European Food Safety Authority

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SCIENTIFIC OPINION

Application (Reference EFSA-GMO-CZ-2005-27) for the placing on the market of the insect-resistant and herbicide-tolerant genetically modified maize MON88017, for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto[1]

Scientific Opinion of the Panel on Genetically Modified Organisms

(Question No EFSA-Q-2005-280)

Adopted on 21April 2009

PANEL MEMBERS[*]

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SUMMARY

Following a request from Monsanto within the framework of Regulation (EC) No 1829/2003 on genetically modified food and feed, the Panel on Genetically Modified Organisms was asked to deliver a scientific opinion on the authorisation of the insect-resistant, glyphosate-tolerant genetically modified maize MON88017 (Unique Identifier MON88Ø17-3).

In delivering its scientific opinion, the GMO Panel considered the application EFSA-GMO-CZ-2005-27, additional information provided by the applicant and the scientific comments submitted by the Member States. The scope of application EFSA-GMO-CZ-2005-27 is for food and feed uses, import and processing of genetically modified maize MON88017 and all derived products, but excluding cultivation in the EU.

The GMO Panel assessed maize MON88017 with reference to the intended uses and the appropriate principles described in the Guidance Document of the Scientific Panel on

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[*] (minority opinion) This opinion is not shared by 0 members of the Panel. / (conflict of interest) 0 members of the Panel did not participate in (part of) the discussion on the subject referred to above because of possible conflicts of interest.

Genetically Modified Organisms for the risk assessment of genetically modified plants and derived food and feed. The scientific assessment included molecular characterisation of the inserted DNA and expression of the new proteins. A comparative analysis of agronomic traits and composition was undertaken and the safety of the newly expressed proteins and the whole food/feed was evaluated with respect to potential toxicity, allergenicity and nutritional quality. An assessment of environmental impacts and the post-market environmental monitoring plan were also undertaken.

Maize MON88017 was developed to express a modified Cry3Bb1 protein rendering maize MON88017 resistant to certain coleopteran pests and the CP4 EPSPS protein derived from *Agrobacterium* sp. strain CP4 which provides tolerance to glyphosate.

The molecular characterisation data establish that the genetically modified maize MON88017 contains one copy of an intact CP4 EPSPS expression cassette and a Cry3Bb1 cassette in a single locus. No other parts of the plasmid used for transformation are present in the transformed plant. Bioinformatic analysis of the open reading frames at the junctions between the inserted DNA and maize genomic DNA did not raise safety concerns. The stability of the inserted DNA and the herbicide tolerance and insect resistance traits were confirmed over several generations.

Based on results of the comparative analysis the EFSA GMO Panel concluded that maize MON88017 is compositionally, phenotypically and agronomically equivalent to the non genetically modified counterpart and conventional maize varieties, except for the presence of Cry3Bb1 and CP4 EPSPS proteins in maize MON88017. In addition, there are no indications of potential toxicity and allergenicity of the Cry3Bb1 and CP4 EPSPS proteins expressed in maize MON88017. A subchronic (90-day) feeding study revealed no indications of adverse effects in rats fed diets containing grains from maize MON88017. In addition, a feeding study in broiler chickens provided evidence of nutritional equivalence of maize MON88017 to conventional maize. The GMO Panel considers that maize MON88017 is as safe and as nutritious as its non-GM counterpart and conventional maize varieties and that it is unlikely that the overall allergenicity of the whole plant is changed by the genetic modification.

The application EFSA-GMO-CZ-2005-27 concerns food and feed uses, import and processing of maize MON88017. There is therefore no requirement for scientific assessment of possible environmental effects associated with the cultivation of this GM maize. There are no indications of increased likelihood of establishment or survival of feral maize plants in case of accidental release into the environment of MON88017 seeds during transportation and processing. Also, the low levels of environmental exposure through other routes indicate that the risk to target and non-target organisms is likely to be extremely low. The scope of the monitoring plan provided by the applicant is in line with the intended uses of maize MON88017.

In conclusion, the Panel considers that the information available for Maize MON88017 addresses the scientific comments raised by the Member States and that it is as safe as its non genetically modified counterpart with respect to potential effects on human and animal health or the environment. Therefore the GMO Panel concludes that MON88017 is unlikely to have any adverse effect on human or animal health or on the environment in the context of its intended uses.

Key words: **GMO, maize, MON88017, glyphosate, human and animal health, environment, import, processing, food, feed, Regulation (EC) No 1829/2003, Cry3Bb1, EPSPS.**

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BACKGROUND

On 10 November 2005, EFSA received from the Competent Authority of Czech Republic an application (Reference EFSA-GMO-CZ-2005-27), for authorisation of the insect-resistant glyphosate-tolerant genetically modified maize MON88017 (Unique Identifier MON-88Ø17-3), submitted by Monsanto within the framework of Regulation (EC) No 1829/2003 on genetically modified food and feed (EC, 2003) for food and feed uses, import and processing.

After receiving the application EFSA-GMO-CZ-2005-27 and in accordance with Articles 5(2)(b) and 17(2)b of Regulation (EC) No 1829/2003, EFSA informed the Member States as well as the European Commission and made the summary of the dossier publicly available on the EFSA website. EFSA initiated a formal review of the application to check compliance with the requirements laid down in Articles 5(3) and 17(3) of Regulation (EC) No 1829/2003. On 21 December 2006, EFSA received additional information requested under completeness check (requested on 05 December 2006) and on 11 January 2007 EFSA declared the application as valid in accordance with Articles 6(1) and 18(1) of Regulation (EC) No 1829/2003.

EFSA made the valid application available to Member States and the European Commission and consulted nominated risk assessment bodies of the Member States, including the national Competent Authorities within the meaning of Directive 2001/18/EC (EC, 2001) following the requirements of Articles 6(4) and 18(4) of Regulation (EC) No 1829/2003, to request their scientific opinion. The Member State bodies had three months after the date of receipt of the valid application (until 11 April 2007) within which to make their opinion known.

The GMO Panel carried out a scientific assessment of genetically modified maize MON88017 taking into account the appropriate principles described in the Guidance Document of the Scientific Panel on Genetically Modified Organisms for the risk assessment of genetically modified plants and derived food and feed (EFSA, 2006a).

On 26 March 2007, 25 June 2007, 12 October 2007, 20 November 2007, 10 December 2007, 16 December 2008 and 28 January 2009 the GMO Panel asked for additional data on maize MON88017. The applicant provided the requested information on 6 June 2007, 19 July 2007, 30 October 2007, 30 November 2007, 7 December 2007, 6 October 2008, 8 January 2009 and 19 February 2009. After receipt and assessment of the full data package, the GMO Panel finalised its risk assessment of maize MON88017.

The GMO Panel carried out a scientific assessment of the GM maize MON88017 for food and feed uses, import and processing in accordance with Articles 6(6) and 18(6) of Regulation (EC) No 1829/2003, taking into consideration the scientific comments of the Member States and the additional information provided by the applicant.

In giving its opinion on GM maize MON88017 to the European Commission, the Member States and the applicant, and in accordance with Articles 6(1) and 18(1) of Regulation (EC) No 1829/2003, EFSA has endeavoured to respect a time limit of six months from the receipt of the valid application. As additional information was requested by the EFSA GMO Panel, the time limit of 6 months was extended accordingly, in line with Articles 6(1), 6(2), 18(1), and 18(2) of Regulation (EC) No 1829/2003.

According to Regulation (EC) No 1829/2003, the EFSA opinion shall include a report describing the assessment of the food and feed and stating the reasons for its opinion and the information on which its opinion is based. This document is to be seen as the report requested under Articles 6(6) and 18(6) of that Regulation and thus will be part of the overall opinion in accordance with Articles 6(5) and 18(5).

TERMS OF REFERENCE

The EFSA GMO Panel was requested to carry out a scientific risk assessment of maize MON88017 for food and feed uses, import and processing in accordance with Articles 6(6) and 18(6) of Regulation (EC) No 1829/2003. Where applicable, any conditions or restrictions which should be imposed on the placing on the market and/or specific conditions or restrictions for use and handling, including post-market monitoring requirements based on the outcome of the risk assessment and, in the case of GMOs or food/feed containing or consisting of GMOs, conditions for the protection of particular ecosystems/environment and/or geographical areas should be indicated in accordance with Articles 6(5)(e) and 18(5)(e) of Regulation (EC) No 1829/2003.

The EFSA GMO Panel was not requested to give a scientific opinion on information required under Annex II to the Cartagena Protocol. Furthermore, the EFSA GMO Panel did also not consider proposals for labelling and methods of detection (including sampling and the identification of the specific transformation event in the food/feed and/or food/feed produced from it), which are matters related to risk management.

ACKNOWLEDGEMENTS

The European Food Safety Authority wishes to thank the members of the Working Groups on Molecular Characterisation, Food Feed and Environment, as well as the ad hoc experts Boet Glandorf, Hans-Jörg Buhk, Philippe Vain, Thomas Frenzel, Gerhard Flachowsky, Sue Hartley for the preparation of this opinion.

ASSESSMENT

1. Introduction

The genetically modified MON88017 maize (Unique Identifier MON88Ø17-3) was assessed with reference to its intended uses, taking account of the appropriate principles described in the Guidance Document of the Scientific Panel on Genetically Modified Organisms for the risk assessment of genetically modified plants and derived food and feed (EFSA, 2006a). In its evaluation the GMO Panel also considered the scientific comments that were raised by Member States on application EFSA-GMO-CZ-2005-27. The risk assessment presented here is based on the information provided in the application relating to maize MON88017 submitted in the EU including additional information from the applicant.

2. Issues raised by Member States

Issues raised by Member States are addressed in Annex G of the overall opinion.

3. Molecular characterisation

3.1 Evaluation of relevant scientific data

3.1.1. Transformation process and vector constructs

Genetically modified maize MON88017 was developed to express a modified Cry3Bb1 protein, derived from *Bacillus thuringiensis* subsp. *kumamotoensis* providing protection against certain coleopteran insect pests, and the CP4 EPSPS protein derived from *Agrobacterium* sp. strain CP4 which provides tolerance to glyphosate.

MON88017 was produced by *Agrobacterium*-mediated transformation of immature embryos of A x Hi-II maize tissue with the PV-ZMIR39 plasmid. PV-ZMIR39 is part of a binary *Agrobacterium tumefaciens* vector system. The T-DNA contains two expression cassettes, one for CP4 EPSPS and one for Cry3Bb1. The CP4 EPSPS cassette contains CP4 *epsps* coding sequence joined to a chloroplast transit peptide and driven by the promoter (P-ract1) and the first intron (*ract1* intron) of the rice actin 1 gene, and the nopaline synthase terminator sequences (NOS 3'). The Cry3Bb1 cassette contains *cry3Bb1* coding sequence, joined to the 5' untranslated leader of the wheat chlorophyll a/b-binding protein and the *ract1* intron and driven by the enhanced 35S plant promoter (P-e35S) and the terminator of the heat shock protein 17.3 (tahsp17 3'). The MON88017 *cry3Bb1* sequence was modified to encode six specific amino acid substitutions with respect to the Cry3Bb1 protein from the wild-type *Bacillus thuringensis* (subsp. *kumamotoensis*) strain EG4691. Moreover, the MON88017 Cry3Bb1 protein is similar to MON863 Cry3Bb1 protein, differing by one of the 653 amino acid residues.

3.1.2. Transgenic constructs in the genetically modified plant

Southern analysis of genomic DNA digested with two different restriction enzymes using four different probes spanning the entire length of the insert showed the presence of a single copy of the introduced DNA at a single insertion locus. The intactness of the two expression cassettes was examined by Southern analysis and was confirmed by PCR amplification of

seven overlapping regions of DNA that span the entire length of the insert. These PCR fragments were sequenced confirming the identity between the sequences inserted in MON88017 and the corresponding sequences of the PV-ZMIR39 plasmid.

The absence of vector backbone sequences in MON88017 plants has been confirmed by Southern analysis using two probes that cover the entire vector backbone.

The sequences of the plant genome adjacent to the 3' and 5' sequences of the insert were determined. 878 bp and 1000 bp flanking the insert at 3' and 5' ends, respectively were amplified by PCR and sequenced. These sequences showed homology to maize DNA. Following an updated analysis of the pre-insertion site in conventional maize it was concluded that a 26 bp fragment of genomic DNA at the target site was deleted and a 20 bp fragment was inserted. The insert lies 174 bp upstream of a region showing high sequence similarity to ESTs annotated as corresponding to putative purine permeases. Phenotypic, agronomic, and compositional analyses showed that MON88017 is equivalent to conventional maize (see sections 4.1.2. and 4.1.3.), except for the expected trait, indicating that the insertion of the transgene has not altered the expression of an essential gene and the insertion of the transgene *per se* does not pose a safety hazard.

3.1.3. Information on the expression of the insert

3.1.3.1. Expression of the introduced genes

Analysis of Cry3Bb1 and CP4 EPSPS proteins was carried out by ELISA using plants grown in three different field locations in the U.S.A. during the 2002 growing season. The tissues and plant samples examined were leaves, whole plant and roots at 4-6 different stages of development. Across the developmental stages examined, the mean Cry3Bb1 protein levels ranged between 260-570 µg/g dw in leaf, 220-500 µg/g dw in the whole plant and 100 -370 µg/g dw in root tissues. CP4 EPSPS protein levels ranged between 150-220 µg/g dw in leaf and 70-150 µg/g dw in root. This plant material was also used to analyse the expression of the proteins in pollen, silk, forage, forage root, grain, stover and senescent roots. The mean Cry3Bb1 protein level in the grain was 15 µg/g dw (range 10-22 µg/g dw) and CP4 EPSPS protein level in grain was 5.8 µg/g dw (range 4.1-7.1 µg/g dw) . The protein expression in the grain was also analysed for plants grown in Argentina during 2003-2004 season confirming the data obtained for the expression of both proteins.

3.1.3.2 Putative open reading frames (ORF)

Bioinformatic analyses were performed to assess the potential for allergenicity, toxicity, or pharmacological activity of putative polypeptides encoded by the 5' and 3' inserted DNA-maize genomic DNA junctions. Sequences spanning the 5' maize genomic DNA-inserted DNA junction and the 3' inserted DNA-maize genomic DNA junction were translated from stop codon to stop codon in all six reading frames. Putative peptides/polypeptides from each reading frame were compared to databases that contained peptides/polypeptides, including allergens and toxins, using bioinformatic tools.

No biologically relevant structural similarities to allergens, toxins, or pharmacologically active proteins were observed for any of the putative polypeptides. Furthermore, no short (eight amino acid) polypeptide matches were shared between any of the putative polypeptides and proteins in the allergen database.

3.1.4. Inheritance and stability of inserted DNA

In order to determine the stability of the integrated DNA, Southern analysis of plant material obtained from seven generations of MON88017 was performed. Probes spanning the entire insert produced the expected bands in all cases demonstrating the stability of the integrated DNA. The phenotypic stability was determined following the segregation of the traits over seven generations of cross-fertilization and three generations of self-pollination. The traits segregated as a Mendelian single dominant locus over seven generations. One exception was described (cross LH198BC0F1 x LH59) and was interpreted as an effect of glyphosate selection during gamete formation (Walker et al., 2006). These results indicate that the inserted DNA and the traits are stable in MON88017 and confirm that MON88017 contains a single locus insertion.

3.2. Conclusion

The molecular characterisation data establish that the genetically modified maize MON88017 contains one copy of an intact CP4 EPSPS expression cassette and a Cry3Bb1 cassette in a single locus. No other parts of the plasmid used for transformation are present in the transformed plant. Bioinformatic analysis of the open reading frames at the junctions between the inserted DNA and maize genomic DNA did not raise safety concerns. The stability of the inserted DNA and the herbicide tolerance and insect resistance traits were confirmed over several generations.

4. Comparative Analysis

4.1. Evaluation of relevant scientific data

Having considered the information provided in the application and the Member States comments, the GMO Panel requested from the applicant additional data on the composition of maize MON88017 not treated with glyphosate in comparison with conventional control maize.

4.1.1. Choice of comparator and production of material for the compositional assessment

Maize MON88017 was compared with a control non-GM line with a comparable genetic background maize LH59XLH198 in the US field trial and with control DKC61-24 maize in the Argentinian field trial treated with other herbicides than glyphosate. In addition to maize MON88017 and the non-GM counterpart, four commercial non-GM varieties were planted at each test site. Grain and forage from plants were harvested from field trials performed at three locations during one season in the United States (2002) and four locations in Argentina during the 2003-2004 season and used in the compositional analysis. Maize MON88017 plants were treated with glyphosate, which is representative of the agricultural practice regarding weed control under commercial cultivation of this maize. Additionally the applicant provided data on the composition of forage and grain of maize MON88017 not treated with glyphosate in comparison with conventional maize controls with comparable background genetics grown during the 2007 growing season at three locations in Germany and at three locations in Spain.

4.1.2. Compositional analysis

The chemical analytical data on composition of material from field trials in the United States (2002 and Argentina (2003-2004) (Mc Cann *et al*, 2007), were statistically analysed for each individual location and for all locations combined. The compounds analysed followed the recommendations of OECD (OECD, 2002).

The data from proximate and mineral analyses (fat, protein, total carbohydrate, acid detergent fibre (ADF), neutral detergent fibre (NDF), ash, moisture, phosphorus, and calcium) of forage from maize MON88017 (treated with glyphosate) were compared to compositional data for forage from the non-GM counterpart, the reference varieties included into the same field trials, and to typical ranges of the analysed constituents in commercial maize varieties reported in the literature and in previous field trials conducted by the applicant. No statistically significant differences between maize MON88017 and the non-GM control were observed in forage from field trials in United States. In samples of forage from field trials in Argentina, significant differences were observed in phosphorus and total fat. However, these differences were detected only in some but not all locations.

The grains of maize MON88017 and its control were analysed for the same proximate parameters as forage, and for total dietary fibre (TDF), amino acids (eighteen amino acids including aromatic amino acids), fatty acids, minerals (calcium, copper, iron, magnesium, manganese, phosphorus, potassium, sodium, and zinc), vitamins (vitamin B1, vitamin B2, vitamin B_6, folic acid, vitamin E and niacin), and other secondary metabolites (phytic acid, raffinose, furfural, *p*-coumaric acid and ferulic acid).

In summary, the compositional analysis of grains from maize MON88017 occasionally revealed statistically significant differences in the levels of some compounds compared to the non-GM control. In most cases differences were observed within one site only and were not consistently observed both each year and at each location. The levels of the compounds that significantly differed from the corresponding levels in the non-GM counterpart were within the ranges reported for conventional maize, including the reference varieties tested within the same field trials, literature data for commercial maize varieties, and data on conventional maize from previous field trials. The isoleucine levels in grains of maize MON88017 and the lysine level in control maize were found to be above the highest values reported in the commercial varieties in field trials in Argentina in 2003-2004. However they still were within the literature and historical ranges for maize grains. The same held true for lower limits of the ranges of p-coumaric acid, vitamin B1, and zinc in grains of maize MON88017 and zinc in control maize, which fell outside the range of reference varieties tested in the same field trial, but not outside the literature and/or historic ranges.

In grains from the field trials in USA 2002, the level of vitamin B1 was consistently significantly lower in grains of maize MON88017 than in grains of the corresponding non-GM control. The reduced levels were observed at each location. However, in the field trial performed in Argentina in 2003-2004, vitamin B1 levels in grains of maize MON88017 were significantly different from the ones in the control in two sites out of four sites only, i.e. they were higher in one location and lower in the other. Notably, all vitamin B1 levels in grains of maize MON88017 and non-GM maize in materials from both years fell within the range reported in the literature and in the range of historical data obtained from previous field trials

provided by the applicant. In addition, grains of maize MON88017 showed statistically significantly higher content of linoleic acid and a lower content of oleic acid in each location and across locations during the field trial in Argentina. Similar differences were observed in the field trials in USA in 2002, but not at each location and for linoleic acid also across all locations. Ranges for both fatty acids fell within ranges reported in the literature and historical ranges. In addition, it is reported in literature that the fatty acid composition of maize grains can vary substantially between maize varieties (e.g. Dunlap et al., 1995).

During the growing season of 2007 the applicant performed on request from the Panel additional compositional analysis of forage and grain from MON88017 maize not treated with the target herbicide (glyphosate). Maize MON88017 was harvested from six replicated field sites, including three sites from across Germany and three sites across Spain, representing northern Europe and southern Europe respectively, each with locally adapted maize varieties into which the event MON88017 had been introduced by plant breeding. One of the Spanish sites was not included in the statistical analysis as too many samples from this site were excluded from the experiment based on contamination with other GMOs. Control maize of a similar genetic background to MON88017 maize, DKC 5143 in Spain and DKC3945 in Germany, were planted along the GM maize, as were 13 different commercial reference maize lines across these 2 European regions. Only some of the commercial maize lines were grown at each field trial site.

In forage 9 different analytical compounds have been measured: proximates (protein, fat, ash, and moisture), alkaline detergent fiber (ADF), neutral detergent fiber (NDF), calcium and phosphorus, as well as carbohydrates by calculation. In grain samples 69 analytical components were analyzed, essentially those analysed in the American field trials. Statistical analysis was performed using a mixed model analysis of variance.

Statistical analysis of the compositional field trial data from Germany showed significant different levels between MON88017 and its non-GM counterpart for potassium and raffinose at all three field trial sites and for vitamin B1 at two sites. However the average values and the range of these parameters fell within the tolerance intervals defined by the reference varieties. Similarly, the statistical analysis of the Spanish data showed significant differences between MON88017 and its control for 4 analytes at both sites, *i.e.* for methionine, iron, beta carotene/vitamin A and vitamin B1. Levels of another 12 analytes differed between MON88017 maize and the non-GM comparator at one site. However, all these statistically significant differences fell within the tolerance intervals defined by the reference varieties.

The GMO Panel considered the observed compositional differences between maize MON88017 and its non-GM comparators in the light of the field trial design, the biological variation and the levels of the compounds in conventional maize varieties, and concludes that maize MON88017 is compositionally equivalent to the its non GM counterpart and conventional maize, except for the introduced trait and statistically significant lower vitamin B1 content measured at each location in the 2002 US field trials. However, vitamin B1 content of MON88017 maize from these trials fell in the range defined by the historical data.

The GMO Panel considered the observed compositional differences between maize MON88017 and its non-GM comparators in the light of the field trial design, the biological variation and the levels of the compounds in conventional maize varieties, and concludes that

maize MON88017 is compositionally equivalent to its non-GM counterpart and conventional maize, except for the introduced trait and statistically significant lower vitamin B1 content measured at each location in 2002 US field trials. However vitamin B1 content from these trials felt in the range of the historical data.

The GMO Panel is of the opinion, that the set of compositional data supplied is in compliance with the principles described in the guidance document of the GMO Panel for the risk assessment of genetically modified plants and derived food and feed (EFSA, 2006a).

4.1.3. Agronomic traits and GM phenotype

During field trials over several seasons and at different locations, phenotypic and agronomic data related to dormancy and germination, emergence and vegetative growth, reproductive growth, seed retention, and stress (*i.e.* disease, biotic and abiotic stressors) were collected.

Statistically significant differences between maize MON88017 and the corresponding non-GM comparator were observed for seedling vigor over two seasons, with a higher average score for MON88017 in one season and a lower score in the other season. Also differences in other agronomic parameters related to vigour were observed between the tested maize varieties but not at all locations. The Panel found it unlikely that these observed differences are of biological significance. The Panel also noticed that the other biological characteristics examined were not consistently changed across all locations.
The GMO Panel concludes that maize MON88017 is equivalent to its non-GM counterpart and conventional maize with regard to phenotypic characteristics and agronomic performance except for the introduced trait.

4.2 Conclusion

Based on results of the compositional analysis of maize samples from field trials located at representative sites and environments, it is concluded that forage and grains of maize MON88017 are compositionally, phenotypically and agronomically equivalent to those of the non-GM counterpart and conventional maize varieties, except for the presence of Cry3Bb1 and CP4 EPSPS proteins in maize MON88017.

5. Food/Feed safety assessment

5.1. Evaluation of relevant scientific data

The GMO Panel requested from the applicant further data with respect to the bioinformatics-supported comparisons of the transgenic proteins expressed in maize MON88017 with sequences of known allergens and toxins.

5.1.1. Product description and intended use

The scope of application EFSA-GMO-CZ-2005-27 includes the import and processing of maize MON88017 and its derived products for use as food and feed. Thus, the possible uses of maize MON88017 include the production of animal feed, but it also includes valuable food products such as, starch, syrups and oils.

The genetic modification of maize MON88017 is intended to improve agronomic performance only and is not intended to influence the nutritional properties, processing characteristics and overall use of maize MON88017 as a crop.

5.1.2 Effects of processing

Since maize MON88017 is compositionally equivalent to conventional maize (see section 4.1.2), except for the newly expressed proteins (see section 3.1.3), the characteristics of processed products derived from this GM maize are not expected to be different from conventional maize varieties.

5.1.3. Toxicology

5.1.3.1. Protein used for the safety assessment

Given the low expression level of the Cry3Bb1 and CP4 EPSPS proteins in maize MON88017 and the very difficult task of isolating a sufficient quantity of purified proteins from this maize for safety testing, proteins produced in a recombinant *Escherichia coli* strain were used.

The equivalence of the Cry3Bb1 protein produced in maize MON88017 grains to the one produced in *E. coli* was demonstrated by SDS PAGE, Western analysis, MALDI-TOF mass spectrometry, protein glycosylation analysis and insect bioactivity assay.

The equivalence of the CP4 EPSPS protein in maize MON88017 grains to the one produced in *E.coli* was proved by SDS PAGE followed by Western analysis, protein glycosylation analysis, and enzymatic activity assay. The identity of the 45-kDa protein identified in plants as CP4 EPSPS was further corroborated with the aid of MALDI-TOF mass spectrometry and N-terminal sequence analysis.

The GMO Panel therefore accepts the *E. coli* derived Cry3Bb1 and CP4 EPSPS proteins as appropriate substitute test materials for the plant Cry3Bb1 and CP4 EPSPS proteins in the safety studies.

5.1.3.2. Toxicological assessment of expressed novel proteins in maize MON88017

MON863 Cry3Bb1, which differs only by one amino acid in sequence from MON88017 Cry3Bb1, has been evaluated previously by the EFSA GMO Panel (EFSA, 2004b, 2004c) and has been regarded as safe. Because of the single amino acid substitution in the Cry3Bb1 protein of MON88017, a risk assessment of this protein has been undertaken.

EPSPS enzymes occur in plants, fungi and microorganisms and are thus consumed as part of the normal diet by humans and animals. No adverse effects associated with the intake of these proteins have been identified. Genetically modified crops containing the EPSPS protein from *Agrobacterium* sp. strain CP4 (CP4 EPSPS) are regarded as being as safe as the respective conventional crops for human and/or animal consumption (ACNFP, 1994; SCP, 1998a, 1998b; EFSA, 2003, 2007b).

Bioinformatic analysis

Bioinformatic analyses of the amino acid sequences of Cry3Bb1 and CP4 EPSPS expressed in maize MON88017 have been carried out using the TOXIN6 database and FASTA algorithm

and databases compiled by the applicant and containing sequences of protein toxins and general public-domain proteins. These analyses revealed no relevant homology between the test proteins and known toxic proteins.

In vitro digestibility

The stability of the Cry3Bb1 and CP4 EPSPS proteins isolated from recombinant *E. coli* were tested *in vitro* with simulated gastric fluid (SGF). No intact Cry3Bb1 protein (ca. 75 kDa) was detected after incubation in SGF for 15 seconds, whereas lower-weight bands transiently occurred but disappeared after four minutes when the samples were analysed using SDS PAGE and protein staining. Using Western analysis after SDS PAGE, no intact protein was detected after incubation in SGF for 15 seconds.

No protein bands due to degradation of CP4 EPSPS protein were observed after 15 seconds of incubation in SGF as demonstrated by SDS PAGE and protein staining and confirmed by Western analysis. In addition, enzymatic activity of CP4 EPSPS was almost lost at the first time point of sampling, *i.e.* after two minutes of incubation.

The degradation of the Cry3Bb1 protein was also tested using *in vitro* simulated intestinal fluid (SIF). Western analysis showed that most of the full length protein was digested within one minute in SIF. Protease resistant fragments were observed until 24 hours. More than 94% of the enzymatic activity of CP4 EPSPS incubated in SIF disappeared within 4.5 hours of incubation.
The *in vitro* digestion experiments demonstrate that the Cry3Bb1 and CP4 EPSPS proteins are rapidly degraded under simulated gastric conditions.

Acute oral toxicity

In single dose toxicity studies using mice no systemic effects were observed after administration of Cry3Bb1 protein and CP4 EPSPS at doses of 1930 mg/kg body weight and 572mg/kg body weight, respectively.

The Panel is of the opinion that the single dose acute oral toxicity study does not add relevant information for the safety assessment of these proteins.

5.1.3.3. Toxicological assessment of constituents other than proteins

Since no new constituents other than the Cry3Bb1 and CP4 EPSPS proteins are expressed in maize MON88017, and no biologically relevant alterations in the levels of endogenous compounds were detected in the comparative compositional analyses, no toxicological assessment of new constituents is required.

5.1.4. Toxicological assessment of the whole GM food/feed

Subchronic oral toxicity

The applicant provided a subchronic (13-week) feeding study in rats using grains of maize MON88017 as a component of the diet. Groups of 20 male and 20 female rats (Crl:CD(SD) IGS BR) were fed diets containing 11% or 33% (w/w) grains from maize MON88017 treated with glyphosate or 33% (w/w) grains from the near isogenic non-GM control maize (LH59xLH198).

Animals were examined twice daily for clinical appearance. Individual body weights and food consumption were recorded weekly. At the end of the experiment clinical pathological evaluation was performed including haematology, serum chemistry and urine analysis. In addition a complete necropsy was carried out including organ weight determinations, macroscopic examinations and histopathology.

There were no statistically significant differences in the mean body weight between the groups and no relevant differences in food consumption.

For haematology parameters a statistically significantly higher mean absolute neutrophil count was observed only in females fed 33% maize MON88017 compared with the control group. There was no difference in the relative neutrophil count between rats fed 33% maize MON88017 and the control group. Since the higher mean absolute neutrophil count was within the range of normal variation and there were no differences in related parameters the observed difference was considered as an incidental finding. There were no findings in serum chemistry parameters, urine analysis, organ weight determinations and microscopic examinations related to feeding rats with diets containing maize MON88017.

The GMO Panel concludes that the 13-week feeding study in rats gave no indication of any adverse effects.

5.1.5. Allergenicity

The strategies used when assessing the potential allergenic risk focus on the characterisation of the source of the recombinant protein, the potential of the newly expressed protein to induce sensitisation or to elicit allergic reactions in already sensitised persons and on whether the transformation may have altered the allergenic properties of the modified food. A weight-of-evidence approach is recommended, taking into account all of the information obtained with various test methods, since no single experimental method yields decisive evidence for allergenicity (EFSA, 2006a; CAC, 2003).

5.1.5.1. Assessment of allergenicity of the newly expressed proteins

Bioinformatics-supported comparisons of the amino acid sequence of the plant-expressed Cry3Bb1 and CP4 EPSPS proteins with sequences of known allergens were performed. Searches using the FASTA algorithm and the allergen database AD8 indicated no similarity of the Cry3Bb1 and CP4 EPSPS proteins with known allergenic proteins. In addition, when the criterion of an identical 8-aa contiguous amino acid stretch was applied, the Cry3Bb1 and CP4 EPSPS sequences yielded no positive outcomes.

The studies on degradation of Cry3Bb1 and CP4 EPSPS proteins with simulated mammalian gastric fluid, which are also relevant for the assessment of potential allergenicity, have been described in section 5.1.3.2. The studies showed that most of the test proteins were degraded by pepsin within seconds.

Based on the available information the EFSA GMO Panel considers that the newly expressed Cry3Bb1 and CP4 EPSPS proteins in maize MON88017 are unlikely to be allergenic. This is in line with previous scientific opinions on events expressing Cry3Bb1 (EFSA, 2004b, 2004c) and CP4 EPSPS (ACNFP, 1994; SCP, 1998a, 1998b; EFSA, 2003, 2007b, 2008a).

5.1.5.2. Assessment of allergenicity of the whole GM plant or crop

The issue of a potential increased allergenicity of maize MON88017 does not appear relevant to the Panel since maize is not considered a common allergenic food. Food allergies to maize are of low frequency and mainly occur in populations of specific geographic areas. Rare cases of occupational allergy to maize dust have been reported. There is no reason to expect that the use of GM maize will significantly increase the intake and exposure to maize. Therefore a possible over-expression of any endogenous protein, which is not known to be allergenic, would be unlikely to alter the overall allergenicity of the whole plant or the allergy risk for consumers (EFSA 2008b, 2009).

5.1.6. Nutritional assessment of GM food/feed

The applicant has provided a 42-day feeding study with broiler chicken to analyse the nutritional value of grain from the maize MON88017 treated with glyphosate, the near isogenic control (LH59xLH198) and five commercial maize varieties. 100 birds per treatment were fed diets containing approximately 55% (w/w) of maize grains during the first half and 60% during the second half of the experiment. Performance, weight gain, feed consumption and carcasses parameters (weight, weight of carcasses parts and compositional analysis of breast and thigh meat) were measured. Out of 56 statistical comparisons performed between the test and the control animals, there were statistically significant differences in feed intake of males, average thigh weight of males and percent drum weight per chill weight of the carcass of males. Although these parameters differed statistically between chickens fed maize MON88017 and the control maize, the parameters were in the biological range of the commercial maize varieties.

The outcomes of the broiler feeding study support the conclusion on the compositional analysis summarized above (section 4.1.2), stating that grains of maize MON88017 are compositionally and therefore nutritionally comparable to grains of the non-GM comparator and commercial maize lines.

5.1.7. Post-market monitoring of GM food/feed

The risk assessment concluded that there is no information to indicate that maize MON88017 is any less safe than its non-GM counterpart and other conventional maize varieties. Furthermore, this maize will be used as any other maize and no increased maize exposure is expected. Therefore, as laid down in the guidance document of the GMO Panel (EFSA, 2006a) a post-market monitoring of the GM food/feed is not considered necessary.

5.2. Conclusion

The Cry3Bb1 and CP4 EPSPS proteins expressed in maize MON88017 showed no homology to known toxic proteins and allergens. Furthermore, they were rapidly degraded in simulated gastric fluid.

A subchronic (90-day) feeding study revealed no indications of adverse effects in rats fed diets containing grains from maize MON88017. In addition, a feeding study in broiler chickens provided evidence of nutritional equivalence of maize MON88017 to conventional maize. These studies, therefore, support the conclusion of the compositional and agronomical comparison that the genetic modification resulted in no unintended effects.

The GMO Panel is of the opinion that maize MON88017 is as safe as conventional maize varieties and considers it unlikely that the overall allergenicity of the whole plant is changed. Maize MON88017 and derived products are unlikely to have any adverse effect on human and animal health in the context of the intended uses.

6. Environmental risk assessment and monitoring plan

6.1. Evaluation of relevant scientific data

6.1.1. Environmental risk assessment

The scope of the application EFSA-GMO-CZ-2005-27 is for food (e.g. starch, syrups, oil) and feed (e.g. maize gluten feed, maize gluten meal) uses, import and processing of maize MON88017 and does not include cultivation. Considering the intended uses of maize MON88017, the environmental risk assessment is concerned with indirect exposure through manure and faeces from the gastrointestinal tracts of animals fed on the GM MON88017 and with accidental release into the environment of MON88017 seeds during transportation and processing.

Maize MON88017 has been developed for protection against specific coleopteran pests (*Diabrotica* spp.) and tolerance to glyphosate. The insect resistance is achieved by expression of the Cry3Bb1 protein from a gene derived from *Bacillus thuringiensis* subspecies *kumamotoensis* and the tolerance to glyphosate is achieved by expression of CP4 EPSPS protein from a gene derived from *Agrobacterium sp.* strain CP4 (see chapter 2.2).

As this application is not for cultivation, concerns regarding the use of glyphosate herbicides on maize MON88017 apply only to imported and processed maize products that may have been treated with these glyphosate herbicides in the countries of origin. However, the regulation and risk assessment of glyphosate herbicides are within the scope of Directive 91/414/EEC concerning the placing of plant protection products on the market (EC, 1991).

6.1.1.1. Potential unintended effects on plant fitness due to the genetic modification

Maize is highly domesticated and generally unable to survive in the environment without cultivation. Maize plants are not winter hardy in most regions of Europe, they have lost their ability to release seeds from the cob and they do not occur outside cultivated land or disturbed habitats in agricultural landscapes of Europe, despite cultivation for many years. In addition, there are no cross compatible wild relatives in Europe, and gene flow via pollen is largely restricted to neighbouring crops.

Insect resistance against certain coleopteran pests, such as corn rootworm larvae (*Diabrotica* spp.), provides a potential advantage in cultivation under infestation conditions on non-rotated maize fields. Tolerance to glyphosate provides an agronomic advantage in cultivation where and when glyphosate is applied. However survival of maize outside of cultivation in Europe is mainly limited by a combination of low competitiveness, absence of a dormancy phase, susceptibility to diseases and adverse climatic conditions. Since these general characteristics of this GM maize are unchanged, the inserted traits, namely insect resistance and herbicide tolerance, are not likely to provide a selective advantage outside of cultivation in Europe. Therefore, it is considered very unlikely that volunteers of this GM maize or its

progeny will differ from conventional maize varieties in their ability to survive until subsequent seasons or to establish feral populations under European environmental conditions.

The applicant carried out field trials in the USA, at 8 locations in 2001 and 10 locations in 2002. These locations provided a range of environmental and agronomic conditions representative of major maize growing regions where commercial production of MON88017 is expected. The across-site analysis for 2001 and 2002 field trials identified two statistically significant differences of the total of 14 phenotypic characteristics: seedling vigour was greater for MON88017 plants at three of the ten sites and days to 50% pollen shed was less then one day shorter for MON88017 plants at one of the ten test sites in 2002. The statistically significant differences observed for seedling vigour in 2001 and 2002 were small in magnitude and not accompanied by consistent across-site differences in stand count, days to pollen shed, or days to silk. This suggests that it is unlikely that the differences observed for seedling vigour are biologically meaningful. The phenotypic data indicate that MON88017 does not confer any detectable selective advantage to maize that would result in increased weed potential, compared to the non-GM maize.

The GMO Panel considers also that the small differences in seedling vigour and time of flowering are unlikely to affect the overall fitness and weed potential of the GM maize. There were no other across-site differences in any of the other phenotypic characteristics of the plants tested. The field data do not provide evidence for changes in invasiveness, enhanced weediness or fitness of maize MON88017 plants, except in the presence of glyphosate and of the specific target organisms. In addition to the data presented by the applicant, the GMO Panel is not aware of any scientific report of increased spread and establishment of the maize MON88017 and any change in survival capacity, including over-wintering.

Since maize MON88017 has no altered survival, multiplication or dissemination characteristics except in the presence of the specific target organisms or glyphosate, the GMO Panel is of the opinion that the likelihood of unintended environmental effects as a consequence of spread of genes from this maize will not differ from that of conventional maize varieties.

6.1.1.2. Potential for gene transfer

A prerequisite for any gene transfer is the availability of pathways for the transfer of genetic material, either through horizontal gene transfer of DNA, or vertical gene flow via seed dispersal and cross-pollination.

(a) Plant to bacteria gene transfer

Based on present scientific knowledge and elaborated in more detail (EFSA, 2004, 2007a), gene transfer from GM plants to microorganisms under natural conditions is extremely unlikely, and its establishment would occur primarily through homologous recombination in microorganisms.

In the case of accidental release and establishment of maize MON88017 in the environment, exposure of microorganisms to transgenic DNA derived from GM maize plants would take place during natural decay of GM plant material and/or pollen in the soil of areas where GM plants establish.

Food and feed products derived from the GM maize could contain transgenic DNA. Therefore microorganisms in the digestive tract of humans and animals may be exposed to transgenic DNA.

The *cry*3Bb1 gene in maize MON88017 is under the control of the enhanced 35S plant promoter (P-e35S) which has limited, if any, activity in prokaryotic organisms (see section 3.1.1). Genes under control of prokaryotic regulatory elements conferring related traits, as expressed in the GM plants, occur in certain microorganisms in natural environments. The *cp4 epsps* gene is under the control of a eukaryotic promoter (rice actin promoter P-act1) with little or no activity in prokaryotic organisms. The CP4 *epsps* genes are derived from naturally occurring agrobacterium (*Agrobacterium* sp. strain CP4) and the *cry3Bb1* genes from the *Bacillus thuringensis* (subsp. *kumamotoensis*)

Taking into account the origin and nature of the *cry3Bb1* gene and *cp4 epsps* gene, the lack of selective pressure in the intestinal tract and the environment, the likelihood that horizontal gene transfer of the *cry3Bb1* gene and *cp4 epsps* gene would confer selective advantage or increased fitness to microorganisms is very limited. For this reason it is very unlikely that genes from maize MON88017 would become transferred and established in the genome of microorganisms in the environment or human and animal digestive tract. In the very unlikely event that such horizontal gene transfer would take place, no adverse effects on human and animal health or the environment are expected, as no principally new traits would be introduced or expressed in microbial communities.

(b) Plant to plant gene transfer

The extent of cross-pollination to conventional maize varieties will mainly depend on the scale of accidental release during transportation and processing. For maize, any vertical gene transfer is limited to other *Zea mays* plants as populations of sexually compatible wild relatives of maize are not known in Europe (OECD, 2003). The flowering of the sporadic GM maize plants originating from accidental release occurring during transportation and processing is unlikely to disperse significant amounts of GM maize pollen to other maize plants.

Insect resistance against certain coleopteran pests, such as corn rootworm larvae (*Diabrotica* spp.), provides an advantage in cultivation under infestation conditions. Tolerance to glyphosate provides an agronomic advantage in cultivation where and when glyphosate herbicide is applied. However survival of maize outside cultivation in Europe is mainly limited by a combination of low competitiveness, absence of a dormancy phase, susceptibility to diseases and to adverse climatic conditions. Since these general characteristics of this GM maize are unchanged, the inserted traits, insect resistance and herbicide tolerance, are not likely to provide a selective advantage outside of cultivation in Europe. Therefore, as any other maize varieties, this GM maize would only survive in subsequent seasons in the warmer regions of Europe and are not likely to establish feral populations under European environmental conditions (see section 5.1.1).

In conclusion, since maize MON88017 has no altered survival, multiplication or dissemination characteristics except when cultivated in the presence of the specific target organism or glyphosate, the GMO Panel is of the opinion that the likelihood of unintended environmental effects as a consequence of spread of genes from this maize is considered to be extremely low.

6.1.1.3. Potential interactions of the GM plant with target organisms

The maize MON88017 was transformed to express the Cry3Bb1 protein from *Bacillus thuringiensis* subsp. *kumamotoensis*. The modified and native Cry3Bb1 proteins behave in a similar way to other Cry proteins (see section 3.1.) and are pore-forming toxins producing ion channels in lipid membranes (Rausell, 2004; Bravo, 2007; Gomez, 2007; Pigott, 2007).

This insecticidal protein is active against larvae of some major coleopteran maize pests, (Siegfried et al., 2000, 2005) particularly against western corn rootworm (*Diabrotica virgifera virgifera* LeConte) and northern corn rootworm (*Diabrotica barberi* Smith and Lawrence).

The intended use of maize MON88017 specifically excludes cultivation, therefore the environmental exposure is limited to exposure through manure and faeces from the gastrointestinal tracts of animals fed on the this GM maize as well as to accidental release into the environment of MON88017 seeds during transportation and processing and subsequently to potential occurrence of sporadic feral plants. Thus the level of exposure of target organisms to the mCry3Bb1 protein is likely to be extremely low and of no biological relevance.

6.1.1.4. Potential interactions of the GM plant with non-target organisms

Considering the intended uses of maize MON88017, the environmental risk assessment is concerned with indirect exposure through manure and faeces from the gastrointestinal tracts of animals fed on the GM maize and with accidental release into the environment of GM seeds during transportation and processing.

The GMO Panel assessed therefore whether the Cry3Bb1 protein might potentially affect non-target organisms by entering the environment *e.g.* in manure and faeces from the gastrointestinal tracts of animals fed on maize MON88017. Because of the selectivity of the Cry proteins, non-target organisms belonging to the same taxonomic group as the target organisms are those most likely to be affected.

Data supplied by the applicant indicate that a limited amount of the Cry3Bb1 protein enters the environment due to low expression (11 and 15 µg/g dry weight) in kernels. In addition, the data show that at least 98% of the full-length of Cry3Bb1 protein was digested within 15 seconds in simulated gastric fluids and at least 99,8% of the full-length Cry3Bb1 protein was digested within 1 minute in simulated intestinal fluids. Therefore most of the Cry protein would be degraded by enzymatic activity in the gastrointestinal tract and only very low amounts of Cry3Bb1 protein would remain intact to pass out in faeces. These data are confirmed by studies of related Cry proteins (Lutz et al., 2005, 2006, and references therein) which indicate that the majority of Cry proteins are degraded in the gastrointestinal tract.

Concerning the environmental exposure of Cry proteins in soils, Cry proteins can bind to humic acids, clays, and the organomineral complex found in soil which may give some protection from degradation. However, a number of studies provided data that there is no persistence or accumulation of Cry proteins from GM crops in soil (Ahmad et al., 2005; Baumgarte and Tebbe, 2005; Dubelman et al., 2005; Head et al., 2002; Herman et al., 2001, 2002; Hopkins and Gregorich, 2005; Icoz and Stotzky, 2008; Krogh and Griffiths, 2007).

In conclusion, exposure of soil and water environments to Cry toxins of maize MON88017 from disposal of animal wastes or accidental spillage of maize kernels is likely to be very low

and localized. Thus exposure of potentially sensitive non-target organisms to the mCry3Bb1 protein is likely to be very low and of no biological relevance.

6.1.1.5. Potential interaction with the abiotic environment and biogeochemical cycles

This point was not considered an issue by the Member States or by the GMO panel considering the intended uses of Maize MON88017, excluding cultivation and the low level of environmental exposure.

6.1.2. Monitoring

The objectives of a monitoring plan according to Annex VII of Directive 2001/18/EC are to confirm that any assumption regarding the occurrence and impact of potential adverse effects of the GMO, or its use, in the environmental risk assessment are correct and to identify the occurrence of adverse effects of the GMO, or its use, on human health or the environment which were not anticipated in the environmental risk assessment.

Monitoring is related to risk management, and thus a final adoption of the monitoring plan falls outside the mandate of EFSA. However, the GMO Panel gives its opinion on the scientific quality of the monitoring plan provided by the applicant (EFSA, 2006b). The potential exposure to the environment of maize MON88017 would be through manure and faeces from the gastrointestinal tracts of animals fed on the GM maize or through accidental release into the environment of GM seeds during transportation and processing.

No specific environmental impact of this GM maize was indicated by the environmental risk assessment and thus no case-specific monitoring is required.

The general surveillance plan proposed by the applicant includes i) the description of an approach involving operators (i.e. grain traders and maize processors), reporting to the applicants any observed adverse effect of GMOs on human health and the environment, ii) a coordinating system newly established by EuropaBio, iii) the use of networks of existing surveillance systems. The applicant will submit a general surveillance report on an annual basis.

The GMO Panel is of the opinion that the general approaches and measures of the monitoring plan proposed by the applicant are in line with the EFSA opinion on post-market environmental monitoring (EFSA, 2006b) as well as with the intended uses of Maize MON88017 since the environmental risk assessment does not cover cultivation and identified no potential adverse environmental effects. The GMO Panel agrees with the reporting intervals proposed by the applicant in the general surveillance plan. The GMO Panel advises that appropriate management systems should be in place to prevent seeds of maize MON88017 entering cultivation as the latter requires specific approval under Directive 2001/18/EC or Regulation (EC) No 1829/2003.

6.2. Conclusion

The scope of the application is for food and feed uses, import and processing of maize MON88017 and does not include cultivation. Considering the intended uses of maize MON88017, the environmental risk assessment is concerned with indirect exposure through manure and faeces from the gastrointestinal tracts of animals fed on the maize MON88017

and with accidental release into the environment of GM seeds during transportation and processing.

Maize is highly domesticated and not able to survive in the environment without cultivation. There are no indications of increased likelihood of establishment or survival of feral maize plants in case of accidental release into the environment of MON88017 seeds during transportation and processing. Taking into account the scope of the application, both the rare occurrence of sporadic feral plants and the low levels of exposure through other routes indicate that the risk to non-target organisms is negligible.

The scope of the monitoring plan provided by the applicant is in line with the intended uses of maize MON88017 since the environmental risk assessment did not cover cultivation and identified no potential adverse environmental effects. Furthermore the GMO Panel agrees with the reporting intervals proposed by the applicant in the general surveillance plan.

CONCLUSIONS AND RECOMMENDATIONS

The molecular characterisation data establish that the genetically modified maize MON88017 contains one copy of an intact CP4 EPSPS expression cassette and a Cry3Bb1 cassette in a single locus. No other parts of the plasmid used for transformation are present in the transformed plant. Bioinformatic analysis of the open reading frames at the junctions between the inserted DNA and maize genomic DNA did not raise safety concerns. The stability of the inserted DNA and the herbicide tolerance and insect resistance traits were confirmed over several generations.

Based on results of the comparative analysis the EFSA GMO Panel concluded that maize MON88017 is compositionally, phenotypically and agronomically equivalent to the non genetically modified counterpart and conventional maize varieties, except for the presence of Cry3Bb1 and CP4 EPSPS proteins in maize MON88017. In addition, there are no indications of potential toxicity and allergenicity of the Cry3Bb1 and CP4 EPSPS proteins expressed in maize MON88017. A subchronic (90-day) feeding study revealed no indications of adverse effects in rats fed diets containing grains from maize MON88017. In addition, a feeding study in broiler chickens provided evidence of nutritional equivalence of maize MON88017 to conventional maize. The GMO Panel considers that maize MON88017 is as safe and as nutritious as its non-GM counterpart and conventional maize varieties and that it is unlikely that the overall allergenicity of the whole plant is changed by the genetic modification.

The application EFSA-GMO-CZ-2005-27 concerns food and feed uses, import and processing of maize MON88017. There is therefore no requirement for scientific assessment of possible environmental effects associated with the cultivation of this GM maize. There are no indications of increased likelihood of establishment or survival of feral maize plants in case of accidental release into the environment of MON88017 seeds during transportation and processing. Also, the low levels of environmental exposure through other routes indicate that the risk to target and non-target organisms is likely to be extremely low. The scope of the monitoring plan provided by the applicant is in line with the intended uses of maize MON88017.

In conclusion, the GMO Panel considers that information available for maize MON88017 addresses the comments raised by the Member States and considers it unlikely that maize MON88017 will have any adverse effect on human and animal health or on the environment in the context of its intended uses.

DOCUMENTATION PROVIDED TO EFSA

1. Letter from the Competent Authority of the Czech Republic, dated 04 November 2005, concerning a request for the placing on the market of maize MON88017 in accordance with Regulation (EC) No 1829/2003 submitted by Monsanto.
2. Acknowledgement letter, dated 07 December 2005, from EFSA to the Competent Authority of Czech Republic (Ref. SR/KL/jq (2005) 1403).
3. Letter from EFSA to applicant, dated 05 December 2006, with request for clarifications under completeness check (Ref. SR/KL/DC/shv (2006) 1865301).
4. Letter from applicant, dated 20 December 2006, providing EFSA with an updated version of the application EFSA-GMO-CZ-2005-27 submitted by Monsanto under Regulation (EC) No 1829/2003.
5. Letter from EFSA to applicant, dated 11 January 2007, delivering the "Statement of Validity" for application EFSA-GMO-CZ-2005-27, maize MON88017 submitted by Monsanto under Regulation (EC) No 1829/2003 (Ref. SR/DC/shv (2007) 1906419).
6. Letter from EFSA to applicant, dated 26 March 2007, with request for additional information (Ref. SR/DC/shv (2007) 2052340).
7. Letter from EFSA to applicant, dated 31 May 2007, with request for additional information from JRC-CRL (Ref. SR/KL/shv (2007) 2169718).
8. Letter from applicant to EFSA, dated 04 June 2007, responding to request for additional information.
9. Letter from EFSA to applicant, dated 25 June 2007, with request for additional information (Ref. SR/DC/shv (2007) 2220569).
10. Letter from applicant to EFSA, dated 18 July 2007, responding to request for additional information.
11. Letter from applicant to EFSA, dated 06 September 2007, sending the MSL 0020940 report spontaneously.
12. Letter from EFSA to applicant, dated 26 September 2007, confirming the reception of MSL 0020940 report (Ref. SR/KL/shv (2007) 2406861).
13. Letter from EFSA to applicant, dated 12 October 2007, with request for additional information (Ref. SR/AC/shv (2007) 2439406).
14. Letter from EFSA to applicant, dated 19 October 2007, accepting the data requested from JRC-CRL (Ref. SR/AC/shv (2007) 2455922).
15. Letter from applicant to EFSA, dated 26 October 2007, responding to request for additional information.
16. Letter from EFSA to applicant, dated 20 November 2007, with request for additional information (Ref. SR/AC/shv (2007) 2516031).
17. Letter from applicant to EFSA, dated 29 November 2007, responding to request for additional information.

18. Letter from applicant to EFSA, dated 05 December 2007, responding to request for additional information.
19. Letter from EFSA to applicant, dated 10 December 2007, with request for additional information (Ref. SR/AC/shv (2007) 2564994).
20. E-mail from applicant to EFSA, dated 23 January 2008, informing about the timeline for the submission of the additional information requested.
21. Letter from applicant to EFSA, dated 15 April 2008, sending additional information spontaneously.
22. Letter from applicant to EFSA, dated 03 October 2008, responding to request for additional information.
23. Letter from EFSA to applicant, dated 12 November 2008, restarting the clock (Ref. PB/AC/md (2008) 3451000).
24. Letter from EFSA to applicant, dated 16 December 2008, with request for additional information (Ref. PB/AC/shv (2008) 3532227).
25. Letter from applicant to EFSA, dated 06 January 2009, responding to request for additional information.
26. Letter from EFSA to applicant, dated 28 January 2009, with request for additional information (Ref. PB/AC/shv (2009) 3628562).
27. E-mail from applicant to EFSA, dated 04 February 2009, informing about the timeline for the submission of the additional information requested.
28. Letter from applicant to EFSA, dated 18 February 2009, responding to request for additional information.
29. Letter from EFSA to applicant, dated 20 March 2009, restarting the clock (Ref. PB/AC/mt (2009) 3817429).

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