Bioveiligheidsraad
Conseil de Biosécurité

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Secretariaat
Secrétariat

O./ref.: WIV-ISP/41/BAC/2018_0056

Advice of the Belgian Biosafety Advisory Council on application EFSA-GMO-RX-004 from Bayer CropScience under Regulation (EC) No. 1829/2003

Context

Application EFSA-GMO-RX-004 was submitted by Bayer CropScience on 9 September 2016 for the renewal of authorisation for the marketing of genetically modified (GM) oilseed rape MS8, RF3 and MS8 x RF3 for food and feed uses, import and processing (excluding cultivation) within the European Union (EU), within the framework of Regulation (EC) No. 1829/2003[1].

Oilseed rape MS8 contains the gene derived from *Bacillus amyloliquefaciens* coding for the ribonuclease Barnase. Oilseed rape RF3 contains the gene derived from *B. amyloliquefaciens* coding for Barstar (Barnase inhibitor). Both also contain the gene derived from *Streptomyces hygroscopicus* coding for the PAT protein conferring tolerance to glufosinate-ammonium herbicides. Oilseed rape MS8 x RF3 was obtained from conventional crossing between the parental lines.

The placing on the market of oilseed rape MS8, RF3 and MS8 x RF3 for food/feed uses, except cultivation, is currently authorised by Commission Decisions 2007/232/EC and 2013/327/EU of 26 March 2007 and 25 June 2013 respectively (applications EFSA-GMO-BE-2010-81 and EFSA-GMO-RX-MS8/RF3), following positive opinions of EFSA on 06/09/2012 and 09/09/2009 (http://www.efsa.europa.eu/en/efsajournal/pub/2875 and http://www.efsa.europa.eu/en/efsajournal/pub/1318), and positive advices of the BAC on 07/12/2012 and 11/12/2009.

The application was officially acknowledged by EFSA on 21 October 2016 and a formal three-month consultation period of the Member States was started, 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 Biosafety and Biotechnology Unit (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.

[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).

Wetenschappelijk Instituut Volksgezondheid | Institut Scientifique de Santé Publique
Dienst Bioveiligheid en Biotechnologie | Service Biosécurité et Biotechnologie
Rue Juliette Wytsmanstraat 14 | B-1050 Brussels | Belgium
T + 32 2 642 52 11 | F + 32 2 642 52 92 | bac@wiv-isp.be | www.bio-council.be

The opinion of the EFSA Scientific Panel on GMOs was adopted on 25 October 2017 (EFSA Journal 2017;15(11):5067, 12 pp[2]), and published on 28 November 2017 together with the responses from the EFSA GMO Panel to comments submitted by the Member States during the three-month consultation period.
On 4 December 2017 the opinion of EFSA was forwarded to the Belgian experts. They were invited to give comments and to react if needed.

The comments formulated by the experts together with the opinion of EFSA, as well as the advices already adopted by the BAC on stacked events containing oilseed rape MS8 and RF3 and the advices already adopted by the BAC on other GM single events expressing the Barnase, Barstar and PAT proteins, form the basis of the advice of the Biosafety Advisory Council given below.

Scientific evaluation

1. Post-market environmental monitoring

The Biosafety Advisory Council welcomes the annual post-market environmental monitoring (PMEM) reports provided by the applicant during the period May 2007 to September 2015, and takes note of the absence of adverse effects reported by the applicant during the authorisation period of oilseed rape MS8, RF3 and MS8 x RF3.

2. Systematic search and evaluation of literature

The Biosafety Advisory Council welcomes the systematic literature search covering the complete duration of the event's authorisation conducted by the applicant following the principles outlined in the relevant EFSA guidance.
The Council agrees with the GMO panel of EFSA that none of the scientific publications relevant for the risk assessment of oilseed rape MS8, RF3 and MS8 x RF3 identified from this literature search raise any new concerns regarding the safety for human or animal health or the environment.

3. Updated bioinformatics

The Biosafety Advisory Council agrees with the GMO panel of EFSA that the updated bioinformatics analyses for GM oilseed rape MS8, RF3 and MS8 x RF3 do not indicate any safety concern, as no known endogenous genes are interrupted by the inserts, the newly expressed proteins do not present significant similarities to known toxins or allergens, and the expression of an open reading frame showing significant similarities to toxins or allergens is highly unlikely.

4. Additional documents or studies

The Biosafety Advisory Council welcomes the reports of additional studies performed by the applicant over the course of the authorisation period with regard to the evaluation of the safety of the food/feed and the risks of the food/feed to humans, animal or the environment from oilseed rape MS8, RF3 and MS8 x RF3.
The Council agrees with the GMO panel of EFSA that this new information does not raise any concern for human and animal health, and the environment.

[2] See https://www.efsa.europa.eu/en/efsajournal/pub/5067

5. Overall assessment

The Biosafety Advisory Council agrees with the GMO panel of EFSA that no new information has given rise to any concern for human or animal health or the environment.

6. Monitoring plan and proposal for improving the conditions of the original authorisation

Since the allergenicity of the whole GM oilseed rape has not been fully assessed, it is recommended to take up monitoring of allergenicity as part of the general surveillance.

Conclusion

Based on the scientific assessment of the dossier done by the Belgian experts, taking into account the opinion of EFSA, the previous advice of the BAC on oilseed rape MS8, RF3 and MS8 x RF3, the advices already adopted by the BAC on stacked events containing oilseed rape MS8 and RF3 and the advices already adopted by the BAC on other GM single events expressing the Barnase, Barstar and PAT proteins, and considering the new information provided by the applicant, the Biosafety Advisory Council is of the opinion that in the context of its proposed uses, oilseed rape MS8, RF3 and MS8 x RF3 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.

In addition, the Biosafety Advisory Council recommends to follow up any unanticipated allergenicity aspects of the GM oilseed rape in the existing allergenicity monitoring systems.

Prof. Maurice De Proft
President *a.i.* of the Belgian Biosafety Advisory Council

Annex I: Compilation of comments of experts in charge of evaluating the application EFSA/GMO/RX-004 and Comments submitted on the EFSAnet on mandate of the Biosafety Council (ref. BAC_2017_0046)

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Compilation of comments of experts in charge of evaluating the application EFSA/GMO/RX-004
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 13 December 2016.
Coordinator: Dr. René Custers
Experts: Eddy Decuypere (KUL), Jacques Dommes (ULg), Patrick du Jardin (ULg), Leo Fiems (ILVO), André Huyghebaert (UGent), Peter Smet (Consultant), Frank Van Breusegem (UGent), Jan Van Doorsselaere (KATO)
SBB: Didier Breyer, Fanny Coppens, Katia Pauwels.

♦ INTRODUCTION

Dossier **EFSA/GMO/RX-004** concerns an application for renewal submitted by the company **Bayer CropScience** for authorisation to place on the market genetically modified **oilseed rape MS8, RF3, MS8 x RF3** 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 3 November 2016.

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
Oilseed rape MS8, RF3 and MS8xRF3 are unlikely to have any adverse effect on the health of humans and animals and the environment in the context of its intended use (exception of cultivation and uses as or in food).

Comment 2
No questions.

Comment 3
No comment.

Comment 4
MS8/RF3 means MS8, RF3 and MS8 x RF3.

Comment 5
No comments.

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
No comment.

Comment 3

1. In the 2015 report, in contrast with the reports of the previous years, the share of GMO cultivation in the country of origin (Canada, as sole exporter) is not given in the section 3.1.1. Although I agree that the exposure assessment is a difficult and quite theoretical exercise, I think that this data is important for such estimation.

Coordinator Comment:
I would not expect large differences with previous years concerning the share of GMO cultivation in country of origin.

2. There is no consolidated report of the annual monitoring reports, which would be appreciated for such a renewal dossier.

3. I wish to point out that the PME environmental monitoring considers accidental spillage and the possibility of volunteers in the context of ports and crushing facilities only, not in field environments. However, since the PMEM plan was approved at the time of the consent, it is deemed sufficient considering the scope of the application which excludes cultivation.

Comment 4
Annual monitoring reports are available for the period 2008 – 2015.
These reports include data on the GM and non-GM imports in the member states of the EU.
The organization of the monitoring system is explained in detail.
With respect to the surveillance, reports from the whole chain of trade and transformation are included: European associations of importers, traders, silo operators, handlers and processors. An annual summary of the information is also available. No incidents in relation to placing on the market of MS8/RF3 have been reported.

No further questions.

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
The assumption of 100% identity of sequence to the originally assessed event is fulfilled; therefor the previous risk assessment is still valid since no new scientific information against the use of MS8 or RF3 B. napus was generated, or that negatively impacted the safety assessment of Brassica napus MS8, RF3 and MS8xRF3.

Comment 2
No comment.

Comment 3
Evaluated, no questions raised.

Comment 4
No comments.

Comment 5
No comments.

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
Bioinformatics analysis on MS8-insertion and RF3-insertion locus sequence reveal the unlikeliness to interrupt or alter transcriptional or translational activity of known endogenous Brassica napus genes, even if the chromosomal location of RF3 insertion locus could not be identified.
Homology searches against the protein database showed matches that corresponded to sequences from ribonuclease inhibitor family for barnase and barstar proteins and to sequences from the acetyltransferases for PAT/bar protein. No allergenic nor toxicological in silico findings associated with barnase, barstar or PAT/bar proteins or with the potential ORF-polypeptides were revealed.

Comment 2
No comment.

Comment 3
In bioinformatic report M-221641-06-1, it is not clear to me, based on the map in figure 1, why the accessions XM_013759299 and XM_013845661 showing high identity with the insertion locus are said to correspond to the 3' flanking region only. The map and alignments displayed in Appendix 3 seem to indicate that both the 3' and 5' flanking regions are in fact involved in the sequence identity. The problem is that 'alignment with the 3' flanking region only' is used as an argument for claiming the absence of interruption of endogenous genes, hence this point should be clarified.

Comment 4
A recent search (2016) revealed no biologically relevant identities with known toxins concerning the Barnase, Barstar and PAT/bar proteins.

Comment 5
No comments.

Comment 6
It is not clear to me, why a BLAT search was performed using the insertion locus as a query sequence. In general, it would be more accurate to indicate the exact parameter settings that were used for the different BLAT and BLAST searches.

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
No comment.

Comment 3
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 or comments.

Comment 2
No comment.

Comment 3
See previous remarks.

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

Comment 1
No questions.

Comment 2
No comment.

Comment 3
No comment.

Comment 4
No further proposal.