Adviesraad voor Bioveiligheid
Conseil consultatif de Biosécurité

Advice of the Belgian Biosafety Advisory Council on application EFSA-GMO-NL-2016-128 (genetically modified soybean MON 87751 x MON 87701 x MON 87708 x MON 89788) from Monsanto under Regulation (EC) No. 1829/2003

10 December 2019
Ref. SC/1510/BAC/2019_1082

Context

Application EFSA-GMO-NL-2016-128 was submitted by Monsanto for the marketing of genetically modified (GM) soybean MON 87751 x MON 87701 x MON 87708 x MON 89788 (Unique Identifier MON-87751-7 x MON-88701-3 x MON-877Ø8-9 x MON-89788-1), 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 soybean MON 87751 x MON 87701 x MON 87708 x MON 89788 was obtained by conventional crossing (no new genetic modification involved) of the corresponding single events:
- MON 87751, expressing the Cry1A.105 and Cry2Ab2 proteins that confer resistance to certain lepidopteran insect pests;
- MON 87701, expressing the Cry1Ac protein that confers resistance to certain lepidopteran insect pests;
- MON 87708, expressing the DMO protein that confers tolerance to herbicide products containing dicamba;
- MON 89788, expressing the CP4 EPSPS protein that confers tolerance to herbicide products containing glyphosate;

The application was validated by EFSA on 22 August 2016. A formal three-month consultation period of the Member States was started, lasting from 25 June 2018 until 24 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 and food/feed aspects of the dossier, chosen from the common list of experts drawn up by the BAC and the Service Biosafety and Biotechnology (SBB). Three experts answered positively to this request and analysed the dossier. None of their comments were forwarded to EFSA. See Annex I for an overview and the general comment that was sent to EFSA.

The opinion of the EFSA Scientific Panel on GMOs was published on 11 November 2019 (EFSA Journal 2019;17(11):5847[2]), together with the responses from the EFSA GMO Panel to comments submitted by the Member States during the three-month consultation period. On 14 November 2019 these two

[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.2019.5847

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documents were forwarded to the Belgian experts. They were invited to give comments and to react if needed.

In delivering the present advice the BAC considered in particular the following information:
- The comments formulated by the experts on application EFSA-GMO-NL-2016-128;
- The opinion of EFSA;
- The advices already adopted by the BAC on the single events. The conclusions of the BAC for the most recent applications for the single events, and two of the lower-order stacks, were as follows:

Event	Application number	BAC advice	Conclusions
MON 87751	EFSA-GMO-NL-2014-121	BAC/2018/0702 (11/09/2018)	Unlikely to pose any risk to human and animal health and the European environment.
MON 87701	EFSA-GMO-BE-2010-79	BAC/2011/0898 (23/09/2011)	Negative advice regarding the health safety of the event. Unlikely to pose any risk to the European environment
MON 87708	EFSA-GMO-NL-2011-93	BAC/201114/0325 (21/05/2014)	No conclusion on the food safety of the event. No risk identified for the European environment.
MON 89788	EFSA-GMO-RX-011	BAC/2018/1090 (11/12/2018)	Unlikely to pose any risk to human and animal health and the environment.
MON 87708 x MON 89788	EFSA-GMO-NL-2012-108	BAC/2015/0811 (08/12/2015)	No conclusion on the food safety of the stacked event. No risk identified for the European environment.
MON 87701 x MON 89788	EFSA-GMO-NL-2009-73	BAC/2012/0444 (27/04/2012)	No advice regarding the health safety of the event. Unlikely to pose any risk to the European environment

All GM soybean 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 soybean MON 87751 x MON 87701 x MON 87708 x MON 89788 (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 soybean MON 87751 x MON 87701 x MON 87708 x MON 89788, when compared with the composition of its conventional counterpart, does not raise safety concerns.

3.2. Assessment of toxicity

The Biosafety Advisory Council has evaluated the safety of the newly expressed Cry1A.105, Cry2Ab2, Cry1Ac and CP4 EPSPS proteins in the context of previous applications, and no safety concerns were identified. In its advice on the single event MON 87708, expressing the DMO protein, the Council had

[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.

expressed some concerns regarding the results of the sub-chronic 90-day rat feeding study with the whole GM soybean: some significant differences in clinical pathology parameters were observed between male rats fed diets containing soybean MON 87708 and control animals. The Council concluded that without further investigation it was not convinced that these differences were incidental. Since no new information has been provided in the current application in relation with the toxicological assessment of the whole food derived from GM soybean MON 87708 or MON 87751 x MON 87701 x MON 87708 x MON 89788, the concerns expressed above are still valid. As a consequence, the Biosafety Advisory Council is unable to determine whether GM soybean MON 87751 x MON 87701 x MON 87708 x MON 89788 is as safe as conventional soybean from a toxicological perspective.

3.3. Assessment of allergenicity

The Biosafety Advisory Council has evaluated the safety of the newly expressed DMO, Cry1A.105, Cry2Ab2, Cry1Ac and CP4 EPSPS proteins in the context of previous applications, and no allergenicity 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 soybean MON 87751 x MON 87701 x MON 87708 x MON 89788 -derived food and feed are not expected to differ from those of conventional soybean varieties.

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 soybean MON 87751 x MON 87701 x MON 87708 x MON 89788 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 BAC, and the advices already adopted by the BAC on the four single events and two lower-order stacks, the Biosafety Advisory Council is of the opinion that as a result of remaining uncertainties concerning the toxicity of the whole food derived from the GM plant, it is not possible to draw a final conclusion on the food safety of soybean MON 87751 x MON 87701 x MON 87708 x MON 89788.

Given the scope of the application of the GM soybean (no cultivation in the EU) and the fact that the establishment of volunteer plants would be unlikely (soybean does not survive without human assistance, nor as a weed in Europe), the potential environmental release of soybean MON 87751 x MON 87701 x MON 87708 x MON 89788 is unlikely to pose any threat to the European environment.

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

Annex I: Outcome of the assessment of application EFSA-GMO-NL-2016-128 and Comments submitted to EFSA on mandate of the Biosafety Council (ref. BAC_2018_0708)

Adviesraad voor Bioveiligheid
Conseil consultatif de Biosécurité

Outcome of the assessment of application EFSA/GMO/NL/2016/128 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)

17 September 2018
Ref. SC/1510/BAC/2018_0708

Mandate for the Group of Experts: Mandate of the Biosafety Advisory Council (BAC) of 29 August 2018.
Coordinator: Geert Angenon
Experts: André Huyghebaert (UGent), Frank Van Breusegem (UGent), Jan Van Doorsselaere (Vives)
SBB: Fanny Coppens

Application: **EFSA/GMO/NL/2016/128**
Applicant: **Monsanto**
GMO: **Soybean MON 87751 x MON 87701 x MON 87708 x MON 89788**
Acknowledgement of receipt by EFSA: **22 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)

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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 indicated in grey. 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.

The following comment from the coordinator/SBB was sent with regards to the toxicological assessment:
The Belgian Biosafety Advisory Council, in its evaluation of the single event MON87708 in 2014, had noted some significant differences in clinical pathology parameters between male rats fed diets containing soybean MON87708 and control animals as a result of the 90-day feeding study. Therefore, in the absence of a sound explanation of these differences, the Council could not conclude on the safety of this single event.
In order to conclude on the safety of the present stacked event soybean MON 87751 x MON 87701 x MON 87708 x MON 89788, the Biosafety Advisory Council asks the applicant to provide any information or evidence that would dispel the concerns arising from the toxicological evaluation of single event MON87708. This could be done for instance by providing the results of a new 90-day feeding study with the single event MON87708, or the results of a 90-day feeding study with the stacked event soybean MON 87751 x MON 87701 x MON 87708 x MON 89788.

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

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

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

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

1.2.4. Conclusions of the molecular characterisation

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

1.3. COMPARATIVE ANALYSIS

1.3.1. Choice of the conventional counterpart and additional comparators

Comment 1
As it is very often the case, the OECD guidelines were followed. Although not included in the guidelines, allergens are also studied.
Due to the growing importance of allergens in human food, this approach is fully justified.
An addition to future guidelines with respect to allergens is to be considered.

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: 1 expert

1.3.3. Selection of material and compounds for analysis

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

1.3.4. Comparative analysis of composition

Comment 1
I agree with the conclusions for the compounds studied: proximate, amino acids, fatty acids, minerals, vitamins, anti-nutrients, isoflavones and allergens (no change in endogenous allergenicity).

As in previous applications, out dated concepts in human nutrition, are applied such as carbohydrates by calculation, fiber in tems of AFD and NFD.

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

Comment 1
The processing steps are described in detail. No particular effect are expected during processing.
I fully agree with the conclusion.

1.3.7. Conclusion

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

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