Adviesraad voor Bioveiligheid
Conseil consultatif de Biosécurité

Advice of the Belgian Biosafety Advisory Council on application EFSA-GMO-NL-2020-171 (genetically modified maize DP4144 x MON 89034 x MON 87411 x DAS-40278-9) from Pioneer under Regulation (EC) No. 1829/2003

30 January 2023
Ref. SC/1510/BAC/2023_0102

Context

Application EFSA-GMO-NL-2020-171 was submitted by Pioneer for the marketing of genetically modified (GM) maize DP4144 x MON 89034 x MON 87411 x DAS-40278-9 (Unique Identifier DP-ØØ4114-3 x MON-89Ø34-3 x MON-87411-9 x DAS-4Ø278-9) for food and feed uses, import and processing (excluding cultivation) within the European Union, under the framework of Regulation (EC) No. 1829/2003[1].

The four-event stack, maize DP4144 x MON 89034 x MON 87411 x DAS-40278-9, was obtained by conventional crossing (no new genetic modification involved) of the corresponding single events:
- DP4144, expressing the *cry1F* gene for resistance to certain lepidopteran insect pests, the *cry34Ab1* and *cry35Ab1* genes for control of corn rootworm pests and the *pat* gene for tolerance to glufosinate herbicide;
- MON 89034, expressing the *cry1A.105* and *cry2Ab2* genes for resistance to certain lepidopteran insect pests;
- MON 87411, expressing the *dvSnf7* dsRNA and *cry3Bb1* gene for resistance to corn rootworm pests and the *cp4 epsps* gene for tolerance to glyphosate;
- DAS-40278-9, expressing the *aad-1* gene conferring tolerance to 2,4-D (2,4-dichlorophenoxyacetic acid) and AOPP (aryloxyphenoxypropionate)-based herbicides.

The application was validated by EFSA on 26 April 2021. A formal three-month consultation period of the Member States was started, lasting until 30 July 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 chosen from the common list of experts drawn up by the BAC and the Service Biosafety and Biotechnology (SBB) to evaluate the molecular data of the four-stack event. Two experts answered positively to this request, and formulated a number of comments to the dossier (see Annex I).

The opinion of the EFSA Scientific Panel on GMOs was published on 9 November 2022 (EFSA Journal 2022;20(11):7619[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 14 November 2022, with an invitation 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.2022.7619

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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-2020-171;
- The opinion of EFSA;
- The advices already adopted by the BAC on the single events and lower-order stacks containing these single events. The conclusions of the BAC for the most recent applications for the single events and the lower-order stacks were as follows:

Event(s)	Application number	BAC advice	Conclusions
DP4144	EFSA-GMO-NL-2014-123	BAC/2018/0463	Unlikely to pose risks to human and animal health, and the European environment.
MON 89034	EFSA-GMO-RX-015	BAC/2019/1085	Unlikely to pose risks to human and animal health, and the European environment.
MON 87411	EFSA-GMO-2015-124	BAC/2018/0704	Unlikely to pose risks to human and animal health, and the European environment.
DAS-40278-9	EFSA-GMO-NL-2010-89	BAC/2017/0066	No conclusion about the food and feed safety of maize DAS-40278-9. No risk identified for the European environment.
MON 89034 x DAS-40278-9	EFSA-GMO-NL-2013-112 EFSA-GMO-NL-2013-113	BAC/2019/0248 BAC/2019/0101	Unlikely to pose risks to human and animal health, and the European environment.
MON 89034 x MON 87411	EFSA-GMO-NL-2013-139 EFSA-GMO-NL-2013-144	BAC/2021/0069 BAC/2019/1083	Unlikely to pose risks to human and animal health, and the European environment.

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

Taking into account the previous assessment of the single events and the additional data on compositional analysis provided by the applicant for the four-stacked event, the Biosafety Advisory Council agrees with the GMO panel of EFSA that the compositional data of maize DP4144 x MON 89034 x MON 87411 x DAS-40278-9 in comparison with its conventional counterpart, do not raise safety concerns.

2.2. Assessment of toxicity

The Biosafety Advisory Council has evaluated the safety of the newly produced Cry1A.105, Cry2Ab2, Cry1F, Cry3Bb1, Cry34Ab1, Cry35Ab1, PAT, CP4 EPSPS and AAD-1 proteins 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 presence of the newly expressed proteins in the stacked event does not raise toxicological concerns.

2.3. Assessment of allergenicity

The Biosafety Advisory Council has evaluated the safety of the newly produced Cry1A.105, Cry2Ab2, Cry1F, Cry3Bb1, Cry34Ab1, Cry35Ab1, PAT, CP4 EPSPS and AAD-1 proteins 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 presence of the newly expressed proteins in the stacked event does not raise concerns regarding allergenicity.

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 DP4144 x MON 89034 x MON 87411 x DAS-40278-9-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 wild relative in the EU. Therefore, the Biosafety Advisory Council is of the opinion that it is unlikely that the accidental release of maize DP4144 x MON 89034 x MON 87411 x DAS-40278-9 (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.

[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

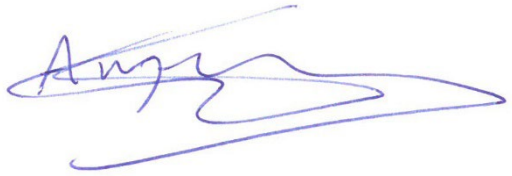
[6] COGEM, 2018. Research report "Are teosinte and feral maize present in the Netherlands?". https://cogem.net/en/publication/are-teosinte-and-feral-maize-present-in-the-netherlands/

[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.

Conclusion

Based on the whole set of data on maize DP4144 x MON 89034 x MON 87411 x DAS-40278-9 provided by the applicant, the scientific assessment of the dossier done by the Belgian experts, the opinion of EFSA and the advices already adopted by the BAC on the single and lower-order stacked events, the Biosafety Advisory Council:

1) Agrees with the GMO panel of EFSA that there is no reason to expect interactions between the newly produced proteins that could impact on the food or feed safety;
2) Agrees with the GMO panel of EFSA that in the context of its proposed uses maize DP4144 x MON 89034 x MON 87411 x DAS-40278-9 is unlikely to pose any risk to human and animal health;
3) Agrees with the GMO panel of EFSA that the spillage of maize DP4144 x MON 89034 x MON 87411 x DAS-40278-9 is unlikely to pose any threat to the European environment;



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

Annex : Outcome of the assessment of the application

Annex : Outcome of the assessment of application EFSA/GMO/NL/2020/171 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)

Coordinator: Lieve Gheysen (Ugent)
Experts: Frank Van Breusegem (VIB-UGent) en Jan Van Doorsselaere (VIVES)
SBB: Adinda De Schrijver

Application: **EFSA/GMO/NL/2020/171**
Applicant: **Pioneer Hi-Bred International, Inc.**
GMO: **maize DP4114 x MON89034 x MON87411 x DAS-40278-9**
Validated by EFSA: **26 April 2021**

The scope of the application is:
(a) GM food
☒ Food containing or consisting of GM plants
☒ Food produced from GM plants or containing ingredients produced from GM plants
(b) GM feed
☒ Feed containing or consisting of GM plants
☒ Feed produced from GM plants
(c) GM plants for food or feed use
☒ Products other than food and feed containing of consisting of GM plants with the exception of cultivation
☐ Seeds and plant propagating material for cultivation in the EU

As this application concerns a stacked event, and all the single events and lower order stacks have previously received a positive advice from the Council, the Biosafety Council decided to evaluate only the specific risk assessment aspects linked to the stacked as mentioned in the Commission Implementing Regulation (EU) No 503/2013, i.e. stability of the traits, expression of the new genes, and interactions between the newly expressed traits.

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.

EFSA will be informed that we do not have any comments and that we consider all the necessary information is present to conduct a robust risk assessment. 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 II - SCIENTIFIC INFORMATION

1. HAZARD IDENTIFICATION AND CHARACTERISATION

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

No feedback provided

1.2. MOLECULAR CHARACTERISATION

1.2.1. Information relating to the genetic modification

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

1.2.2. Information relating to the genetically modified plant

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

1.2.3. Conclusions of the molecular characterisation

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

OTHER COMMENTS

Comment:
The combination of the events in the stacks is stable and the expression of the events is not different from the individual events.