Adviesraad voor Bioveiligheid
Conseil consultatif de Biosécurité

Advice of the Belgian Biosafety Advisory Council on application EFSA-GMO-NL-2020-170 (maize MON 95379) from Bayer under Regulation (EC) No. 1829/2003

2 February 2023
Ref. SC/1510/BAC/2023_0106

Context

Application EFSA-GMO-NL-2020-170 was submitted by Bayer for the authorisation for the marketing of genetically modified (GM) maize MON 95379 (Unique Identifier MON-95379-3) for food and feed uses, import and processing (excluding cultivation) within the European Union, within the framework of Regulation (EC) No. 1829/2003[1].

Maize MON 95379 contains the *cry1B.868* and *cry1Da_7* genes which are derived from genes from *Bacillus thuringiensis* (Bt) which are expressed to produce the Cry1B.868 and Cry1Da_7 proteins for resistance to certain lepidopteran pests.

The application was validated by EFSA on 9 April 2021 and a formal three-month consultation period of the Member States was started, lasting until 9 September 2021, 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, contacted experts to evaluate the dossier, chosen from the common list of experts drawn up by the BAC and the Service Biosafety and Biotechnology (SBB). Six experts answered positively to this request, and formulated a number of comments to the dossier. See Annex I for an overview of all the comments and the comments sent to EFSA on 2 July 2021.

The opinion of the EFSA Scientific Panel on GMOs was published on 15 November 2022 (EFSA Journal 2022;20(11):7588[2]) together with the responses from the EFSA GMO Panel to comments submitted by the Member States during the three-month consultation period. Those documents were forwarded to the experts on 09/01/2023, with an invitation to react if needed.

In delivering the present advice, the BAC considered in particular the comments formulated by the experts on application EFSA-GMO-NL-2020-170 and the opinion of EFSA.

[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://www.efsa.europa.eu/en/efsajournal/pub/7588

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Scientific evaluation

1. 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.

2. Assessment of food/feed safety and nutritional value

2.1. Assessment of compositional analysis

The Biosafety Advisory Council agrees with the GMO panel of EFSA that the compositional data of GM maize MON 95379, in comparison with its conventional counterpart, do not raise safety concerns.

2.2. Assessment of toxicity

The Biosafety Advisory Council agrees with the GMO panel of EFSA that the available data on the toxicity of GM maize MON 95379, in comparison with its conventional counterpart, does not raise safety concerns.

2.3. Assessment of allergenicity

The Biosafety Advisory Council agrees with the GMO panel of EFSA that the available data on the allergenicity of GM maize MON 95379, in comparison with its conventional counterpart, does not raise safety concerns.

2.4. 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 95379-derived food and feed are not expected to differ from those of conventional maize varieties.

3. Environmental risk assessment

Field observations indicate that maize grains can sometimes overwinter and germinate in certain regions of the EU (e.g. Palaudelmàs *et al*., 2009[3]; COGEM, 2011[4]; Pascher, 2016[5]). As a result, volunteer maize plants do sometimes occur in subsequent crops. There is also evidence of the rare occurrence of feral maize plants (e.g. Pascher, 2016; COGEM, 2018[6]). However, volunteer maize has been shown to grow weakly and is not considered an agricultural problem. The occurrence of feral maize plants has not resulted in the establishment of self-sustaining populations, mainly because maize is highly domesticated, has no weedy characteristics and is not tolerant to frost. Thus, the occurrence of volunteer and feral maize in the EU is currently limited and transient. In addition, maize has no sexual compatible

[3] Palaudelmàs M., *et al*., 2009. Effect of volunteers on maize gene flow. Transgenic Res.18(4):583-594. doi:10.1007/s11248-009-9250-7

[4] COGEM, 2011. Research report "Crop volunteers and climate change. Effects of future climate change on the occurrence of maize, sugar beet and potato volunteers in the Netherlands". https://cogem.net/en/publication/crop-volunteers-and-climate-change-effects-of-future-climate-change-on-the-occurrence-of-maize-sugar-beet-and-potato-volunteers-in-the-netherlands/

[5] Pascher K., 2016. Spread of volunteer and feral maize plants in Central Europe: recent data from Austria. Environ. Sci Eur.28(1):30. doi:10.1186/s12302-016-0098-1

[6] COGEM, 2018. Research report "Are teosinte and feral maize present in the Netherlands?". https://cogem.net/en/publication/are-teosinte-and-feral-maize-present-in-the-netherlands/

wild relative in the EU. Therefore, the Biosafety Advisory Council is of the opinion that it is unlikely that the accidental release of maize MON 95379 (i.e. during transport and/or processing) into the European environment[7] will lead to environmental harm.

4. Monitoring

With regard to monitoring, the Biosafety Advisory Council is of the opinion that the information provided is sufficient.

Conclusion

Based on the whole set of data on maize MON 95379 provided by the applicant, the scientific assessment of the dossier done by the Belgian experts, the opinion of EFSA, and the answers of the EFSA GMO panel to the questions raised by the Belgian experts, the Biosafety Advisory Council:

1) Agrees with the GMO panel of EFSA that the potential environmental release of maize MON 95379 is unlikely to pose any threat to the European environment;
2) Agrees with the GMO panel of EFSA that in the context of its proposed uses, maize MON 95379 is as safe as its conventional counterpart and the tested non-GM maize reference varieties with respect to potential effects on human and animal health and the environment;
3) The BAC wishes to additionally note that maize MON 95379 is not to be commercialised as a stand-alone product for food and feed uses, import and processing. Instead only stacks containing maize MON 95379 are the aimed commercial products. One can question the relevance of assessing such hypothetical products. The BAC is of the opinion that it would be good to discuss this with the European Commission and EFSA.

Dr. ir. Geert Angenon
President of the Belgian Biosafety Advisory Council

Annex : Outcome of the assessment of the application and comments sent to EFSA

[7] As the application doesn't imply cultivation of the GM crop in the EU, a full environmental assessment, as in the case of a cultivation dossier, is not warranted.

Annex : Outcome of the assessment of application EFSA-GMO-NL-2020-170 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) and feedback from the EFSA GMO Panel

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Experts: Eddy Decuypere (KUL), Jacques Dommes (ULg), Leo Fiems (ILVO), Peter Smet (Consultant), Frank Van Breusegem (UGent), Jan Van Doorsselaere (Vives)
SBB: Fanny Coppens

Application: **EFSA-GMO-NL-2020-170**

Applicant: **Bayer**

GMO: **Maize MON 95379**

Validation of dossier by EFSA: **9 April 2021**

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.

Comments sent to EFSA are highlighted in grey, with the answers from the GMO Panel from EFSA provided underneath.

List of comments/questions received from the experts

PART I - GENERAL COMMENTS

Comment 1
The authors clearly demonstrate that maize MON 95379 contains one T-DNA with two cry genes that are expressed. The construct is stably maintained during several generations.

Comment 2
Special caution is required with respect to the possible development of resistance of fall armyworm against the new Cry1 proteins in MON 95379 maize. These new Cry1 proteins may not be a risk for human and animal health.

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: 5 experts

1.2. MOLECULAR CHARACTERISATION

1.2.1. Information relating to the genetic modification

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

Comment 1
-The conventional counterpart (LH244 x HCL617) and the original transformation line (LH244) have both similar genetic backgrounds to Mon95379
-In 1.2.1.3., as for the function of the Cry-proteins for protection against insects, it is stated that the specific receptors are not present in mammals or humans, nor in most of the non-target insects: this last part of the sentence seems a bit vague; what do they mean by “most of non-target insects”?

Coordinator comment: It is true that this last part is a bit vague, and in case this would be a cultivation dossier that required a full environmental risk assessment here in Europe, then it would be important to have this specified in more detail. For this dossier it is not a ‘need-to-know’.

1.2.2. Information relating to the genetically modified plant

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

Comment 1
Minor comment. On p35, I think it’s more accurate to state (underlined): “The sporadic low-level detection of plasmid sequences such as OR-ori-pBR322 has previously been described (Zastrow-Hayes et al., 2015), and reported in Yang et al. (2013), and is most likely due to the presence of environmental bacteria in tissue samples used in the preparation of genomic DNA used for library construction.” To my knowledge, no evidence is provided that these two reads are due to a sample contamination.

Coordinator comment: I agree that a lack of evidence that the two read are due to a sample contamination, should prompt the applicant to be less conclusive in its conclusions about this.

Comment 2
The cry1B.868 & Cry1Da-7 give protection against lepidopteran pests. By proteolysis, the active insecticide domain sets free in 3 structural domains, respectively for binding to specific receptors, for oligomerization and for insertion into the plasma membrane of enterocytes and pore-formation, leading to loss of cell integrity: again, how specific is this process against some of the insect pests of maize, but not for other insects or more specifically, for other lepidoptera?

Coordinator comment: See comment above. Only in case of cultivation in Europe this information would be a need-to-know. The proposed import as food or feed is not likely to result in exposure of non-target lepidoptera in Europe.

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: 4 experts

1.3. COMPARATIVE ANALYSIS

1.3.1. Choice of the conventional counterpart and additional comparators

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

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

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

1.3.3. Selection of material and compounds for analysis

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

Comment 1
Why were trypsin inhibitor, furfural and inositol not tested?

Feedback from the EFSA GMO Panel: Forage and grain harvested from the field trials were analysed for 78 constituents (nine in forage and 69 in grain), including those recommended by OECD (OECD, 2002). The statistical analysis was not applied, among other constituents to furfural because its concentration in more than half of the samples were below the limit of quantification. Reference: OECD (Organisation for Economic Co-operation and Development), 2002. Consensus document on

compositional considerations for new varieties of maize (Zea mays): key food and feed nutrients, anti-nutrients and secondary plant metabolites. Series on the safety of novel foods and feeds, No. 6-ENV/JM/MONO(2002)25.

1.3.4. Comparative analysis of composition

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

1.3.5. Comparative analysis of agronomic and phenotypic characteristics

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

1.3.6. Effects of processing

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

1.3.7. Conclusion

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

1.4. TOXICOLOGY

1.4.1. Testing of newly expressed proteins

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

1.4.2. Testing of new constituents other than proteins

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

1.4.3. Information on natural food and feed constituents

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

1.4.4. Testing of the whole genetically modified food or feed

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

1.4.5. Conclusion of the toxicological assessment

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

Comment 1
The chance that the new proteins of MON 95379 maize (Cry1B.868 and Cry1Da_7) will pose serious risks for toxicity is rather negligible. Bt proteins have demonstrated its safety as a biocontrol agent over more than five decades (Palma et al., 2014).

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

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

1.6.2. Nutritional assessment of the genetically modified feed

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

1.6.3. Conclusion of the nutritional assessment

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

Comment 1
There is no reason to assume that the nutritional value of the feed and the food derived from MON 95379 maize is affected by the insertion of the Cry1B.868 and Cry1Da_7 proteins.

2. EXPOSURE ASSESSMENT — ANTICIPATED INTAKE OR EXTENT OF USE

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

3. RISK CHARACTERISATION

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

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

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

5. ENVIRONMENTAL RISK ASSESSMENT (ERA)

5.1. INTRODUCTION

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

5.2. GENERAL APPROACH OF THE ERA

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

5.3. SPECIFIC AREAS OF RISK

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

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

5.3.2. Plant to micro-organisms gene transfer

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

5.3.3. Interactions of the GM plant with target organisms

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

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

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

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

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

5.3.6. Effects on biogeochemical processes

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

5.3.7. Effects on human and animal health

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

5.3.8. Overall risk evaluation and conclusions

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

Comment 1
The applicant mentioned that resistance development by Spodoptera frugiperda against Bt proteins could be a potential concern (P.89 Main text of the Dossier). Cross-Resistance between Cry1 proteins in Spodoptera frugiperda may affect the sustainability of pyramided Bt maize varieties (Blanco et al., 2010; Bernardi et al., 2015). Furthermore, the migratory capacity of fall armyworm may play an important role in the spread of resistant alleles (Gutierrez-Moreno et al., 2020). The cultivation of MON 95379 maize in the EU is not intended. Nevertheless, the consciousness that the resistance against Cry1 proteins may be more than a local problem in the EU, but that it may become a global problem, can cause some concern. Experiments of Horikoshi et al. (2021) showed that Cry1B.868 and Cry1Da_7 proteins in MON 95379 maize protected maize against larval feeding by Spodoptera frugiperda. When Cry1Da_7 and Cry1B.868 proteins are pyramided together, as in MON 95379 maize, they may provide durability against Spodoptera frugiperda (Wang et al., 2019). So, *vigilance is required with regard to* the resistance of Spodoptera frugiperda against Cry1B.868 and Cry1Da_7 proteins.

Coordinator comment: This is a general comment about possible resistance development that will not affect the current risk assessment or imply that EFSA should request additional information. But the comment could be shared with EFSA as a general remark for information purposes.

Feedback from the EFSA GMO Panel: The scope of the present application does not include cultivation of maize MON 95379. Feral populations of genetically modified maize of this event could arise due to accidental spillage of seeds during import and processing, and through viable seeds present either in organic matter or in faeces of animals fed with maize of this event. However, measures are in place to minimize incidental spillage of maize, resulting in a very low probability of occurrence of feral maize MON 95379 plants in the European Union. Additionally, Spodoptera frugiperda is a European Union quarantine pest listed in Annex II Part A of Commission Implementing Regulation (EU) 2019/2072. Member States need to implement a set of strict emergency measures laid down in Commission Implementing Decision (EU) 2018/638 aimed at preventing the introduction and spread of this pest species. The GMO Panel considers that the absence of established populations of S. frugiperda in continental Europe combined with the expected very rare presence of feral plants of maize MON 95379 indicate that there is no risk of resistance development to the toxins Cry1B.868 and Cry1Da_7 expressed by maize MON 95379 in fall armyworm in the European Union. Therefore, there is no need to consider a risk management strategy.

6. POST-MARKET ENVIRONMENTAL MONITORING PLAN (PMEM)

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

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

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

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

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

Comment 1
With regard to the resistance of Spodoptera frugiperda against Cry1B.868 and Cry1Da_7 proteins, *vigilance is required; see 5.3.8.*

6.4. REPORTING THE RESULTS OF PMEM

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

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

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

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