Bioveiligheidsraad
Conseil de Biosécurité

30-01-2018

Secretariaat
Secrétariat

O./ref.: WIV-ISP/41/BAC/2018_0058

Advice of the Belgian Biosafety Advisory Council on application EFSA-GMO-RX-005 from Syngenta Crop Protection NV/SA under Regulation (EC) No. 1829/2003

Context

Application EFSA-GMO-RX-005 was submitted by Syngenta Crop Protection NV/SA on 10 November 2016 for the renewal of authorisation for the marketing of genetically modified (GM) maize GA21 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].

Maize GA21 expresses a mutated EPSPS protein (mEPSPS) for tolerance to glyphosate herbicides.
The placing on the market of maize GA21 for food/feed uses, except cultivation, is currently authorised by Commission Decision 2008/280/EC of 28 March 2008 (applications EFSA-GMO-UK-2005-19 and EFSA-GMO-RX-GA21), following a positive opinion of EFSA on 13/09/2007[2]. The Belgian Biosafety Advisory Council (BAC) already issued two positive advices on this event: a first one on the two above-mentioned applications (with a reservation of some members about the health safety of the event) on 07/12/2007[3], and a second one on 10/02/2012 on application EFSA-GMO-UK-2008-60[4].

The application was officially acknowledged by EFSA on 7 April 2017 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 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). Seven experts answered positively to this request, and formulated a number of comments to the dossier, none of which concerned the risk assessment of the GM maize. Therefore no comments were sent to EFSA by the BAC during the consultation period of the Member States.

[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 http://www.efsa.europa.eu/en/efsajournal/pub/541
[3] Ref. WIV-ISP/BAC/2007_SC_614
[4] Ref. WIV-ISP/41/BAC/2012_0216

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The opinion of the EFSA Scientific Panel on GMOs was adopted on 21 September 2017 (EFSA Journal 2017;15(10):5006[5]), and published on 24 October 2017 together with the responses from the EFSA GMO Panel to comments submitted by the Member States during the three-month consultation period.
The opinion of EFSA, as well as the advices already adopted by the BAC on stacked events containing maize GA21 and the advices already adopted by the BAC on other GM single events expressing the mEPSPS protein, 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 March 2008 to July 2016, and takes note of the absence of adverse effects reported by the applicant during the authorisation period of maize GA21.

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 maize GA21 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 maize GA21 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 maize GA21.
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.

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.

[5] See http://www.efsa.europa.eu/en/efsajournal/pub/5006

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

Since the allergenicity of the whole GM maize 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 advices of the BAC on maize GA21, the advices already adopted by the BAC on stacked events containing maize GA21 and the advices already adopted by the BAC on other GM single events expressing the mEPSPS protein, 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, maize GA21 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 maize could pose to the European environment.

In addition the Biosafety Advisory Council recommends following up any unanticipated allergenicity aspects of the GM maize 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-005 on mandate of the Biosafety Council (ref. BAC_2017_0594)

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02/08/2017

Secretariaat
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Compilation of comments of experts in charge of evaluating the application EFSA/GMO/RX-005
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 25 April 2017.
Coordinator: Dr. Marc De Loose
Experts: Leo Fiems (ILVO), Johan Grooten (UGent), André Huyghebaert (UGent), Peter Smet (Consultant), Frank Van Breusegem (UGent), Michel Ghanem (ICARDA), Jacques Dommes (ULg)
SBB: Didier Breyer, Fanny Coppens, Katia Pauwels.

- **INTRODUCTION**

Dossier **EFSA/GMO/RX-005** concerns an application for renewal submitted by the company Syngenta for authorisation to place on the market genetically modified **maize GA21** 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 07 April 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
The chance that the genetic modification of GA21 maize is detrimental for animal and human health and the environment is neglectable.
Because the genetic modification of GA21 maize is intended to the application of glyphosate in maize for weed management, it is interesting that a maximum residue level of 1.0 mg/kg for glyphosate is respected.
Although GA21 maize is not intended for cultivation in the EU, the intensive use of other glyphosate-tolerant GM crops beside GA21 maize around the world can result in a fast development of glyphosate-tolerant weeds, so that the sustainability of GA21 maize is questionable.
Because of the debate concerning the safety of glyphosate the post-market surveillance should pay attention to this issue.

SBB Comment:
The assessment of pesticide use is not within the remit of the Biosafety Advisory Council.

Comment 2
No comments.

Comment 3
No particular comments.

Comment 4
No comments.

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 concerns regarding risk to human and animal health have emerged from the monitoring reports.

Comment 2
The post-market monitoring system is described in detail. The file contains annual reports of the monitoring.
The applicant concludes that no adverse effects have been observed. Previous conclusions about the safety are confirmed. There is also no reason to modify the PMEM system.

The surveillance network consists of:
- importers and traders,
- silo operators,
- processors like crushers and meal- and vegetable oil processors.

It seems that end- users of the wet and dry milling products are not involved in the network. In this case the end-user is not the consumer but the food and feed industry.

As end users involved in product development and quality assurance are very familiar with the properties of the products obtained, any shift or modification in the properties would be certainly observed.

I wonder if end-users, in one or another way, could not be involved in the surveillance system.

B.3. NEW INFORMATION

B.3.1. SYSTEMATIC SEARCH AND EVALUATION OF LITERATURE:

Comment 1

A comprehensive and systematic search of scientific peer-reviewed, open literature has been performed covering the last ten years. This analysis did not reveal concerns relating to human and animal health.

Comment 2

No question or remark.

Comment 3

No comments.

Comment 4

No new data that changes anything compared to previous results.

B.3.2. UPDATED BIOINFORMATICS

Comment 1

The updated sequence similarity assessment to known allergens by bioinformatics analyses yielded no significant amino acid sequence similarities with any known allergens.

Comment 2

ORFs contained between stop codons within the GA21 insert DNA were identified. Each hypothetical or real ORF sequence, which included the mEPSPS sequence, was translated to amino acid sequence and was evaluated for the presence of alignments with proteins from an allergen database. Each full length ORF was also evaluated for the presence of alignments with proteins from the Syngenta toxin database. Results support the conclusion that putative amino acid translations show no biologically relevant sequence similarity to any known or putative protein allergens or toxins of mammalian concern. Study dates from 2016, so no further questions.

Comment 3

No comments.

Comment 4

BLASTN analyses complete. No particular comment.

Comment 5

The applicant did bioinformatics analyses using appropriate tools and settings, and updated databases. The results confirm the previous analyses and support the following conclusions:

- the insertion of foreign DNA did not disrupt an essential nuclear maize gene;
- amino acid sequences obtained by translation of the DNA sequences spanning the junctions between insert and maize genomic DNA did not show similarity to any toxin or allergen;
- amino acid sequences obtained by translation of the insert sequence (all reading-frames) did not show relevant similarity to any known toxin or allergen;
- the sequence of the insert did not show relevant similarities on at least two stretches of minimum 200 bp of microbial DNA, suggesting a very low probability of recombination with the DNA of microbes.

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

Comment 1
No comments.

Comment 2
No particular comments in this section compared to previous reported results.

C. OVERALL ASSESSMENT

Comment 1
While a discussion is on-going on the health risk of extended glyphosate usage, this discussion in essence does not relate to the health risk of the transgenic mEPSPS protein. It may raise however the issue of glyphosate residue levels on glyphosate resistant GA21 maize, which clearly is an entirely different, yet highly relevant discussion.
No further remarks.

Comment 2
No particular comments regarding new hazards or new scientific uncertainties.
No issues concerning potential new risks.

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

Comment 1
I agree with the conclusion of the applicant that no adverse effects have been identified.

Comment 2
No particular comment.