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Assessment of genetically modified maize NK603 x MON810 for renewal of authorisation under Regulation (EC) No 1829/2003 (application EFSA-GMO-RX-007)

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Abstract

Following the submission of application EFSA-GMO-RX-007 under Regulation (EC) No 1829/2003 from Monsanto, the Panel on Genetically Modified Organisms of the European Food Safety Authority (GMO Panel) was asked to deliver a scientific risk assessment on the data submitted in the context of the renewal of authorisation application of the herbicide-tolerant and insect-resistant genetically modified maize NK603 x MON810. The data received in the context of this renewal application contained post-market environmental monitoring reports, a systematic search and evaluation of literature, updated bioinformatic analyses, and additional documents or studies performed by or on behalf of the applicant. The GMO Panel assessed these data for possible new hazards, modified exposure or new scientific uncertainties identified during the authorisation period and not previously assessed in the context of the original application. Under the assumption that the DNA sequence of the events in maize NK603 x MON810 considered for renewal is identical to the sequence of the originally assessed events, the GMO Panel concludes that there is no evidence in the renewal application EFSA-GMO-RX-007 for new hazards, modified exposure or scientific uncertainties that would change the conclusions of the original risk assessment on maize NK603 x MON810.

Keywords: maize, NK603 x MON810, renewal, articles 11 and 23, Regulation (EC) No 1829/2003

Requestor: European Commission (DG SANTE)

Question number: EFSA-Q-2017-00028

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Summary

Following the submission of application EFSA-GMO-RX-007 under Regulation (EC) No 1829/2003[1] from Monsanto, the Panel on Genetically Modified Organisms of the European Food Safety Authority (GMO Panel) was asked to deliver a scientific opinion on the data submitted in the context of the renewal of authorisation application of the herbicide-tolerant and insect-resistant genetically modified (GM) maize NK603 x MON810. The scope of the renewal application EFSA-GMO-RX-007 is for food and feed uses, import and processing, but excludes cultivation within the European Union (EU).

In delivering its scientific opinion, the GMO Panel took into account application EFSA-GMO-RX-007, additional information provided by the applicant, scientific comments submitted by the Member States and relevant scientific publications. The data received in the context of the renewal application EFSA-GMO-RX-007 contained: post-market environmental monitoring reports, an evaluation of the literature retrieved by a systematic search, updated bioinformatic analyses and additional documents or studies performed by or on behalf of the applicant. The GMO Panel assessed these data for possible new hazards, modified exposure or new scientific uncertainties identified during the authorisation period and not previously assessed in the context of the original application.

Under the assumption that the DNA sequence of the events in maize NK603 x MON810 considered for renewal is identical to the sequence of the originally assessed events, the GMO Panel concludes that there is no evidence in the renewal application EFSA-GMO-RX-007 for new hazards, modified exposure or scientific uncertainties that would change the conclusions of the original risk assessment on maize NK603 x MON810.

[1] Regulation (EC) No 1829/2003 of the European Parliament and of the Council of 22 September 2003 on genetically modified food and feed. OJ L 268, 18.10.2003, p. 1–23.

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1. Introduction

1.1. Background

On 22 December 2016, the European Food Safety Authority (EFSA) received from the European Commission (DG SANTE) the application EFSA-GMO-RX-007 by Monsanto for the renewal of authorisation of genetically modified (GM) maize NK603 x MON810 (maize MON-ØØ6Ø3-6 x MON-ØØ81Ø-6) for food and feed uses, import and processing within the framework of Regulation (EC) No 1829/2003. Before sending the application to EFSA, the European Commission (DG SANTE) confirmed whether the data submitted in the context of this renewal application were in line with the legal requirements laid down in Articles 11 and 23 of Regulation (EC) No 1829/2003.

After receiving the application EFSA-GMO-RX-007, and in accordance with Articles 5(2)(b) and 17(2)(b) of Regulation (EC) No 1829/2003, EFSA informed Member States and made the summary of the application available to the public on the EFSA website.[2]

On 18 April 2017, EFSA declared the application 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 Member States, including national Competent Authorities within the meaning of Directive 2001/18/EC following the requirements of Articles 6(4) and 18(4) of Regulation (EC) No 1829/2003, to request their scientific opinion. Member States had 3 months after the opening of the Member State commenting period (until 1 August 2017) to make their opinion known.

Following the submission of application EFSA-GMO-UK-2004-01 and the publication of the EFSA scientific opinion (EFSA, 2005), the placing on the market of maize NK603 x MON810 for food/feed uses, except cultivation, was authorised by Commission Decision 2007/701/EC.[3] A copy of this authorisation was provided by the applicant.[4]

EFSA requested additional information on 12 July 2017 and 28 November, and the applicant submitted the replies on 13 September 2017 and 11 January 2018, respectively. On 5 October, EFSA received from the European Commission the post-market environmental monitoring plan submitted by the applicant to the risk managers.

In giving its scientific opinion 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 6 months from the acknowledgement of the valid application. As additional information was requested by the 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, this scientific opinion 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 EFSA overall opinion in accordance with Articles 6(5) and 18(5).

1.2. Terms of Reference as provided by the requestor

The GMO Panel was requested to carry out a scientific risk assessment on the data submitted in the context of a renewal of authorisation application for maize NK603 x MON810 for food and feed uses, import and processing in accordance with Articles 11 and 23 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 GMO Panel was not requested to give an opinion on information required under Annex II to the Cartagena Protocol. Furthermore, the GMO Panel did not consider proposals for labelling and methods of detection (including sampling and the identification of the specific transformation events in the food/feed and/or food/feed produced from it), which are matters related to risk management.

[2] Available online: http://registerofquestions.efsa.europa.eu/roqFrontend/questionDocumentsLoader?question=EFSA-Q-2017-00028

[3] Commission Decision of 24 October 2007 authorising the placing on the market of products containing, consisting of, or produced from genetically modified maize NK603 x MON810 (maize MON-ØØ6Ø3-6xMON-ØØ81Ø-6) pursuant to Regulation (EC) No 1829/2003 of the European Parliament and of the Council. (2007/701/EC); OJ L 285, pp 37–41.

[4] Annex 1 of the dossier.

2. Data and methodologies

2.1. Data

The data for application EFSA-GMO-RX-007 provided by the applicant at the time of submission, or in reply to requests for additional information, are specified below.

No new sequencing data were submitted among the studies performed by or on behalf of the applicant. Therefore, in accordance with the GMO Panel guidelines for renewal of applications of GM food/feed authorised under Regulation (EC) No 1829/2003 (EFSA GMO Panel, 2015), the GMO Panel evaluated the data provided in the context of NK603 x MON810 renewal application under the assumption that the events' sequence is identical to the sequence of the originally assessed events.

In addition the GMO Panel noted that the assumption was supported by information on the sequence of event NK603 in commercial varieties of maize NK603 x MON810 that has been published (Castan et al., 2017). The applicant has confirmed that the NK603 sequence in NK603 x MON810 commercial varieties is identical to that of the original event (EFSA, 2005, 2009).[5]

2.1.1. Post-market monitoring reports[6]

Based on the outcome of the initial food and feed risk assessment, a post-market monitoring plan for monitoring of GM food/feed was not required by the authorisation decision. The implementation of a post-market environmental monitoring (PMEM) plan, consisting of a general surveillance plan to check for any adverse effects on the environment arising from maize NK603 x MON810, was a condition for the authorisation. As no potential adverse environmental effects were identified in the environmental risk assessment (ERA) of maize NK603 x MON810 (EFSA, 2005), case-specific monitoring was not considered necessary by the GMO Panel.

The applicant provided eight annual PMEM reports covering a reporting period from March 2008 to July 2016. The annual PMEM plans submitted by the applicant included (1) the description of a centralised system established by EuropaBio for the collection of information recorded by various operators (federations involved in maize (or bulk grain) import and processing) on any observed adverse effect(s) on human health and the environment arising from handling of maize possibly containing maize NK603 x MON810; (2) the reports of the surveillance activities conducted by such operators; and (3) the review of relevant scientific peer-reviewed studies retrieved from literature searches.

2.1.2. Systematic search and evaluation of literature[7]

The applicant performed a systematic literature search of studies published between 2007 and 2016, relevant to the food/feed and environmental safety assessments of maize NK603 x MON810, following the principles outlined in the EFSA guidance on the application of systematic review methodology for food and feed safety assessment (EFSA, 2010). In total, 28 publications using the identified search terms relevant to maize NK603 x MON810 were identified. After applying the eligibility/inclusion criteria defined *a priori* by the applicant, no primary research studies were identified that was relevant for the food and feed risk assessment, and the ERA risk assessment.

2.1.3. Updated bioinformatic data[8]

At the time of submission of the renewal dossier, the applicant provided a bioinformatics data package for maize NK603 x MON810 including an analysis of the insert and flanking sequences and an analysis of the potential similarity to allergens or toxins of the newly expressed proteins and of all possible open reading frames (ORFs) within the insert and spanning the junction sites and an analysis of possible horizontal gene transfer (HGT). The bioinformatic data were obtained using the original sequence submitted by the applicant. The outcome of the updated bioinformatics is presented in Section 3.3.

[5] Additional information 11/1/2018.
[6] Annex 2 of the dossier.
[7] Annex 3.1 of the dossier.
[8] Annex 3.2 of the dossier and additional information 13/9/2017.

2.1.4. Additional documents or studies provided by the applicant[9]

The applicant provided an overview on the worldwide approvals of maize NK603 x MON810 and the full reports of all studies performed by or on behalf of the applicant over the course of the authorisation period and not previously submitted to the EU (Appendix A).

The relevance of the listed studies for molecular characterisation, human and animal safety and the environment was assessed by the applicant.

2.1.5. Overall assessment as provided by the applicant[10]

In line with the requirements listed in the renewal guidance (EFSA GMO Panel, 2015), the applicant provided an overall assessment concluding that information provided in the application for renewal of the authorisation of maize NK603 x MON810 for food and feed use and processing in the EU, do not change the outcome of the original risk assessment (EFSA, 2005).

2.1.6. Monitoring plan and proposal for improving the conditions of the original authorisation[11]

The applicant indicated in the dossier that the environmental monitoring plan is appropriate and does not need any changes.

2.2. Methodologies

The GMO Panel assessed the application for the renewal of the authorisation of maize NK603 x MON810 for food and feed uses, import and processing in accordance with Articles 11 and 23 of Regulation (EC) No 1829/2003. The GMO Panel took into account the requirements described in its guideline for the risk assessment of renewal applications of GM food and feed authorised under Regulation (EC) No 1829/2003 (EFSA GMO Panel, 2015).

The comments raised by Member States are addressed in Annex G of EFSA's overall opinion[12] and were taken into consideration during the scientific risk assessment.

3. Assessment

3.1. Evaluation of the post-market environmental monitoring reports

During the general surveillance activities covering the authorisation period of maize NK603 x MON810, no adverse effects were reported by the applicant.

3.2. Evaluation of the systematic search and evaluation of literature

The GMO Panel assessed the systematic literature search carried out by the applicant and acknowledged that no publication has been identified raising a safety concern for human and animal health and the environment which would change the original risk assessment conclusions on maize NK603 x MON810 (EFSA, 2005).

Due to the date of the publication, the publication by Castan et al. (2017) was not included in the systematic literature search. This publication is discussed in Section 2.1

3.3. Evaluation of the updated bioinformatic data

The results of the updated bioinformatic analyses on maize events NK603 and MON810 confirmed previous assessments (EFSA, 2005) that no known endogenous genes were disrupted by the inserts. Analyses of the amino acid sequence of the newly expressed CP4 EPSPS and Cry1Ab proteins revealed no significant similarities to toxins and allergens. In addition, bioinformatic analyses of the newly created ORFs within the insert or spanning the junctions with genomic DNA revealed no significant similarities to toxins and allergens.

The sequence identity analysis of the regions of bacterial origin in maize NK603 x MON810 did not identify elements with sufficient length and identity to support homologous recombination. There is no

[9] Annex 3.3 of the dossier and additional information: 6/7/2017.
[10] Annex 3 of the dossier.
[11] Additional information: 5/10/2017.
[12] Available online: http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2017-00028

information that would change the previous conclusion of the GMO Panel that the unlikely, but theoretically possible, horizontal transfer of recombinant genes from maize NK603 x MON810 to bacteria does not raise any environmental safety concern.

3.4. Evaluation of the additional documents or studies provided by the applicant

The GMO Panel evaluated the full reports of the additional studies provided and listed in Appendix A. This new information did not raise any concern for human and animal health and the environment, which would change the original risk assessment conclusions on maize NK603 x MON810.

3.5. Evaluation of the overall assessment as provided by the applicant

The GMO Panel evaluated the overall assessment provided by the applicant and confirmed that there is no evidence in the renewal application EFSA-GMO-RX-007 indicating new hazards, relevant changes in exposure or scientific uncertainties.

3.6. Evaluation of the monitoring plan and proposal for improving the conditions of the original authorisation

The PMEM plan followed by the applicant consists mainly of general surveillance of imported GM maize plant material, including maize NK603 x MON810.[11] This general surveillance is coordinated by EuropaBio and implemented by selected operators (federations involved in maize import and processing). As mentioned in Section 2.1.6, the applicant considers that this plan does not need any changes. The GMO Panel is of the opinion that the scope of the plan provided by the applicant is consistent with the scope of maize NK603 x MON810 but reminds that monitoring is related to risk management, and thus the final adoption and implementation of the PMEM plan falls outside the mandate of EFSA.

4. Conclusions

Under the assumption that the DNA sequence of the two events in maize NK603 x MON810 considered for renewal is identical to the sequence of the originally assessed events, the GMO Panel concludes that there is no evidence in the renewal application EFSA-GMO-RX-007 for new hazards, modified exposure or scientific uncertainties that would change the conclusions of the original risk assessment on maize NK603 x MON810 (EFSA, 2005).

Documentation provided to EFSA

1) Letter from the European Commission to EFSA received on 22 December 2016 for the continued marketing of genetically modified maize NK603 x MON810 in accordance with articles 11 and 23 of Regulation (EC) No 1829/2003 by Monsanto (EFSA-GMO-RX-007).
2) Acknowledgement letter dated 11 January 2017 from EFSA to European Commission.
3) Letter from EFSA to applicant dated 20 February 2017 requesting additional information under completeness check.
4) Letter from applicant to EFSA received on 23 March 2017 providing additional information under completeness check.
5) Letter from EFSA to applicant dated 18 April 2017 delivering the 'Statement of Validity' for application EFSA-GMO-RX-007.
6) Letter from EFSA to applicant dated 12 July 2017 requesting additional information and stopping the clock.
7) Letter from applicant to EFSA received on 13 September 2017 providing additional information.
8) Email from EFSA to applicant dated 14 September 2017 re-starting the clock on 6 July 2017.
9) Letter from the European Commission to EFSA received on 5 October 2017 providing the post-market environmental monitoring plans submitted by Monsanto.
10) Letter from EFSA to applicant dated 28 November 2017 requesting additional information and stopping the clock.
11) Letter from applicant to EFSA received on 11 January 2018 providing additional information.

References

Castan M, Ben Ali SE, Hochegger R, Ruppitsch W, Haslberger AG and Brandes C, 2017. Analysis of the genetic stability of event NK603 in stacked corn varieties using high-resolution melting (HRM) analysis and Sanger sequencing. European Food Research and Technology, 2017(243), 353–365. https://doi.org/10.1007/s00217-016-2749-2

EFSA (European Food Safety Authority), 2005. Opinion of the Scientific Panel on Genetically Modified Organisms on an application (Reference EFSA-GMO-UK-2004-01) for the placing on the market of glyphosate-tolerant and insect-resistant genetically modified maize NK603 x MON810, for food and feed uses under Regulation (EC) No 1829/2003 from Monsanto. EFSA Journal 2005;3(12):309, 22 pp. https://doi.org/10.2903/j.efsa.2005.309

EFSA (European Food Safety Authority), 2009. Scientific Opinion of the Panel on Genetically Modified Organisms on applications (EFSA-GMO-NL-2005-22 and EFSA-GMO-RX-NK603) for the placing on the market of the genetically modified glyphosate tolerant maize NK603 for cultivation, food and feed uses and import and processing, and for renewal of the authorisation of maize NK603 as existing product. EFSA Journal 2009;7(6):1137, 50 pp. https://doi.org/10.2903/j.efsa.2009.113

EFSA (European Food Safety Authority), 2010. Application of systematic review methodology to food and feed safety assessments to support decision making. EFSA Journal 2010;8(6): 1637, 90 pp. https://doi.org/10.2903/j.efsa.2010.1637

EFSA GMO Panel (EFSA Panel on Genetically Modified Organisms), 2015. Guidance for renewal applications of genetically modified food and feed authorised under Regulation (EC) No 1829/2003. EFSA Journal 2015;13(6):4129, 8 pp. https://doi.org/10.2903/j.efsa.2015.4129

Abbreviations

EPSPS	5-enolpyruvylshikimate-3-phosphate synthase
ERA	environmental risk assessment
GM	genetically modified
GMO	genetically modified organisms
HGT	horizontal gene transfer
ORFs	open reading frames
PMEM	post-market environmental monitoring report

Appendix A – List of additional studies performed by or on behalf of the applicant over the course of the authorisation period and not previously submitted to the EU with regard to the evaluation of the safety of the food/feed for humans, animal or the environment from maize NK603 x MON810

Study identification	Title
Report N°: MSL0021504	Compositional Analyses of Corn Forage and Grain from NK603, MON 810 x NK603, MON 88017, MON 89034, MON 89034 x MON 88017, and MON 89034 x NK603 Produced in European Field Trials during the 2007 Growing Season
Report N°: MSL0020890	Assessment of the Cry1Ab and CP4 EPSPS Protein Levels in Tissues from Maize MON 810 x NK603 Produced in 2005–2006 Brazil Field Trials
Report N°: RAR-09-204	Compositional Analysis of Grain from RSA Maize (MON 810 x NK603 and NK603) and Conventional Maize Produced in Republic of South Africa during 2009
Report N°: MSL0021367	Assessment of the CP4 EPSPS and Cry1Ab Protein Levels in Tissues of Corn NK603 x MON 810 Produced in European Field Trials During 2007
Report N°: MSL0020739	Compositional Analyses of Forage and Grain Collected from Maize MON 810 x NK603 Grown in 2005–2006 Brazil Field Trials