Bioveiligheidsraad
Conseil de Biosécurité

7-12-2012

Secretariaat
Secrétariat

O./ref.: WIV-ISP/41/BAC/2012_1009

Title: Advice of the Belgian Biosafety Advisory Council on the application EFSA/GMO/NL/2010/78 from Monsanto under Regulation (EC) No. 1829/2003

Context

The application EFSA/GMO/NL/2010/78 was submitted by Monsanto on 18 February 2010 for the marketing of genetically modified soybean MON87705 for food and feed uses, import and processing within the framework of Regulation (EC) No. 1829/2003[1]. Soybean MON87705 contains a FAD2-1A/ FATB1A suppression cassette resulting in an altered fatty-acid profile of the soybean seed and expresses the cp4 epsps conferring tolerance to glyphosate- based herbicides.

The application was officially acknowledged by EFSA on 10 August 2010. On the same date EFSA started the formal three-month consultation period of the Member States, 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 Biosafety and Biotechnology Unit (SBB). Six experts answered positively to this request, and formulated a number of comments to the dossier, which were edited by the coordinator. See Annex I for an overview of all the comments and for the list of comments actually placed on the EFSAnet on 30 October 2012.

The opinion of the EFSA Scientific Panel on GMOs was adopted on 28 September 2012 (EFSA Journal 2012; 10(10):2909[2], and published together with the responses from the EFSA GMO Panel to comments submitted by the experts during the three-month consultation period.

On 5 November 2012 the opinion of EFSA was forwarded to the Belgian experts. They were invited to give comments and to react if needed to the answers given by the EFSA GMO Panel, in particular in case the comments formulated in their initial assessment of the dossier were not taken into account in the opinion of EFSA. The comments formulated by the experts together with the opinion of EFSA including the answers of the EFSA GMO Panel form the basis of the advice of the Biosafety Advisory Council given below.

[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 http://www.efsa.europa.eu/en/efsajournal/pub/2560.htm

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Scientific evaluation

1. Environmental risk assessment

According to the Biosafety Advisory Council no major risks were identified concerning the environment[3].

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 is of the opinion that the composition of the GM soybean MON87705 only shows biologically relevant differences with conventional soybean in its fatty acid profile, and the additional expression of the EPSPS protein, as intended.

The Biosafety Advisory Council also considers that, although not required by the OECD Document on compositional considerations for new varieties of soybean (OECD, 2001), it lacks the analysis on dietary fibre. The Biosafety Advisory Council recommends the analysis on dietary fibre since this concept is widely accepted in human food studies and recommends the adaptation of the OECD consensus document accordingly.

3.2. Assessment of toxicity

The applicant provided different data to substantiate that the CP4-EPSPS protein is not toxic. Additionally, the applicant provided the results of a 90-day rat feeding study, even though the EFSA guidelines on the safety assessment of food and feed from GM crops do not require such a study in this particular case. The Biosafety Advisory Council considered this study and noted that only one test dose was used, where the EFSA guidelines require at least two doses to be included in such a study. Even though the study does not allow a dose-response relationship to be established, it does confirm that consumption of GM soybean MON87705 at the studied dose does not lead to any signs of toxicity. The used dose represents a very substantial safety margin compared with the amounts humans are likely to consume, and humans have been consuming oils with a more high-oleic fatty acid profile already for a very long period of time.

Therefore, with regard to toxicity the Biosafety Advisory Council is of the opinion that the information provided is sufficient and does not raise safety concerns.

3.3. Assessment of allergenicity

The potential allergenicity of the newly expressed proteins (CP4EPSPS is the only newly expressed protein in MON87705) has been assessed as well as the allergenicity of the whole GM soybean. It is unlikely that the new expressed proteins changed the allergenicity of the whole crop.

[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 achieved.

3.4. Nutritional value

The Biosafety Advisory Council is of the opinion that soybean MON 87705 do not raise nutritional concerns in the context of the intended use, which does not target its use for commercial frying (high temperature and repeated frying). The Council agrees with EFSA that an additional nutritional assessment should be performed in case the intended use of MON 87705 soybean covers commercial frying. Additionally, the BAC considers that the claimed anticipated nutritional benefits associated with an increase of oleic acid at the expense of linoleic acid are not supported by a full scientific consensus.

4. Monitoring

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

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 is of the opinion that in the context of its proposed uses, MON 87705 is unlikely to pose any risk to human and animal health. For other uses, such as high temperature, repeated frying an additional nutritional assessment should be performed.

Given the scope of the application of this herbicide tolerant soybean with altered fatty-acid profile(no cultivation in EU) and the fact that the establishment of volunteer plants would be unlikely (soybean cannot survive without human assistance and is not capable of surviving as a weed in Europe), the potential environmental release of MON87705 is unlikely to pose any threat to the environment.

p.o. Dr. Thierry Hermann

Prof. D. Reheul
President of the Belgian Biosafety Advisory Council

Annex I: Full comments of experts in charge of evaluating application EFSA/GMO/NL/2009/78 and *comments submitted on the EFSAnet (ref. BAC_2010_1064)*

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Conseil de Biosécurité

17-11-2010

Secretariaat
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N./réf. : WIV-ISP/41/BAC_2010_1064
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Compilation of comments of experts in charge of evaluating the application EFSA/GMO/NL/2010/78
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 27 August 2010
Coordinator: René Custers
Experts: Armand Christophe (UGent), Johan Grooten (UGent), André Huyghebaert (UGent), Peter Smet (Consultant), Frank Van Breusegem (VIB), Johan Van Waes (ILVO)
Domains of expertise of experts involved: Genome analysis, genetic engineering, transgene expression, human nutrition, biochemistry of food/feed, analysis of food/feed, industrial processing, toxicology, immunology, alimentary allergology , plant allergens, agronomy, agro-ecology, herbicide tolerance, soybean
Secretariat (SBB): Didier Breyer, Adinda De Schrijver, Martine Goossens, Philippe Herman, Katia Pauwels

INTRODUCTION

Dossier **EFSA/GMO/NL/2010/78** concerns an application of the company **Monsanto** for the marketing authorisation of the genetically modified **Soybean MON87705** for food and feed applications under Regulation (EC) 1829/2003.
The application has been officially acknowledged by EFSA on 13 August 2010.

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

According to the dossier the scope of application does not include the authorization for the cultivation of MON 87705 soybean products in the EU. It can however be valuable to give some remarks on the different topics, dealing with cultivation and survivability of seeds, in the case that the applicant should ask in the near future for an extension for the scope of cultivation, especially for cultivation in some southern European countries.
So as agronomical expert I will also give some comments in this questionnaire, related to cultivation and the environmental aspect.
Remark SBB, agreed by coordinator
Comments related to cultivation of this GMO could indeed be useful for information purpose, but should not be communicated to EFSA as they are out of scope for the risk assessment of the current application.

Comment 2

1) Some of the claimed anticipated nutritional benefits from the fatty acid changes are not equivocal. While there is general agreement that reduction of saturated fatty acids is beneficial, it is not clear whether achieving this by an increase of oleic acid at the expense of linoleic acid will have a positive effect on cardiovascular risk factors (part I, page 49). Moreover there is no consensus in literature that increasing oleic acid intake above a certain level is indicated (e.g. Degirolamo et al, 2009). Thus the term "nutritionally-improved soybean oil" (e.g. part I, page 212) could be misleading. Of course, this comment has no bearing on the safety of MON87705.

2) One of the main reasons for the intended modification is obtaining an oil which has a higher oxidative stability for technological reasons. Major factors determining the oxidative stability of an oil are its fatty acid composition and the nature and level of its antioxidants. Vitamin E is the only antioxidant, and even not the most abundant antioxidant in soybean oil, that was determined (Evans et al., 2002). Therefore it would be expected that the oxidative stability of the oil would have been determined directly. This is not the case.

Additional comment from the coordinator

The applicant has sticked to the OECD recommendations, and has only looked at vitamin E.
The comment is correct, that one would expect the applicant to have looked at the oxidative stability of the oil directly. Maybe they have done so, but it is not part of this dossier.
To my opinion it also has no bearing on the safety assessment.

Comment 3

The information relating to the GM plant and its parent, to the genetic modifications inserted and to the functional outcome of these genetic modifications was found to be adequate in general and specifically in relation to the allergenicity feature of the GM plant, the focus of the present report.

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

Under "3. Survivability – ability to form structures for survival or dormancy" it is mentioned that mature soybean seeds have no innate dormancy, are sensitive to cold and are not likely to survive from one growing season to the next if left in the field over winter. My question is : are there data available of overwintering of seed of soybean for example in Southern Europe and in that case how were the volunteers be destroyed?

Remark SBB, agreed by coordinator

Suggestion not to forward this comment to EFSA, because it is not relevant in the context of the current application (no cultivation). Same comment in a previous soybean dossier (2009/73 and 2009/76) has not been sent to EFSA.

Moreover, it should be noted that, for commercial reasons, MON87769 will be processed in dedicated facilities and therefore it is not expected that significant quantities of this GM soybean will commingle with general soybean supply in the EU.

Comment 2

No comments.

C. INFORMATION RELATING TO THE GENETIC MODIFICATION

Comments/Questions of the expert(s)

Comment 1

No comments.

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.

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

Comments/Questions of the expert(s)

Comment 1

No comments.

D.3. INFORMATION ON THE EXPRESSION OF THE INSERT

Comments/Questions of the expert(s)

Comment 1

No comments.

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.

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

Comments/Questions of the expert(s)

Comment 1

No comments.

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

Comments/Questions of the expert(s)

Comment 1

No comments.

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

Question: Most of the concentrations of the fatty acids are below the LOQ. Is this also the case in the reference lines?

Comment 2

Question

Reported mean values for lignoceric acid in seed at Site CdT are 0.15 for both MON87705 and its control (Table 17, page 131). Yet a mean difference between these values (reported to be -3.24%) would exist and would be significant. Is there a printing mistake? (this does not impact on the nutritional value or safety considerations).

Suggestion. As pointed out in previous evaluation reports, it is suggested that a recommendation would be made about the way carbohydrates are best determined and reported. Calculation values "by difference" (as is done in this report) is not the most indicated way from a nutritional point of view. Why not reporting "available carbohydrates" (as is done for instance in the NUBEL food table).

Above comment as rephrased by the coordinator:
It is noted that the carbohydrates are reported in values 'by difference'. This way of reporting is no longer accepted for the inclusion in nutrient labels. We recommend to alter this into reporting in the form of 'available carbohydrates'.

Comments

1) Due to the intended fatty acid modification, it is likely that the fatty acid compositions of crude lecithin and especially in phospholipids fractions derived from it will be different in phospholipids derived from MON87705 than in conventional soybean varieties. Thus the claim that MON 87705 lecithin is considered compositionally equivalent to conventional soybean lecithin (Part I, page 190) can be challenged. Recently, soy lecithin has been used for the cryopreservation of human sperm

(Reed et al., 2009), to improve the productive and reproductive performance of hens, (Attia et al., 2009), and to change the fatty acid composition of milk (Gaby, 2009). Soy derived phospholipids are incorporated in infant formula and marketed as dietary supplements (e.g. Jorissen et al., 2002).

2) Minor comment:
Printing error in 1 (vi) (Part I, page 122) **Forage** proximate …levels …in harvested **seed** .

Comment 3

For the assessment of potential allergenic effects of the GM plant, the GM MON87705 was compared to the parent A3525 soybean plant. Both were grown at different field sites and growing seasons. Also commercially available conventional soybean varieties that are already on the market and are being used for human consumption, were included in the comparative assessment where appropriate. This broad reference panel with respect to agronomic conditions and non-GM cultivars is crucial in setting a 'baseline' for assessing the potential allergenicity of the GM plant and is in line with the recommendation by the EFSA GMO panel scientific opinion on the assessment of allergenicity of GM plants (EFSA Journal 2010; 8(7): p69).

Comment 4

Compositional assessment
The OECD document on compositional assessment for soybean was followed. The applicant presents results of an in detail analysis of nutrients and known anti-nutrients and toxicants. Levels of constituents in seeds an forage of biotechnology derived and conventional soybeans are compared in order to provide an equal or increased assurance of safety.
Results obtained for biotechnology derived crops are compared with those from a non-modified comparator and with natural ranges from commercial varieties and literature data. These include analyses of material from two growing seasons in Chile and the US.
Seed and forage from the biotechnology-derived crop and the conventional control were obtained from soybeans grown at five sites during the 2007/2008 season in Chile. In addition twenty conventional varieties were also included in the study.
Analyis of soybean seeds included:

- Proximates: moisture, fat, protein, ash and carbohydrates by difference
- Acid and neutral detergent fiber
- Amino acids
- Fatty acids
- Anti-nutrients: trypsin inhibitors, phytic acid, lectin
- Isoflavones: daidzein, glycetein, genistein
- Vitamin E
- Flatulence factors: raffinose, stachyose

Analysis of forage included

- Proximates: moisture, fat, protein, ash, carbohydrates by calculation
- Acid and neutral detergent fiber

General comments:
1. Known nutrients and anti-nutrients are covered. However at a first view no data are presented for minerals. With respect to vitamins analyses are limited to vitamin E.

2. Minerals: due to the wide range of geographical locations and different growing conditions such as soil, fertilizers..., data on minerals would be an additional demonstration of equivalence.

3. Vitamins: I fully agree that vitamin E is an important vitamin in soybean. As it is a fat soluble constituent, it will affect the oxidative stability of the oil. However if the biotechnology-derived soybean is intended for other uses, such as soy drinks and others for humans, information of the levels of other vitamins would be welcome.

4. The approach selected for carbohydrates is no longer up-to-date in the assessment of the nutritional value of foods. To my knowledge this approach is well acceptable for feed. For food however there are a range of well accepted methods to determine the level of sugars, other than raffinose and stachyose, and for digestible carbohydrates (starch). Results for carbohydrates obtained by difference, among others, are not accepted for the inclusion in nutrients tables.
As mentioned before the OECD document needs an urgent update in order to be in line with the actual demands for nutrient data. This applies also for the analysis of fiber constituents.

Further results Chile production

Fatty acids

The modification in fatty acid composition is in line with the objective of improving the oxidative stability. This is realized by a decrease in saturated fatty acids and linoleic acid with a corresponding increase in oleic acid. A reduction of linolenic acid is also observed.
No further comment

Non-fatty acid nutrients

No statistically significant difference was observed for most of the nutrients with the exception of total fat, arginine and cystine. As the differences are rather limited I agree with the conclusion that the biotechnology derived soybean is compositionally equivalent to the conventional one.

Anti-nutrients

The compositional equivalences is demonstrated.

Forage

The compositional equivalence is also demonstrated.

Results US production

Results are in general in the same line as the Chile samples. Glyphosate-untreated and treated soybeans are also included in the comparison.

I agree with the general conclusion that the biotechnology-derived soybean is compositionally equivalent, as far as the analyzed nutrients and anti-nutrients is concerned, with the conventional one.

D.7.2 Production of material for comparative assessment

Comments/Questions of the expert(s)

Comment1

No further comments.

D.7.3 Selection of material and compounds for analysis

Comments/Questions of the expert(s)

Comment 1

Suggestions.

1) As pointed out in previous evaluation reports, it is suggested that saponins would be included in the compositional analysis of soybean. Indeed, saponins are present in soy in relatively high quantities (Berhow et al., 2003) and although poorly absorbed in humans (Hu et al., 2004) they can cause bloat in ruminants (Van Haver et al., 2003) and induce enteritis in salmon (Knudsen et al., 2007). Recently it has been shown that soy saponins inhibit human renin activity (Takahashi et al., 2010). Soya sapogenols, obtained by hydrolysis of saponins, clearly have important biological effects (e.g. Zhang et al., 2008).
2) Determination of the fatty acid composition of the major phospholipids classes seems indicated (see above).
3) That desmethyltocopherols are present in soybean oil and that they have important biological properties is mentioned in the application (Part I, page 204). Yet, these compounds, which are more prevalent in soybean oil than Vitamin E (Seguin et al., 2009) were not determined. It is suggested that these compounds would be determined.
4) As previously mentioned phytosterols and phytosterol glycosides are bioactive in humans and because soy phytosterols are used in food applications; Jones et al.; 1997) it has been suggested in literature that they should be analysed (Lin et al. , 2009)

Above comments rephrased by the coordinator:

Although the OECD consensus document on "Compositional considerations for new varieties of soybean: key food and feed nutrients and anti-nutrients" does not prescribe the analysis of saponins, desmethyltocopherols, phytosterols and phytosterol glycosides, one expert has suggested to include these components in the compositional analysis. It is also recommended that the same OECD consensus document is adjusted on the point of the analyses of fibres, and that for human food uses, the requirement will become to determine dietary fibre instead of ADF and NDF. And that the document should consider more recent soybean foods such as soybean drinks and derived foods. These types of foods may make it more relevant to look at other vitamins, instead of only vitamin E.

Comment 2

The genetic modifications implemented are twofold, namely (i) a gene encoding the newly expressed protein, CP4 EPSPS, from *Agrobacterium* sp. CP4 and (ii) a *FAD2-1A/FATB1-A* suppression cassette

encoding for dsRNA. dsRNA by itself is unlikely to encode protein, a feature that is further prohibited by the presence of a hairpin secondary structure. Therefore the analysis of allergenic potential correctly focused on the CP4 EPSPS newly expressed protein and the GM plant itself. The CP4 EPSPS protein assayed was produced in *E. coli*. The physicochemical and functional equivalence of the plant- and bacteria-produced protein was verified by N-terminal sequence analysis, MALDI-TOF mass spectrometry, SDS-PAGE apparent molecular weight, western blot immunoreactivity, enzymatic activity, and (absence) of glycosylation. Although western blotting for comparison of immunoreactivity between two proteins is a rather crude and ineffective method, the results from the MALDI-TOF mass spectrometry and glycosylation and enzymatic analyses are sufficiently convincing to demonstrate the physicochemical and functional equivalence of the MON87705 and *E.coli* expressed CP4 EPSPS protein.

Comment 3

See above.

D.7.4 Agronomic traits

Comments/Questions of the expert(s)

Comment 1

It is mentioned that from field trials MON 87705 soybean is equivalent to the traditional soybean, except for the introduced trait.
From this information we can conclude that there is no significant difference in the agronomical value between the MON 87705 soybean and the traditional type. Is this conclusion correct?
Remark SBB, agreed by coordinator
In this context, equivalence relates to the composition of the GMO, not to its agronomical value.

D.7.5 Product specification

Comments/Questions of the expert(s)

Comment 1

No questions

D.7.6 Effect of processing

Comments/Questions of the expert(s)

Comment 1

No questions

Comment 2

Biotechnology-derived and conventional soybeans have been processed according to the generally applied technology. Intermediate and end products obtained include toasted defatted soybean meal, refined, bleached and deodorized soybean oil, protein isolate and crude lecithin. Fractions were analyzed according the above mentioned OECD document.
Nutrients and anti-nutrients analyzed are mainly the same as in the compositional analysis. In addition the lecithin fraction was analyzed for the major fosfatides.
From the results it can be derived that, except for the intended modifications, no statistical differences are observed. In some cases small differences are found. They are however not relevant from a nutrition or safety point of view.

Comment:
The application covers the major soybean products and fractions. Some products like soybean drinks and derived foods are not included in the study. It is not expected that the conclusion would be influenced by the study of these more recent soybean foods. However it is recommended to included them in a future revision of the OECD document.

D.7.7 Anticipated intake/extent of use

Comments/Questions of the expert(s)

Comment 1

Minor comment: In contrast with what is said on page 213, estimated consumption of food products derived from soybean are available for European countries (Keinan-Boker et al., 2002).

Comment 2

No particular comment.

D.7.8 Toxicology

Comments/Questions of the expert(s)

Comment 1

CP4 EPSPS protein content in MON 87705 is comparable to other CP4 EPSPS containing GMOs.

D. 7.8.1 Safety assessment of newly expressed proteins

Comments/Questions of the expert(s)

Comment 1

a) Degradation of the CP4 EPSPS protein in simulated gastric fluid ().

CP4 EPSPS was shown to be rapidly degraded in both an *in vitro* simulated gastric fluid (SGF) digestion model and an *in vitro* simulated intestinal fluid (SIF) model.

b) Degradation of the CP4 EPSPS protein in simulated intestinal fluid ().

See above.

c) CP4 EPSPS: Acute Oral Toxicity Study in Mice ().

There were no treatment-related adverse effects in mice administered the CP4 EPSPS protein by oral gavage at dosages up to 572 mg/kg.
There were no statistically significant ($p \leq 0.05$) differences in body weight, cumulative body weight, or food consumption between the vehicle and bovine serum albumin protein control groups and CP4 EPSPS protein-treated groups.

d) CP4 EPSPS: Assessment of Amino Acid Sequence Homology with Known Toxins ()

The results of the bioinformatic analyses demonstrated that no structurally relevant similarity exists between the CP4 EPSPS protein and any known toxic or other biologically active proteins that would be harmful to human or animal health.

Comment 2

There is no indication that the expressed protein in the level envisaged to be consumed is not safe.
It can not be excluded that due to the genetic modification certain naturally occurring proteins could be expressed more or less. However there is no indication that this occurs in proteins that may pose a health hazard.

D.7.8.2 Testing of new constituents other than proteins

Comments/Questions of the expert(s)

Comment 1

There are no indications that new constituents other than proteins are present in MON87705.

D.7.8.3 Information on natural food and feed constituents

Comments/Questions of the expert(s)

Comment 1

Comment

Several of the studies mentioned in Table 42 (page234) do not support strictu sensu high oleic acid intake. These studies are substitution studies which show that oleic acid is better than saturated fatty acids or trans fatty acids. The important question from a nutritional point of view would be whether the effects of MON 87705 soybean oil would be different from those of conventional soybean oil. Taking into account the amount of soybean oil in the diet that is expected to be replaced by MON 87705 (1 % of energy; page 257), difference in fatty acid composition (ΔS=~7%; ΔP=~53%) and literature data (recently reviewed by Sanders, 2009), I assume that differences in effect, if any, would be negligible.

D.7.8.4 Testing of the whole GM food/feed

Comments/Questions of the expert(s)

Comment 1

a) 42-day feeding study in broiler chickens (**From CBI**: CQR-08-271, 2009).

Broiler mortality

From Day 7 - 42 bird mortality averaged 1.3% and ranged from 0 to 2.0% across all treatment groups. Mortality from Day 7 - 42 was 1.0% for birds receiving diets containing soybean meal produced from MON 87705.

Performance measurements

No unexpected effects on broiler performance were observed when broilers were fed diets formulated with soybean meal produced from MON 87705 compared to diets formulated with control or reference soybean meal.

Carcass measurements

Within sex analyses detected no difference (P ≥ 0.05) for any of these parameters between birds fed diets containing soybean meal produced from MON 87705 and conventional control soybean for male or female birds, with exception of average breast weight for male birds (0.562 versus 0.592 kg/bird, respectively)

CONCLUSION

There were no biologically relevant differences in broiler performance, carcass yield or meat composition between broilers fed diets containing SBM produced from MON 87705 and those fed diets containing SBM produced from conventional control soybean.

b) 90-Day rat feeding study (**From CBI:** WIL-50357, 2010).

Question: Only one dosing regimen was used in this study. Why? As such, no dose-response relationship can be established or excluded.

Above sentence as rephrased by the coordinator:
The question was raised by why only one dosing regimen was used in this study. This has as a consequence that no dose-response relationship can be established or excluded.

Comment 2

Long term feeding of defatted meal in 2 different species revealed no negative effects.

D.7.9 Allergenicity

Comments/Questions of the expert(s)

Comment 1

As allergenicity of a given protein or mix of proteins is hard to predict, the EFSA proposed a weight-of-evidence approach that integrates multiple, with allergenicity associated parameters for a given protein. The analysis of allergenic potential of MON87705 has been performed in agreement with this recommendation.

Allergenicity risk evaluation of newly expressed CP4 EPSPS protein:
Sensitivity to proteolysis (trypsin; simulated gastric fluids) and lack of shared amino acid sequence with known allergens (FASTA sequence alignment using the FARRP_2010 Database; eight-amino acid sliding window search using the FARRP_2010 Database) both indicate that the CP4 EPSPS protein does not pose an increased risk for allergenicity. Whereas CP4 EPSPS protein constitutes a relatively small portion of the total plant protein (mean value 0,042%), a considerable expression range in the order of 40 – 1000 µg/g dwt is observed for crops from different locations and countries (Chile, USA). Common sense would predict the lower the expression, the better. However, from diverse population studies it remains unclear to what extend high versus low level exposures directly correlate with allergic sensitization. Therefore, it is difficult to conclude from CP4 EPSPS protein expression levels per se to what extend the reported expression levels increase or not the risk for allergic sensitization.

Additional comment from the coordinator:
If a protein does not have an allergic potential, its expression levels do not matter.
CP4 EPSPS has been extensively looked at in earlier dossiers, and has been consumed on a very large scale.

Allergenicity risk evaluation of the whole GM plant:
Because soybean is known to be allergenic as such, it is imperative to verify to what extend the genetic modifications implemented caused a change in the expression of endogenous allergenic proteins. This was correctly verified by IgE binding assays (ELISA) using sera from soybean allergic

individuals. The baseline was set by comparison with a reference panel of conventional soybean varieties and the parent plant. This analysis was complemented with an allergic protein-selective assay using two-dimensional western blot analysis. Both analyses convincingly showed that the genetic modifications did not result in quantitative or qualitative changes in the expression levels of allergenic proteins in MON87705 compared to conventional soybean.

Conclusion.
The analysis of multiple parameters associated with or indicative of allergenic potential does not indicate individually or combined an increased risk for allergenicity of the MON87705 GM plant.

D.7.10 Nutritional assessment of GM food/feed

Comments/Questions of the expert(s)

Comment 1

Comments

1) There are no indications that the use of MON87705 soy bean oil in humans would pose any hazard. The same is true for the use of MON87705 soybean meal in animals (broiler chickens).
2) Some of the sentences in the application are suggestive of what is not true. For instance Part I, page 259 last paragraph above Table 45) suggests that the effect of reducing saturated fat intake by the use of MON 87705 oil would be greater in reality than “based on the highly conservative approach taken”. The reverse is true. If less MON87705 would be used, the effect would be smaller, not greater. Anyhow the effects on the fatty acid composition of the total diet are so small that they are not expected to have a considerable health effect if any.

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)

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

No negative effects expected.

D.9.7 Effects on animal health

Comments/Questions of the expert(s)

Comment 1

No negative effects expected.

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)

Comment 1

In this paragraph it is mentioned again that the scope of application does not include cultivation of soybean plants in the EU. Nevertheless I give some remarks in the case that the applicant should ask in the near future for an extension for the scope of cultivation. In the framework of the EU- regulation 2002/53 a new variety have to be submitted to DUS (Distinctness, Uniformity, Stability) and VCU (Value for Cultivation and Use) tests before the variety can be commercialised. The new variety has to be compared with the best existing standard varieties. So my question here is : can the GM- soybean be incorporated in normal VCU trials, without adapting the field conditions for the specific trait?
Remark SBB, agreed by coordinator
Suggestion not to forward this comment to EFSA, because it is not relevant in the context of the current application (no cultivation). Similar comment in a previous soybean dossier (2009/73 and 2009/76) has not been sent to EFSA.

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)

Comment 1

The proposed environmental monitoring plan is OK.

D.11.2 Interplay between environmental risk assessment and monitoring

Comments/Questions of the expert(s)

Comment 1

Based on the scope of application (no cultivation) I can agree with the remark of this chapter.

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)

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