Adviesraad voor Bioveiligheid
Conseil consultatif de Biosécurité

Advice of the Belgian Biosafety Advisory Council on application EFSA-GMO-BE-2015-125 from Monsanto under Regulation (EC) No. 1829/2003

Adopted on 29 May 2018
Ref. SC/1510/BAC/2018_0328

Context

Application EFSA-GMO-BE-2015-125 was submitted by Monsanto on 26 June 2015 for the marketing of genetically modified (GM) maize MON87403 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 MON 87403 was developed by *Agrobacterium tumefaciens*-mediated transformation and expresses the truncated protein AtHB17Δ113 from *Arabidopsis thaliana*, a transcription factor that modulates HD-Zip II regulated pathways in the ear leading to increase in ear growth and grain yield at harvest.

The application was officially acknowledged by EFSA on 2 October 2015 and a formal three-month consultation period of the Member States was started, lasting until 2 January 2016, 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). Nine 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 8 March 2018 (EFSA Journal 2018;16(3):5225[2]), and published on 28 March 2018 together with the responses from the EFSA GMO Panel to comments submitted by the Member States during the three-month consultation period. On 18 April 2018 the opinion of EFSA was forwarded to the Belgian experts. They were invited to give comments and to react if needed.

In delivering the present advice the Biosafety Advisory Council considered in particular the comments formulated by the experts on application EFSA-GMO-BE-2015-125 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://www.efsa.europa.eu/en/efsajournal/pub/5225

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Scientific evaluation

1. Environmental risk assessment

The Biosafety Advisory Council is of the opinion that it is unlikely that the accidental release of maize MON87403 (i.e. during transport and/or processing) into the European environment[3] will lead to any unwanted effects.

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

The Biosafety Advisory Council agrees with the GMO panel of EFSA that the compositional data of GM maize MON87403, in comparison with its conventional counterpart, does not raise safety concerns.

3.2. Assessment of toxicity

The Biosafety Advisory Council agrees with the GMO panel of EFSA that the available data on the toxicity of GM maize MON87403, in comparison with its conventional counterpart, does not raise safety concerns.

3.3. Assessment of allergenicity

The Biosafety Advisory Council agrees with the GMO panel of EFSA that the available data on the allergenicity of GM maize MON87403, in comparison with its conventional counterpart, does not raise safety concerns.

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 maize MON87403-derived food and feed 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.

[3] As the application doesn't imply a cultivation of the GM crop in the EU, a full environmental assessment is not required in EFSA procedure and was not performed.

Conclusion

Based on the scientific assessment of the dossier done by the Belgian experts, taking into account the opinion of EFSA, the answers of the EFSA GMO panel to the questions raised by the Belgian experts, the answers of the applicant to the EFSA GMO panel questions and considering the data presently available, the Biosafety Advisory Council:

1) Agrees with the GMO panel of EFSA that the potential environmental release of maize MON87403 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, maize MON87403 is unlikely to pose any risk to human and animal health;

In addition the Biosafety Advisory Council recommends following up any unanticipated allergenicity aspects of the GM maize in the existing allergenicity 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/BE/2015/125 and Comments submitted on the EFSAnet on mandate of the Biosafety Council (ref. BAC_2016_003)

Bioveiligheidsraad
Conseil de Biosécurité

04/01/2016

Secretariaat
Secrétariat

O./ref.: WIV-ISP/41/BAC_2016_0003
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Compilation of comments of experts in charge of evaluating the application EFSA/GMO/BE/2015/125
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 20 October 2015.
Coordinator: Geert Angenon
Experts: Jacques Dommes (ULg), Patrick du Jardin (ULg), Leo Fiems (ILVO), Johan Grooten (UGent), André Huyghebaert (UGent), Peter Smet (Consultant), Frank Van Breusegem (UGent), Jan Van Doorsselaere (KATO), Hadewijch Vanhooren (KUL)
Domains of expertise of experts involved: Molecular characterisation, DNA/RNA/protein analysis, herbicide tolerance, analysis of food/feed, food/feed processing, toxicology, general biochemistry, statistics, immunology, alimentary allergology, plant allergens, maize, breeding techniques, agronomy, plant biology.
SBB: Didier Breyer, Fanny Coppens, Katia Pauwels

♦ INTRODUCTION

Dossier **EFSA/GMO/BE/2015/125** concerns an application submitted by the company **Monsanto** for authorisation to place on the market genetically modified **Maize MON 87403** 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 2 October 2015.

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/questions received from the experts

GENERAL COMMENTS

Comment 1
Based on the data and the information presented in this dossier by the applicant it is unlikely that MON 87403 maize will exert adverse effects on human and animal health and the environment in the context of its intended use in the EU.

Comment 2
None.

Comment 3
No comments.

A. HAZARD IDENTIFICATION AND CHARACTERISATION

A.1. INFORMATION RELATED TO THE RECIPIENT OR (WHERE APPROPRIATE) THE PARENTAL PLANT

Comment 1
No comments.

Comment 2
No comment. Adequate information was provided.

Comment 3
None.

Comment 4
No comments.

A.2. MOLECULAR CHARACTERISATION

A.2.1. INFORMATION RELATING TO THE GENETIC MODIFICATION including:

- Description of the methods used for the genetic modification
- Source and characterization of nucleic acid used for transformation
- Nature and source of vector(s) used

Comment 1
No comments.

Comment 2
No comment. Adequate information was provided.

Comment 3
The applicant performs a similarity search with the ATHB17Δ113 protein newly expressed in this GM maize as a query and a complete protein database PRT_2015. A highly significant hit is found with

patented plant sequences but the applicant concludes that there is no biologically relevant similarity with bioactive peptides, hence no indication of potential adverse effect (main text page 34 and FROM CBI: Basu and Silvanovich, 2015d). However, in the absence of any information regarding the function of these patented sequences, such conclusion is not substantiated. The applicant should be asked to develop his argumentation in this regard.

Comment 4
No comments.

A.2.2. INFORMATION RELATING TO THE GM PLANT including:

- Description of the trait(s) and characteristics which have been introduced or modified
- Information on the sequences actually inserted or deleted
- Information on the expression of the insert
- Genetic stability of the inserted/modified sequence and phenotypic stability of the GM plant

Comment 1
Page 36: has it been investigated which genes/proteins are up-regulated as a consequence of the overexpression of the transcription factor ATHB17-113? It is shown that this protein poses no risk with respect to toxicity/allergenicity, but is it known which down-stream genes are upregulated?

Page 61: the ATHB17-113 protein level (gene expression under the control of the 35S promotor) is (to my opinion) low (eg 0,001 microgram/gDW). Data from other dossiers show that – in general - expression of genes driven by the 35S promotor are in the range of microgram/gDW. What could be the explanation for this low protein level? Position effects?

Comment 2
Adequate information was provided, and adequate sequencing and bioinformatic evaluations were carried out. The results of the molecular characterization do not raise any safety concern.

Comment 3
Comment #1.
NGS/JSA is used for the molecular characterization, i.e. for insert number determination, control of absence of unintended DNA sequences from plasmid vector, and for generational study of insert stability. However, the applicant provides limited information allowing the risk assessor to validate the method in the particular case of the application. In particular, Garnaat et al. say (main text page 14) : *The depth of coverage (the median number of times each base of the genome is independently sequenced) was ≥75x for each genome. It has previously been demonstrated that 75x coverage of the soybean genome is adequate to provide comprehensive coverage and ensure detection of inserted DNA (Kovalic et al., 2012) and similarly 75x coverage provides comprehensive coverage of the maize genome (Clarke and Carbon, 1976). The level of sensitivity of this method was demonstrated by detection of a positive control spiked at 1/10th copy-per-genome equivalent.*
It is unclear how the paper (Clarke and Carbon, 1976) was used to determine coverage depth of the maize genome. Positive controls (spiked DNA) are mentioned but a missing information is the variablity of coverage depth *across* the genome. Indeed, depending on eu-/heterochormatic regions, GC contents etc., variability is expected in sequencing efficacy and coverage depth along the genomic DNA and how this is taken into consideration is unclear. Considering that NGS/JSA methodology is rather new in the risk assessment of GMO, detailed justification of the assumptions made should be

provided. This is needed for the quality check which is expected from risk assessors when analyzing the applicants' dossiers.

Coordinator comment
How the methodology mentioned in reference Clarke and Carbon, 1976 is used to calculate that 75X coverage is appropriate, is indeed unclear.

Comment #2.
When searching for backbone alignments of NGS reads (main dossier page 48), a few of such reads are found but discarded on the basis of a high ratio (ca.1000 fold) between 'intended' (T-DNA) reads and 'unintended' (backbone) reads. The applicant should justify his rationale and indicate which threshold values in such ratios would be used to conclude on significant vs. non-significant reads alignments. Again (cfr. previous comment), such clarification would be helpful to build up a sound risk assessment of GMOs using NGS.

Comment #3.
Since the newly expressed protein is quite a « new one » in RA and belongs to a family of plant transcriptional regulators, the quality and specificity of the antibodies as claimed by the applicant should be supported by experimental data, i.e. western blots where potential cross reactions with native HD-Zip II proteins could be assessed. The applicant should provide such western blots (only western blots against purified preparations are displayed, e.g. figure 15 of main dossier).

Coordinator comment
In non-confidential reference (Rice et al. 2014 a) Western blot is shown that includes an extract from a WT plant; there is 40kDa band in extracts of WT and transgenic lines, which is thus an endogenous cross-reacting protein. The size of this cross-reacting protein is very different from that of full length and truncated ATHB17.

Comment 4
No major comments. But in the CBI Reference Garnaat et al., 2014 that describes in more detail the methodology and results of the NGS/JSA analysis on the insertion position of the integrated plasmid DNA is mentioning on p14: ….75x coverage of the soybean genome is adequate to provide comprehensive coverage and ensure detection of the inserted DNA (Kovalic et al 2012) and similarly 75x coverage provides comprehensive coverage of large genomes such as maize (Clarke and Carbon **1976**). This is an awkward reference. I could not access the paper, but based on the title it relates to the analysis of E.coli genomes……In 1976, no data on coverage needs of NGS based sequences were at hand for plant genomes….

Coordinator and SBB comment
This comment is similar to the one above, which was submitted to EFSA.

A.3. COMPARATIVE ASSESSMENT

A.3.1. CRITERIA FOR THE SELECTION OF COMPARATOR(S)

Comment 1
None.

Comment 2
Maize 87403 is compared with a variety with similar genetic background. The breeding program is described in detail. Several conventional varieties with a history of safe use were also included.

No remarks.

A.3.2. FIELD TRIALS: EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS

Comment 1
For agronomic and phenotypic analysis, MON 87403 and MPA640B maize, and reference varieties were planted in a randomized complete block design with four replicates at each of eight field sites in the US during the 2012 season (P.71 of the technical dossier). How many hectares have been involved in the maize production to carry out the agronomic and phenotypic analyses and the compositional analysis?

Comment 2
None.

Comment 3
No remarks.

A.3.3. COMPOSITIONAL ANALYSIS

Comment 1
Sixty-two different components were effectively analysed. Differences were only observed between MON 87403 maize and the conventional counterpart at the 10% significance level for vitamin B2 in the grain, and calcium and NDF in the forage. However, these ranges of vitamin B2, calcium and NDF values for MON 87403 maize overlapped with the ranges of vitamin B2, calcium and NDF values for the conventional counterpart, so that the differences are not relevant from a feed and food perspective.

Comment 2
The compositional analysis was performed on grain and forage from maize 87403, the conventional counterpart and 17 reference varieties.
The OECD document from 2002 was followed for the selection of compounds for analysis.
Grain samples were assessed for proximates, carbohydrates, fibre, amino acids, fatty acids, minerals, vitamins, anti-nutrients, and secondary metabolites.
Forage samples were analyses for proximates, carbohydrates, fibre and minerals.
I will not repeat my comments on the selection of compounds and the methods used as the answer to my remark is that the OECD guidelines from 2002 were followed.

In the statistical analysis it was demonstrated that maize 87403 is equivalent to the set of reference maize samples. The values for most compounds were found to be in equivalence category I outcome type 1. Two nutrients of grains, vitamin B2 and moisture were in category I outcome type 2. This was also the case for calcium in forage. A significant difference was found for the NDF fraction in forage, but not in grain. The applicant discussed these results obtained according to the EFSA guidelines for statistical evaluation.

The applicant concludes that maize 87403 is compositionally similar to the conventional maize comparators.

I agree with this conclusion.

Comment 3
No comments.

A.3.4. AGRONOMIC AND PHENOTYPIC CHARACTERISTICS

Comment 1
Although MON 87403 maize is not intended for cultivation in the EU, the agricultural benefits of the use of MON 87403 maize are not clearly described. P.36 of the technical dossier refers to the potential for an increased grain yield at harvest, but this is not confirmed by the data of Table 11 of the technical dossier, although a significant increase in the ear weight at silking in transgenic events in comparison with conventional maize has been reported (Rice et al., 2014).

Coordinator comment
Comment 2 below is similar.

Comment 2
The applicant describes the intended trait resulting from the genetic modification in the following terms (technical dossier page 36) :
« Thus, ear biomass, which is set during early reproductive stages, is considered an important determinant of reproductive success and a larger ear biomass at early reproductive stages is associated with increased grain yield at harvest. »

However the agronomic characteristics assessed in the comparative analysis do not indicate any yield increase (see table on page 85), raising the question of whether the intended trait was properly expressed in the analysed materials. The applicant should comment on this.

Comment 3
In section 1.3.5.3 Environmental interaction evaluations it is mentioned that no differences were observed between maize 87403 and the conventional counterpart for the assessed diseases amongst others for *Fusarium* sp. This is an important conclusion as maize is known to be sensitive to the presence of particular mycotoxins.

A.3.5. EFFECTS OF PROCESSING

Comment 1
The wet and dry milling processes for converting maize into consumption products are reviewed. The applicant concludes that it is highly likely that maize 87403 and its derived food and feed products are not different from the equivalent foods originating from the conventional maize.

I fully agree.

It is striking that in the discussion attention is given to xanthofyll the yellow pigment of maize. Xanthofyll is an important constituent in maize as well in human as animal nutrition. Remarkably xanthofyll is not included in the OECD list.

A.4. TOXICOLOGICAL ASSESSMENT

A.4.1. METHODOLOGY USED FOR TOXICITY TESTS

A.4.2. ASSESSMENT OF NEWLY EXPRESSED PROTEINS including:

- Molecular and biochemical characterisation of the newly expressed proteins
- Up-to-date bioinformatic search for homology
- Information on the stability of the protein under the relevant processing and storage conditions for the food and feed derived from the GM plant
- Data concerning the resistance of the newly expressed protein to proteolytic enzymes
- Repeated dose toxicity studies using laboratory animals

Comment 1

The applicant stated that DNA released by plant tissues will be mostly degraded during the digestive processes (P.155 in the technical dossier). However, Sharma et al. (2006) reported that transgenic feed-ingested DNA fragments can survive the gastrointestinal tract and uptake into gut epithelial tissues can occur.

Nevertheless, based on the weight of evidence in this dossier:

- the lack of structural or functional relationship of MON 87403 ATHB17∆113 to proteins that adversely affect human or animal health
- the history of safe use of proteins with a high sequence identity to the ATHB17∆113 protein and its source organism
- the negligible human exposure to MON 87403 ATHB17∆113 protein from maize consumption: mean ATHB17∆113 protein concentration in MON 87403 of 0.0018 µg/g dry weight in forage and below the limit of detection in grain
- the digestibility of MON 87403 ATHB17∆113
- the reduced activity of E. coli-produced ATHB17∆113 upon heat treatment
- the lack of acute toxicity of the ATHB17∆113 protein at doses several orders of magnitude higher than anticipated human exposure: no test substance-related effects were found on survival, clinical observations, body weight, food consumption, locomotor activity parameters, clinical pathology, or ophthalmic observations after a 90-d study in Sprague-Dawley rats,

it is unlikely that MON 87403 maize will pose serious risks for toxicity.

Comment 2

The introduced ATHB17Δ113 DNA binding protein was extensively characterised. An up-to-date bioinformatic search for homology to toxins was provided. The equivalence of the plant and the *E. coli* produced protein used in the tests (stability, resistance to proteolytic enzymes, acute toxicity) was shown. No 28-day repeated oral toxicity study with the protein was conducted. However, we support the view that no additional study should be made available. There is an acute toxicity study available that is used to calculate the anticipated intake of the ATHB17Δ113 protein and there is a 90-day feeding study provided conducted with rats using 33% MON88403 ground maize grain meal. Taken all data together, there are no indications that the ATHB17Δ113 protein would have toxic effects.

No further comments or questions.

Comment 3
Figure 15 (main dossier page 103) shows a western blot where the immunoreactive bands have apparent molecular masses below 20 kDA, whilst the stained purified proteins shown in figure 14 and the expected MW are above 20 kDa (22 kDa). Why this discrepancy ?

Comment 4
7a) Degradation of the ATHB17Δ113 protein in simulated gastric and intestinal fluid (Wang, 2014).

The *E. coli*-produced ATHB17Δ113 purified protein was rapidly degraded in simulated gastric fluid (SGF) as demonstrated by Wang. More than 97.5% degraded within 30 seconds.

Digestion in simulated intestinal fluid (SIF) was also assessed. More than 93.5% degraded within 5 minutes.

7c) 28 Day Repeat Dose Toxicity Study by Oral Gavage in Rats. ().

Not performed. No further testing is needed.

7d) ATHB17Δ113: Sequence homology with known toxins (Basu and Silvanovich, 2015d)

The results of this analysis indicate that no biologically relevant sequence similarities were observed between the MON 87403 ATHB17Δ113 protein and any toxin, or biologically active proteins that would be harmful to human or animal health.

A.4.3. ASSESSMENT OF NEW CONSTITUENTS OTHER THAN PROTEINS

Comment 1
No comments or questions.

A.4.4. ASSESSMENT OF ALTERED LEVELS OF FOOD AND FEED CONSTITUENTS

Comment 1
An extensive comparative compositional analysis was conducted in grain and forage with the components analyses according to the OECD consensus documents for maize composition (OECD 2002) and statistics according to EFSA guidelines and EFSA scientific opinion (equivalence and difference tests). Based on the results of the statistic tests, MON 87403 was found compositional similar to the conventional maize reference varieties grown in the same study. No further comments or questions.

A.4.5. ASSESSMENT OF THE WHOLE FOOD AND/OR FEED DERIVED FROM GM PLANTS

Comment 1
A 90-day feeding study was made available conducted with rats using 33% MON88403 or 33% MPA640B ground maize grain meal. The study was designed according the OECD 1998a OECD guideline 408 and according the scientific opinion EFSA 2011c. No adverse effects were detected. No further comments or questions.

Comment 2

b) 90-Day rat feeding study (WIL-50414, 2014).

33% grain from MON 87403 (16M + 16F)
33% control (16M + 16F)

Survival: OK.

There were no test substance-related clinical observations.
There were no test substance-related effects on body weights.
There were no test substance-related effects on food consumption.
There were no test substance-related alterations in hematology and coagulation parameters.
There were no test substance-related alterations in serum chemistry parameters.
Urinalysis parameters were unaffected by test substance administration.
No ophthalmic lesions indicative of toxicity were observed in any of the test substance-treated groups.
Review of the gross necropsy observations revealed no observations that were considered to be associated with administration of the test substance.
There were no test substance-related alterations in organ weights.
There were no test substance-related or statistically significantly different histologic changes.

No further testing is needed.

A.5. ALLERGENICITY ASSESSMENT

A.5.1. ASSESSMENT OF ALLERGENICITY OF THE NEWLY EXPRESSED PROTEIN including:

- Amino acid sequence homology comparison between the newly expressed protein and known allergens using a comprehensive database
- Specific serum screening
- Pepsin resistance and in vitro digestibility tests
- Additional tests

Comment 1
Based on the weight of evidence in this dossier:
- the safe consumption of near relatives of *A. thaliana* by humans and animals
- the lack of biologically relevant sequence similarities to allergens when the ATHB17Δ113 protein sequence was used as a query for a FASTA search
- ATHB17Δ113 protein is rapidly digested in SGF and SIF

it is assumed that MON 87403 maize does not pose a serious allergenic risk, and that it is comparable with conventional maize with regard to allergenicity.

Comment 2
Adequate bioinformatic analyses and experiments were carried out. No safety concern.

Comment 3
None.

Comment 4
As indicated by the applicant, the present GM maize is most likely to be commercialized as part of a stacked event and may thus be prone to recurrent reviews.

The transgenic ATHB17_113 protein has no traits indicative of constituting a risk for increased allergenicity as based on the various bioinformatics analyses appropriately performed by the applicant. Especially the significant sequence identity and structural similarity the ATHB17_113 protein shares with proteins present in frequently consumed food plants and the below detection expression level in maize grain strongly argue against an increased risk for allergenicity from ATHB17_113 protein expressed in the GMO.

I have no further comments.

A.5.2. ASSESSMENT OF ALLERGENICITY OF THE WHOLE GM PLANT

Comment 1
No comment.

Comment 2
In their assessment of allergenicity of the **WHOLE** GM plant, the applicants exclusively focused on the ATHB17_113 protein as such, disregarding the biologic activity of the protein. Reportedly acting as a dominant negative mutant of a transcription factor with gene repressor activity, the transgenic protein serves as a repressor of a repressor. As a consequence, an increased expression of genes controlled by endogenous maize HDZipII repressor activity is anticipated. Increased protein expression may constitute a risk for allergenicity. The applicant in his assessment largely neglects this feature. A listing of target genes susceptible to loss of suppression by ATHB17_113 protein and data on their expression levels (mRNA, protein if feasible) would allow for a more rationalistic assessment of allergenicity of the whole GM plant.

Coordinator comment
Similar remark as comment 1 in A.2.2.
The applicants briefly discuss the possibility of overexpression of endogenous proteins, but consider it unlikely this would alter allergenicity. See 1.5.2, p. 125 technical dossier.
"Maize is not considered a common allergenic food. Food allergies to maize are of low frequency and mainly occur in populations of specific geographic areas. Rare cases of occupational allergy to maize dust have been reported. There is no reason to expect that the use of MON 87403 will significantly increase the intake and exposure to maize. Therefore a possible overexpression of any endogenous protein, which is not known to be allergenic, would be unlikely to alter the overall allergenicity of the whole plant or the allergy risk for consumers."

A.5.3. ADJUVANTICITY

Comment 1
No comment.

Comment 2
No comments.

A.6. NUTRITIONAL ASSESSMENT

A.6.1. NUTRITIONAL ASSESSMENT OF FOOD DERIVED FROM GM PLANTS

Comment 1
Based on the compositional equivalence, and the non-significant differences for vitamin B2, calcium and NDF (P>0.05; Section 1.3.4 of this dossier) there is no reason to assume that the genetic modification has affected the nutritional value of food derived from MON 87403 maize.

A.6.2. NUTRITIONAL ASSESSMENT OF FEED DERIVED FROM GM PLANTS

Comment 1
Based on the compositional equivalence, or the non-significant differences for vitamin B2, calcium and NDF (P>0.05) there is no reason to assume that the genetic modification has affected the nutritional value of feed derived from MON 87403 maize.

B. EXPOSURE ASSESSMENT - ANTICIPATED INTAKE/EXTENT OF USE

Comment 1
The reference used for the estimation of animal feed intake is not clear: OECD (2009) is not mentioned in the reference list of the technical dossier (P.185-186). This is rather a question of negligence of the applicant, because the estimation of animal feed intake will be of main importance, due to the small chance of MON 87403 maize for risks of toxicity and allergenicity: see A.4.2., A.5.1. and A.6.2.

Comment 2
No comment.

C. RISK CHARACTERISATION

Comment 1
No comment.

D. POST MARKET MONITORING (PMM) OF FOOD AND FEED DERIVED FROM GM PLANTS

E. ENVIRONMENTAL RISK ASSESSMENT

E.1. INTRODUCTION

Comment 1
No comment.

Comment 2
None.

E.2. GENERAL APPROACH OF THE ERA

Comment 1
No comment.

Comment 2
None.

E.3. SPECIFIC AREAS OF RISK

As stated in the EFSA guidance on the environmental risk assessment of genetically modified plants (EFSA Journal 2010, 8(11):1879) the objective of the ERA is on a case-by-case basis to identify and evaluate potential adverse effects of the GM plant, direct and indirect, immediate or delayed (including cumulative long-term effects) on the receiving environment(s) where the GM plant will be released.
For each specific risk the ERA consists of the six steps described in Directive 2001/18/EC:
1. Problem formulation including hazard identification,
2. Hazard characterisation,
3. Exposure characterisation,
4. Risk characterisation,
5. Risk management strategies,
6. Overall risk evaluation and conclusions.

E.3.1. PERSISTENCE AND INVASIVENESS INCLUDING PLANT-TO-PLANT GENE FLOW

Comment 1
No safety concern.

Comment 2
None.

E.3.2. PLANT TO MICRO-ORGANISMS GENE TRANSFER

Comment 1
No safety concern.

Comment 2
None.

E.3.3. INTERACTION BETWEEN THE GM PLANT AND TARGET ORGANISMS

Comment 1
No safety concern.

E.3.4. INTERACTION BETWEEN THE GM PLANT AND NON-TARGET ORGANISMS (NTOS)

Comment 1
No safety concern.

E.3.5. IMPACTS OF SPECIFIC CULTIVATION AND MANAGEMENT AND HARVESTING TECHNIQUES

Comment 1
No safety concern.

Comment 2
None.

E.3.6. Effects on biogeochemical processes

Comment 1
No safety concern.

Comment 2
None.

E.3.7. Effects on human and animal health

Comment 1
There is no reason to assume that MON 87403 will exert detrimental effects on human and animal health.

Comment 2
No safety concern.

E.3.8. Overall risk evaluation and conclusions

Comment 1
It is assumed that the likelihood for any adverse effects occurring in humans and animals as a result of the ATHB17Δ113 protein in MON 87403 maize is negligible.

Comment 2
No safety concern.

Comment 3
None.

E.4. Post Market Environmental Monitoring plan

E.4.1. Interplay between environmental risk assessment and monitoring

Comment 1
None.

E.4.2. Case-specific GM plant monitoring

Comment 1
None.

E.4.3. General surveillance for unanticipated adverse effects

Comment 1
None.

E.4.4. REPORTING THE RESULTS OF MONITORING

Comment 1
None.

References

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