Adviesraad voor Bioveiligheid
Conseil consultatif de Biosécurité

Advice of the Belgian Biosafety Advisory Council on application EFSA-GMO-NL-2014-121 (soybean MON 87751) from Monsanto under Regulation (EC) No. 1829/2003

11 September 2018
Ref. SC/1510/BAC/2018_0702

Context

Application EFSA-GMO-NL-2014-121 was submitted by Monsanto for the marketing of genetically modified (GM) soybean MON 87751 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 MON 87751 was developed to confer resistance against certain lepidopteran pests. This is achieved by the expression of the *cry1A.105* and *cry2Ab2* genes from *Bacillus thuringiensis*.

The application was validated by EFSA on 22 January 2015 and a formal three-month consultation period of the Member States was started, lasting until 4 July 2015, 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). Ten 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 published on 2 August 2018 (EFSA Journal 2018;16(8):5346[2]) together with the responses from the EFSA GMO Panel to comments submitted by the Member States during the three-month consultation period. On 13 August 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 BAC considered in particular the information below:
- The comments formulated by the experts on application EFSA-GMO-NL-2014-121; 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] https://doi.org/10.2903/j.efsa.2018.5346

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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 soybean MON 87751 seeds (*i.e.* during transport and/or processing) into the European environment[3] 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

The Biosafety Advisory Council agrees with the GMO panel of EFSA that the compositional data of soybean MON 87751, in comparison with its conventional counterpart, do 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 soybean MON 87751, 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 soybean MON 87751, 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 soybean MON 87751-derived food and feed are not expected to differ from those of conventional soybean 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 cultivation of the GM crop in the EU, a full environmental assessment is as in the case of a cultivation file is not warranted.

Conclusion

Based on the whole set of data on soybean MON 87751 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 environmental release of soybean MON 87751 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 MON 87751 is unlikely to pose any risk to human and animal health.

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-NL-2014-121 (ref. BAC_2015_0255)

Bioveiligheidsraad
Conseil de Biosécurité

Secretariaat
Secrétariat

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24/04/2015

Compilation of comments of experts in charge of evaluating the application EFSA/GMO/NL/2014/121 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 10 February 2015.
Coordinator: René Custers
Experts: Jan Van Doorsselaere (KATO), Leo Fiems (ILVO), Eddy Decuypere (KUL), André Huyghebaert (UGent), Hadewijch Vanhooren (KUL), Birgit Mertens (WIV-ISP), Peter Smet (Consultant), Johan Grooten (UGent), Michel Van Koninckxloo (HEP Hainaut-Condorcet), Jacques Dommes (ULg).
Domains of expertise of experts involved: Molecular characterisation, DNA/RNA/protein analysis, herbicide tolerance, animal and human nutrition, food/feed processing, toxicology, general biochemistry, statistics, immunology, alimentary allergology, plant allergens, agronomy, ecology, oilseed rape, breeding techniques, plant biology.
SBB: Didier Breyer, Adinda De Schrijver, Martine Goossens, Aiko Gryspeirt, Philippe Herman, Katia Pauwels.

♦ INTRODUCTION

Dossier **EFSA/GMO/NL/2014/121** concerns an application submitted by the company **Monsanto** for authorisation to place on the market genetically modified **soybean MON 87751** 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 22 January 2014.

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
The safety of the Cry1A.105 and Cry2Ab2 proteins has already been previously established. Therefore, MON 87751 soybean is considered as safe as conventional soybean in animal and human nutrition.

Comment 2
Cry1A.105, a chimaeric protein from Cry1Ab, Cry1F derived from soil bacteria *Bacillus thuringiensis* with 100% homology for the protease-resistant core between MON 87751- and MON 89034-produced Cry1A.105 protein. This holds also for the Cry2Ab2 protein of MON 89034 and MON 87751. The levels of these proteins are mainly expressed in forage and less in seeds of soybean plants, this because the expression of the Cry-proteins are targeted to chloroplasts.

Comment 3
The information provided in the application is sufficient.

Comment 4
No comment, adequate information is provided.

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 comments

Comment 3
The information provided in the application is sufficient.

Comment 4
No comment, adequate information is provided.

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 questions

Comment 2

No comments

Comment 3

The information provided in the application is sufficient.

Comment 4

No comment, adequate information is provided.

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

No questions

Comment 2

No comments

Comment 3

Adequate information is provided.

If I understood well, there is a small typo on page 73 of the document 'Part II – Scientific information'. Under the title 1.2.2.3. Information on the expression of the insert(s), subtitle (a) The methods used..., lines 9-10 of first paragraph: it should be read "...per gram (g) fresh weight (fw) basis." instead of "...per gram (g) dry weight (dw) basis." This does not modify the conclusions drawn from the molecular characterisation of this event.

A.3. COMPARATIVE ASSESSMENT

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

Comment 1

No questions

Comment 2

The information provided in the application is sufficient.

Comment 3
MON 87751 will be further referred to as MON exp.
MON exp was compared to a conventional soybean A3555 with similar background genetics and with other conventional soybean varieties. This approach is in line with previous applications.
No further comments.

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

Comment 1
No questions

Comment 2
Comment: in Table 10. Field and planting information on the 2012 US field trials (Hoi and Donelson, 2014c), and in Hoi and Donelson (2014c), we find for the site NCBD, 29.9 % OM. This value is unusually high and highly unlikely in sandy loam soil.
Nevertheless, the information provided in the application is sufficient.

Comment 3
No particular comments on the experimental design and the statistical analysis.

A.3.3. COMPOSITIONAL ANALYSIS

Comment 1
The compositional analysis showed some differences between MON 87751 soybean and its conventional counterpart, but mean values were within the range of reference soybean varieties, so that differences are not relevant from a food or feed safety perspective.

Comment 2
No differences, or no meaningful differences from those of conventional counterpart and equivalency to the values from the conventional reference varieties.
Comment 3
The information provided in the application is sufficient.

Comment 4
As usual the OECD guidelines were followed in the selection of the key nutrients and other nutritionally important constituents. Seed and forage of MON exp, the conventional counterpart and 19 reference varieties have been analyzed.

The analysis of soybean seeds covers nutrients, including proximates, amino acids, fatty acids, vit E as α-tocopherol, vitamin K1 as phylloquinon, and minerals calcium and phosphorous. The anti-nutrients include the well known anti-nutrient compounds in soya: lectin, phytic acid, raffinose, stachyose, trypsin inhibitors and other components such as isoflavones.
The range of compounds analyzed in forage is somewhat more restricted.

Some comments on the selection of constituents for analysis:
- the OECD document is followed but I repeat my previous comments on carbohydrates and fibre constituents,
- the amino acid and fatty acid analysis cover the nutritionally important acids,
- the analysis of vitamins is limited to α-tocopherol; soy is an important source of vitamin E; I regret however that other tocopherols and tocotrienols are not included; there is growing interest in the contribution of these constituents to vitamin E activity and to antioxidative activity; in particular soybeans are a good source of ó-tocopherol among others; due to the shift towards more unsaturated fats and oils in human nutrition, antioxidative properties are of growing importance,
- on the other hand the dossier contains information on vitamin K1, in line with recent insights in human nutrition,
- isoflavones, previously described as anti-nutrients, are classified as other components; the debate on the properties as pseudo-estrogens is probably at the basis of this modified classification.

Results are discussed in detail and are classified “as equivalent” (fifty components) to the counterpart or “more likely than not equivalent” (methionine) to the counterpart. No constituents are classified as “non-equivalent more likely than not” or as “non-equivalent”.

The applicant concludes that Mon exp is compositionally similar to the conventional counterpart.

I agree with this overall conclusion.

A.3.4. AGRONOMIC AND PHENOTYPIC CHARACTERISTICS

Comment 1
No questions

Comment 2
The information provided in the application is sufficient.

A.3.5. EFFECTS OF PROCESSING

Comment 1
No questions

Comment 2
The information provided in the application is sufficient.

Comment 3
No differences are to be expected in the processing of MON exp in comparison with the conventional counterpart with the exception of the insect-protection trait.

Different steps in the processing of soybeans and the products obtained are briefly reviewed.

The applicant concludes that it is highly likely that Mon exp and its derived food and feed products are not different from the equivalent food and feed products obtained from the conventional counterpart.

I agree with this conclusion.

A.4. TOXICOLOGICAL ASSESSMENT

A.4.1. METHODOLOGY USED FOR TOXICITY TESTS

Comment 1

- The amino acid sequences of both MON 87751 Cry1A.105 and Cry2Ab2 proteins are not similar to any of the antinutritional proteins or to any other known protein toxins
- History of safe use
- Rapid digestion in gastric mode systems together with negligible human exposure from soybean consumption and deactivation by heat treatment of soybeans; Therefore the conclusion that no 28-day oral toxicity studies are needed, is warranted.

Comment 2

No comments

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 concludes that the probability of any foreign DNA entering and recombining with the host DNA in humans and animals is negligible (Technical dossier, P.81). However, it cannot be completely excluded that meal-derived DNA fragments, which are large enough to carry complete genes, can avoid degradation and enter the human circulation system through an unknown mechanism (Spisák et al., 2013).

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

- Cry1A.105 and Cry2Ab2 proteins have a demonstrated history of safe use
- Cry1A.105 and Cry2Ab2 proteins have no structural similarity to known toxins or other biologically active proteins that could cause adverse effects in humans or animals, using FASTA algorithm
- deactivation of Cry1A.105 and Cry2Ab2 upon heat treatment
- Cry1A.105 and Cry2Ab2 proteins are rapidly digested in simulated digestive fluids

it is unlikely that MON 87751 soybean will pose serious risks for toxicity.

Comment 2

The inserted genes in MON 87751 soybean encode for two new proteins, i.e. Cry 1A.105 and Cry2Ab2. No 28-day oral toxicity studies with the MON 87751 Cry1A.105 and Cry2Ab2 proteins were performed as both proteins were considered safe based on the following evidence:

- the lack of structural or functional relationship of MON 87751 Cry1A.105 and Cry2Ab2 to proteins that adversely affect human or animal health;

- the history of safe use of the Cry1A.105 and Cry2Ab2 proteins and their source organism;
- the negligible human exposure to MON 87751 Cry1A.105 and Cry2Ab2 proteins from soybean consumption;
- the digestibility of MON 87751 Cry1A.105 and Cry2Ab2
- the deactivation of MON 87751 Cry1A.105 and Cry2Ab2 upon heat treatment.

Comment 3
No questions

Comment 4
Repeated dose toxicity testing (28-d toxicity testing with the newly expressed proteins) was not performed. The applicant argues that the safety of the highly similar Cry1A.105 and Cry2Ab2 proteins from MON 89034 maize (EFSA Journal (2008) 909, 1-30) were already assessed in the context of different applications. I can agree that no further repeated dose toxicity testing is needed as the outcome of the other studies performed, did not reveal any motivation for further testing.

Comment 5
Using the Cry1A.105 protein as the query sequence to search the PRT_2014 database, numerous alignments were recovered. The top twelve alignments displaying 100% identity with an *E*-score of 0 positively identified Cry1A.105
→ What is the identity of the other proteins which display a significant identity with Cry1A.105?

Using Cry2Ab2 as the query sequence to search the PRT_2014 database a total of 4043 alignments yielded an *E*-score less than or equal to one and of those 1039 sequences yielded an alignment with an *E*-score of 0. The top sixteen alignments displayed 100% identity in a window of 633 or 634 amino acids with an *E*-score of 0. One of the top alignments using GenBank sequence annotation positively identified Cry2Ab2 (GI-27311145).
→ What other proteins display 100% identity?

No further studies are included and no toxicity testing is performed. In dossier 37 I raised the following concerns about these proteins:

Macroscopic examination:
- Urinary calculi were found in the bladders of 2 high-dose (33%) females which resulted in histologic alterations.

Organ weights:
- A low thyroid/parathyroid weight relative to final body weight was observed in the 33% test diet group females.

Microscopic examination:
- The kidneys of the high-dose (33%) test group females showed findings not found or at lower incidence in the control group. One rat was found dead on day 14. There were 5 findings of chronic progressive nephropathy, 3 findings of transitional cell hyperplasia, 2 cases of subacute inflammation and hydronephrosis, papillary necrosis and tubular necrosis. Most of these findings were attributable to the two rats which were found to have calculi (see Macroscopic examination).

It is worth discussing these items and have a closer look, whether these findings are solely due to chance. In case any doubt remains, further testing is recommended.

The EFSA answered these remarks as follows:
Microscopic findings in organs and tissues were almost equally distributed and no statistically significant differences between males and females of the high dose group and the controls were noted. A numerically higher incidence of kidney alterations in females of the high dose group was attributable to two rats (one died at day 14 of unknown cause, the other survived to the end of the study). The alterations in these two rats included minimal chronic progressive nephropathy, minimal/moderate transitional cell hyperplasia, minimal sub-acute inflammation and moderate hydronephrosis. The animal that died on day 14 additionally showed mild papillary necrosis and minimal tubular necrosis. Both rats had urinary bladder calculi and the study pathologist concluded that the lesions observed most likely were linked to these calculi.
It seems unlikely that the urinary bladder calculi and associated kidney alterations could have been induced by the tested maize in 14 days. A low incidence of urinary bladder calculi is known to occur in this rat strain and may be considered a spontaneous finding in sub-chronic studies. According to historical control data supplied in the application, the incidence of urinary bladder calculi in high dose females in this study was also found in female control rats in previous studies conducted with CD rats in the same testing laboratory. The Panel therefore considers the urinary bladder calculi as well as the associated kidney alterations as incidental findings which were not related to administration of maize MON89034. The same applies to the nephroblastomas, a very rare tumour of the kidney, which were observed in two female animals of the control group.

Up till now, no further toxicity testing for these two proteins has been conducted. Besides a homology search, no other data are provided in this dossier so my concerns remain.

A 28-day repeat dose toxicity study in rats could provide the necessary scientific data to have a closer look at the possible effects of both proteins.

Comment Coordinator / SBB :
The comments above were already provided by the expert for the dossier 37 but were not transmitted to EFSA. For the sake of consistency they are not transmitted for this application.

A.4.3. ASSESSMENT OF NEW CONSTITUENTS OTHER THAN PROTEINS

Comment 1
Since no new constituents other than the Cry 1A.105 and Cry2Ab2 were expressed in MON 87751, a toxicological assessment of new constituents other than proteins is not applicable.

Comment 2
Not relevant because no new other constituents than the 2 Cry-proteins is expressed in MON 87751.

Comment 3
No comments.

Comment 4
The information provided in the application is sufficient.

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

Comment 1
The levels of antinutrients present in MON 87751 were shown to be comparable to those present in conventional soybean.

Comment 2
No questions

Comment 3
The compositional analyses of MON 87751 seed and forage showed clearly that the levels of food and feed components were not altered. Results of both equivalence and difference tests: only methionine was equivalence cat II at the 95% confidence level and showed significant differences at the 10% sign. Level (outcome type 2), however the MON 87751 methionine data fell within the range seen in the reference data.

Comment 4
The information provided in the application is sufficient.

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

Comment 1
Although the applicant questioned its scientific value, a 90-day feeding study with processed soybean meal from MON 87751 was performed as required by the Commission Implementing Regulation (EU) No 503/2013. No test substance-related effects on clinical observations, body weight, food consumption, FOB parameters, locomotor activity parameters, clinical pathology endpoints, or ophthalmic observations were observed in this study. In addition, there were no test substance-related macroscopic findings, histologic findings, or differences in organ weights.

Comment 2
Given the lack of biological or compositional difference between MON 87751 and the conventional counterparts, whole food feeding studies are not necessary.
Cry1A.105 and Cry2Ab2 have no synergistic or antagonistic effects since the mode and sites of biological activity are different.
Nevertheless a 90-day feeding study was performed on (tumor sensitive-)Sprague-Dawley rats, with no effects on growth or health, or nervous, endocrine, reproductive and immunological systems.

Comment 3
A 90-d feeding study in Sprague Dawley rats (16/sex/group, pair-housed, randomized complete block design) was performed using 1 control group (30% soybean meal from A3555, accepted as conventional soybean counterpart) and 1 test group (30% soybean meal from MON 87751) and using the in-house historical control data (15%, 30% soybean meal, pair-housed data, individual data) according to OECD guideline 408 and EFSA guidance (EFSA Journal 2011; 9(12):2438) but was initiated before the EFSA explanatory statement (EFSA Journal 2014; 12(10):3871). The weakness of this testing strategy is that it cannot reveal any dose-response.
The significant differences seen between the test and control group on haematology, serum chemistry, urinalyses, organ weight, and histopathology could not been seen as meaningful as there was no

consistency over sexes and the parameters tested (haematology: ♂ ↓abs. neutrophil count, ♀ ↓RBC count, haemoglobin conc., reticulocyte conc., ↑MCV, ↓abs. monocyte count; serum chemistry: ♂ ↓mean albumin, total protein, ♀ ↓ALP; Urinalyses: ♀ ↑mean specific gravity, ↓pH; organ weight: ♂ ↓brain weight, ♀ ↓liver weight; histopathology: ♂ ↓ sperm in epididymidis, hypospermatogenesis in the testes (1 animal), ♀ ↓incidence of tubular basophilia in kidneys). The differences that were detected between the test and control diets were also within the range seen in the in-house historical control data.
In addition, the compositional analyses did not demonstrate any biologically differences.

Comment 4
The information provided in the application is sufficient.

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:
- Cry1A.105 and Cry2Ab2 proteins lack structural similarity to known allergens, using FASTA
- Cry1A.105 and Cry2Ab2 proteins are rapidly digested in simulated digestive fluid

it is assumed that MON 87751 soybean does not pose a serious allergenic risk, and that it is comparable with conventional soybean with regard to allergenicity.

Comment 2
No further comments.

Comment 3
The applicant performed all assays required by EFSA to assess the potential for allergenicity of both introduced proteins with the exception of specific serum screening. While I comply with the applicant's arguments for not performing the latter test (prior evaluations by EFSA, long history of safe use, ...), I find it a pity and a missed opportunity not to use the full array of scientific tools available to assess the potential risk of a GMO. In fact when 90 days feeding studies are being done with rats as is the case with most dossiers, why not perform on these animals some simple non-endpoint tests for assaying besides toxicity also allergenicity such as a DTH assay and an ELISA for detecting antibodies against the introduced proteins. Could this not be proposed to EFSA. I quite understand that human sera are limited but such animal assays may be equally revealing.
Specifically regarding this application and with the exemption of my remarks above, I agree with the applicant's conclusion that the Cry1A.105 protein and Cry2Ab2 protein are unlikely to be allergenic.
Comment Coordinator :
It is suggested to discuss this issue in a more broader way between the Council's members, in particular in light of the outcome of the workshop on allergenicity of GM plants that EFSA is organizing on 17 June 2015.

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

Comment 1
No questions.

Comment 2
Soybean being an allergenic food, the applicants performed here a thorough analysis of the impact of the genetic manipulation on endogenous allergen levels. This analysis was performed using sera from soybean allergic donors and testing of GMO and parental soybean protein extracts for reactivity using ELISA and 1D and 2D PAGE. The results of these analyses are satisfactory, indicating that the MON 87751 GMO is not likely to be more allergenic that its parental counterpart.

A.5.3. ADJUVANTICITY

Comment 1
No questions.

Comment 2
No comments. No indications for a risk of adjuvancy of the introduced Cry1A.105 and Cry2Ab2 proteins.

A.6. NUTRITIONAL ASSESSMENT

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

Comment 1
No differences between MON 87751 and conventional counterpart except for the newly expressed Cry-proteins; the conclusion that additional nutritional studies for food or feed use are not warranted , is justified.

Comment 2
The information provided in the application is sufficient.

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

Comment 1
There is no reason to assume that the nutritional value of MON 87751 soybean is different from its conventional counterpart.

Comment 2
Id. As A.6.1

Comment 3
The information provided in the application is sufficient.

B. EXPOSURE ASSESSMENT - ANTICIPATED INTAKE/EXTENT OF USE

Comment 1
No questions.

Comment 2
The information provided in the application is sufficient.

C. RISK CHARACTERISATION

Comment 1
No questions.

Comment 2
The information provided in the application is sufficient.

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

Comment 1
No comments.

Comment 2
The information provided in the application is sufficient.

E. ENVIRONMENTAL RISK ASSESSMENT

E.1. INTRODUCTION

Comment 1
No comments.

Comment 2
The information provided in the application is sufficient.

E.2. GENERAL APPROACH OF THE ERA

Comment 1
The applicant concludes that the long-term adverse environmental effects are negligible (Technical dossier, P.204). However, this exposure cannot be completely excluded. Zhang et al. (2014) detected fragments of Cry1Ab in steamed rice with 217 bp. The continuous discoveries of novel mobile genetic elements and mechanisms of HGT, together with the findings of unexpectedly high HGT rates in natural ecosystems, indicate that the true extent of HGT in nature is not yet completely understood (Aminov, 2011).

Comment 2
No comments (see also on section A4.1 and A4.5).

Comment 3
The information provided in the application is sufficient.

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
In the text of list of comments on p6/9 under E3 Specific areas of risk, it is stated that “the objective of ERA is to identify and evaluate potential adverse effects of the GM-plant, direct and indirect, immediate or delayed”.
However the sentence “intended or unintended” is omitted here; this should perhaps by added here , especially for those applications where the impact and processing is foreseen, but excluding the cultivation of the plants/crops.
Comment Coordinator :
No need to add this sentence. If one speaks about the ‘potential adverse effects of the GM plant, …’ then this automatically includes intended and unintended effects.

Comment 2
The information provided in the application is sufficient.

Comment 3
No comment, adequate information is provided.

E.3.2. PLANT TO MICRO-ORGANISMS GENE TRANSFER

Comment 1
No comments.

Comment 2
The information provided in the application is sufficient.

Comment 3
No comment, adequate information is provided.

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

Comment 1
Not relevant

Comment 2
The information provided in the application is sufficient.

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

Comment 1
No questions.

Comment 2
The information provided in the application is sufficient.

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

Comment 1
Not relevant.

Comment 2
The cultivation of MON 87751 in the EU is not in the scope of this application

E.3.6. EFFECTS ON BIOGEOCHEMICAL PROCESSES

Comment 1
Not relevant.

Comment 2
The information provided in the application is sufficient.

E.3.7. EFFECTS ON HUMAN AND ANIMAL HEALTH

Comment 1
It is assumed that MON 87751 soybean represents negligible risk to human and animal health.

Comment 2
No further questions or comments; see also A4.1 and A4.5.

Comment 3
The information provided in the application is sufficient.

E.3.8. Overall risk evaluation and conclusions

Comment 1
No questions.

Comment 2
The information provided in the application is sufficient.

E.4. Post Market Environmental Monitoring plan

E.4.1. Interplay between environmental risk assessment and monitoring

Comment 1
Not relevant.

Comment 2
The information provided in the application is sufficient.

E.4.2. Case-specific GM plant monitoring

Comment 1
Not relevant.

Comment 2
The information provided in the application is sufficient.

E.4.3. General surveillance for unanticipated adverse effects

Comment 1
No questions.

Comment 2
The information provided in the application is sufficient.

E.4.4. Reporting the results of monitoring

Comment 1
No questions.

Comment 2
The information provided in the application is sufficient.

References

- Aminov, R.I. 2011. Horizontal gene exchange in environmental microbiota. Front. Microbiol. 2, Article 158.
- Spisák, S., Solymosi, N., Ittzés, P., Bodor, A., Kondor, D., Vattay, G., Barták, B.K., Sipos, F., Galamb, O., Tulassay, Z., Szállási, Z., Rasmussen, S., Sicheritz-Ponten, T., Brunak, S., Molnár, B., Csabai, I., 2013. Complete genes may pass from food to human blood. PLoS ONE 8, e69805.
- Zhang, W., Xing, F., Selvaraj, J.N., Liu, Y., 2014. Degradation of endogenous and exogenous genes of genetically modified rice with Cry1Ab during food processing. J. Food Sci. 79, T1055-T1066.