Adviesraad voor Bioveiligheid
Conseil consultatif de Biosécurité

Advice of the Belgian Biosafety Advisory Council on application EFSA-GMO-DE-2010-86 (maize Bt11 x MIR162 x 1507 x GA21) from Syngenta under Regulation (EC) No. 1829/2003

11 September 2018
Ref. SC/1510/BAC/2018_0701

Context

Application EFSA-GMO-DE-2010-86 was submitted by Syngenta for the marketing of genetically modified (GM) maize Bt11 x MIR162 x 1507 x GA21 (Unique Identifier SYN-BT011 x SYN-IR162-4 x DAS-01507 x MON-00021-9), as well as three subcombinations (Bt11 x MIR162 x 1507, MIR162 x 1507 x GA21 and MIR162 x 1507) independently of their origin, for food and feed uses, import and processing (excluding cultivation) within the European Union, within the framework of Regulation (EC) No. 1829/2003[1].

The four-event stack maize Bt11 x MIR162 x 1507 x GA21 was obtained by conventional crossing (no new genetic modification involved) of the corresponding single events:
- Bt11, expressing the Cry1Ab protein for control of certain lepidopteran pests and the PAT protein that confers tolerance to herbicide products containing glufosinate ammonium;
- MIR162, expressing the Vip3Aa20 protein for control of certain lepidopteran pests and the PMI protein, which acts as a selectable marker;
- 1507, expressing the Cry1F protein which confers protection against certain lepidopteran pests and the PAT protein that confers tolerance to herbicide products containing glufosinate ammonium;
- GA21, expressing the mEPSPS protein that confers tolerance to herbicide products containing glyphosate.

The application was validated by EFSA on 14 June 2012 and a formal three-month consultation period of the Member States was started, lasting until 18 September 2012, 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). Seven 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 forwarded to EFSA.

The opinion of the EFSA Scientific Panel on GMOs was published on 11 July 2018 (EFSA Journal 2018;16(7):5309[2]) 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] https://doi.org/10.2903/j.efsa.2018.5309

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

In delivering the present advice the BAC considered in particular the following information:
- The comments formulated by the experts on application EFSA-GMO-DE-2010-86;
- The opinion of EFSA;
- The advices already adopted by the BAC on the single events and seven subcombinations (stacked events). The conclusions of the BAC for the most recent applications for the single events were as follows:

Event	Application number	BAC advice	Conclusions
Bt11	EFSA-GMO-RX-Bt11	BAC/2009/0904 (17/03/2009)	No major risks for human and animal health or concerning the environment were identified.
MIR162	EFSA-GMO-DE-2010-82	BAC/2012/0785 (29/08/2012)	No major risks for human and animal health or concerning the environment were identified. (a concern about the potential allergenicity of the PMI protein was raised at that time, but this issue has been solved in the meantime)
1507	EFSA-GMO-RX-001	BAC/2017/0186 (21/03/2017)	Unlikely to pose any risk to human and animal health. No risk identified for the European environment.
GA21	EFSA-GMO-RX-005	BAC/2018/0058 (30/01/2018)	Unlikely to pose any risk to human and animal health. No risk identified for the European environment.

All GM maize mentioned in the table above are authorised in the EU for food and feed uses[3], as well as seven combinations of two or more events.

Scientific evaluation

1. Environmental risk assessment

The Biosafety Advisory Council is of the opinion that it is unlikely that the accidental release of maize Bt11 x MIR162 x 1507 x GA21 (i.e. during transport and/or processing) into the European environment[4] will lead to environmental harm.

2. Molecular characterisation

With regard to the molecular characterisation, the Biosafety Advisory Council is of the opinion that the information provided is sufficient and does not raise safety concerns.

3. Assessment of food/feed safety and nutritional value

3.1. Assessment of compositional analysis

Taking into account the previous assessment of the single events and the new data on compositional analysis provided by the applicant for the four-stacked event, the Biosafety Advisory Council agrees with the GMO panel of EFSA that the compositional data of GM maize Bt11 x MIR162 x 1507 x GA21, in comparison with its conventional counterpart, do not raise safety concerns.

[3] See EU register of GM food and feed: http://ec.europa.eu/food/dyna/gm_register/index_en.cfm
[4] As the application doesn't imply cultivation of the GM crop in the EU, a full environmental assessment is as in the case of a cultivation file is not warranted.

3.2. Assessment of toxicity

The Biosafety Advisory Council has evaluated the safety of the newly expressed mEPSPS, PAT, Cry1Ab, Cry1F, Vip3Aa20, and PMI proteins in the context of previous applications, and no safety concerns were identified. Taking into account the updated information considered in the current application, the Council is of the opinion that its previous conclusions remain valid.
The Biosafety Advisory Council is also of the opinion that the combined expression of the newly expressed proteins in the stacked event does not raise toxicological concerns.

3.3. Assessment of allergenicity

The Biosafety Advisory Council has evaluated the safety of the newly expressed mEPSPS, PAT, Cry1Ab, Cry1F, Vip3Aa20, and PMI proteins in the context of previous applications, and no concerns were identified. Since no new information on allergenicity of these proteins has become available, the Council is of the opinion that its previous conclusions remain valid.
Previous advices of the Biosafety Council on GM maize's expressing the PMI protein (see applications EFSA/GMO/UK/2005/11, EFSA/GMO/UK/2007/48, EFSA/GMO/UK/2007/50, EFSA/GMO/UK/2008/56 and EFSA/GMO/DE/2010/82) reflected the concerns expressed by some of the members about the potential allergenicity of the PMI protein due to a possible cross-reactivity with a moderately important latex allergen, Hev b13. On the basis of updated expert opinions (see advice of 23 February 2016 on application EFSA/GMO/DE/2009/66, ref WIV-ISP/41/BAC/2016_0122), the Council concluded that further testing of the potential allergenicity of the PMI protein in humans was not needed from the safety viewpoint.
The Biosafety Advisory Council is also of the opinion that the combined expression of the newly expressed proteins in the stacked event does not raise concerns regarding the allergenicity.

3.4. Nutritional value

The Biosafety Advisory Council is of the opinion that the information provided is sufficient to conclude that the nutritional characteristics of food and feed derived from maize Bt11 x MIR162 x 1507 x GA21 are not expected to differ from those of conventional maize varieties.

4. Monitoring

With regard to monitoring, the Biosafety Advisory Council is of the opinion that the information provided is sufficient.

Conclusion

Based on the whole set of data on maize Bt11 x MIR162 x 1507 x GA21 provided by the applicant, the scientific assessment of the dossier done by the Belgian experts, the opinion of EFSA, the answers of the EFSA GMO panel to the questions raised by the Belgian experts, and the advices already adopted by the BAC on the four single events and seven subcombinations, the Biosafety Advisory Council:

1) Agrees with the GMO panel of EFSA that the potential environmental release of maize Bt11 x MIR162 x 1507 x GA21 is unlikely to pose any threat to the European environment;
2) Agrees with the GMO panel of EFSA that there is no reason to expect interactions between the newly expressed proteins that could impact on the food or feed safety;
3) Agrees with the GMO panel of EFSA that in the context of its proposed uses, maize Bt11 x MIR162 x 1507 x GA21 is unlikely to pose any risk to human and animal health;
4) Considers that the conclusions of the Biosafety Advisory Council on the single events that have been assessed previously (Bt11, MIR162, 1507 and GA21 - see table on page 2) remain unchanged.

In addition, the Biosafety Advisory Council recommends following up any unanticipated allergenicity aspects of the GM maize in monitoring systems.

Dr. Corinne Vander Wauven
President of the Belgian Biosafety Advisory Council

Annex I: Compilation of comments of experts in charge of evaluating the application EFSA/GMO/DE/2010/86 and Comments submitted on the EFSAnet on mandate of the Biosafety Council (ref. BAC_2012_0837)

Bioveiligheidsraad
Conseil de Biosécurité

17/09/2012

Secretariaat
Secrétariat

N./réf. : WIV-ISP/41/BAC_2012_0837
Email. : bac@wiv-isp.be

Compilation of comments of experts in charge of evaluating the application EFSA/GMO/DE/2010/86 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 15 June 2012
Coordinator: Prof. dr. ir. Dirk Reheul
Experts: Leo Fiems (ILVO), Rony Geers (KUL), Johan Grooten (UGent), André Huyghebaert (UGent), Peter Smet (Consultant), Jan Van Doorsselaere (KH Zuid-West Vlaanderen), Bart Van Droogenbroeck (ILVO)
Domains of expertise of experts involved: Genetics, genome analysis, molecular characterisation, genetic engineering, transgene expression, human nutrition, analysis food/feed, substantial equivalence, animal nutrition, toxicology in vitro, general biochemistry, allergology, herbicide tolerance
Secretariat (SBB): Didier Breyer, Adinda De Schrijver, Martine Goossens, Philippe Herman, Katia Pauwels

INTRODUCTION

Dossier **EFSA/GMO/DE/2010/86** concerns an application of the company **Syngenta Crop Protection** for the marketing of the genetically modified **maize Bt11 x MIR162 x 1507 x GA21** for food and feed applications under Regulation (EC) 1829/2003.
The application has been officially acknowledged by EFSA on 14 June 2012.
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 genetically modified plant considered in the application on its 1) molecular, 2) environmental, 3) allergenicity, 4) toxicity and/or 5) food and feed aspects. It was expected that the expert should evaluate if 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.

The comments are structured as in the "Guidance document of the scientific panel on genetically modified organisms for the risk assessment of genetically modified plants and derived food and feed" (EFSA Journal (2004), 99, 1-94). 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 received from the experts

GENERAL COMMENTS

Comments/Questions of the expert(s)

Comment 1

Plants with multiple insertion events are likely to have more transformation-induced mutations and thus carry a greater risk of exhibiting unintended consequences. Genetically modified maize Bt11 x MIR162 x 1507 x GA21 is obtained by traditional breeding of four genetically modified maize lines. So, the chance of mutations is limited.
Most individual events have been assessed and approved by EFSA (2005, 2007, 2012) or are currently under review.
The applicant put forward that potential adverse effects to human and animal health arising from Cry1Ab, PAT, Vip3Aa20, PMI, Cry1F and mEPSPS have previously been assessed and concludes that the potential toxic effects to humans and animals of these proteins could be considered negligible.
Nevertheless, some caution is necessary with regard to safety.

A. GENERAL INFORMATION

Comments/Questions of the expert(s)

Comment 1

No comments.

B. INFORMATION RELATING TO THE RECIPIENT OR (WHERE APPROPRIATE) PARENTAL PLANTS

Comments/Questions of the expert(s)

Comment 1

No comments.

Comment 2

No comments. All provided information is clear.

C. INFORMATION RELATING TO THE GENETIC MODIFICATION

Comments/Questions of the expert(s)

Comment 1

No comments.

Comment 2

No major comments. All the necessary information is provided.

One small remark: In Table C.2.1 (pg. 31) the applicant describes the origin of the 35S promoters used in the "active ingredient cassette" and the "selectable marker cassette, respectively.
For the 35S promotor in the "active ingredient cassette" with a size of 509 bp, the following description is given:
"Promoter from the cauliflower mosaic virus (CaMV) (Gardner *et al.*, 1981), supplemented with the intron sequence 6 (471 bp) from the alcohol dehydrogenase 1S (*adh1*) gene from maize."
This could give the reader the idea that the intron sequence might be part of the promoter sequence. To avoid confusion it is better not to include the information of the intron sequence in the functional description of the promoter sequence. The intron itself is discussed as the second functional element in Table C.2.1 anyway. The same remark applies to the selectable marker cassette.
SBB: We agree with this comment, but as this is more a remark to the applicant (to adapt text), we wonder if it is relevant to send this remark to EFSA?
Plus as said in comment below: the traits have been described previously in the application.

D. INFORMATION RELATING TO THE GM PLANT

D.1 DESCRIPTION OF THE TRAITS AND CHARACTERISTICS WHICH HAVE BEEN INTRODUCED OR MODIFIED

Comments/Questions of the expert(s)

Comment 1

No comments.

Comment 2

No comments or questions.
The traits and characteristics present in the stacked event Bt11 x MIR162 x 1507 x GA21 have been described previously in the application of the four single events. For three of the four events (B11, 1507 and GA21), the information has been previously reviewed by EFSA. Event MIR162 and stacked event Bt11 x MIR162 x GA21 are currently under scientific review.
All necessary information about the traits and characteristics was provided as a summary of the relevant sections of the dossier of the single events.

D.2. INFORMATION ON THE SEQUENCES ACTUALLY INSERTED OR DELETED

Comments/Questions of the expert(s)

Comment 1

No comments.

Comment 2

No major comments or questions.

- I agree with the conclusions from Appendix 2 regarding "The copy number of all detectable inserts, both complete and partial", confirming the intactness of the of events combined by crossing in the stacked event:
"... the analyses showed that the predicted DNA hybridization patterns from each individual event were confirmed in Bt11 x MIR162 x 1507 x GA21 maize, demonstrating preservation of the integrity of the transgenic insert from each individual event to Bt11 x MIR162 x 1507 x GA21 maize"

- In addition, it is clear from the information derived from new BLASTN and BLASTX analyses that have been performed on the genomic sequences flanking the Bt11, MIR162, 1507 and GA21 maize inserts, using up-to-date nucleotide and protein databases, that none of the inserts in the stacked event disrupts known endogenous maize genes, as was the case in the single events.

D.3. INFORMATION ON THE EXPRESSION OF THE INSERT

Comments/Questions of the expert(s)

Comment 1

No comments.

Comment 2

Minor remarks:
- The heading of table D.3(a)-1 is a bit confusing as it lists the protein expressed per event, while the data in the table is given in a different order. This is specifically confusing to interpret the PAT expression data, the only protein that in the stacked maize contains two functional copies of the pat gene and is therefore not expected to contain the same concentration of PAT protein as the single events Bt11 and 1507 maize, each with one functional copy of the pat gene.
SBB: We don't grasp this comment. We think it is because PAT appears in two events that the data on PAT have been addressed as last (on p.61 of Technical Dossier), so that one can see the expression levels in the single events and the stack?
- The applicants mentions significant differences in protein expression in the text, e.g. on pg 58 it is stated: "*Although some statistically significant differences were seen, these differences were small or*

not consistent across the growing season." A detailed explanation about the experimental setup and statistical method used is only included in Appendix 9. For reasons of clarity these can be repeated in the body of the dossier as well. The significant differences observed are not indicated in the table. Why not?

SBB: Again, this is more a comment to the applicant to adapt text/table. So not really a relevant comment for EFSA to address...

All information on statistical difference is indeed available in Appendix 9.

D.4. INFORMATION ON HOW THE GM PLANT DIFFERS FROM THE RECIPIENT PLANT IN: REPRODUCTION, DISSEMINATION, SURVIVABILITY

Comments/Questions of the expert(s)

Comment 1

No comments. All provided information is clear.

D5. GENETIC STABILITY OF THE INSERT AND PHENOTYPIC STABILITY OF THE GM PLANT

Comments/Questions of the expert(s)

Comment 1

No comments. All provided information is clear.

- From the conclusions formulated on pg 47, based on the Southern blot analysis described in Appendix 2, I agree with the following statement about the stability of the inserts in the stacked event: "*The results of this study demonstrate that Bt11 x MIR162 x 1507 x GA21 maize produced by conventional breeding crosses combining Bt11, MIR162, 1507 and GA21 maize have stably inherited the cry1Ab and pat genes from Bt11 maize, the vip3Aa20 and pmi genes from MIR162 maize, the cry1F and pat genes from 1507 maize and the mepsps gene from GA21 maize, retaining the hybridization patterns as predicted."*

- In addition I agree with the statement formulated on pg. 66-67, which is based on ELISA expression study of the stacked and single events "*The results also confirm that there is no evidence for any potential interactions or adverse effects arising from the combined expression of the introduced proteins in the higher order stack...."*

D.6. ANY CHANGE TO THE ABILITY OF THE GM PLANT TO TRANSFERR GENETIC MATERIAL TO OTHER ORGANISMS

Comments/Questions of the expert(s)

D.7. INFORMATION ON ANY TOXIC, ALLERGENIC OR OTHER HARMFUL EFFECTS ON HUMAN OR ANIMAL HEALTH ARISING FROM THE GM FOOD/FEED

D.7.1 Comparative assessment

Comments/Questions of the expert(s)

Comment 1

Maize Bt11 x MIR162 x 1507 x GA21 is a combined trait obtained by conventional breeding. In previous assessments EFSA concluded that the single events are compositionally equivalent to their near-isogenic conventional counterparts.

The applicant states that there is no reason to indicate that the combination by conventional breeding would result in changes in the composition of maize.

D.7.2 Production of material for comparative assessment

Comments/Questions of the expert(s)

Comment 1

The approach chosen is equivalent to the previous dossiers. A comparative study was conducted with maize Bt11 x MIR162 x 1507 x GA21 and the corresponding non-transgenic near-isogenic control maize. Maize was grown at six locations in the US.

The levels of nutrients in grain and forage of maize Bt11 x MIR162 x 1507 x GA21 was compared with the near-isogenic counterparts. The ILSI database, 2009, was also used as a reference.

No further comment.

D.7.3 Selection of material and compounds for analysis

Comments/Questions of the expert(s)

Comment 1

Nutrients studied in grain and forage are comparable to previous applications and include proximates, starch, minerals, vitamins, amino acids, fatty acids, secondary metabolites and antinutrients.

The overall conclusion of the applicant is that the composition of maize Bt11 x MIR162 x 1507 x GA21 is equivalent to conventional maize apart from the introduced traits.

I agree with this conclusion.

D.7.4 Agronomic traits

Comments/Questions of the expert(s)

D.7.5 Product specification

Comments/Questions of the expert(s)

Comment 1

No further comment.

D.7.6 Effect of processing

Comments/Questions of the expert(s)

Comment 1
The applicant refers to previous applications. Wet and dry milling are traditional processing techniques for maize. As the composition of maize Bt11 x MIR162 x 1507 x GA21 is equivalent to commercial maize there is no reason to suggest that the processing techniques would be influenced.

I agree with this conclusion.

D.7.7 Anticipated intake/extent of use

Comments/Questions of the expert(s)

D.7.8 Toxicology

Comments/Questions of the expert(s)

Comment 1

No new genetic modification occurred in Bt11 x MIR162 x 1507 x GA21 maize because of conventional breeding. Therefore, it can be assumed that there are no extra risks compared to the single GM events: Cry1Ab, PAT, Vip3Aa20, PMI, Cry1F and mEPSPS. This is not be a guarantee that the effect of a combination of events on toxicity is negligible, taking into account that in the expression level of the introduced traits the GM stacked event might be different from that of the GM parental lines (De Schrijver et al., 2007).

SBB: According to the information in the application, the expression levels are comparable... Thus this reasoning is not applicable here...

A multi-generation study, performed with mice, showed that average litter size and weight, as well as number of weaned pups, were lower in NK603 x MON810 maize, compared to the near isogenic line, and differences were statistically significant in the 3rd and 4th litters (Velimirov et al., 2008).

SBB: We do not see why a multi-generation should be asked for. Considering the spectrum activity of the traits, there is no reason to believe that combining the traits will affect human/animal health.

Further, as far as we are aware the BAC has never raised the issue that multi-generation studies are necessary. Up till now, short-term feeding trials have been considered appropriate as a first step to assess potential adverse effects on animal health (before deciding if any further testing, e.g. multi-generation studies, is necessary.

Comment 2

General conclusion:

1. The single events are considered as save due to earlier notifications
2. The amounts of expressed proteins in the stacked event are comparable to the single events
3. The amounts of secondary metabolites and antinutrients are comparable to the non-modified comparator
4. No new toxicological data are available.

At this moment no further testing is needed.

D. 7.8.1 Safety assessment of newly expressed proteins

Comments/Questions of the expert(s)

D.7.8.2 Testing of new constituents other than proteins

Comments/Questions of the expert(s)

D.7.8.3 Information on natural food and feed constituents

Comments/Questions of the expert(s)

D.7.8.4 Testing of the whole GM food/feed

Comments/Questions of the expert(s)

D.7.9 Allergenicity

Comments/Questions of the expert(s)

Comment 1

It is assumed that it is unlikely that any interaction between the newly expressed proteins would alter the pattern of expression of endogenous proteins/potential allergens.

Comment 2

This dossier is highly similar in nature and scope of modifications and intended applications (resistance to pests and herbicides) with dossier GMO/DE/2011/99. Accordingly, the same remarks and concerns raised in dossier GMO/DE/2011/99 are also of relevance for the present application.

The potential for allergenicity of the individual traits has already been assessed in separate EFSA applications on the basis of an evaluation of the allergenicity of the source organisms, amino acid sequence comparisons, and the physicochemical properties and abundance of the individual proteins. This resulted in the conclusion of a low allergenicity risk for either of the individual traits. Combining these traits did not significantly alter the expression levels of the individual proteins except for the PAT protein where modestly increased expression levels were observed that however are unlikely to significantly affect uptake levels and hence allergenicity.

On p94, top paragraph, the applicants indicate the likelihood that "*any interactions between the newly expressed proteins and metabolic pathways of maize would alter the pattern of expression of endogenous proteins/potential allergens*" are unlikely based on a conclusion reached by the EFSA GMO panel in reference EFSA, 2010. I looked up this exhaustive document but did not find the conclusion referred to. I may have missed it and therefore would like a more precise reference for this strong statement.

SBB: The citation done by the applicant as EFSA, 2010 refers to the Scientific Opinion on application EFSA-GMO-UK-2008-56 and more precisely on point 5.1.5.2 relating to the assessment of the allergenicity of the whole GM plant.

A final remark concerns enzymatic breakdown products from the targeted herbicides. As I already mentioned in a previous report (report on dossier GMO/NL/2011/91), such breakdown products may accumulate in (parts of) the GM plant, cause toxicity upon consumption and/or modify endogenous proteins with increased risk for allergenicity. Yet, this feature is not addressed at all by the applicants although logic suggests an increased risk as a result of an increased resistance range of the GM plant.

SBB: The remark above relates to the still open discussion on where this kind of assessment should be made (pesticide legislation or GMO legislation).

Additional comment from SBB:
There are doubts regarding the potential allergenicity of PMI protein (Advice BAC on dossier EFSA/GMO/DE/2010/82). The applicant refers to sequence homology and the three-dimensional spatial structure of the PMI protein to conclude on absence of potential allergenic effect. The question remains why the applicant has not performed in vitro and/or in vivo tests which could have taken away the doubts?

D.7.10 Nutritional assessment of GM food/feed

Comments/Questions of the expert(s)

Comment 1

Bt11 x MIR162 x 1507 x GA21 maize forage and grain may not be materially different in nutrient composition than forage and grain from the maize reference hybrids grown under the same conditions.
However, in genetic modified maize, in which the expression of Cry1Ab protein is introduced, principal component analysis showed metabolic variations involving 50% changes in osmolytes and branched amino acids (Manetti et al., 2006).

D.7.11 Post-market monitoring of GM food/feed

Comments/Questions of the expert(s)

D.8. MECHANISM OF INTERACTION BETWEEN THE GM PLANT AND TARGET ORGANISMS (IF APPLICABLE)

Comments/Questions of the expert(s)

D.9. POTENTIAL CHANGES IN THE INTERACTIONS BETWEEN THE GM PLANT WITH THE BIOTIC ENVIRONMENT RESULTING FROM THE GENETIC MODIFICATION

D.9.1. Persistence and invasiveness

Comments/Questions of the expert(s)

D.9.2 Selective advantage or disadvantage

Comments/Questions of the expert(s)

D.9.3 Potential for gene transfer

Comments/Questions of the expert(s)

Comment 1

This item is not relevant, as the application of maize Bt11 x MIR162 x 1507 x GA21 is not intended for cultivation.

D.9.4 Interactions between the GM plant and target organism

Comments/Questions of the expert(s)

D.9.5 Interactions of the GM plant with non-target organism

Comments/Questions of the expert(s)

D.9.6 Effects on human health

Comments/Questions of the expert(s)

Comment 1

Because of some long-term effects in animals (see comments with regard to D.7.8 and D.9.7), it is questionable if Bt11 x MIR162 x 1507 x GA21 maize will not exert a long-term effect in humans.

D.9.7 Effects on animal health

Comments/Questions of the expert(s)

Comment 1

No information found for evaluation on experimental design.
SBB: No whole GM food/feed tests were performed (see also comment below).

Comment 2

As far as can be verified from the Technical dossier, no animal performance experiments have been conducted. Referring to Bt11 x 59122 x MIR604 x 1507 x GA21 maize, it can be assumed that Bt11 x MIR162 x 1507 x GA21 maize will not exert an adverse effect in short-term feeding trials. However, short-term feeding experiments may not always be appropriate. Feeding MON810 maize, containing Cry1Ab protein, is safe for pigs, but there was a tendency for an increase in kidney weight (Walsh et al., 2012). Spiroux de Vendômois et al. (2009) detected GM-maize linked effects due to Cry1Ab either after 14 weeks of consumption or at a high GM feed dose in the diet. Blood cells, adrenal gland and kidney weights, blood urea nitrogen and spleen weight were affected. They observed a sex-dependency for the measured parameters in liver and kidneys.

SBB: see comment above on long-term feeding studies

D.9.8 Effects on biogeochemical processes

Comments/Questions of the expert(s)

D.9.9 Impacts of the specific cultivation, management and harvesting techniques

Comments/Questions of the expert(s)

D.10. POTENTIAL INTERACTIONS WITH THE ABIOTIC ENVIRONMENT

Comments/Questions of the expert(s)

D.11. ENVIRONMENTAL MONITORING PLAN

D.11.1 General

Comments/Questions of the expert(s)

D.11.2 Interplay between environmental risk assessment and monitoring

Comments/Questions of the expert(s)

D.11.3 Case-specific GM plant monitoring

Comments/Questions of the expert(s)

D.11.4 General surveillance of the impact of the GM plant

Comments/Questions of the expert(s)

D.11.5 Reporting the results of monitoring

Comments/Questions of the expert(s)

References

De Schrijver, A., Devos, Y., Van den Bulcke, M., Cadot, P., De Loose, M., Reheul, D., Sneyers, M. 2007. Risk assessment of GM stacked events obtained from crosses between GM events. Trends Food Sci. Technol. 18: 101-109.

EFSA, 2005. Opinion of the Scientific Panel on Genetically Modified Organisms on a request from the Commission related to the notification (Reference C/F/96/05.10) for the placing on the market of insect resistant genetically modified maize Bt11, for cultivation, feed and industrial processing, under Part C of Directive 2001/18/EC from Syngenta Seeds. EFSA Journal 3: (231) 1-33

EFSA, 2007. Opinion of the Scientific Panel on Genetically Modified Organisms on applications (references EFSA-GMO-UK-2005-19 and EFSA-GMO-RX-GA21) for the placing on the market of glyphosate-tolerant genetically modified maize GA21, for food and feed uses, import and processing and for renewal of the authorisation of maize GA21 as existing product, both under Regulation (EC) No 1829/2003 from Syngenta Seeds S.A.S. on behalf of Syngenta Crop Protection AG. EFSA Journal 5: (541) 1-25

EFSA, 2012. Scientific Opinion on application (EFSA-GMO-DE-2010-82) for the placing on the market of insect-resistant genetically modified maize MIR162 for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Syngenta. EFSA Journal 10: (2756) 1-27.

Manetti, C., Bianchetti, C., Casciani, L., Castro, C., Di Cocco, M.E., Miccheli, A., Motto, M., Conti, F. 2006. A metabonomic study of transgenic maize (Zea mays) seeds revealed variations in osmolytes and branched amino acids. J. Exp. Bot. 57: 2613-2625.

Spiroux de Vendômois, J.,Roullier, F., Cellier, D., Séralini, G.E. 2009. A Comparison of the effects of three GM corn varieties on mammalian health. Int. J. Biol. Sci. 5: 706-726.

Velimirov, A., Binter, C., Zentek, J. 2008. Biological effects of transgenic maize NK603xMON810 fed in long term reproduction studies in mice. Available online: http://www.biosicherheit.de/pdf/aktuell/zentek_studie_2008.pdf (accessed on 18 July 2012).

Walsh, M.C., Buzoianu, S.G., Gardiner, G.E., Rea, M.C., Ross, R.P., Cassidy, J.P., Lawlor, P.G. 2012. Effects of short-term feeding of Bt MON810 maize on growth performance, organ morphology and function in pigs. Br. J. Nutr. 107: 364-371.