Bioveiligheidsraad
Conseil de Biosécurité

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Secretariaat
Secrétariat

O./ref.: WIV-ISP/41/BAC/2018_0059

Advice of the Belgian Biosafety Advisory Council on application EFSA-GMO-RX-006 from KWS SAAT SE and Monsanto Company under Regulation (EC) No. 1829/2003

Context

Application EFSA-GMO-RX-006 was submitted by KWS SAAT SE and Monsanto Company on 22 December 2016 for the renewal of authorisation for the marketing of genetically modified (GM) sugar beet H7-1 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].

Sugar beet H7-1 produces the CP4 EPSPS protein for tolerance to glyphosate herbicides. The placing on the market of sugar beet H7-1 for food/feed uses, except cultivation, is currently authorised by Commission Decision 2007/692/EC of 24 October 2007 (application EFSA-GMO-UK-2004-08), following a positive opinion of EFSA on 14/12/2006 (https://www.efsa.europa.eu/en/efsajournal/pub/431). On this dossier the Belgian Biosafety Advisory Council (BAC) issued a positive advice on 21 June 2007 (ref. WIV-ISP/BAC/2007_SC_544) but only related to the marketing of dried products produced from sugar beet H7-1. The BAC was of the opinion that if other products were to be placed on the market, further assessment was needed about the toxicity of undried material likely to contain proteins.

Application EFSA-GMO-RX-006 was officially acknowledged by EFSA on 18 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). 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.

The opinion of the EFSA Scientific Panel on GMOs was adopted on 26 October 2017 (EFSA Journal 2017;15(11):5065[2]), and published on 16 November 2017 together with the responses from the EFSA GMO Panel to comments submitted by the Member States during the three-month consultation period.

[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://www.efsa.europa.eu/en/efsajournal/pub/5065

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

On 20 November 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 sugar beet H7-1 and on other GM single events expressing the CP4 EPSPS protein, form the basis of the advice of the Biosafety Advisory Council given below.

Scientific evaluation

1. Post-market environmental monitoring

Since no post-market environmental monitoring reports were required by Commission Decision 2007/692/EC, no reports were submitted in the frame of this application and no evaluation was performed.

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 sugar beet H7-1 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 sugar beet H7-1 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 sugar beet H7-1.
These studies include an assessment of CP4 EPSPS protein levels in pollen, and leaf and root (Brei) tissues of event H7-1, as well as a compositional analysis of leaf and root.
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.

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

No monitoring plan was required by the authorisation decision, and the Biosafety Advisory Council agrees with the GMO Panel of EFSA that a monitoring plan is still not needed.

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 sugar beet H7-1 and the advices already adopted by the BAC on other GM single events expressing the CP4 EPSPS 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, sugar beet H7-1 is unlikely to pose any risk to human and animal health.

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-006 and Comments submitted on the EFSAnet on mandate of the Biosafety Council (ref. BAC_2017_0595)

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

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O./ref.: WIV-ISP/41/BAC_2017_0595
Email. : bac@wiv-isp.be

Compilation of comments of experts in charge of evaluating the application EFSA/GMO/RX-006
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. Philippe Baret
Experts: Leo Fiems (ILVO), Johan Grooten (UGent), André Huyghebaert (UGent), Peter Smet (Consultant), Frank Van Breusegem (UGent), Michel Ghanem (ICARDA), Jacques Dommes (ULg), Patrick duJardin (ULg)
SBB: Didier Breyer, Fanny Coppens, Katia Pauwels.

♦ INTRODUCTION

Dossier **EFSA/GMO/RX-006** concerns an application for renewal submitted by the companies **KWS SAAT SE and Monsanto** for authorisation to place on the market genetically modified **sugar beet H7-1** 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 18 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
It is assumed that the genetically modified H7-1 sugar beet as such is not detrimental for animal and human health and the environment is neglectable.
Because the genetic modification of H7-1 sugar beet is intended to the application of glyphosate in beet for weed management, it would be interesting to mention a maximum residue level for glyphosate.
Although H7-1 sugar beet is not intended for cultivation in the EU, the intensive use of other glyphosate-tolerant GM crops beside H7-1 sugar beet around the world can result in a fast development of glyphosate-tolerant weeds, so that the sustainability of H7-1 sugar beet maize is questionable.
Because of the concerns about 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
Overall, this dossier was poorly structured. Being just a collection of separate files through which one has to navigate in order to retract the info needed, this is clearly not an example of a dossier that provides the required info in a well-structured and transparent manner.

Comment 3
No comment or question

Comment 4
No comments.

Comment 5
No comments.

Comment 6
No comment, adequate information was provided

Comment 7
The information provided in the application for the renewal requested by KWS SAAT SE and Monsanto is sufficient.
Data have been provided concerning a literature update and DNA sequence flanking the gene of interest.

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 comments.

Comment 3
No comment, no safety concern

B.3. NEW INFORMATION

B.3.1. SYSTEMATIC SEARCH AND EVALUATION OF LITERATURE:

Comment 1
Because most new information is quasi uniquely provided by the applicant, some vigilance is desirable.

Comment 2
A systematic search of scientific peer-reviewed literature has been performed covering the period of 2007 to March 2017. This analysis reportedly did not reveal concerns relating to human and animal health. However, because the applicants merely provide a list of publications without any further assessment of these publications, it is hard to judge from such a listing to what extend this proposition is indeed the case.

Comment 3
No comment

Comment 4
No comments

Comment 5
No comments.

Comment 6
Adequate literature survey was made. No safety concern.

Comment 7
New literature provided. New data do not bring any change to the previous results.

B.3.2. UPDATED BIOINFORMATICS

Comment 1

Because most new information dealing with Bioinformatics is quasi uniquely provided by the applicant, some vigilance is desirable.

Comment 2
The updated sequence similarity assessment to known allergens by bioinformatics analyses yielded no significant amino acid sequence similarities with any known allergens.

Comment 3
A bioinformatic analysis performed using the six reading frames translated from the T-DNA was performed. The results of this analysis positively identified CP4 EPSPS and other intended genetic elements, but revealed no structurally relevant sequence similarities between the six reading frames translated from the T-DNA with allergens, toxins, or other relevant biologically active proteins that could affect human or animal health. (Studies date from 2016)

Comment 4
No comments

Comment 5

1. The bioinformatic searches use the sequence of the insert and flanks found in the report "Kraus 2003 amended 2011". However, this report does not describe which amendments were actually brought in 2011 to the initial study (2003). Whether there are any changes in the nucleotide sequence as compared with that used in the previous risk assessment (EFSA scientific opinion of 2006) is unclear. The applicant should be asked to clarify which amendments were brought to the description of the insert and flanking sequences as compared with their previous risk assessments. Furthermore, from the same report it is unclear whether the insert sequence described in figure 3 was obtained from the transformation event as in sugar beet H7-1 or was just a 'copy and paste' of the sequence from the transformation vector. Indeed, the report describes the PCR amplification of the flanking regions for sequence analysis but there is no indication of how the insert sequence itself was determined. The applicant should clarifiy this as well.

2. The applicant has identified a possibly interrupted gene at the 5' extremity of the insert, by both BlastN and BlastX analysis, corresponding to a MATE efflux transporter protein (Menze and Davenport 2016). One of the hits of the bioinformatic analysis corresponds to a sugar beet EST, suggesting that the interrupted gene is possibly expressed in non-GM sugar beet. This was apparently not identified by the previous risk assessment (it would have been commented by the EFSA scientific opinion for sure). However, I consider that this raises no safety issue, following the arguments of the applicant, considering the nature of these MATE transporters, their encoding by multiple gene families, and the agronomic, phenotypic and compositional analysis of H7-1 sugar beet which did not indicate (significant) unintended changes as compared with its non-GM comparator (NB: argued by the applicant but not double-checked).

Comment 6
Bioinformatics analyses were repeated using updated databases (year 2016). They confirmed the analyses made for the first application: they did not rise any safety concern.

Comment 7
Updated bioinformatics evaluation of the flanking DNA sequences of the insertion site provided and seems comprehensive. No additional remarks.

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

Comment 1
No comments

Comment 2
No comments

Comment 3
Expression of the CP4 EPSPS protein was assessed in leaf and root tissues (European field trials), as well as in pollen (USA field trials). These studies confirmed previous data.
Phenotypic characteristics were also evaluated in field trials in USA. No significant difference was found with non-transgenic counterparts. So these additional studies do not rise any safety concern.

Comment 4
Applicant provide latest data from 2013.
The claim that the results demonstrate that there were no relevant changes in the phenotype is not supported by the data given the large and significant differences between transgenics and non-transgenics, when it comes to germination, flowering and branching.

C. OVERALL ASSESSMENT

Comment 1
No further specific comments.

Comment 2
It seems important to clarify the origin of the DNA sequences used in the bioinformatic analyses, as explained before.

Comment 3
The data do not identify any new hazard, nor modified exposure, nor any new scientific uncertainty. The data confirm the previous risk assessment.

Comment 4
No particular comments regarding new hazards or new scientific uncertainties.

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

Comment 1
No comments

Comment 2

The applicant concludes that “there is no reason to assume any change in the conclusions of the original risk assessment. Product produced from sugar beet H7-1 are unlikely to have any adverse effect on human or animal health”.
I agree with this conclusion.

Comment 3
None.

Comment 4
No comment

Comment 5
No particular comment.