Bioveiligheidsraad
Conseil de Biosécurité

03-02-2009

Secretariaat
Secrétariat

O./ref.: WIV-ISP/BAC/2009_880

Title: Advice of the Belgian Biosafety Advisory Council on the application EFSA/GMO/NL/2007/37 from Monsanto under Regulation (EC) No. 1829/2003

Context

The application EFSA/GMO/NL/2007/37 was submitted by Monsanto on 31 January 2007 for the marketing (import and processing) of the insect resistant genetically modified (GM) maize MON89034 for food and feed uses under Regulation (EC) No. 1829/2003[1].

The application was officially acknowledged by EFSA on 24 August 2007. On the same date EFSA started the formal three-month consultation 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 (GMOs) being part of the products).

Within the framework of this consultation, the Belgian Biosafety Advisory Council, under the supervision of a coordinator and with the assistance of its Secretariat, contacted experts chosen from the common list of experts drawn up by the Biosafety Advisory Council and the Division of Biosafety and Biotechnology (SBB) to evaluate the dossier. Seven 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 20 November 2007.

The opinion of the EFSA Scientific Panel on GMOs was adopted on 3 December 2008 (The EFSA Journal, 2008, 909, 1-30)[2], and published together with the responses of the EFSA GMO Panel to comments submitted by the experts during the three-month consultation period.

On 22 December 2008 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/EFSA/efsa_locale-1178620753812_1211902216540.htm>

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 Belgian experts are of the opinion that information received is sufficient.

3. Food/feed safety assessment

3.1. Following the comments submitted by the Belgian experts, the Biosafety Advisory Council considers that even if the compositional analysis of the GM food/feed was performed according to the OECD consensus document[4], 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.

3.2. The Biosafety Advisory Council observes that the allergenicity of the whole GM maize has not been evaluated. The introduction of the transforming DNA might interfere with the expression levels of other maize proteins, including allergens. Therefore, it might be relevant to analyze whether the expression levels of allergens is increased and to carry out IgE binding studies.

[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.
[4] OECD, 2001. Consensus Document on Compositional Considerations for New Varieties of Soybean: Key Food and Feed Nutrients and Anti-Nutrients. ENV/JM/MONO(2001)15.
http://www.olis.oecd.org/olis/2001doc.nsf/c5ce8ffa41835d64c125685d005300b0/

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 notifier to the EFSA GMO Panel questions and considering the data presently available, the Biosafety Advisory Council,

Agrees with the GMO panel of EFSA that
a) No major risks concerning the environment were identified.
b) No major risks for human and animal health were identified.

In addition, the Biosafety Advisory Council recommends:
1) To adapt the OECD consensus documents to include the analysis of dietary fibre in the compositional analysis of food;
2) To consider introducing assessment of allergenicity of the whole GM crops in the frame of the revision of the EFSA guidance document on Food/Feed safety assessment.

p.o.

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

Annex: Full comments of experts in charge of evaluating application EFSA/GMO/NL/2007/37 *and comments submitted on the EFSAnet (ref: BAC_2007_PT_603)*

Bioveiligheidsraad
Conseil de Biosécurité

20 November 2007

Secretariaat
Secrétariat

N./réf. : WIV-ISP/BAC/2007_PT_603
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Compilation of comments of experts in charge of evaluating the application EFSA/GMO/NL/2007/37 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 5 September 2007
Coordinator: Prof. dr. ir. Dirk Reheul
Experts: Dr. Pascal Cadot (Consultant), Prof. Dr. ir. François Chaumont (UCL), Prof. Dr. Jacques Dommes (ULg), Prof. Jean-Pierre Maelfait (UGent), Prof. Robert Renaville (FUSAGx), Dr. Peter Smet (Consultant), Prof. Wim Stevens (UIA)
Domains of expertise of experts involved: Biochemistry, genetics, genetic engineering, , improvement of plants, genome analysis, GMO traceability, transgene integration pattern, transgene expression, toxicology, immunology, alimentary allergology, animal nutrition, ecology, plant-insect relations, nature conservation, biosafety research.
Secretariat: Didier Breyer, Adinda De Schrijver, Martine Goossens, Philippe Herman

INTRODUCTION

Dossier **EFSA/GMO/NL/2007/37** concerns an application of the company **Monsanto** for the marketing of the genetically modified **maize MON 89034** for food and feed applications under Regulation (EC) 1829/2003.
The application has been officially acknowledged by EFSA on 24 August 2007.
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. Comments placed on the EFSAnet are indicated in grey.

List of comments received from the experts

A. GENERAL INFORMATION

Comments/Questions of the expert(s)

Comment 1

The notification concerns the authorization of MON 89034 maize for import, processing, and food and feed use and not for cultivation.

Comment 2

General Comment
As MON 89034 will enter in the food chain as normal maize it'll probably also enter in the diet of mothers and kids. Therefore toxicity studies are lacking on gravid animals to assess possible teratogenic effects as well as effects on neonates.

Maize is usually consumed all over the year and doesn't present a seasonal ingestion so that humans and animals will be exposed to MON 89034 for long periods of time even all life long. The duration of toxicity assays are therefore too limited and should be prolonged for more that 90 days to assess chronic effects.

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

Comments/Questions of the expert(s)

Comment 1

The recipient plant is maize (*Zea mays* L.) that has been widely and extensively cultivated worldwide.

C. INFORMATION RELATING TO THE GENETIC MODIFICATION

Comments/Questions of the expert(s)

Comment 1

MON 89034 was obtained by *Agrobacterium*-mediated transformation of maize using a single vector containing two T-DNAs. The first one includes two *cry* genes (*cry1A.105* and *cry2Ab2*) with specific regulatory elements and the second one contains a selectable marker (*ntpII* gene encoding the neomycin phosphotransferase enzyme). The use of 2T-DNA system allows to generate marker-free plants by segregation during the breeding. MON 89034 contains only the T-DNA for the expression of the *cry* genes.

The description of the vector including the source of the different DNA fragments is complete. However, the rationale to use a modified Cry1A protein including the domain III of Cry1F was not explained. Similarly, contrary to the Cry1A.105 protein, Cry2Ab2 was fused to a chloroplast transit peptide to address the protein to the chloroplast. The reason to target the two Cry proteins to different subcellular localizations was not explained.

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

See above. The combination of Cry1A.105 and Cry2Ab2 proteins was done to mainly improve insect control.

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

Comments/Questions of the expert(s)

Comment 1

Two remarks :

- The applicant did not describe the strategy and methods used to determine the sequence of plant genomic DNA flanking the insert.
- Southern blot hybridisation carried out to show the presence of the HSP70 intron in the insert (Technical dossier: figure 15) : additional bands are due to hybridisation on endogenous genes, but why were these hybridisation signals not observed when using a set of probes spanning the whole insert (Technical dossier: figure 9) ?

However the data presented in this section are sufficient to support the claims of the applicant.

Comment 2

Molecular analysis is fully documented and has been carried out with all the required controls. Many Southern blots with adequate DNA probes have been performed to demonstrate the size, copy number and integrity of the T-DNA containing the *cry* genes. Similarly, the absence of the T-DNA including the selectable marker and the plasmid PV-ZMIR245 backbone was demonstrated using probes covering the whole target sequence.
It was however difficult to understand directly why the applicants mentioned (p42 and p43 of Technical dossier) the presence of a Left border^{r1} and an e35S^{89} promoter sequence instead of a right border and P-e35S, respectively at 5' of the T-DNA insert. They should have mentioned or referred to the genetic modification at the 5' T-DNA flanking region detected by PCR fragments sequencing (described p65-67) at this place.

The way the site of T-DNA insertion and the flanking genomic DNA were identified is not described in the technical dossier. The modification detected at the 5' junction was detailed. However how the modification in e35S promoter affects the RNA expression was not investigated. The detection of high amount of Cry1A.105 proteins in the different parts of the plant suggests that the rearrangement in the promoter did not prevent protein expression.
The presence of a putative gene in the flanking regions was not reported in the original document but a subsequent bio-informatics analysis indicates that there are no hits with known genes.
It is of my opinion that the conclusions raised are in full agreement with the molecular results.

Comments summarized by the coordinator

1. Southern blot hybridisation carried out to show the presence of the HSP70 intron in the insert (Technical dossier: figure 15) : additional bands are due to hybridisation on endogenous genes, but why were these hybridisation signals not observed when using a set of probes spanning the whole insert (Technical dossier: figure 9) ?
2. It was difficult to understand directly why the applicants mentioned (p42 and p43 of Technical dossier) the presence of a Left border^{r1} and an e35S^{89} promoter sequence instead of a right border and P-e35S, respectively at 5' of the T-DNA insert. They should have mentioned or referred to the genetic modification at the 5' T-DNA flanking region detected by PCR fragments sequencing (described p65-67) at this place.
3. The way the site of T-DNA insertion and the flanking genomic DNA were identified is not described in the technical dossier. The modification detected at the 5' junction was detailed. However how the modification in e35S promoter affects the RNA expression was not investigated. The detection of high amount of Cry1A.105 proteins in the different parts of the plant suggests that the rearrangement in the promoter did not prevent protein expression.
   The presence of a putative gene in the flanking regions was not reported in the original document but a subsequent bio-informatics analysis indicates that there are no hits with known genes.

D.3. INFORMATION ON THE EXPRESSION OF THE INSERT

Comments/Questions of the expert(s)

Comment 1

The expression of the Cry proteins was assessed using an enzyme-linked immunosorbent assay (ELISA) in various plant tissues of MON 89034 produced in 2005 in the US. The expression of potential fusion proteins has been excluded from bio-informatics analysis. RT-PCR or Northern blot experiments using primers/probes from the flanking regions will be useful to confirm the bioinformatics analysis.

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 statistical differences between MON 89034 and conventional maize have been detected.

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

Comments/Questions of the expert(s)

Comment 1

The stability of the insert was demonstrated through multiple breeding generations (self-pollination and back-cross using segregation data and Southern blot analysis. In addition the absence of the second T-DNA containing the *npt* marker was shown.
On p109 (Technical dossier), the data allowing the estimation of the size (11.8 kb) of the band coming from a putative partial digestion of the flanking region was not mentioned. In addition the background signals using probes 18-23 in Figure 26 differs from the one observed in Figure 9 (Technical dossier). The explanations were not clear.

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

Comments/Questions of the expert(s)

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

D.7.1 Comparative assessment

Comments/Questions of the expert(s)

D.7.2 Production of material for comparative assessment

Comments/Questions of the expert(s)

D.7.3 Selection of material and compounds for analysis

Comments/Questions of the expert(s)

D.7.4 Agronomic traits

Comments/Questions of the expert(s)

D.7.5 Product specification

Comments/Questions of the expert(s)

D.7.6 Effect of processing

Comments/Questions of the expert(s)

D.7.7 Anticipated intake/extent of use

Comments/Questions of the expert(s)

D.7.8 Toxicology

Comments/Questions of the expert(s)

Comment 1

Only acute studies were done, some effects can only be seen after a long period of exposure so chronic studies are needed.

D. 7.8.1 Safety assessment of newly expressed proteins

Comments/Questions of the expert(s)

Comment 1

Acute oral toxicity study in mice with Cry1A.105 protein (Bonnette *et al.*, 2005).
Under the conditions of this test, no test article-related mortality or other toxicity was observed in the Cry1A.105 protein group.

Acute oral toxicity study in mice with Cry2Ab2 protein (Bonnette *et al.*, 2006).
Under the conditions of this test, no test article-related mortality or other toxicity was observed in the Cry2Ab2 protein group.

Digestibility of Cry1A.105 in simulated gastric fluid (SGF).
99.3% of full-length protein was degraded within 30 seconds. In the first 20 minutes trace amounts of a small fragment (4.5 kDa) was present. This fragment was undetectable in the 30 minute time point and beyond.

Digestibility of Cry1A.105 in simulated intestinal fluid (SIF).
The full-length Cry1A.105 was digested within 5 minutes, yielding fragments with molecular weights of approximately 62, 32 and 30 kDa. The major proteolytic fragment was observed for up to 24 hours (longest time point tested).

Digestibility of Cry2Ab2 in simulated gastric fluid (SGF).
99.4% of full-length protein was digested within 30 seconds. A small amount of a 5 kDa fragment was detected up till 2 minutes. Thereafter no bands were visible.

Digestibility of Cry2Ab2 in simulated intestinal fluid (SIF).
97.5% of full-length protein was digested within 15 minutes. Proteolytic bands with approximate molecular weight of 60, 55, 50, 40, 12 and 10 kDa were observed at the 5 minute time point. Several new bands (< 50 kDa) were detectable beginning at the 4 hour time point.

Although these proteins do not seem to be readily degradable in SIF, the digestibility studies in SGF and acute toxicity testing in mice indicate the absence of acute toxic effects.

Comment 2

It is well-known that the pesticides are endocrinal disruptors. In clinical investigations, endocrine measures are considered routine measures in assessing patient health. In this dossier there are no mentions of any endocrine tests! Endocrine axis is the first to be disrupted in illness so that they can not be removed from a toxicity study.

D.7.8.2 Testing of new constituents other than proteins

Comments/Questions of the expert(s)

D.7.8.3 Information on natural food and feed constituents

Comments/Questions of the expert(s)

D.7.8.4 Testing of the whole GM food/feed

Comments/Questions of the expert(s)

Comment 1

Comparison of broiler performance and carcass parameters when fed diets containing MON89034, control or commercial corn (Davis *et al.*, 2006).
There were no biologically relevant differences in the parameters measured between broilers fed the MON89034 diet and the control diet.

13-Week feeding study in rats (Kirkpatrick *et al.*, 2006).
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 sub-acute 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.

Comment 2

In the broiler study, feed conversion was statistically different between MON 89034 and control. This difference is not justified by the fact that there was no differences between MON 89034 and the other

treatments (commercial lines). There's a need of further investigation to understand this effect on feed conversion. Moreover Monsanto should provide the weights of organs like kidneys and liver.
Only acute studies were done, some effects can only be seen after a long period of exposure so chronic studies are needed.

Comments summarized by the coordinator

1.Tests with broilers

In the broiler study, feed conversion was statistically different between MON 89034 and control, while there were no differences between MON 89034 and the other treatments (commercial lines). There is a need of further investigation to understand this effect on feed conversion in order to conclude about the biological relevance of the differences. Moreover Monsanto should provide the weights of organs like kidneys and liver.
Only acute studies were done, some effects can only be seen after a long period of exposure so chronic studies are needed.

2. 13-Week feeding study in rats (Kirkpatrick *et al.*, 2006).

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 sub-acute 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.

D.7.9 Allergenicity

Comments/Questions of the expert(s)

Comment 1

To study the allergenicity of the Cry1A.105 and Cry2Ab2 proteins Monsanto has used the following criteria to test for allergenicity:

1. the protein is from a non-allergenic source: hitherto there are no reports on allergenic properties of Bt proteins.

2. the protein does not share structural similarities to known allergen based on the amino acid sequence: no relevant matches were found using the AD6 database for both proteins ore aminoacid sequences. There is no significant similarity between Cry1A.105 and a kiwi fruit protein. There were no alignments of at least 8 aminoacids found for Cry1A.105.
3. the protein is rapidly digested in simulated gastric fluid (SGF).
4. the protein represents only a very small portion of the total protein in the grain.

Nevertheless these rules are not absolute (Ebo and Stevens, 2001):

- a protein or polypeptide inserted in an other protein can end up with conformational changes of the original protein. Allergens are non only linear epitopes but can be formed by conformational epitopes.
- The rapid digestibility of a protein does not warrant non-allergenicity; some labile proteins are allergenic (eg. Mal d 1 form apple)
- The quantity of the protein in food is not absolutely related to allergenicity: allergic reactions can be induced by minute amounts of allergen

Post marketing surveillance remains necessary.

Comment 2

Assessment of the allergenicity of the introduced traits

The fact that Cry1A.105 shows 24.2% identity over 318 aa with actinidin, the major allergen of kiwi (Pastorello et al, 1998), might be a concern. Of course, this does not exceed the threshold of 35% over 80 aa, as recommended in the FAO/WHO guidelines, but this represents a sufficient number of aminoacids to form common conformational epitopes with actinidin when folded in the 3-D structure, which is not taken into account with single alignment searches. Kiwi allergy is not uncommon in Europe. It might be relevant and not difficult to perform skin tests with purified Cry1A.105 on kiwi-sensitized patients (the right kiwi-sensitized population must be chosen (Lucas et al, 2007)).

Likewise, potential cross-reactivity of Cry2Ab2 with Cop c 1 (Brander et al, 1999) should be further evaluated, though basidiomycetes-sensitized patients might be more difficult to find.

Testing the resistance to digestion is not useful in the assessment of allergenicity since there are multiple examples of labile allergens.

Assessment of the allergenicity of the whole GM plant or crop

In section 7.9.2, the allergenicity of the genetically modified maize itself has not been evaluated. The reviewer wishes to emphasize that the rationale of this section is not to take the new traits into consideration, but to evaluate, due to the introduction of the new traits, possible changes in the allergenicity of the recipient plant when this plant is known as an allergenic source.

Although not frequent, food allergy to maize has been described and major allergens have been determined (Pastorello et al. 2003; Pasini et al. 2002), and other potential allergens have been detected (Weichel et al. 2006). The introduction in the plant of Cry1A.105 and Cry2Ab2 and the effects thereof might interfere with the expression levels of other maize proteins, including allergens. For that reason, it is relevant to analyze whether the expression levels of known major allergens is increased in genetically modified MON89034 maize grains. Patient IgE binding to maize grain extract or titration of known major allergens of maize should be carried out.

Comments summarized by the coordinator

1. General comments

To study the allergenicity of the Cry1A.105 and Cry2Ab2 proteins Monsanto has used the following criteria to test for allergenicity:

1. the protein is from a non-allergenic source: hitherto there are no reports on allergenic properties of Bt proteins.
2. the protein does not share structural similarities to known allergen based on the amino acid sequence: no relevant matches were found using the AD6 database for both proteins ore aminoacid sequences. There is no significant similarity between Cry1A.105 and a kiwi fruit protein. There were no alignments of at least 8 aminoacids found for Cry1A.105.
3. the protein is rapidly digested in simulated gastric fluid (SGF).
4. the protein represents only a very small portion of the total protein in the grain.

Nevertheless these rules are not absolute (Ebo and Stevens, 2001):

- a protein or polypeptide inserted in an other protein can end up with conformational changes of the original protein. Allergens are non only linear epitopes but can be formed by conformational epitopes.
- The rapid digestibility of a protein does not warrant non-allergenicity; some labile proteins are allergenic (eg. Mal d 1 form apple)
- The quantity of the protein in food is not absolutely related to allergenicity: allergic reactions can be induced by minute amounts of allergen

Post marketing surveillance remains necessary.

2. Comments on the allergenicity of the introduced traits and of the whole GM plant

2.1 Assessment of the allergenicity of the introduced traits

The fact that Cry1A.105 shows 24.2% identity over 318 aa with actinidin, the major allergen of kiwi (Pastorello et al, 1998), might be a concern. Of course, this does not exceed the threshold of 35% over 80 aa, as recommended in the FAO/WHO guidelines, but this represents a sufficient number of aminoacids to form common conformational epitopes with actinidin when folded in the 3-D structure, which is not taken into account with single alignment searches. Kiwi allergy is not uncommon in Europe. It might be relevant and not difficult to perform skin tests with purified Cry1A.105 on kiwi-sensitized patients (the right kiwi-sensitized population must be chosen (Lucas et al, 2007)).
Likewise, potential cross-reactivity of Cry2Ab2 with Cop c 1 (Brander et al, 1999) should be further evaluated, though basidiomycetes-sensitized patients might be more difficult to find.

2.2 Assessment of the allergenicity of the whole GM plant or crop

In section 7.9.2, the allergenicity of the genetically modified maize itself has not been evaluated. The reviewer wishes to emphasize that the rationale of this section is not to take the new traits into consideration, but to evaluate, due to the introduction of the new traits, possible changes in the allergenicity of the recipient plant when this plant is known as an allergenic source.
Although not frequent, food allergy to maize has been described and major allergens have been determined (Pastorello et al. 2003; Pasini et al. 2002), and other potential allergens have been detected (Weichel et al. 2006). The introduction in the plant of Cry1A.105 and Cry2Ab2 and the effects thereof might interfere with the expression levels of other maize proteins, including allergens. For that reason,

it is relevant to analyze whether the expression levels of known major allergens is increased in genetically modified MON89034 maize grains. Patient IgE binding to maize grain extract or titration of known major allergens of maize should be carried out.

D.7.10 Nutritional assessment of GM food/feed

Comments/Questions of the expert(s)

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

Comments/Questions of the expert(s)

Comment 1

As no long term toxicity studies has been done, it is not possible to exclude long term effect of GMO consumption. That's why it is required to do a follow-up of the GM food post-market.

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)

Comment 1

Provided information: sufficient.

D.9.2 Selective advantage or disadvantage

Comments/Questions of the expert(s)

Comment 1

Provided information: sufficient.

D.9.3 Potential for gene transfer

Comments/Questions of the expert(s)

Comment 1

Provided information: sufficient.

D.9.4 Interactions between the GM plant and target organism

Comments/Questions of the expert(s)

Comment 1

Not applicable

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

Comments/Questions of the expert(s)

Comment 1

Provided information: sufficient.

D.9.6 Effects on human health

Comments/Questions of the expert(s)

D.9.7 Effects on animal health

Comments/Questions of the expert(s)

D.9.8 Effects on biogeochemical processes

Comments/Questions of the expert(s)

Comment 1

Provided information: sufficient.

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

Comments/Questions of the expert(s)

Comment 1

Not applicable

D.10. POTENTIAL INTERACTIONS WITH THE ABIOTIC ENVIRONMENT

Comments/Questions of the expert(s)

Comment 1

Provided information: sufficient.

D.11. ENVIRONMENTAL MONITORING PLAN

D.11.1 General

Comments/Questions of the expert(s)

Comment 1

We support the recommendation of ACRE (2006) that provision of detailed arrangements for general surveillance post-market monitoring plans for the import and processing of grain from GM maize should be made a condition of any consent. These should include which and when information should be provided to EFSA and how the applicant can ensure this to happen.
Although resistance to insect attack is not the only factor preventing maize to grow outside the agricultural environment, the (indeed low) possibility of the establishment of maize protected against insect larvae in the wild in Europe should be a point of particular interest in a more detailed general surveillance plan.

D.11.2 Interplay between environmental risk assessment and monitoring

Comments/Questions of the expert(s)

D.11.3 Case-specific GM plant monitoring

Comments/Questions of the expert(s)

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

Comments/Questions of the expert(s)

D.11.5 Reporting the results of monitoring

Comments/Questions of the expert(s)

References

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