Adviesraad voor Bioveiligheid
Conseil consultatif de Biosécurité

Advice of the Belgian Biosafety Advisory Council on application EFSA-GMO-NL-2018-153 (soybean GMB151) from BASF under Regulation (EC) No. 1829/2003

1 June 2021
*Ref. SC/1510/BAC/2021*_0523

Context

Application EFSA-GMO-NL-2018-153 was submitted by BASF for the authorisation for the marketing of genetically modified (GM) soybean GMB151 for food and feed uses, import and processing (excluding cultivation) within the European Union, within the framework of Regulation (EC) No. 1829/2003[1].

Soybean GMB151 contains a single insert consisting of the *cry14Ab-1.b* and *hppdPf-4Pa* gene cassettes, conferring resistance to soybean cyst nematode and tolerance to HPPD inhibitor herbicides, respectively.

The application was validated by EFSA on 4 March 2019 and a formal three-month consultation period of the Member States was started, lasting until 8 June 2019, 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). Four 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 23 May 2019.

The opinion of the EFSA Scientific Panel on GMOs was published on 19 April 2021 (EFSA Journal 2021;19(4):6424[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 28 April 2021, 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-2018-153 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.2021.6424

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Scientific evaluation

1. Molecular characterisation

After request for more information on a potential altered expression of the *BAP1* gene at the insertion site and on the bioinformatics search for similarities at protein and allergen level, the BAC is of the opinion that the molecular characterisation data do not raise safety concerns.

2. Assessment of food/feed safety and nutritional value

2.1. Assessment of compositional analysis

The BAC agrees with the GMO panel of EFSA that the compositional data of GM soybean GMB151, in comparison with the non-GM reference varieties showed no differences that would require further assessment with respect to their possible impact on food and feed safety and nutritional properties. Hence no clear hypothesis for further testing can be formulated. The BAC therefore considers that further testing of the whole food/feed (i.e. 90-day feeding trial) did not bring any added value to this particular dossier.

2.2. Assessment of toxicity

The BAC agrees with the GMO panel of EFSA that the available data on the toxicity of GM soybean GMB151, in comparison with its conventional counterpart, do not raise safety concerns.

2.3. Assessment of allergenicity

The BAC agrees with the GMO panel of EFSA that the available data on the allergenicity of the Cry14Ab-1.b and HppdPf-4Pa proteins, as expressed in soybean GMB151, and on the overall allergenicity of soybean GMB151, do not raise safety concerns.

2.4. Nutritional value

The BAC is of the opinion that the information provided is sufficient to conclude that the nutritional characteristics of soybean GMB151-derived food and feed are not expected to differ from those of conventional soybean varieties.

3. Environmental risk assessment

The BAC is of the opinion that it is unlikely that the accidental release[3] of soybean GMB151 seeds (i.e. during transport and/or processing) into the European environment will lead to environmental harm.

4. Monitoring

With regard to monitoring, the BAC is of the opinion that the information provided is sufficient.

[3] As the application doesn't imply cultivation of the GM crop in the EU, a full environmental assessment, as in the case of a cultivation dossier, is not warranted.

Conclusion

Based on the whole set of data on soybean GMB151 provided by the applicant, the scientific assessment of the dossier done by the Belgian experts, the opinion 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 accidental environmental release of soybean GMB151 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, soybean GMB151 is unlikely to pose any risk to human and animal health.

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-NL-2018-153 (ref. BAC_2019 0485).

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Outcome of the assessment of application EFSA/GMO/NL/2018/153 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)

23 May 2019
Ref. SC/1510/BAC/2019_0485

Coordinator: Bruno Schiffers
Experts: Jacques Dommes (ULg), André Huyghebaert (UGent), Patrick du Jardin (ULg), Peter Smet (Consultant)
SBB: Adinda De Schrijver

Application: **EFSA/GMO/NL/2018/153**
Applicant: **BASF**
GMO: **soybean GMB151**
Acknowledged of receipt by EFSA: **6 July 2018**

The scope of the application is:
(a) GM food
☒ Food containing or consisting of GM plants
☒ Food produced from GM plants or containing ingredients produced from GM plants
(b) GM feed
☒ Feed containing or consisting of GM plants
☒ Feed produced from GM plants
(c) GM plants for food or feed use
☒ Products other than food and feed containing of consisting of GM plants with the exception of cultivation
☐ Seeds and plant propagating material for cultivation in the EU

Given the characteristics of the GMO and its intended uses, experts were consulted to cover the following areas of expertise:
☒ Molecular characterisation
☒ 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.

Comments placed on the EFSAnet are indicated in grey. 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

GENERAL INFORMATION

No comments received

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: 2 experts

1.2. MOLECULAR CHARACTERISATION

1.2.1. Information relating to the genetic modification

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

1.2.2. Information relating to the genetically modified plant

Comment 1

1- Analysis of the insertion locus indicates that the insertion of T-DNA sequences in the GMB151 soybean is located in the 3' untranslated region of a putative endogenous gene annotated as a BON1-associated protein 1-like protein (BAP1, main text page 46 and report 18-RSVLS011). This gene seems to encode a protein involved in a signal transduction cascade. The quoted reference Yang et al. 2006 seems to be missing in the dossier and should have been provided. After retrieving this reference from the Scopus database, it becomes evident that, despite the fact that the BAP1 protein seems to be encoded by a multigene family, a single mutation in the *BAP1* gene causes phenotypes in Arabidopsis which are related to programmed cell death and disease resistance. In the case of the GMB151 soybean, it remains unclear whether insertion in the 3' untranslated region as shown in the dossier is expected to alter the expression of the gene. The applicant should have discussed this point based on the bioinformatic data and should have commented on the possible effects on the GMB151 soybean which might be relevant from a risk assessment point of view.

2- When searching the new ORFs for allergen similarities the following conclusions are given (main text page 47): *the 80-mer sliding window search identified one 80-mer from GMB151_ORF.572 having low identity of 35.4%, with a very high E-value of 99, with a 77 amino acid stretch of Asp f 22 enolase from Aspergillus fumigatus. This match was just above the conservative threshold of >35 homology with E-value of ≤100. A sequence identity of more than 50% between homologous allergens has been reported to be necessary in order to exhibit cross-reactivity*. This last statement (the '50 % identity' issue) is not supported by references, and I am not aware of such a criterion in EFSA / FAO guidance documents. It is also unclear in the absence of indication of the length over which the identity should be calculated. Could the applicant justify this quite general statement? Nevertheless, when applying the criteria used by EFSA, considering the high E-value of this alignment and the further arguments presented by the applicant, I see no safety concern, but a methodological concern.

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: 2 experts

Comment 1

All this information is presented later in the dossier, in section 5.

1.2.4. Conclusions of the molecular characterisation

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

Comment 1

See my comments above.

1.3. COMPARATIVE ANALYSIS

1.3.1. Choice of the conventional counterpart and additional comparators

Have evaluated this section and consider the information adequate: 3 experts

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

Comment 1

Compounds for analysis were selected according to the OECD consensus document, revised edition, Particular attention was given to metabolites of the tyrosine pathway: tocopherols and vitamin K.

In addition to soybean 153 and the conventional counterpart other soybean varieties were also considered.

My comments are related to grain and not to forage.

1.3.4. Comparative analysis of composition

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

Comment 1

The usual approach is followed in the discussion of the results: classification according to no statistically different, statistically different with particular outcome.
The following items are considered;
- proximate and fiber,
- amino acids,
- fatty acids,
- minerals,
- vitamins,
- anti-nutrients,
- endogenpus allergens,
- tyrosine pathway metabolites.

Analytes classified as outcome 1, 2 and 3 were not further evaluated.

Palmitic acid in soybean 153 was found to be significantly different to the conventional counterpart. The mean value was however only slightly lower than the minimum reference variety and within the range of values in the Ilsi data bank;

Heptadecenoic acid, C17:1 was also found to be significantly different. Due to the low content of this particular fatty acid, it is stated that any lack of statistically equivalence would not affect the impact of food and feed utilization.

The values for trypsin inhibitor are not significantly different but equivalence between soybean 153 is less likely than not. The mean values are however within the range of reference varieties.

Vitamin A, assessed as beta-carotene, was found to be significantly different. The mean value is within the range of reference varieties. It is concluded that the values are within the range of natural variability. Further on the lack of equivalence especially for higher levels of beta-carotene, would not affect the food utilization.

Tyrosine pathway metabolites such as beta tocopherols, gamma tocopherols and total tocopherols were found not to be statistically different. Delta tocopherol was statistically different but equivalence was demonstrated

I regret that tocotrienols are not included in the study. Tocotrienols are a range of constituents structurally related to tocopherols. They hav no vitamine activity like alpha tocopherols but are well known antioxidants with a growing importance in human nutrition. Tocotrienols are not included in the OECD consensus paper..

The applicant conludes from the comparative assessment that there are no biologically relevant differences between the 153 soybean and the comparators taking into account natural variation.

I agree with this conclusion.

1.3.5. Comparative analysis of agronomic and phenotypic characteristics

Have evaluated this section and consider the information adequate: Patrick du Jardin

1.3.6. Effects of processing

Comment 1

As soybean 151 is compositionally equivalent to reference soybean, it is expected that processing will not be affected.

1.3.7. Conclusion

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

Comment 1

I agree with the conclusion of the applicant

Comment 2

We agree with the conclusions of the applicant that the comparative assessment of GMB151 soybean, the conventional counterpart, and the non-GM reference varieties showed no differences that would require further assessment with respect to their possible impact on food and feed safety and nutritional properties. Hence no clear hypothesis for further testing can be formulated. We therefore consider that further testing of the whole food/feed (i.e. 90-day feeding trial) is not needed.

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

1.4.3. Information on natural food and feed constituents

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

1.4.4. Testing of the whole genetically modified food or feed

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

1.4.5. Conclusion of the toxicological assessment

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

1.5. ALLERGENICITY

1.5.1. Assessment of allergenicity of the newly expressed protein

Comment 1

The same remark as in section 1.2.2 before, on the allergenicity assessment of Cry14AB-1, is valid here (cfr page 149 on main dossier, where the same bioinformatic criteria are indicated).

1.5.2. Assessment of allergenicity of the whole genetically modified plant

Have evaluated this section: 0 experts

1.5.3. Conclusion of the allergenicity assessment

Comment 1

The same remark as in section 1.2.2 before, on the allergenicity assessment of Cry14AB-1, impacts the general conclusions.

1.6. NUTRITIONAL ASSESSMENT

1.6.1. Nutritional assessment of the genetically modified food

Have evaluated this section: 0 experts

1.6.2. Nutritional assessment of the genetically modified feed

Have evaluated this section: 0 experts

1.6.3. Conclusion of the nutritional assessment

Have evaluated this section: 0 experts

2. EXPOSURE ASSESSMENT — ANTICIPATED INTAKE OR EXTENT OF USE

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

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

5. ENVIRONMENTAL RISK ASSESSMENT (ERA)

5.1. INTRODUCTION

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

5.2. GENERAL APPROACH OF THE ERA

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

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: 2 experts

5.3.2. Plant to micro-organisms gene transfer

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

Comment 1

The report M-618502-01 detailing the HGT analysis concludes: "*Although the cry14Ab-1.b gene originates from Bacillus thuringiensis and the hppdPf-4Pa gene originates from Pseudomonas fluorescens, no hits were obtained in the BLASTN searches. This is due to the fact that the nucleotide sequences of the cry14Ab-1.b and the hppdPf-4Pa genes were changed, thereby significantly reducing the % identity of these genes to their native sequences".* However, both the *cry14Ab-1.b* and *hppdPf-4P* genes were amplified from bacterial DNA and the dossier provides no indication of re-synthesis with codon optimisation which would significantly alter the nucleotide sequences. The "changes" mentioned by the applicant seem thus minor and the similarity search between the inserted sequences and bacterial sequences in the databases should have spotted these two genes of bacterial origin. The applicant should provide a more convincing explanation for the absence of hits in this bioinformatic analysis, e.g. by providing the percentages of similarity between the native and changed sequences as inserted in the plant. Indeed the absence of these hits allows to question the validity of the bioinformatic searches.

5.3.3. Interactions of the GM plant with target organisms

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

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

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

5.3.5. Impacts of the specific cultivation, management and harvesting techniques

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

5.3.6. Effects on biogeochemical processes

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

5.3.7. Effects on human and animal health

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

5.3.8. Overall risk evaluation and conclusions

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

Comment 1

See my comments above.

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)

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

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

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

6.4. REPORTING THE RESULTS OF PMEM

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

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

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