Adviesraad voor Bioveiligheid
Conseil consultatif de Biosécurité

Advice of the Belgian Biosafety Advisory Council on application EFSA-GMO-NL-2020-169 (oilseed rape MON 94100) from Monsanto under Regulation (EC) No. 1829/2003

18 October 2022
Ref. SC/1510/BAC/2022_1179

Context

Application EFSA-GMO-NL-2020-169 was submitted by Monsanto for marketing authorisation of genetically modified (GM) oilseed rape MON 94100 (Unique Identifier MON-941ØØ-2) for food and feed uses, import and processing (excluding cultivation) within the European Union, within the framework of Regulation (EC) No. 1829/2003[1].

Oilseed rape MON 94100 contains a single insert consisting of the *dmo* gene cassette, conferring tolerance to the herbicide dicamba. MON 94100 is going to be used to produce stacked events via conventional breeding and will not be commercialized as a stand-alone product. The assessment and opinion by the Belgian Biosafety Advisory Council (BAC) presented below are therefore for a hypothetical product.

The application was validated by EFSA on 25 March 2021 and a formal three-month consultation period of the Member States was started, lasting until 28 June 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 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). Five 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 22 June 2021.

The opinion of the EFSA Scientific Panel on GMOs was published on 22 July 2022 (EFSA Journal 2022;20(7):7411[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 1 August 2022, 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-2020-169 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://doi.org/10.2903/j.efsa.2022.7411

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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 oilseed rape MON 94100, 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 expressed DMO (dicamba mono-oxygenase) protein variants, (DMO and DMO+27 protein) in the context of a previous application (EFSA/GMO/NL/2011/93) expressing soybean MON 88708-derived DMO protein variants with respect to their toxicity. Taking into account the information on the possible toxicity of the DMO protein considered in the current application, which includes a 90-day rodent feeding study, the Council is of the opinion that the studies with the DMO protein do not point to a safety issue.

Further, the Biosafety Advisory Council agrees with the GMO panel of EFSA that the available data on the toxicity of GM oilseed rape MON 94100, in comparison with its conventional counterpart, does not raise safety concerns.

2.3. Assessment of allergenicity

The Biosafety Advisory Council has evaluated the safety of the newly expressed DMO protein variants, (DMO and DMO+27 protein) in the context of a previous application (EFSA/GMO/NL/2011/93) expressing soybean MON 88708-derived DMO protein variants and no concerns were identified with respect to their allergenicity. Since no new information on the potential allergenicity of this protein has become available, the Council is of the opinion that its previous conclusion remains valid.

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 oilseed rape MON 94100-derived food and feed are not expected to differ from those of conventional maize varieties.

3. Environmental risk assessment

Spilled oilseed rape seeds have the ability to survive in the soil for several years and to establish populations outside agricultural areas, mainly in semi-natural managed habitats (e.g. roadside, mowed areas). In undisturbed natural habitats, feral populations are transient and decline over a few years' time (e.g. Busi and Powles, 2016[3] and references therein). Oilseed rape does not have the capacity to outcompete plants in such habitats.
The herbicide tolerance trait of MON 94100 could provide a selective advantage when these oilseed rape plants are exposed to herbicides that contain dicamba as the sole active ingredient. In such case, the abundance of herbicide-tolerant plants in managed environments treated with dicamba may increase locally. However, this fitness advantage will not allow oilseed rape MON 94100 to overcome the biological and abiotic factors limiting the plant's persistence and invasiveness in time.

[3] Busi R and Powles SB, 2016. Transgenic glyphosate-resistant canola (*Brassica napus*) can persist outside agricultural fields in Australia. Agriculture, Ecosystems and Environment, 220, 28–34.

The main applications of dicamba, a broadleaf herbicide, is in crop – especially maize – and on grassland, which is also the focus of the authorisations of dicamba. In Belgium the use along roadsides, railways and alike, is not permitted.
The Biosafety Advisory Council is of the opinion that oilseed rape MON 94100 will be equivalent to conventional oilseed rape varieties in their ability to survive and establish feral populations under European environmental conditions in case of accidental release into the environment of viable oilseed rape MON 94100 seeds. It is therefore unlikely that the accidental release of oilseed rape MON 94100 (i.e. during transport and/or processing) into the European environment will lead to environmental harm.

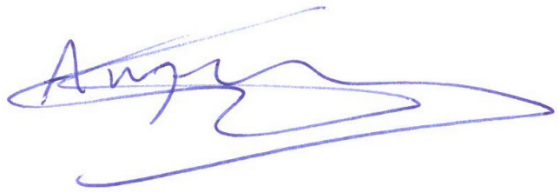
4. Monitoring

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 oilseed rape MON 94100 provided by the applicant, the scientific assessment of the dossier done by the Belgian experts, the opinion and complementing statement 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 oilseed rape MON 94100 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, oilseed rape MON 94100 is unlikely to pose any risk to human and animal health;
3) The BAC wishes to additionally note that oilseed rape MON94100 is not to be commercialised as a stand-alone product for food and feed uses, import and processing. Instead only stacks containing MON 94100 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 EFSA-GMO-NL-2020-169 and comments sent to EFSA.

Minority declaration of P. Baret

On point 3 of this advice (Environmental risk assessment), the potential introgression of herbicide tolerance to non-transgenic populations of rapeseed is acknowledged. Considering the wide distribution of rapeseed in semi-natural and cultivated habitats, a science-based assessment of this introgression on biodiversity should have been made. In absence of a comprehensive assessment of the potential consequences of introgression of transgenic trait in these populations, a risk for biodiversity cannot be excluded and it is impossible to conclude that there is no environmental risk. My minority advice is in line with the non-authorization of rapeseed transgenic plants in Norway ((Myhr, Grønsberg, and Okoli 2020).

Myhr, Anne Ingeborg, Idun Merete Grønsberg, and Arinze Stanley Okoli. 2020. "Norway—The Norwegian Gene Technology Act: Presenting Case Studies to Illustrate the Act's Advances in Protecting Biodiversity." In *GMOs*, 641–49. Springer.

Annex: Outcome of the assessment of application EFSA/GMO/NL/2020/169 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 EFSA GMO Panel

Coordinator: René Custers (VIB)
Experts: Eddy Decuypere (KULeuven), Jacques Dommes (ULiege), André Huyghebaert (UGent), Peter Smet (Consultant), Jan Van Doorsselaere (VIVES)
SBB: Adinda De Schrijver

Application: EFSA/GMO/NL/2020/169
Applicant: Bayer CropScience LP
GMO: oilseed rape MON 94100
Validation of dossier by EFSA: 25 March 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.

The comments indicated in grey 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: 5 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: 3 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: 1 expert

Comment:
The DMO enzyme is from *Stentrophomonas maltophilia* which occurs ubiquitous in the environment, also in water, milk and milk products; the enzymes catalyses demethylation of dicamba-herbicide to dichlorosalicyclic acid & formaldehyde which are safe (FAO-WHO); working mechanisms are well explained and no further comments are needed.

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

1.3. COMPARATIVE ANALYSIS

1.3.1. Choice of the conventional counterpart and additional comparators

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

Comment:
This applies for oilseed rape MON 94100, the conventional counterpart and the commercial reference hybrids.

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: 1 expert

Comment:
The compositional assessment was performed for oilseed rape MON 94100, the conventional counterpart and 13 reference hybrids. Grain was analyzed for nutrients and anti-nutrients. The comparison included oilseed rape MON 94100, treated with herbicide and non treated.

1.3.4. Comparative analysis of composition

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

Comment 1:
In this section the info as such makes it difficult to evaluate, but refereeing to Taylor et al (2020), and after evaluation of the Amended report for MSL0030457, Taylor, Scaife & Meng (2020a) "compositional analyses of Canola seed harvested from Monsanto 94100 grown at 8 field sites in USA and Canada during the 2018 season", Monsanto Co, TRR0000591, I can agree with the conclusions of equivalence between the GMO and reference.

Comment 2:
The applicant concludes that the differences observed have no compositional relevance from a food or feed perspective. In particular the differences observed are small in comparison with the wide range of values, observed for the compositional counterpart and other commercial oilseeds. He concludes that oilseed rape MON 94100 is compositionally similar to the conventional counterpart. I agree with this overall conclusion.

Nutrients were selected according to the OECD document (2011). The study includes proximate, amino,acids, fatty acids, carbohydrates, fiber, ash, minerals and vitamins. Assessment of anti-nutrients includes glucosinolates, phytic acid, sinapine and tannins.

Results of the statistical analysis are summarized in 14 tables. Methods used for analysis are well established.

- Proximates: no problem with moisture, fats, ash and proteins. With respect to fiber and carbohydrates, methods used are suitable for feed analysis, but not for food. This is not a problem as the major use of oilseed rape cake is animal feed. In the framework of protein transition in human nutrition there is interest to apply oilseed rape proteins for humans as well.
- Amino acids: the whole range of essential and non essential amino acids are studied.
- Fatty acids: no comment on the ccomponents studied
- Minerals: calcium, phosphorous
- Vitamins: tocopherols: alpha, gamma and delta, expressed as alpha-tocopherol, vitamin K1
- Phytic acid
- Glucosinolates
- Sinapine
- Tannins:
  no further commenst taking into account the main use of oilseed rape: oil as a human food and the oilseed cake as an animal feed.

Results were statistically evaluated. In case significant differences were observed between oilseed rape MON 94100 and the counterpart, the relevance of the differences was assessed by evaluating the magnitude of the difference and the range of individual replicate values.

As a result the applicant concludes that no significant differences are observed for most constituents. In case of a significant difference is observed it is concluded that this difference is of no compositional relevance for a food or feed perspective.

As a general conclusion the applicant states that oilseed rape MON 94100 is compositional similar to conventional oilseed rape. I agree with this overall conclusion.

I have the following comment. The whole study of equivalence is based on the OECD guidelines. The main objective of this document is to give guidance for the compositional study of new varieties. It takes into account the major use of the oil as a human food and the cake as an animal feed. There are however studies for the application of the protein fraction as a human food. This potential future use, in the framework of the protein transition is not considered in the application.

SBB and coordinator comment: We will forward this comment to the OECD so that in future revisions of the consensus documents, the application of protein fraction is taken into account.

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: 1 expert

Comment:
The applicant concludes that the effect of processing of oilseed rape MON 94100 is not expected to be different from conventional oilseed rape. I agree with this 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: 2 experts

1.4.2. Testing of new constituents other than proteins

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

Comment:
Not relevant

1.4.3. Information on natural food and feed constituents

Comment:

Not relevant

1.4.4. Testing of the whole genetically modified food or feed

Comment 1:

Not needed but nevertheless done and reported in TRR0000324 a-d

Comment 2:

Liver weight is significantly increased in both the low and high dose group and falls outside the range of the historical control data. Microscopic examination of the liver mentions an infiltrate in several test cases in both control and high dose group, but not in the low dose group. Apparently, there is no correlation between the two findings.

Reexamination of the 90-day rat study in dossiers 140 and 161 did not reveal a similar effect on liver weight. No significant increase in liver weight between the control group and the high dose group was observed.

SBB and coordinator comment: The expert was asked if he can agree with the following: "*Although these mean values were above the Historical Control Data range for group mean, these differences were also not considered test substance-related because the control group value was also outside of the range, the observed differences were small (≤ 6%) compared to the control group, there was not a dose response, and there were no correlating microscopic findings"* ? The expert replied that on the basis of the data provided in the dossier, no adverse effect is expected, but noted that the fact that the data observed fall outside the historical range, is unusual. On the basis of the feedback on 1.4.4 received, the following was forwarded to EFSA:
We agree with the conclusion that the composition of GM soybean MON 94100, in comparison with the non-GM reference varieties, is equivalent. Hence, as no clear hypothesis for further testing can be formulated, we consider that testing of the whole food/feed (i.e. 90-day feeding trial) does not bring any added value to this particular dossier. We also agree with the conclusion that the 90-day study does not point to a safety issue. However, we want to note that for the liver weight (relative to the body weight) the data reported for the control group (and the test groups) fall outside of the range of the historical control data (see Table 24 of TRR0000324, 2020a), which is an unusual observation.

Feedback from the EFSA GMO Panel: The GMO Panel assessed the design and results of the 90-day toxicity study in rodents with the whole GM food and feed and was able to conclude that no treatment related adverse effects were observed in rats after feeding diets containing oilseed rape MON 94100 meal at 5 % or 15% of inclusion level, for 90 days.

1.4.5. Conclusion of the toxicological assessment

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

1.5. ALLERGENICITY

No feedback received

1.6. NUTRITIONAL ASSESSMENT

No feedback received

2. EXPOSURE ASSESSMENT — ANTICIPATED INTAKE OR EXTENT OF USE

No feedback received

3. RISK CHARACTERISATION

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

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

No feedback received

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: 1 expert

5.3.2. Plant to micro-organisms gene transfer

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

5.3.3. Interactions of the GM plant with target organisms

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

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

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

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: 1 expert

5.3.8. Overall risk evaluation and conclusions

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

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)

Comment:

For monitoring any unanticipated adverse effects, the authorization holder will maintain a website dedicated to operators. This website will be hosted on the EuropaBio website. However the link to the monitoring website does not work (Error 404, “the page you are looking for does not exist”). It is therefore not possible to check which informations and instructions will be given to the operators, nor how they will report on possible adverse effects.

Feedback from the EFSA GMO Panel: The GMO panel thanks Belgium for the comment. When trying the link it opened the webpage of EuropaBio. Therefore, the problem that is reported seems to be related to the browser or internet settings.

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

Comment:

See comment on section 6.2. It is not possible to evaluate correctly this point without knowing the content of the website that is an important tool for the monitoring.

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

No feedback received