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SCIENTIFIC OPINION

Application (EFSA-GMO-RX-1507) for renewal of authorisation for the continued marketing of existing products produced from maize 1507 for feed use, under Regulation (EC) No 1829/2003 from Pioneer Hi-Bred International, Inc./Mycogen Seeds [1]

Scientific Opinion of the Panel on Genetically Modified Organisms

(Question No EFSA-Q-2007-144)

Adopted on 28 May 2009

PANEL MEMBERS[*]

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SUMMARY

This document provides the scientific opinion of the Panel on Genetically Modified Organisms (GMO Panel) of the European Food Safety Authority (EFSA) on an application submitted under Regulation (EC) No 1829/2003 (reference EFSA-GMO-RX-1507) for renewal of the authorisation of existing products derived from genetically modified maize 1507.

The scope of this application covers the continued marketing of existing feed produced from maize 1507 (feed materials and feed additives), which were lawfully placed on the market in the Community before the date of entry into force of Regulation (EC) No 1829/2003. After the date of entry into force of Regulation (EC) 1829/2003 these products were notified to the European Commission according to Article 20 of that Regulation and included in the Community Register of genetically modified food and feed[2].

Maize 1507 was developed to provide protection against specific lepidopteran pests and tolerance to the herbicide glufosinate by the introduction of Cry1F and PAT proteins.

The EFSA GMO Panel has previously issued scientific opinions related to notifications C/NL/00/10 for the placing on the market of maize 1507 for import and processing and C/ES/01/01 for the placing on the market of maize 1507 for import, feed and industrial processing and cultivation, under Part C of Directive 2001/18/EC. In addition to this, a scientific opinion for food use of maize 1507 under Regulation (EC) No 1829/2003 was issued

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[*] 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.

[2] http://ec.europa.eu/food/dyna/gm_register/gm_register_auth.cfm?pr_id=2

and published. In these scientific opinions the EFSA GMO Panel concluded that maize 1507 will not have an adverse effect on human and animal health or the environment in the context of its proposed uses. In addition, maize 1507 has been assessed in several applications related to stacked events.

In delivering its opinion the EFSA GMO Panel considered the information provided in the renewal application (reference EFSA-GMO-RX-1507) as well as additional information submitted by the applicant on request of the Panel. In accordance with the Guidance Document for renewal of authorisations of existing EFSA GMO products, the EFSA GMO Panel has taken into account the new information, experience and data, which have become available during the authorisation period.

According to information provided by the applicant, feed products produced from maize 1507 and from maize containing 1507 event stacked with other GM events that have been approved in the EU, have been consumed without reports of adverse effects. Scientific publications, which have become available since the previous evaluation of maize 1507 by the EFSA GMO Panel, did not raise safety issues. Additional bioinformatics studies using updated databases have confirmed the results of the previous studies showing that no relevant similarities exist between the newly expressed proteins Cry1F and PAT and known toxic proteins for human and mammals or allergens. Bioinformatics analysis of the flanking regions showed homology to retrotransposable elements which raises no safety concern.

The scope of this application is for feed materials and feed additives which are produced from maize 1507. Thus the scope only includes products produced from maize 1507 which contain no viable plant parts. Therefore, there are no requirements for scientific information on environmental safety assessment of accidental release or cultivation of maize 1507. A post market environmental monitoring plan for maize 1507 is not required.

The EFSA GMO Panel concludes that the new information provided by the applicant and a review of the scientific literature that has been published since the previous opinions of the EFSA GMO Panel does not require changes of the previous scientific opinions on maize 1507 and addresses the scientific comments raised by the Member States. Therefore, the EFSA GMO Panel reiterates the previous conclusions that genetically modified maize 1507 is unlikely to have an adverse effect on human and animal health or the environment in the context of its proposed uses. This includes the use of feed materials and feed additives produced from maize 1507.

Key words: GMO, maize, *Zea mays*, 1507, insect protection, Cry1F, PAT, feed safety, animal health, Regulation (EC) No 258/97, Regulation (EC) No 1829/2003, Directive 70/524/EEC, Directive 2001/18/EC, renewal, existing product.

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BACKGROUND

On 29 June 2007, EFSA received from the European Commission an application for renewal of the authorisation of existing products derived from maize 1507 (EFSA-GMO-RX-1507) for feed use, submitted by Pioneer Hi-Bred International, Inc./Mycogen Seeds within the framework of Regulation (EC) No 1829/2003. The scope of this application covers the continued marketing of existing feed materials and feed additives produced from maize 1507, which were lawfully placed on the market in the Community before the date of application of Regulation (EC) No 1829/2003. After the date of application of Regulation (EC) 1829/2003 the products were notified to the Commission according to Article 20 of that Regulation and included in the Community Register of genetically modified food and feed[3]. Feed produced from 1507 maize (feed materials and feed additives) was notified as existing feed falling within the scope of Article 20(1)(b) of Regulation (EC) No 1829/2003 namely as feed materials and feed additives (subject to Directive 70/524/EEC) which are produced from a genetically modified organism (GMO).

The EFSA GMO Panel has previously issued scientific opinions related to notifications C/NL/00/10 for the placing on the market of maize 1507 for import and processing and C/ES/01/01 for the placing on the market of maize 1507 for import, feed and industrial processing and cultivation, under Part C of Directive 2001/18/EC (EFSA 2004a, 2005b). Furthermore, a scientific opinion for food use of maize 1507 under Regulation (EC) No 1829/2003 was issued and published (EFSA 2005a). In these scientific opinions the EFSA GMO Panel concluded that maize 1507 will not have an adverse effect on human and animal health or the environment in the context of its proposed uses.

After receiving the application EFSA-GMO-RX-1507 and in accordance with Article 17(2)(b) of Regulation (EC) No 1829/2003, EFSA informed the Member States and the European Commission and made the summary of the dossier available to the public on the EFSA website. EFSA initiated a formal review of the application to check compliance with the requirements laid down in Articles 8 and 20 of Regulation (EC) No 1829/2003. On 15 April 2008 EFSA declared the application as valid in accordance with Article 18(1) of Regulation (EC) No 1829/2003[4].

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 Article 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 within which to make their scientific comments known.

On 24 April 2008, 19 September 2008 and 6 November 2008 the GMO Panel asked the applicant for additional data or clarifications on maize 1507. The applicant provided the requested information on 1 September 2008, 3 October 2008 and 19 December 2008. After receipt and assessment of the full data package, the GMO Panel finalised its opinion.

The EFSA GMO Panel carried out a scientific assessment of the renewal application on maize 1507 according to the guidance document on renewal of applications (EFSA, 2006a) taking into consideration the scientific comments of the Member States and the additional information provided by the applicant.

[3] http://ec.europa.eu/food/dyna/gm_register/gm_register_auth.cfm?pr_id=2
[4] See section Documentation provided to EFSA

In giving its opinion on maize 1507 to the European Commission, the Member States and the applicant, and in accordance with Article 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 18(1), and 18(2) of Regulation (EC) No 1829/2003.

According to Regulation (EC) No 1829/2003, the EFSA opinion shall include an assessment report stating the reasons for its opinion and the information on which this opinion is based, including the opinions of the competent authorities when consulted in accordance with Article 18(4) of Regulation (EC) No 1829/2003. This document is to be seen as the report requested under Article 18(6) of that Regulation and thus will be part of the overall opinion in accordance with Article 18(5).

TERMS OF REFERENCE

The EFSA GMO Panel was requested to issue a scientific opinion on an application for renewal of the authorisation for continued marketing of existing feed materials and feed additives produced from maize 1507 that were notified, according to Article 20(1)(b) of Regulation (EC) No 1829/2003 on genetically modified food and feed, and that has now been submitted under Article 20(4) of Regulation (EC) No 1829/2003. This application fulfils the requirements of Article 23(2) of Regulation (EC) No 1829/2003.

The EFSA GMO Panel was not requested to give an opinion on information required under Annex II to the Cartagena Protocol. Furthermore, the 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

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ASSESSMENT

1. Introduction

Summary of the conclusions of the previous scientific opinions (EFSA, 2004a, 2005a,b).

Regarding the information which has already been evaluated in the context of the previous applications on maize 1507, the EFSA GMO Panel refers to the respective opinion (EFSA, 2004a, 2005a,b). The scientific assessment included the transformation process, the vectors used and the transgenic constructs in the genetically modified plants. A comparative analysis of agronomic traits and composition was undertaken and the safety of the new proteins and the whole food/feed was evaluated with respect to toxicology and allergenicity. A nutritional assessment and an environmental assessment including monitoring plans were undertaken. The EFSA GMO Panel concluded that maize 1507 is unlikely to have an adverse effect on human and animal health or the environment in the context of its proposed uses (EFSA, 2004a, 2005a,b).

The assessment presented here is based on the information provided by the applicant in its application for renewal EFSA-GMO-RX-1507 and the additional information submitted by the applicant in reply to questions from the EFSA GMO Panel.
The EFSA GMO Panel has assessed the new information in relation to the data which have already been evaluated by the GMO Panel in the context of the previous applications for maize 1507 (EFSA, 2004a, 2005a,b).

2. Issues raised by the Member States

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

3. Evaluation of relevant new scientific data

3.1. Molecular Characterisation

The new molecular data included updated bioinformatics analysis of the border regions of the 1507 insert and of all putative reading frames (defined from STOP codon to STOP codon) spanning the 5' and 3' insert – genomic DNA junctions or resulting from rearrangement of the original construct intended for insertion (e.g. junctions between the complete and/or partial copies of the PHI8999A original insert). Homology searches with the flanking regions as query sequences identified high scores with maize genomic DNA, homologous to retrotransposable elements, which raises no safety concern. *In silico* analysis of all reading frames at all new junctions resulting from the insertion, using updated databases, identifed 61 putative peptides with no similarity to known allergens, toxins or other bioactive peptides.

Updated Southern analysis, using several probe/enzyme combinations and recent seed materials from backross generations containing the 1507 event, indicated that both the insert and the flanking regions were stable. Stability of expression was analysed by measuring the Cry1F and PAT protein contents of grains from field experiments in USA in 2008. The new data do not indicate any safety concern.

3.1.1. Conclusion

The updated molecular and bioinformatic analyses together with protein expression data do not indicate any safety concerns with regard to maize event 1507.

3.2. Food and Feed safety assessment

In this new application, new studies have been performed with regards to the potential allergenicity of Cry1F and PAT proteins of GM maize 1507. Ladics *et al.* (2006) assessed the potential cross-reactivity of the proteins Cry1F from maize and Der p7 from dust mite with human sera positive for Der p7-IgE. The rationale for this was an identical sequence of six contiguous amino acids shared by Cry1F with Der p7. In this study, nonetheless, no cross-reactivity between the two proteins tested, i.e. no binding to Cry1F of the sera positive for Der p 7, was evidenced supporting previous reports that the 6-amino-acid threshold for bioinformatics-supported comparisons of novel protein sequences with allergens likely leads to many false positives.

In addition to this, the applicant was asked to provide the outcome of bioinformatics-supported comparisons of the amino acids sequences of PAT and Cry1F proteins with updated data bases of known toxins and allergens. New bioinformatics studies using updated databases have confirmed the results of studies already evaluated by the EFSA GMO Panel, showing that no homologies exist between the newly expressed proteins Cry1F and PAT and known toxic proteins or allergens.

3.2.1. Conclusion

New information from the literature and from additional studies performed by the applicant does not prompt the EFSA GMO Panel to change its previous opinion on maize 1507.

3.3. Environmental assessment

The scope of this application is for feed materials and feed additives which are produced from maize 1507. Thus the scope only includes products produced from maize 1507 which contain no viable plant parts. Therefore, there are no requirements for scientific information on environmental safety assessment of accidental release or cultivation of maize 1507.

3.3.1. 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. Considering the scope of the current application, the possible pathway is limited to horizontal gene transfer from plant material to bacteria.

Plant material to bacteria gene transfer

Based on the current scientific knowledge and elaborated recently in more detail (EFSA, 2004b, 2007), horizontal gene transfer from GM plant materials to microorganisms under natural conditions is extremely unlikely, and that its establishment would occur primarily through homologous recombination in microorganisms (Keese, 2008).

The *cry1F* gene and the *pat* gene expressed in maize 1507 are under the control of eukaryotic promotors with limited if any activity in prokaryotic organisms. Genes under control of prokaryotic regulatory elements conferring the same traits as expressed in the GM plants are widespread in microorganisms in natural environments.

Taking into account the origin and/or nature of *cry1F* and *pat* genes and the lack of selective pressure in the intestinal tract and/or the environment, the likelihood that horizontal gene transfer would result in increased fitness on microorganisms or other selective advantages is very small. For this reason, it is very unlikely that *cry1F* and *pat* genes from maize 1507 would become established in the genome of microorganisms in the environment or in the human and animal digestive tract. In the very unlikely event that such a 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 into microbial communities.

3.3.2. Interactions between the GM plant material and non-target organisms

The EFSA GMO Panel assessed whether the Cry1F protein might potentially affect non-target organisms by entering the environment through manure and faeces from the gastrointestinal tracts of animals fed maize 1507. Due to the selectivity of the Cry protein, non-target organisms most likely to be affected by the Cry1F protein are those belonging to a similar taxonomic group as that of the target organisms.

Most Cry proteins are degraded by enzymatic activity in the gastrointestinal tract, meaning that only low amounts of Cry proteins would remain intact to pass out in faeces (e.g., Einspanier et al., 2004; Lutz et al., 2005, 2006; Wiedemann et al., 2006; Guertler et al., 2008). There would subsequently, be further degradation of the Cry1F protein in the manure and faeces due to microbial processes.

Exposure of soil and water environments to the Cry1F protein from disposal of animal wastes of maize kernels is likely to be very low and localized. While Cry proteins can bind to clay minerals and humic substances in soil, thereby reducing their availability to microorganisms for degradation, a number of studies revealed that there is no accumulation of Cry proteins from GM crops in soil (reviewed by Icoz and Stotzky, 2008).

Considering the scope of the application, it can be concluded that the exposure of potentially sensitive non-target organisms to the Cry1F protein is likely to be very low and of no biological relevance.

3.3.3. Monitoring

Considering the scope of the application EFSA-GMO-RX-1507 for feed materials and feed additives which are produced from maize 1507, a post market environmental monitoring plan for maize 1507 is not required

3.3.4. Conclusion

The scope of this application is for feed materials and feed additives which are produced from maize 1507. Thus the scope only includes products produced from maize 1507 which contain no viable plant parts. Therefore, there are no requirements for scientific information on environmental risks associated with the accidental release or cultivation of maize 1507. A post market environmental monitoring plan for maize 1507 is not required.

CONCLUSIONS AND RECOMMENDATIONS

The EFSA GMO Panel was requested to deliver a scientific opinion for renewal of the authorisation of existing products from maize 1507 (EFSA-GMO-RX-1507) for feed use under Regulation (EC) No 1829/2003. The scope of this application covers the continued marketing of existing feed materials and feed additives produced from maize 1507, which were lawfully placed on the market in the Community before the date of application of Regulation (EC) No 1829/2003 and included in the Community Register of genetically modified food and feed.

In its previous opinions the EFSA GMO Panel concluded that the maize 1507 will not have an adverse effect on human and animal health or the environment in the context of its proposed use (EFSA 2004a, 2005a, b).

The updated molecular and bioinformatic analyses provided for the maize 1507 event do not indicate any safety concerns.

New information from the scientific literature and from additional studies performed by the applicant does not prompt the Panel to change its previous opinion that maize 1507 is as safe and nutritious as the non-GM counterparts.

The EFSA GMO Panel considers that there is no requirement for scientific information on environmental risk assessment associated with the accidental release or cultivation of maize 1507. A post market environmental monitoring plan for maize 1507 is not required.

The EFSA GMO Panel concludes that the new information provided by the applicant and a review of the scientific literature that has been published since the previous opinions of the EFSA GMO Panel does not require changes of the previous scientific opinions on maize 1507 and addresses the scientific comments raised by the Member States. Therefore, the EFSA GMO Panel reiterates the previous conclusions that genetically modified maize 1507 is unlikely to have an adverse effect on human and animal health or the environment in the context of its proposed uses (EFSA 2004a, 2005a, b). This includes the use of feed materials and feed additives produced from maize 1507.

DOCUMENTATION PROVIDED TO EFSA

1. Letter from the European Commission, dated 29 June 2007, concerning a request for renewal of authorisation for the placing on the market of maize 1507 in accordance with Regulation (EC) No. 1829/2003.
2. Acknowledgement letter, dated 20 July 2007, from EFSA to the European Commission.
3. Letter from EFSA to applicant, dated 10th April 2008, delivering the 'Statement of Validity' for application EFSA-GMO-RX-1507 maize 1507 submitted by Pioneer under Regulation (EC) No. 1829/2003.
4. Letter from EFSA to applicant, dated 24 April 2008, with request for clarifications/additional information.
5. Letter from applicant to EFSA, dated 03 September 2008, providing additional information upon EFSA request.
6. Letter from EFSA to applicant, dated 19 September 2008, with request for clarifications/additional information.
7. Letter from applicant to EFSA, dated 06 October 2008, providing additional information upon EFSA request.
8. Letter from EFSA to applicant, dated 06 November 2008, with request for clarifications/additional information.
9. Letter from applicant to EFSA, dated 22 December 2008, providing additional information upon EFSA request.
10. Letter from EFSA to applicant, dated 03 March 2009, re starting the clock.

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