Adviesraad voor Bioveiligheid
Conseil consultatif de Biosécurité

Advice of the Belgian Biosafety Advisory Council on application EFSA-GMO-NL-2017-144 (genetically modified maize MON 87427 x MON 89034 x MIR162 x MON 87411) from Monsanto under Regulation (EC) No. 1829/2003

10 December 2019
Ref. SC/1510/BAC/2019_1083

Context

Application EFSA-GMO-NL-2017-144 was submitted by Monsanto for the marketing of genetically modified (GM) maize MON 87427 x MON 89034 x MIR162 x MON 87411 (Unique Identifier MON-87427-7 × MON-89Ø34-3 × SYN-IR162-4 × MON 87411-9), for food and feed uses, import and processing (excluding cultivation) within the European Union, within the framework of Regulation (EC) No. 1829/2003[1].

The four-event stack maize MON 87427 x MON 89034 x MIR162 x MON 87411 was obtained by conventional crossing (no new genetic modification involved) of the corresponding single events:
- MON 87427, expressing the CP4 EPSPS protein that confers tolerance to herbicide products containing glyphosate;
- MON 89034, expressing the Cry1A.105 and Cry2Ab2 proteins for resistance to lepidopteran insect pests;
- MIR162, expressing the Vip3Aa20 protein, conferring resistance to certain lepidopteran insect pests, and the PMI protein, a selectable marker;
- MON 87411, expressing the CP4 EPSPS protein that confers tolerance to herbicide products containing glyphosate, the Cry3Bb1 protein for resistance against certain coleopteran insect pests, and the DvSnf1 dsRNA for protection against corn rootworm.

The application was validated by EFSA on 13 July 2017. A formal three-month consultation period of the Member States was started, lasting from 1 June 2018 until 3 September 2018, in accordance with Articles 6.4 and 18.4 of Regulation (EC) No. 1829/2003 (consultation of national Competent Authorities within the meaning of Directive 2001/18/EC designated by each Member State in the case of genetically modified organisms being part of the products).

Within the framework of this consultation, the Belgian Biosafety Advisory Council (BAC), under the supervision of a coordinator and with the assistance of its Secretariat, analysed its past advices on the single events, the issues that were identified and the new information that is provided in the present application. Based on this, experts were contacted to evaluate the molecular aspects of the dossier, chosen from the common list of experts drawn up by the BAC and the Service Biosafety and Biotechnology (SBB). Four experts answered positively to this request and analysed the dossier. None of their comments were forwarded to EFSA. See Annex I for an overview of the outcome of the assessment.

The opinion of the EFSA Scientific Panel on GMOs was published on 7 November 2019 (EFSA Journal 2019;17(11):5848 [2]), which was forwarded to the Belgian experts on 12 November 2019. They were invited to give comments and to react if needed.

[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).
[2] See https://doi.org/10.2903/j.efsa.2019.5848

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In delivering the present advice the BAC considered in particular the following information:
- The comments formulated by the experts on application EFSA-GMO-NL-2017-144;
- The opinion of EFSA;
- The advices already adopted by the BAC on the single events and the lower-order stacks, which were as follows:

Event	Application number	BAC advice	Conclusions
MON 87427	EFSA-GMO-BE-2012-110	BAC/2015/0585 (08/09/2015)	Unlikely to pose any risk to human and animal health. No risk identified for the European environment.
MON 89034	EFSA-GMO-NL-2007-37	BAC/2009/0880 (03/02/2009)	No major risks for human and animal health or for the environment.
MIR162	EFSA-GMO-DE-2010-82	BAC/2012/0785 (29/08/2012)	No major risks for animal health or for the environment, no conclusion on human health. The PMI protein has been positively assessed in subsequent applications.
MON 87411	EFSA-GMO-NL-2015-124	BAC/2018/0704 (11/09/2018)	Unlikely to pose any risk to human and animal health. No risk identified for the European environment.
MON 89034 x MIR162	EFSA-GMO-BE-2013-117	BAC/2017/0741 (19/09/2017)	Unlikely to pose any risk to human and animal health. No risk identified for the European environment.
MON 87427 x MON 89034 x MIR162 and subcombinations	EFSA-GMO-NL-2016-131	BAC/2019/0745 (17/09/2019)	Unlikely to pose any risk to human and animal health. No risk identified for the European environment.

All GM maize events mentioned in the table above are authorised in the EU for food and feed uses[3].

Scientific evaluation

1. Environmental risk assessment

The Biosafety Advisory Council is of the opinion that it is unlikely that the accidental release of maize MON 87427 x MON 89034 x MIR162 x MON 87411 (i.e. during transport and/or processing) into the European environment[4] will lead to environmental harm.

2. Molecular characterisation

With regard to the molecular characterisation, the Biosafety Advisory Council is of the opinion that the information provided is sufficient and does not raise safety concerns.

3. Assessment of food/feed safety and nutritional value

3.1. Assessment of compositional analysis

Taking into account the previous assessment of the single events and the new data on the composition of the four-stacked event, provided by the applicant, the Biosafety Advisory Council agrees with the GMO panel of EFSA that the compositional data of GM maize MON 87427 x MON 89034 x MIR162 x MON 87411, when compared with the composition of its conventional counterpart, does not raise safety concerns.

[3] See EU register of GM food and feed: http://ec.europa.eu/food/dyna/gm_register/index_en.cfm
[4] As the application doesn't imply cultivation of the GM crop in the EU, a full environmental assessment is as in the case of a cultivation file is not warranted.

3.2. Assessment of toxicity

The Biosafety Advisory Council has evaluated the safety of the newly expressed CP4 EPSPS, Cry1A.105, Cry2Ab2, Vip3Aa20 and Cry3Bb1 proteins and the DvSnf1 dsRNA in the context of previous applications, and no safety concerns were identified. Taking into account the updated information considered in the current application, the Council is of the opinion that its previous conclusions remain valid.
The Biosafety Advisory Council is also of the opinion that the combined expression of the newly expressed proteins in the stacked event does not raise toxicological concerns.

3.3. Assessment of allergenicity

The Biosafety Advisory Council has evaluated the safety of the newly expressed CP4 EPSPS, Cry1A.105, Cry2Ab2, Vip3Aa20 and Cry3Bb1 proteins and the DvSnf1 dsRNA in the context of previous applications, and no concerns were identified. Since no new information on allergenicity of these proteins has become available, the Council is of the opinion that its previous conclusions remain valid.
The Biosafety Advisory Council is also of the opinion that the combined expression of the newly expressed proteins in the stacked event does not raise concerns regarding the allergenicity.

3.4. Nutritional value

The Biosafety Advisory Council is of the opinion that the information provided is sufficient to conclude that the nutritional characteristics of maize MON 87427 x MON 89034 x MIR162 x MON 87411-derived food and feed are not expected to differ from those of conventional maize varieties.

4. Monitoring

Since the allergenicity of the whole GM maize has not been fully assessed, it is recommended to take up monitoring of allergenicity as part of the general surveillance.

Conclusion

Based on the whole set of data on maize MON 87427 x MON 89034 x MIR162 x MON 87411 provided by the applicant, the scientific assessment of the dossier done by the Belgian experts, the opinion of EFSA, the answers of the EFSA GMO panel to the questions raised by the Belgian experts, and the advices already adopted by the BAC on the four single events and lower-order stacks, the Biosafety Advisory Council:

1) Agrees with the GMO panel of EFSA that the potential environmental release of maize MON 87427 x MON 89034 x MIR162 x MON 87411 and its subcombinations is unlikely to pose any threat to the European environment;
2) Agrees with the GMO panel of EFSA that there is no reason to expect interactions between the newly expressed proteins that could impact on the food or feed safety;
3) Agrees with the GMO panel of EFSA that in the context of its proposed uses, maize MON 87427 x MON 89034 x MIR162 x MON 87411 and its subcombinations are unlikely to pose any risk to human and animal health;

Dr. Corinne Vander Wauven
President of the Belgian Biosafety Advisory Council

Annex I: Outcome of the assessment of application EFSA/GMO/NL/2017/144 (ref. BAC_2018_0654)

Adviesraad voor Bioveiligheid
Conseil consultatif de Biosécurité

Outcome of the assessment of application EFSA/GMO/NL/2017/144 by the Biosafety Advisory Council during the formal consultation of the Member States (3-month commenting period in accordance with Articles 6.4 and 18.4 of Regulation (EC) No 1829/2003)

3 September 2018
Ref. SC/1510/BAC/2018_0654

Mandate for the Group of Experts: Mandate of the Biosafety Advisory Council (BAC) of 18 June 2018.
Coordinator: René Custers
Experts: Jacques Dommes (ULg), Frank Van Breusegem (UGent), Jan Van Doorsselaere (Vives), Bart Van Droogenbroeck (ILVO)
SBB: Fanny Coppens

Application: **EFSA/GMO/NL/2017/144**
Applicant: **Monsanto**
GMO: **Maize MON 87427 x MON 89034 x MIR162 x MON 87411**
Acknowledgement of receipt by EFSA: **1st June 2018**

Scope of the application:
☒ GM plants for food use
☒ Food containing or consisting of GM plants
☒ Food produced from GM plants or containing ingredients produced from GM plants
☒ GM plants for feed use
☒ Feed produced from GM plants
☒ Import and processing (Part C of Directive 2001/18/EC)
☐ Seeds and plant propagating material for cultivation in European Union (Part C of Directive 2001/18/EC)

Given the characteristics of the GMO and its intended uses, experts were consulted to cover the following areas of expertise:
☒ Molecular characterization
☐ Environmental aspects
☐ Allergenicity
☐ Toxicology
☐ Food and Feed aspects

The experts were asked to evaluate whether the information provided in the application is sufficient in order to state that the marketing of the genetically modified plant for its intended uses, will not raise any problems for the environment or human or animal health. If information is lacking, the expert was asked to indicate which information should be provided and what the scientifically reasoning is behind this demand.

None of the comments formulated by the experts were sent to EFSA. It should be noted that all the comments received from the experts are considered in the evaluation of this dossier and in formulating the final advice of the Biosafety Advisory Council.

List of comments/questions received from the experts

PART I - GENERAL INFORMATION

Have evaluated this section and consider the information adequate: 2 experts

PART II - SCIENTIFIC INFORMATION

1. HAZARD IDENTIFICATION AND CHARACTERISATION

1.1. INFORMATION RELATING TO THE RECIPIENT OR (WHERE APPROPRIATE) PARENTAL PLANTS

Have evaluated this section and consider the information adequate: 4 experts

1.2. MOLECULAR CHARACTERISATION

1.2.1. Information relating to the genetic modification

Have evaluated this section and consider the information adequate: 4 experts

1.2.2. Information relating to the genetically modified plant

Have evaluated this section and consider the information adequate: 3 experts

Comment 1
Comment: p31; it is somewhat surprising to see that in the stack the PMI protein is approx. 4x higher (in forage) while 3x lower (in grain), as compared to single event.

Coordinator comment: It is not unusual that protein expression levels change after conventional crosses.

1.2.3. Additional information relating to the genetically modified plant required for the environmental safety aspects

Have evaluated this section and consider the information adequate: 4 experts

1.2.4. Conclusions of the molecular characterisation

Have evaluated this section and consider the information adequate: 3 experts

Comment 1
With regard to the molecular characterisation, the Expert is of the opinion that the information provided is sufficient and does not raise safety concerns, for the stacked event described in the application, as well as for the subcombinations that were not previously assessed.

1.3. COMPARATIVE ANALYSIS

1.3.1. Choice of the conventional counterpart and additional comparators

1.3.2. Experimental design and statistical analysis of data from field trials for comparative analysis

1.3.3. Selection of material and compounds for analysis

1.3.4. Comparative analysis of composition

1.3.5. Comparative analysis of agronomic and phenotypic characteristics

1.3.6. Effects of processing

1.3.7. Conclusion

1.4. TOXICOLOGY

1.4.1. Testing of newly expressed proteins

Have evaluated this section and consider the information adequate: 1 expert

1.4.2. Testing of new constituents other than proteins

Have evaluated this section and consider the information adequate: 1 expert

1.4.3. Information on natural food and feed constituents

Have evaluated this section and consider the information adequate: 1 expert

1.4.4. Testing of the whole genetically modified food or feed

Have evaluated this section and consider the information adequate: 1 expert

1.4.5. Conclusion of the toxicological assessment

Have evaluated this section and consider the information adequate: 1 expert

1.5. ALLERGENICITY

1.5.1. Assessment of allergenicity of the newly expressed protein

Have evaluated this section and consider the information adequate: 1 expert

1.5.2. Assessment of allergenicity of the whole genetically modified plant

Have evaluated this section and consider the information adequate: 1 expert

1.5.3. Conclusion of the allergenicity assessment

Have evaluated this section and consider the information adequate: 1 expert

1.6. NUTRITIONAL ASSESSMENT

1.6.1. Nutritional assessment of the genetically modified food

1.6.2. Nutritional assessment of the genetically modified feed

1.6.3. Conclusion of the nutritional assessment

2. EXPOSURE ASSESSMENT — ANTICIPATED INTAKE OR EXTENT OF USE

3. RISK CHARACTERISATION

4. POST-MARKET MONITORING ON THE GENETICALLY MODIFIED FOOD OR FEED

5. ENVIRONMENTAL RISK ASSESSMENT (ERA)

5.1. INTRODUCTION

5.2. GENERAL APPROACH OF THE ERA

5.3. SPECIFIC AREAS OF RISK

5.3.1. Persistence and invasiveness including plant-to-plant gene flow

5.3.2. Plant to micro-organisms gene transfer

5.3.3. Interactions of the GM plant with target organisms

5.3.4. Interactions of the GM plant with non-target organisms (NTOs)

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

5.3.6. Effects on biogeochemical processes

5.3.7. Effects on human and animal health

5.3.8. Overall risk evaluation and conclusions

6. POST-MARKET ENVIRONMENTAL MONITORING PLAN (PMEM)

6.1. INTERPLAY BETWEEN ENVIRONMENTAL RISK ASSESSMENT, RISK MANAGEMENT AND PMEM

6.2. CASE-SPECIFIC GM PLANT MONITORING (STRATEGY, METHOD AND ANALYSIS)

6.3. GENERAL SURVEILLANCE FOR UNANTICIPATED ADVERSE EFFECTS (STRATEGY, METHOD)

6.4. REPORTING THE RESULTS OF PMEM

7. ADDITIONAL INFORMATION RELATED TO THE SAFETY OF THE GENETICALLY MODIFIED FOOD OR FEED