*-maize fields compared with non-*Bt*-maize fields. The potential for larval movement between *Bt*-maize and refuge plants, and the exposure of later instars to sublethal doses of the toxin may reduce the efficacy of IRM strategies relying on seed blends (also termed seed mixtures or refuge in a bag), as these factors may lower the selective differential between susceptible and resistant genotypes, and increase the effective dominance of resistance by producing more heterozygote individuals (Mallet and Porter, 1992; Goldstein et al., 2010; Onstad et al., 2011). The findings reported by Razze and Mason (2012) will be useful in evaluating the efficacy of seed blends for *Bt*-maize and ECB as refuge strategy for managing ECB resistance in *Bt*-maize. The EFSA GMO Panel previously indicated that seed blends may not be an appropriate strategy for managing resistance evolution when *Bt*-maize events express a single *Bt*-toxin and are truly high dose, and/or when larval movement of the target insect pests is substantial (EFSA, 2012a; Siegfried and Hellmich, 2012).

- Siegfried and Hellmich (2012) reviewed all available data in terms of laboratory-, greenhouse- and field-selected resistance in ECB to plant-produced *Bt*-toxins from *Bt*-maize events targeting this pest. According to Siegfried and Hellmich (2012), evidence supports the high dose nature of *Bt*-maize events (including 1507) and the functional recessiveness of resistance in ECB to these plants. However, in the case of *Bt*-maize 1507, the authors indicated that the frequency of Cry1F resistance may be higher than that observed for Cry1Ab in field populations of ECB. As there is no indication that the frequency of Cry1F resistance has increased in the US corn belt following maize 1507 cultivation, the authors concluded that the HDR strategy may be robust enough to delay resistance evolution even when the frequency of resistance is higher than anticipated. Overall, Siegfried and Hellmich (2012) noted that the predictions from initial theoretical models about the sustainability of the technology when deployed in a manner consistent with the HDR strategy appear to have been realised.

6.2.1.3. Conclusion

Results reported by Alyokhin (2011), Coates et al. (2011), Buschman and Ramaswamy (2012), Head and Greenplate (2012), Razze and Mason (2012) and Siegfried and Hellmich (2012) do not contain new information that would invalidate the previous recommendations on risk mitigation measures made by the EFSA GMO Panel. Therefore, the EFSA GMO Panel considers that its previous conclusions on maize 1507 remain valid and applicable.

Findings reported by Burkness et al. (2011) indicate that pollen-mediated gene flow between *Bt*-maize fields and refuges may theoretically reduce the efficacy of the HDR strategy due to sublethal exposure of ECB larvae to the *Bt*-toxin (as previously highlighted by Chilcut and Tabashnik, 2004). However, recent model predictions by Glaum et al. (2012) and Kang et al. (2012) estimated that pollen-mediated gene flow from *Bt*-maize to refuge plants has little impact on the evolution of resistance of the target insect pests.

Findings reported by Ghimire et al. (2011) suggest that the mode of action of Cry1Ab and Cry1F could overlap, and therefore should be accounted for when developing IRM strategies for maize 1507. When defining measures to delay resistance evolution to the Cry1F protein from maize 1507 in target insect pests, risk managers should consider that Cry1Ab-expressing maize events (such as MON 810) are approved for cultivation in the EU. The EFSA GMO Panel recommends that, in regions where maize 1507 and Cry1Ab-expressing maize events would be cultivated together, refuge areas equivalent to 20% of the total Lepidoptera-active *Bt*-maize area are established due to the potential for cross-resistance between Cry1Ab and Cry1F.

6.2.2. Post-market environmental monitoring

Upon request of the European Commission, the EFSA GMO Panel recently updated its previous evaluation of the initial PMEM plan for maize 1507 and made several recommendations to strengthen the PMEM plan proposed by the applicant (EFSA, 2005b, 2011d, 2012b). In addition, the PMEM plan required amendments for consistency with the updated EFSA GMO Panel Scientific Opinion on the PMEM of GM plants which provides applicants and risk managers with guidance on the strategy, methodology and reporting of PMEM of GM plants (EFSA, 2011b).

6.2.2.1. Summary of previous conclusions by the EFSA GMO Panel

The EFSA GMO Panel indicated that risk management measures should be undertaken for both of the risks identified in section 6.2, above, and it recommended case-specific monitoring (CSM) in both cases to confirm the assumptions underlying the ERA and development of appropriate risk management measures (EFSA, 2011d). The EFSA GMO Panel made specific recommendations to the applicant to strengthen the IRM plan proposed by the applicant (e.g., non-*Bt-refugia* for clusters of maize 1507 fields greater than 5 ha, sampling over time in areas with high uptake of maize 1507 and multivoltine target pests) in 2011 (EFSA, 2011a, 2012a,b).

With regard to general surveillance (GS), the EFSA GMO Panel requested that its proposals (e.g., farmer questionnaires, existing monitoring networks) to strengthen GS, in order to detect possible unanticipated adverse effects of maize 1507 cultivation, are implemented (EFSA, 2011a,d, 2012a).

6.2.2.2. Results from the literature search

From the literature search, the following two new peer-reviewed scientific publications containing evidence specific to maize 1507 for this specific area were identified and scrutinised for their possible relevance for the monitoring of maize 1507:

- van Kretschmar et al. (2011) developed an alternative method to the standard insect diet biosassays that typically rely on mortality or growth inhibition as endpoints to detect resistance in target insect populations to plant-produced *Bt*-toxins. This method is based on feeding disruption arising from the insecticidal activity of the *Bt*-toxin on the target insect pest, and is measured through reduced faecal production. The authors applied this approach to *Heliothis virescens* and *H. zea* by exposing neonates to a diagnostic dose of Cry1F containing blue indicated dye. Cry1F resistant individuals were able to consume the diagnostic dose and produced blue faecal pellets, while susceptible ones did not. The authors concluded that this method based on feeding disruption is appropriate for the detection of resistance in pests, subject to some improvements to the methodology.

- Using leaf disk feeding bioassays, dose-response bioassays and plant seedling assays, Farinós et al. (2012) measured the susceptibility of field-collected MCB populations from representative maize growing EU areas (such as France, Greece, Italy) and Turkey to Cry1F, and established the first baseline susceptibility data of MCB to Cry1F in the EU. The EFSA GMO Panel considers that the development of baseline susceptibility data represents the first step toward the development of a monitoring program designed to detect changes in susceptibility that may result from repeated and prolonged exposure to *Bt*-toxins (Siegfried et al., 2000). In this study, mortality and growth inhibition were followed as endpoints. Results indicated that the nine MCB populations had a very low variability, with a 3-fold difference between the LC_{50} of the most tolerant and most susceptible population (see also Gaspers et al., 2011). This low variability of observed susceptibility was attributed to natural variation in Cry1F susceptibility among MCB populations rather than variation caused by prior exposure to selection pressures. Therefore, the authors concluded that MCB is susceptible to Cry1F across most of its geographic range. Based on the baseline susceptibility data generated by Farinós et al. (2012), future variation in susceptibility of MCB populations to Cry1F and resistance evolution can be documented. Several authors (Siegfried et al., 2007; Siegfried and Hellmich, 2012) indicated that baseline susceptibility data will serve as a benchmark against which future changes in susceptibility can be measured when monitoring for the evolution of resistance.

6.2.2.3. Conclusion

Results reported by van Kretschmar et al. (2011) and Farinós et al. (2012) do not contain new information that would invalidate the previous recommendations on monitoring made by the EFSA GMO Panel. Therefore, the EFSA GMO Panel considers that its previous conclusions on maize 1507 remain valid and applicable.

Overall Conclusions and Recommendations

Following a search of the scientific literature published between 2005 and September 2012, the EFSA GMO Panel identified 61 peer-reviewed publications containing evidence specific to the risk assessment and/or management of maize 1507, of which 25 publications were discussed and cited in previous EFSA GMO Panel scientific outputs. From the remaining 36 publications, two were relevant for the food and feed safety assessment of maize 1507, and 34 for the environmental risk assessment and/or risk management of maize 1507.

The EFSA GMO Panel did not identify new peer-reviewed scientific publications reporting new information that would invalidate its previous conclusions on the safety of maize 1507. Therefore, the EFSA GMO Panel considers that its previous risk assessment conclusions on maize 1507, as well as its previous recommendations for risk mitigation measures and monitoring, remain valid and applicable.

When defining measures to delay resistance evolution to the Cry1F protein from maize 1507 in target insect pests, risk managers should consider that Cry1Ab-expressing maize events (such as MON 810) are approved for cultivation in the EU. The EFSA GMO Panel recommends that, in regions where maize 1507 and Cry1Ab-expressing maize events would be cultivated together, refuge areas equivalent to 20% of the total Lepidoptera-active *Bt*-maize area are established due to the potential for cross-resistance between Cry1Ab and Cry1F.

DOCUMENTATION PROVIDED TO EFSA

Letter from the Deputy Director General for the Health and Consumers of the European Commission, dated 20 June 2012, to the EFSA executive Director requesting an EFSA opinion gathering all available information related to the environmental risk assessment of maize 1507 for cultivation.

Acknowledgement letter, dated 11 July 2012, from the EFSA executive Director to the Director General for the Health and Consumers of the European Commission.

Letter, dated 27 September 2012, from the EFSA executive Director to the Director General for the Health and Consumers of the European Commission prioritising the Commission mandates in the area of GMOs currently pending with EFSA and requesting to provide additional evidence to support previous EFSA Opinions on maize 1507, Bt11 and MON 810.

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APPENDICES

A. PUBLICATIONS OBTAINED FROM ISI WEB OF KNOWLEDGE USING KEYWORD SEARCHES, AND FROM TARGETED SEARCHES OF PEER-REVIEWED JOURNALS

Authors of publication	Title of publication	Journal	Publication year	Issue in the remit of the EFSA GMO Panel and relevant to this EC mandate	Peer-reviewed publication	Publication in English	Publication previously discussed and cited in relevant maize 1507-related applications and/or scientific outputs of the EFSA GMO Panel
Abbott A, Schiermeier Q	Showdown for Europe	Nature	2007	NO	-	-	-
Ali S, Hameed S, Masood S, Ali GM, Zafar Y	Status of *Bt* cotton cultivation in major growing areas of Pakistan	Pakistan Journal of Botany	2010	NO	-	-	-
Alyokhin A	Scant evidence supports EPA's pyramided Bt corn refuge size of 5%	Nature Biotechnology	2011	YES	YES	YES	NO
Appenzeller LM, Malley L, MacKenzie SA, Hoban D, Delaney B	Subchronic feeding study with genetically modified stacked trait lepidopteran and coleopteran resistant (DAS-1507-1 × DAS-59122-7) maize grain in Sprague-Dawley rats	Food and Chemical Toxicology	2009	YES	YES	YES	YES[14]
Armstrong JS, Adamczyk JJ, Greenberg SM	Efficacy of single and dual gene cotton *Gossypium hirsutum* events on neonate and third instar fall armyworm *Spodoptera frugiperda* development based on tissue and meridic diet assays	Florida Entomologist	2011	NO	-	-	-

[14] GM plant market registration application with reference EFSA-GMO-NL-2005-15 / Additional information received on 15/04/2008 / MacEnzie (2006) / Note: the full study initially reported by MacEnzie (2006) was subsequently published as Appenzeller et al. (2009)

Armstrong JS, Gore J, Adamczyk JJ	Efficacy of single and dual gene cotton *gossypium hirsutum* (l.) events on yellow-striped armyworm (Lepidoptera: Noctuidae) in south Texas and the Mississippi delta	Florida Entomologist	2011	NO	-	-	-
Baig DN, Bukhari DA, Shakoori AR	Cry genes profiling and the toxicity of isolates of *Bacillus thuringiensis* from soil samples against American bollworm *Helicoverpa armigera*	Journal of Applied Microbiology	2010	NO	-	-	-
Balog A, Szenasi A, Szekeres D, Palinkas Z	Analysis of soil dwelling rove beetles (Coleoptera: Staphylinidae) in cultivated maize fields containing the Bt toxins Cry34/35Ab1 and Cry1F × Cry34/35Ab1	Biocontrol Science and Technology	2011	YES	YES	YES	YES
Blanco CA, Storer NP, Abel CA, Jackson R, Leonard R, Lopez JD, Payne G, Siegfried BD, Spencer T, Teran-Vargas AP	Baseline susceptibility of tobacco budworm (Lepidoptera: Noctuidae) to Cry1F toxin from *Bacillus thuringiensis*	Journal of Economic Entomology	2008	NO	-	-	-
Buntin GD	Corn expressing cry1ab or cry1f endotoxin for fall armyworm and corn earworm (Lepidoptera: noctuidae) management in field corn for grain production	Florida Entomologist	2008	YES	YES	YES	NO
Burkness EC, O'Rourke PK, Hutchison WD	Cross-pollination of nontransgenic corn ears with transgenic Bt corn: efficacy against lepidopteran pests and implications for resistance management	Journal of Economic Entomology	2011	YES	YES	YES	NO
Buschman LL, Ramaswamy SB	How to build the non-host plant for stability in insect resistance management	GM Crops and Food: Biotechnology in Agriculture and the Food Chain	2012	YES	YES	YES	NO
Carstens K, Anderson J, Bachman P, De Schrijver A, Dively G, Federici B, Hamer M, Gielkens M, Jensen P, Lamp W, Rauschen S, Ridley G, Romeis J, Waggoner A	Genetically modified crops and aquatic ecosystems: considerations for environmental risk assessment and non-target organism testing	Transgenic Research	2012	YES	YES	YES	YES

Cheeke TE, Rosenstiel TN, Cruzan MB	Evidence of reduced arbuscular mycorrhizal fungal colonization in multiple lines of *Bt* maize	American Journal of Botany	2012	YES	YES	YES	NO
Chen L, Guo J, Wang Q, Kai G, Yang L	Development of the visual loop-mediated isothermal amplification assays for seven genetically modified maize events and their application in practical samples analysis	Journal of Agricultural and Food Chemistry	2011	NO	-	-	-
Coates BS, Sumerford DV, Lopez MD, Wang H, Fraser LM, Kroemer JA, Spencer T, Kim KS, Abel CA, Hellmich RL, Siegfried BD	A single major QTL controls expression of larval Cry1F resistance trait in *Ostrinia nubilalis* (Lepidoptera: Crambidae) and is independent of midgut receptor genes	Genetica	2011	YES	YES	YES	NO
Crespo ALB, Rodrigo-Simon A, Siqueira HAA, Pereira EJG, Ferre JS, Blair D	Cross-resistance and mechanism of resistance to Cry1Ab toxin from *Bacillus thuringiensis* in a field-derived strain of European corn borer *Ostrinia nubilalis*	Journal of Invertebrate Pathology	2011	YES	YES	YES	NO
Dryzga MD, Yano BL, Andrus AK, Mattsson JL	Evaluation of the safety and nutritional equivalence of a genetically modified cottonseed meal in a 90-day dietary toxicity study in rats	Food and Chemical Toxicology	2007	NO	-	-	-
Edgerton MD, Fridgen J, Anderson JR, Ahlgrim J, Criswell M, Dhungana P, Gocken T, Li Z, Mariappan S, Pilcher CD, Rosielle A, Stark SB	Transgenic insect resistance traits increase corn yield and yield stability	Nature Biotechnology	2012	NO	-	-	-
Eichenseer H, Strohbehn R, Burks J	Frequency and severity of western bean cutworm (Lepidoptera: Noctuidae) ear damage in transgenic corn hybrids expressing different *Bacillus thuringiensis* cry toxins	Journal of Economic Entomology	2008	YES	YES	YES	YES

Farinos GP, de la Poza M, Ortego F, Castanera P	Susceptibility to the Cry1F toxin of field populations of *Sesamia nonagrioides* (Lepidoptera: Noctuidae) in mediterranean maize cultivation regions	Journal of Economic Entomology	2012	YES	YES	YES	NO
Faust M, Smith B, Rice D, Owens F, Hinds M, Dana G, Hunst P	Performance of lactating dairy cows fed silage and grain from a maize hybrid with the cry1F trait versus its non-biotech counterpart	Journal of Dairy Science	2007	YES	YES	YES	YES
Gao Y, Fencil KJ, Xu XP, Schwedler DA, Gilbert JR, Herman RA	Purification and characterization of a chimeric Cry1F delta-endotoxin expressed in transgenic cotton plants	Journal of Agricultural and Food Chemistry	2006	NO	-	-	-
Gaspers C, Siegfried BD, Spencer T, Alves AP, Storer NP, Schuphan I, Eber S	Susceptibility of European and North American populations of the European corn borer to the Cry1F insecticidal protein	Journal of Applied Entomology	2011	YES	YES	YES	YES
Ghimire MN, Huang F, Leonard R, Head GP, Yang Y	Susceptibility of Cry1Ab-susceptible and -resistant sugarcane borer to transgenic corn plants containing single or pyramided *Bacillus thuringiensis* genes	Crop Protection	2011	YES	YES	YES	NO
Gingras JL, Mitchell EA, Grattan KE	Fetal homologue of infant crying	Archives of Disease in Childhood-Fetal and Neonatal Edition	2005	NO	-	-	-
Glaum PR, Ives AR, Andow DA	Contamination and management of resistance evolution to high-dose transgenic insecticidal crops	Theoretical Ecology	2011	YES	YES	YES	NO
Gong Y, Wang C, Yang Y, Wu S, Wu Y	Characterization of resistance to *Bacillus thuringiensis* toxin Cry1Ac in *Plutella xylostella* from China	Journal of Invertebrate Pathology	2010	NO	-	-	-
Gouffon C, Van Vliet A, Van Rie J, Jansens S, Jurat-Fuentes JL	Binding sites for *Bacillus thuringiensis* Cry2Ae toxin on heliothine brush border membrane vesicles are not shared with Cry1A, Cry1F, or Vip3A toxin	Applied and Environmental Microbiology	2011	NO	-	-	-

Gryspeirt A, Gregoire JC	Effects of two varieties of *Bacillus thuringiensis* maize on the biology of *Plodia interpunctella*	Toxins	2012	YES	YES	YES	NO
Gupta M, Nirunsuksiri W, Schulenberg G, Hartl T, Novak S, Bryan J, Vanopdorp N, Bing J, Thompson S	A non-PCR-based invader (R) assay quantitatively detects single-copy genes in complex plant genomes	Molecular Breeding	2008	NO	-	-	-
Hardke JT, Leonard BR, Huang F, Jackson RE	Damage and survivorship of fall armyworm (Lepidoptera: Noctuidae) on transgenic field corn expressing *Bacillus thuringiensis* Cry proteins	Crop Protection	2011	YES	YES	YES	NO
Head GP, Greenplate J	The design and implementation of insect resistance management programs for Bt crops	GM Crops and Food: Biotechnology in Agriculture and the Food Chain	2012	YES	YES	YES	NO
Heide BR, Dromtorp SM, Rudi K, Heir E, Holck AL	Determination of eight genetically modified maize events by quantitative, multiplex PCR and fluorescence capillary gel electrophoresis	European Food Research and Technology	2008	NO	-	-	-
Herman RA, Storer NP, Phillips AM, Prochaska LM, Windels P	Compositional assessment of event DAS-59122-7 maize using substantial equivalence	Regulatory Toxicology and Pharmacology	2007	NO	-	-	-
Higgins LS, Babcock J, Neese P, Layton RJ, Moellenbeck DJ, Storer N	Three-year field monitoring of Cry1F, event DAS-1507-1, maize hybrids for nontarget arthropod effects	Environmental Entomology	2009	YES	YES	YES	YES
Holck AL, Dromtorp SM, Heir E	Quantitative, multiplex ligation-dependent probe amplification for the determination of eight genetically modified maize events	European Food Research and Technology	2009	NO	-	-	-

Hutchison W, Burkness E, Mitchell P, Moon R, Leslie T, Fleischer S, Abrahamson M, Hamilton KL, Steffey KL, Gray ME, Hellmich RL, Kaster LV, Hunt TE, Wright RJ, Pecinovsky K, Rabaey TL, Flood RB, Raun ES	Areawide suppression of European corn borer with Bt maize reaps savings to non-Bt maize growers	Science	2010	YES	YES	YES	NO
Jackson RE, Gore J, Abel C	Bollworm (Lepidoptera: Noctuidae) behavior on transgenic cotton expressing Cry1Ac and Cry1F proteins	Journal of Entomological Science	2010	NO	-	-	-
Kang J, Onstad DW, Hellmich RL, Moser SE, Hutchison WD, Prasifka JR	Modeling the impact of cross-pollination and low toxin expression in corn kernels on adaptation of European corn borer (Lepidoptera: Crambidae) to transgenic insecticidal corn	Transgenic Plants and Insects	2012	YES	YES	YES	NO
Kerns DL, Kesey BJ	Evaluation of seedling transgenic cotton containing *Bacillus thuringiensis* toxins to saltmarsh caterpillar *Estigmene acrea* (Drury)	Southwestern Entomologist	2009	NO	-	-	-
Kim JH, Song HS, Heo MS, Lee WY, Lee SH, Park SH, Park HK, Kim MC, Kim HY	Detection of eight different events of genetically modified maize by multiplex PCR method	Food Science and Biotechnology	2006	NO	-	-	-
Kim JH, Kim SY, Lee H, Kim YR, Kim HY	An event-specific DNA microarray to identify genetically modified organisms in processed foods	Journal of Agricultural and Food Chemistry	2010	NO	-	-	-
Kim YH, Hwang CE, Kim T, Lee SH	Risk assessment system establishment for evaluating the potential impacts of imported *Bacillus thuringiensis* maize on a non-target insect, *Tenebrio molitor*	Journal of Asia-Pacific Entomology	2012	YES	NO	-	-
Kim YH, Hwang CE, Kim TS, Lee JH, Lee S	Assessment of potential impacts due to unintentionally released Bt maize plants on non-target aphid *Rhopalosiphum padi* (Hemiptera: Aphididae)	Journal of Asia-Pacific Entomology	2012	YES	YES	YES	NO

Kullik SA, Sears M, Schaafsma AW	Sublethal effects of Cry1F *Bt* corn and clothianidin on black cutworm (Lepidoptera: Noctuidae) larval development	Journal of Economic Entomology	2011	NO	-	-	-
La Paz J, Garcia-Muniz N, Nadal A, Esteve T, Puigdomenech P, Pla M	Interlaboratory transfer of a real-time polymerase chain reaction assay for quantitative detection of genetically modified maize event TC-1507	Journal of AOAC International	2006	YES	YES	YES	YES
Ladics GS, Bardina L, Cressman RF, Mattsson JL, Sampson HA	Lack of cross-reactivity between the *Bacillus thuringiensis* derived protein Cry1F in maize grain and dust mite Der p7 protein with human sera positive for Der p7-IgE	Regulatory Toxicology and Pharmacology	2006	YES	YES	YES	YES
Lertwiriyawong B, Pinthong K, Chanpaisaeng J, Saksoong P, Huehne PS	Analysis of the insecticidal crystal gene type 1 of *Bacillus thuringiensis* isolates affecting lepidopterans	Science Asia	2010	NO	-	-	-
Lee SH, Kang SH, Park YH, Min DM, Kim YM	Quantitative analysis of two genetically modified maize lines by real-time PCR	Journal of Microbiology and Biotechnology	2006	NO	-	-	-
Li X, Yang L, Zhang J, Wang S, Shen K, Pan L, Zhang D	Simplex and duplex polymerase chain reaction analysis of Herculex (R) RW (59122) maize based on one reference molecule including separated fragments of 5' integration site and endogenous gene	Journal of AOAC International	2009	NO	-	-	-
Lu XB, Wu HB, Wang M, Li BD, Yang CL, Sun HW	Developing a method of oligonucleotide microarray for event specific detection of transgenic maize (*Zea mays*)	Acta Agronomica Sinica	2009	NO	-	-	-
MacKenzie SA, Lamb I, Schmidt J, Deege L, Morrisey MJ, Harper M, Layton RJ, Prochaska LM, Sanders C, Locke M, Mattsson JL, Fuentes A, Delaney B	Thirteen week feeding study with transgenic maize grain containing event DAS-1507-1 in Sprague-Dawley rats	Food and Chemical Toxicology	2007	YES	YES	YES	YES

Martinez C, Ibarra JE, Caballero P	Association analysis between serotype cry gene content and toxicity to *Helicoverpa armigera* larvae among *Bacillus thuringiensis* isolates native to Spain	Journal of Invertebrate Pathology	2005	NO	-	-	-
Mason CE, Sheldon JK, Pesek J, Bacon H, Gallusser R, Radke G, Slabaugh B	Assessment of *Chrysoperla plorabunda* longevity fecundity and egg viability when adults are fed transgenic Bt corn pollen	Journal of Agricultural and Urban Entomology	2008	YES	YES	YES	NO
Meihls LN, Higdon ML, Ellersieck M, Hibbard BE	Selection for resistance to mCry3A-expressing transgenic corn in western corn rootworm	Journal of Economic Entomology	2011	NO	-	-	-
Meng Y, Liu X, Wang S, Zhang D, Yang L	Applicability of plasmid calibrant pTC1507 in quantification of TC1507 maize: an interlaboratory study	Journal of Agricultural and Food Chemistry	2012	NO	-	-	-
Ngo DB, Nguyen XC, Nguyen TAN, Nguyen DT, Pham KT, Nguyen TTH, Asano S, Ohba M	Characterization of *Bacillus thuringiensis* strains in the Vietnam *Bacillus thuringiensis* collection	Proceedings of the 6th Pacific Rim Conference on the Biotechnology of *Bacillus thuringiensis* and its environmental impact	2007	NO	-	-	-
Oppert B, Ellis RT, Babcock J	Effects of Cry1F and Cry34Ab1/35Ab1 on storage pests	Journal of Stored Products Research	2010	YES	YES	YES	NO
Oguchi T, Onishi M, Mano J, Akiyama H, Teshima R, Futo S, Furui S, Kitta K	Development of multiplex PCR method for simultaneous detection of four events of genetically modified maize: DAS-59122-7, MIR604, MON863 and MON88017	Food Hygiene and Safety Science	2010	NO	-	-	-
Onishi M, Matsuoka T, Kodama T, Kashiwaba K, Futo S, Akiyama H, Maitani T, Furui S, Oguchi T, Hino A	Development of a multiplex polymerase chain reaction method for simultaneous detection of eight events of genetically modified maize	Journal of Agricultural and Food Chemistry	2005	NO	-	-	-

Park KW, Lee B, Kim CG, Kim Y, Park Y, Ko EM, Jeong SC, Choi KH, Yoon WK, Kim HM	Monitoring the occurrence of genetically modified maize at a grain receiving port and along transportation routes in the Republic of Korea	Food Control	2010	YES	YES	YES	YES
Pereira EJG, Lang BA, Storer NP, Siegfried BD	Selection for Cry1F resistance in the European corn borer and cross-resistance to other Cry toxins	Entomologia Experimentalis et Applicata	2008	YES	YES	YES	YES
Pereira EJG, Siqueira HAA, Zhuang M, Storer NP, Siegfried BD	Measurements of Cry1F binding and activity of luminal gut proteases in susceptible and Cry1F resistant *Ostrinia nubilalis* larvae (Lepidoptera: Crambidae)	Journal of Invertebrate Pathology	2010	YES	YES	YES	NO
Pereira EJG, Storer NP, Siegfried BD	Fitness costs of Cry1F resistance in laboratory-selected European corn borer (Lepidoptera: Crambidae)	Journal of Applied Entomology	2011	YES	YES	YES	YES
Pereira EJG, Storer NP, Siegfried BD	Inheritance of Cry1F resistance in laboratory-selected European corn borer and its survival on transgenic corn expressing the Cry1F toxin	Bulletin of Entomological Research	2008	YES	YES	YES	YES
Perry JN, Devos Y, Arpaia S, Bartsch D, Ehlert C, Gathmann A, Hails RS, Hendriksen NB, Kiss J, Messean A, Mestdagh S, Neemann G, Nuti M, Sweet JB, Tebbe CC	Estimating the effects of Cry1F Bt-maize pollen on non-target Lepidoptera using a mathematical model of exposure	Journal of Applied Ecology	2012	YES	YES	YES	YES
Prashanth S, Katageri IS, Vamadevaih HM, Khadi BM	Effect of external damage on regeneration of cotton explants (*Gossypium arboreum* and *G. barbadense*)	Karnataka Journal of Agricultural Sciences	2011	NO	-	-	-
Prihoda KR, Coats JR	Examination of the fate of Bt Cry1F protein in an aerobic aquatic system	Abstracts of Papers of The American Chemical Society	2006	NO	-	-	-
Qi XF, Li MS, Choi JY, Kim YS, Wang Y, Kang JN, Choi HK, Je YH, Song JZ, Li JH	Molecular characterization of a novel *Bacillus thuringiensis* strain from China	International Journal of Industrial Entomology	2005	NO	-	-	-

Raybould A, Higgins LS, Horak MJ, Layton RJ, Storer NP, De La Fuente JM, Herman RA	Assessing the ecological risks from the persistence and spread of feral populations of insect-resistant transgenic maize	Transgenic Research	2012	YES	YES	YES	YES
Razze JM, Mason CE	Dispersal behavior of neonate European corn borer (Lepidoptera: Crambidae) on Bt corn	Journal of Economic Entomology	2012	YES	YES	YES	NO
Reavy-Jones FPF, Wiatrak P	Evaluation of new transgenic corn hybrids producing multiple *Bacillus thuringiensis* toxins in South Carolina	Journal of Entomological Science	2011	YES	YES	YES	NO
Reavy-Jones FPF, Wiatrak P, Greene JK	Evaluating the performance of transgenic corn producing *Bacillus thuringiensis* toxins in South Carolina	Journal of Agricultural and Urban Entomology	2009	YES	YES	YES	NO
Rimachi GLF, Alcantara DJ, Aquino VY, Ortiz R	Detecting adventitious transgenic events in a maize center of diversity	Electronic Journal of Biotechnology	2011	NO	-	-	-
Schaafsma AW, Holmes ML, Whistlecraft J, Dudley SA	Effectiveness of three Bt corn events against feeding damage by the true armyworm (*Pseudaletia unipuncta* Haworth)	Canadian Journal of Plant Science	2007	YES	YES	YES	NO
Scheideler SE, Rice D, Smith B, Dana G, Sauber T	Evaluation of nutritional equivalency of corn grain from DAS-1507-1 (Herculex* I) in the diets of laying hens	Journal of Applied Poultry Research	2008	YES	YES	YES	YES[15]
Schmidt NR, Haywood JM, Bonning BC	Toward the physiological basis for increased *Agrotis ipsilon* multiple nucleopolyhedrovirus infection following feeding of *Agrotis ipsilon* larvae on transgenic corn expressing Cry1Fa2	Journal of Invertebrate Pathology	2009	YES	YES	YES	NO
Shan G, Embrey SK, Herman RA, Mccormick R	Cry1F protein not detected in soil after three years of transgenic *Bt* corn (1507 corn) use	Environmental Entomology	2008	YES	YES	YES	YES

[15] GM plant market registration application with reference EFSA-GMO-2008-CZ-62 / Additional information received on 23/06/2009 / Scheideler et al. (2008)

Shan G, Embrey SK, Schafer BW	A highly specific enzyme-linked immunosorbent assay for the detection of Cry1Ac insecticidal crystal protein in transgenic widestrike cotton	Journal of Agricultural and Food Chemistry	2007	NO	-	-	-
Siebert MW, Babock JM, Nolting S, Santos AC, Adamczyk JJ, Neese PA, King JE, Jenkins JN, McCarty J, Lorenz GM, Fromme DD, Lassiter RB	Efficacy of cry1f insecticidal protein in maize and cotton for control of fall armyworm (Lepidoptera: noctuidae)	Florida Entomologist	2008	YES	YES	YES	NO
Siebert MW, Tindal KV, Leonard BR, Van Duyn JW, Babcock JM	Evaluation of corn hybrids expressing Cry1F (Herculex (R) I insect protection) against fall armyworm (Lepidoptera: Noctuidae) in the southern United States	Journal of Entomological Science	2008	YES	YES	YES	NO
Siebert MW, Nolting S, Leonard BR, Braxton LB, All JN, Van Duyn JW, Bradley JR, Bacheler J, Huckaba RM	Efficacy of transgenic cotton expressing Cry1Ac and Cry1F insecticidal protein against Heliothines (Lepidoptera: Noctuidae)	Journal of Economic Entomology	2008	NO	-	-	-
Siebert MW, Patterson TG, Gilles GJ, Nolting SP, Braxton LB, Leonard BR, Van Duyn JW, Lassiter RB	Quantification of Cry1Ac and Cry1F *Bacillus thuringiensis* insecticidal proteins in selected transgenic cotton plant tissue types	Journal of Economic Entomology	2009	NO	-	-	-
Siebert MW, Nolting SP, Hendrix W, Dhavala S, Craig C, Leonard BR, Stewart SD, All J, Musser FR, Buntin GD, Samuel L	Evaluation of corn hybrids expressing Cry1F, Cry1A.105, Cry2Ab2, Cry34Ab1/Cry35Ab1, and Cry3Bb1 against southern United States insect pests	Journal of Economic Entomology	2012	YES	YES	YES	NO
Siegfried BD, Hellmich RL	Understanding successful resistance management - The European corn borer and Bt corn in the United States	GM Crops and Food: Biotechnology in Agriculture and the Food Chain	2012	YES	YES	YES	NO
Sindt J, Drouillard J, Loe E, Kessen T, Sulpizio M, Montgomery S, Rice D, Hinds M, Smith B, Owens F, Dana G, Hunst P	Effect of corn containing the Cry1F protein on performance of beef heifers fed a finishing diet based on steam-flaked corn	Professional Animal Scientist	2007	YES	YES	YES	NO

Stein HH, Sauber TE, Rice DW, Hinds MA, Smith BL, Dana G, Peters DN, Hunst P	Growth performance and carcass composition of pigs fed corn grain from das-1507-1 (herculex i) hybrids 1	Professional Animal Scientist	2009	YES	YES	YES	NO
Storer NP, Babcock JM, Schlenz M, Meade Ts Thompson GD, Bing JW, Huckaba RM	Discovery and characterization of field resistance to Bt maize: *Spodoptera frugiperda* (Lepidoptera: Noctuidae) in Puerto Rico	Journal of Economic Entomology	2010	YES	YES	YES	YES
Storer NP, Kubiszak ME, King J	Status of resistance to Bt maize in *Spodoptera frugiperda*: Lessons from Puerto Rico	Journal of Invertebrate Pathology	2012	YES	YES	YES	NO
Storer NP, Thompson GD, Head GP	Application of pyramided traits against Lepidoptera in insect resistance management for Bt crops	GM Crops and Food: Biotechnology in Agriculture and the Food Chain	2012	YES	YES	YES	NO
Tabashnik BE, Van Rensburg JBJ, Carriere Y	Field-evolved insect resistance to Bt crops: definition theory and data	Journal of Economic Entomology	2009	YES	YES	YES	YES
Takabatake R, Futo S, Minegishi Y, Watai M, Sawada C, Nakamura K, Akiyama H, Teshima R, Furui S, Hino A, Kitta K	Evaluation of quantitative PCR methods for genetically modified maize (MON863, NK603, TC1507 and T25)	Food Science and Technology Research	2010	NO	-	-	-
Takacs E, Fonagy A, Juracsek J, Kugler N, Szekacs A	Characterisation of tritrophic effects of DAS-59122-7 maize on the seven-spotted ladybird (*Coccinella septempunctata*) feeding on the bird cherry-oat aphid (*Rhopalosiphum padi*)	IOBC/WPRS Bulletin	2012	NO	-	-	-
Tan SY, Cayabyab BF, Alcantara EP, Ibrahim YB, Huang F, Blankenship EE, Siegfried BD	Comparative susceptibility of *Ostrinia furnacalis Ostrinia nubilalis* and *Diatraea saccharalis* (Lepidoptera: Crambidae) to *Bacillus thuringiensis* Cry1 toxins	Crop Protection	2011	YES	YES	YES	NO
Thompson GD, Dalmacio SC, Criador AR, Alvarez ER, Hechanova RF	Field performance of TC1507 transgenic corn hybrids against Asian corn borer in the Philippines	Philippine Agricultural Scientist	2010	YES	YES	YES	NO

Thuler A MG, Thuler RT, Cicero ES, Bortoli SA, de Lemos MVF	The study of genic variability in *Bacillus thuringiensis* Brazilian strains for use in the biological control of *Plutella xylostella*	Boletin de Sanidad Vegetal Plagas	2007	NO	-	-	-
Tian JC, Collins HL, Romeis J, Naranjo SE, Hellmich RL, Shelton AM	Using field-evolved resistance to Cry1F maize in a lepidopteran pest to demonstrate no adverse effects of Cry1F on one of its major predators	Transgenic Research	2012	YES	YES	YES	NO
Tindall KV, Siebert MW, Leonard BR, All J, Haile FJ	Efficacy of Cry1Ac:Cry1F proteins in cotton leaf tissue against fall armyworm, beet armyworm and soybean looper (Lepidoptera: Noctuidae)	Journal of Economic Entomology	2009	NO	-	-	-
Valicente FH, de Toledo Picoli EA, Vilaca de Vasconcelos MJ, Carneiro NP, Carneiro AA, Guimaraes CT, Lana UG	Molecular characterization and distribution of *Bacillus thuringiensis* cry1 genes from Brazilian strains effective against the fall armyworm *Spodoptera frugiperda*	Biological Control	2010	NO	-	-	-
van Kretschmar JB, Bailey WD, Arellano C, Thompson GD, Sutula CL, Roe RM	Feeding disruption tests for monitoring the frequency of larval lepidopteran resistance to Cry1Ac Cry1F and Cry1Ab	Crop Protection	2011	YES	YES	YES	NO
Virla EG, Alvarez A, Loto F, Pera LM, Baigori M	Fall armyworm strains (Lepidoptera: Noctuidae) in Argentina their associate host plants and response to different mortality factors in laboratory	Florida Entomologist	2008	YES	YES	YES	NO
Virla EG, Casuso M, Frias EA	A preliminary study on the effects of a transgenic corn event on the non-target pest *Dalbulus maidis* (Hemiptera: Cicadellidae)	Crop Protection	2010	YES	YES	YES	YES
Wolt JD	A mixture toxicity approach for environmental risk assessment of multiple insect resistance genes	Environmental Toxicology and Chemistry	2011	YES	YES	YES	YES

Wolt JD, Hellmich RL, Prasifka JR, Sears MK	Global regulatory perspectives regarding transgenic crop risks to nontarget insects: the case of Cry1F maize and butterflies	Bulletin OILB/SROP	2006	YES	NO	-	-
Wolt JD, Conlan CA, Majima K	An ecological risk assessment of Cry1F maize pollen impact to pale grass blue butterfly	Environmental Biosafety Research	2005	YES	YES	YES	YES
Wu HB, Sun HW, Li BD, Yang CL, Lu XB	Detection of genetically modified maize by multiplex PCR-gene chip	Journal of Agricultural Biotechnology	2009	NO	-	-	-
Xiaolei Z, Lili C, Ping S, Junwei J, Dabing Z, Litao Y	High sensitive detection of Cry1Ab protein using a quantum dot-based fluorescence-linked immunosorbent assay	Journal of Agricultural and Food Chemistry	2011	NO	-	-	-
Xu L, Wang Z, Zhang J, He K, Ferry N, Gatehouse AMR	Cross-resistance of Cry1Ab-selected Asian corn borer to other Cry toxins	Journal of Applied Entomology	2010	YES	YES	YES	YES
Yang L, Guo J, Pan A, Zhang H, Zhang K, Wang Z, Zhang D	Event-specific quantitative detection of nine genetically modified maizes using one novel standard reference molecule	Journal of Agricultural and Food Chemistry	2007	NO	-	-	-
Zhu X, Chen L, Shen P, Jia J, Zhang D, Yang L	High sensitive detection of Cry1Ab protein using a quantum dot-based fluorescence-linked immunosorbent assay	Journal of Agricultural and Food Chemistry	2011	NO	-	-	-