Adviesraad voor Bioveiligheid
Conseil consultatif de Biosécurité

Advice of the Belgian Biosafety Advisory Council on application EFSA-GMO-RX-002 (oilseed rape GT73) from Monsanto under Regulation (EC) No. 1829/2003

30 September 2020
Ref. SC/1510/BAC/2020_0869

Context

Application EFSA-GMO-RX-002 was submitted by Monsanto for the renewal of authorisation for the marketing of genetically modified (GM) oilseed rape GT73 for feed containing or consisting of GM oilseed rape GT73, and products other than food and feed containing or consisting of it, excluding cultivation within the European Union within the framework of Regulation (EC) No. 1829/2003[1].

Oilseed rape GT73 expresses the CP4 EPSPS and GOXv247 proteins which confer tolerance to glyphosate herbicides.
The placing on the market of oilseed rape GT73 for food containing or consisting of genetically modified oilseed rape GT73, or food and feed produced from that genetically modified organism, is currently authorised by Commission Implementing Decision 2015/701/EU of 24 April 2015. Feed and other products containing or consisting of GT73 oilseed rape with the exception of cultivation are currently authorised by Commission Decision 2005/635/EC of 31 August 2005, following a positive opinion of EFSA (EFSA Journal 2004; 29, 1-19)[2] published on 1 March 2004 following notification C/NL/98/11.

The renewal application was validated by EFSA on 15 December 2016 and a formal three-month consultation period of the Member States was started, lasting from 9 January 2017 until 10 April 2017, 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). Eight 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 10/04/2017.

The opinion of the EFSA Scientific Panel on GMOs was published on 29 July 2020 (EFSA Journal 2020;18(7):6199)[3], together with the responses from the EFSA GMO Panel to comments submitted by the Member States during the three-month consultation period.

The comments formulated by the experts on the renewal application, together with the answers of the EFSA GMO Panel and the assessment of the application made by EFSA, as well as the previous advice of the BAC on oilseed rape GT73 (BAC_2010_0158)[4] form the basis of the advice of the Biosafety Advisory Council on application EFSA-GMO-RX-002 given below.

[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] http://www.efsa.europa.eu/en/efsajournal/pub/29
[3] https://www.efsa.europa.eu/en/efsajournal/pub/5347
[4] http://www.bio-council.be/Advices/BAC_2010_0158.pdf

Biosafety Advisory Council - Secretariat • Service Biosafety and Biotechnology (SBB)
Sciensano • Rue Juliette Wytsmanstraat 14 • B-1050 Brussels • Belgium
T + 32 2 642 52 93 • bac@sciensano.be • www.bio-council.be

Scientific evaluation

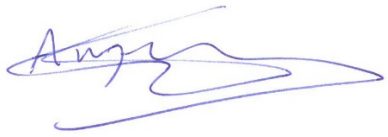
The data for application EFSA-GMO-RX-002 provided by the applicant at the time of submission included the annual post-market environmental monitoring (PMEM) reports covering the years of import, several systematic literature searches covering the complete duration of the event's authorisation, an updated bioinformatic package including an analysis of the insert and flanking sequences, an analysis of the potential similarity to allergens and toxins of the newly expressed proteins and of all possible open reading frames (ORFs) within the insert and spanning the junction sites, and an analysis of possible horizontal gene transfer and reports of additional studies performed by the applicant over the course of the authorisation period.

The Belgian experts and the members of the BAC raised questions on the bio-informatics analysis performed on the sequences flanking the insert. These questions were addressed by the applicant by providing additional information to EFSA. This additional information provided reassurance that no endogenous genes were interrupted and that all predicted ORFs spanning the insert and flanking sequences have no similarities with known toxins or allergens. The BAC is of the opinion that no information elements in the renewal application EFSA-GMO-RX-002 raise a safety concern for human or animal health or the environment.

Conclusion

Based on the whole set of data on oilseed rape GT73 provided by the applicant, the scientific assessment of the dossier done by the Belgian experts, the opinion of EFSA, and the previous advice of the BAC on oilseed rape GT73, the Biosafety Advisory Council is of the opinion that in the context of its proposed uses, oilseed rape GT73 is unlikely to pose any risk to human and animal health.

The Biosafety Advisory Council did not identify any risk that the import and processing of this GM oilseed rape could pose to the European environment.



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

Annex I: Compilation of comments of experts in charge of evaluating the application EFSA/GMO/RX-002 (ref. BAC_2017_0155)

Bioveiligheidsraad
Conseil de Biosécurité

10/04/2017

Secretariaat
Secrétariat

O./ref.: WIV-ISP/41/BAC_2017_0155
Email. : bac@wiv-isp.be

Compilation of comments of experts in charge of evaluating the application EFSA/GMO/RX-002
and
Comments submitted on the EFSAnet on mandate of the Biosafety Council

Mandate for the Group of Experts: Mandate of the Biosafety Advisory Council (BAC) of 31 January 2017.
Coordinator: Dr René Custers
Experts: Eddy Decuypere (KUL), Patrick du Jardin (ULg), Leo Fiems (ILVO), André Huyghebaert (UGent), Peter Smet (Consultant), Frank Van Breusegem (UGent), Jan Van Doorsselaere (KATO) Hadewijch Vanhooren (KUL)
SBB: Didier Breyer, Fanny Coppens, Katia Pauwels.

♦ INTRODUCTION

Dossier **EFSA/GMO/RX-002** concerns an application for renewal submitted by the company **Monsanto** for authorisation to place on the market genetically modified **oilseed rape GT73** in the European Union, according to Regulation (EC) No 1829/2003 on genetically modified food and feed. The application has been officially acknowledged by EFSA on 9 January 2017.

The scope of the application is:
☒ 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)

Depending on their expertise, the experts were asked to evaluate the renewal submission, which should contain (1) a copy of the authorisation for placing the food/feed on the market, (2) a report on the results of the monitoring, if so specified in the authorisation (3) any other new information, which has become available, with regard to the evaluation of the safety of the food/feed and the risks of the food/feed to humans, animals or the environment, (4) where appropriate, a proposal for amending or complementing the conditions of the original authorisation, inter alia the conditions concerning future monitoring. Those aspects were evaluated with regards to their molecular, environmental, allergenicity, toxicity and/or food and feed aspects. If information was lacking, the expert was asked to

indicate which information should be provided and what the scientifically reasoning is behind this demand.

The comments are structured as in the "Guidance for renewal applications of genetically modified food and feed authorised under Regulation (EC) 1829/2003" (EFSA Journal 2015;13(6):4129). Items are left blank when no comments have been received either because the expert(s) focused on other related aspects, or because for this dossier the panel of experts who accepted to evaluate the dossier didn't have the needed expertise to review this part of the dossier.
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. Comments placed on the EFSAnet are indicated in grey.

List of comments/questions received from the experts

A. GENERAL COMMENTS

Comment 1
No comments.

Comment 2
The risk for human and animal health and the environment of using oilseed rape GT73 is considered negligible, the increased use of glyphosate-tolerant oilseed rape GT73 may have an indirect effect on human and animal health and the environment through the presence of residues. Proper cultivation of oilseed rape GT73 and application of glyphosate-based herbicides is of utmost importance.

Comment 3
The applicant starts with the statement that the GM oilseed rape is not different from the conventional rape seed, with the exception of the introduced trait.

Comment 4
On a general note on the dossier: a more clear and detailed table of content would save a lot of time in assessing the application compared to the mere presentation of individual references.

B. DATA REQUIREMENTS

B.1. COPY OF AUTHORISATION FOR PLACING THE FOOD/FEED ON THE MARKET

N/A

B.2. POST-MARKET MONITORING AND POST-MARKET ENVIRONMENTAL MONITORING REPORTS

Comment 1
No comments.

Comment 2
Comparing the annual monitoring reports (Annexe CI, PMEM) and the conclusions of the renewal application (in document “GT73_renewal.pdf”) identifies some inconsistency : the monitoring report 2015 concludes that “In view of the results given in this report, no revisions to the general surveillance plan are considered necessary for any Monsanto GM oilseed products”, whilst the renewal application states “Therefore, Monsanto believes that a revision of the current monitoring plan is appropriate”. It is my opinion that the surveillance plan is of a very general nature and that a modification of the procedure can be hardly envisaged.

Comment 3
From the annual reports of post market monitoring it is concluded that there is no new elements to modify the conclusions of the original risk assessment.

The report contains import data of GM and non-GM oilseed rape.
The network of surveillance consists of importers/traders, silo operators and processors. They report on an annual basis.

No adverse effects are mentioned.
Careful attention is given to minimize spills during handling.

At the end of the chain, the end users of the food and feed industry seems to be not involved in the surveillance reports. On the other hand, any obvious adverse effect observed, would certainly be reported.

No further questions or remarks.

Comment 4
No comment.

B.3. NEW INFORMATION

B.3.1. SYSTEMATIC SEARCH AND EVALUATION OF LITERATURE:

- search for new scientific information in a comprehensive and structured manner.
- search in all available databases, since the date of authorisation of the event.
- relevant for the three main areas of risk assessment (molecular characterisation, food and feed safety, and the environment).

Comment 1
No questions.

Comment 2
The information is split over different documents and folders, making the assessment uneasy. Moreover, the document 20161123_EFSA_GT73_renewal_cc.pdf presents the methodology and results of the literature review, indicating (page 6) "*Retrieved articles were assessed according to the procedures (…) leading to the conclusion that only two are deemed relevant (…). Also, these two references are the same as the ones identified from the literature searches performed and documented in the frame of each of the yearly PMEM reports (see our response of 30 September 2016)"*. I could not identify these two references, nor the "response of 30 September 2016". Are these two references Caine et al. 2007 and Reuter et al. 2007 (subfolder Literature in folder 2016-10-03)? (**SBB Comment**: yes indeed) I guess that the conclusions were indeed previously analysed by the EFSA GMO panel during its assessment of yearly monitoring reports, but I could not double check this.

Overall, more clarity in the presentation of the literature search would be appreciated. A renewal application should be a stand-alone dossier, avoiding cross references to previous risk assessments and monitoring reports.

Comment 3
The original risk assessment is confirmed. There is no new information available to modify the conclusions from the original authorization.

Comment 4

The updated search for scientific information/literature in the available databases did not reveal food/feed safety concerns.
No comments or further questions.

Comment 5
No comments.

Comment 6
No more comment (after having spotted) the extra info in the “Missing parts” folder.

B.3.2. UPDATED BIOINFORMATICS

- similarity searches for known toxic and/or allergenic proteins, using up-to-date databases, for all ORFs between stop codons without applying a size limit.
- information on the similarities of DNA sequences inserted in the plant genome with microbial DNA sequences, with an assessment of potentially altered likelihood for horizontal gene transfer, together with an evaluation of the consequences for human and animal health and the environment.

Comment 1
A bioinformatics search has been conducted (2015). No similarities with known toxins (CP4 EPSPS and GOXv247) were found.

Comment 2
No questions or comments.

Comment 3
I have no remarks on any of the bioinformatics reports.

Comment 4
The updated bioinformatics did not reveal any safety concerns.
No comments or further questions.

Comment 5
No comments.

Comment 6
The presented sequence of the insertion locus is rather small (100 bp at each site). Why was no new BLAT or BLAST analysis done on the *Brassica* genome sequence to reassess the insertion position and check for the interruption of genes or ORF? As a query sequence towards the allergenicity and toxicity databases, it would be more accurate to also use all ORFs (starting from the start codon of the interrupted gene or from any potential start triplet in the flanking regions). In Figure 2 (p12) of Kessenich and Silvanovich, 2016, only one peptide stemming from the junction regions can be seen. Why?

B.3.3. ADDITIONAL DOCUMENTS OR STUDIES PERFORMED BY OR ON BEHALF OF THE APPLICANT

- any prohibition or restriction imposed by any third country in which the food/feed is placed on the market.

- all unpublished studies performed or sponsored by the applicant and not previously submitted to the EU, with a review and assessment of their relevance for molecular characterisation, human and animal safety and the environment.

Comment 1
No questions.

Comment 2
The unpublished studies found in Annex 3 (non-CI) are errata to studies included in previous application dossiers. Although it must be stressed that these errata do not raise safety issues, the question remains if these amendments would have been ever communicated in the absence of this renewal application? Which are the regulatory provisions in this respect?

Comment 3
No comments or further questions.

Comment 4
No comments.

C. OVERALL ASSESSMENT

- potential identification of new hazards or modified exposure, or new scientific uncertainties, challenging the previous risk assessment.
- new studies in case required by the elements above.

Comment 1
No questions.

Comment 2
Oilseed rape GT73 can be considered as safe for human and animal health and the environment. The modified crop has been approved for more than 20 years in some countries, and can make up more than 90% of the total cultivation area in these countries. However, residues of glyphosate can be detrimental for the rumen physiology of ruminants and the nutritional efficiency of diets containing glyphosate residues (Reuter et al., 2007). On the other hand, there is no evidence that the transgene encoding glyphosate tolerance will be incorporated into feed particle- or fluid-associated rumen bacteria. Rapeseed meal is used as a high quality animal feed after removing the oil from the seed (±43%).

Comment 3
No comment.

Comment 4
No comments or further questions.

D. MONITORING PLAN AND PROPOSAL FOR IMPROVING THE CONDITIONS OF THE ORIGINAL AUTHORISATION

Comment 1

No questions.

Comment 2

The applicant “proposes to discontinue the PMEM efforts”, having regard to the monitoring information collected so far and the confirmation of the absence of adverse effects. We highlight this standpoint, which seems to call for a consistent answer throughout all renewal applications confirming the absence of adverse effects at the end of the monitoring period.

Comment 3

The applicant proposes an amendment to the original authorization and to discontinue the PMEM monitoring.

No objection to this proposal.

References

Reuter, T., Alexander, T.W., Martínez, T.F. McAllister, T.A. 2007. The effect of glyphosate on digestion and horizontal gene transfer during in vitro ruminal fermentation of genetically modified canola. J. Sci. Food Agric. 87, 2837-2843.