Bioveiligheidsraad
Conseil de Biosécurité

06-11-2009

Secretariaat
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O./ref.: WIV-ISP/BAC/2009_01491

Title: Advice of the Belgian Biosafety Advisory Council on the application EFSA/GMO/CZ/2006/33 from Monsanto under Regulation (EC) No. 1829/2003

Context

The application EFSA/GMO/CZ/2006/33 was submitted by Monsanto on 3 January 2006 for the placing on the market of the insect resistant and glyphosate-tolerant genetically modified MON88017 x MON810 maize under Regulation (EC) No. 1829/2003[1]. The scope of the application covers food and feed uses, import and processing of the GM maize and all derived products, but excludes cultivation in the EU.

The application was officially acknowledged by EFSA on 21 February 2007. 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 (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 to evaluate the dossier, chosen from the common list of experts drawn up by the Biosafety Advisory Council and the Division of Biosafety and Biotechnology (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 21 May 2007.

The opinion of the EFSA Scientific Panel on GMOs was adopted on 2 July 2009 (The EFSA Journal, 2009, 1192, 1-27)[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 21 August 2009 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_1211902691146.htm>

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In addition, the scientific evaluations of the single events, namely maize line MON810 (EFSA/GMO/RX-MON810) and maize line MON88017 (EFSA/GMO/CZ/2005/27), are taken into account in this advice[3]. The Biosafety Advisory Council formulated a positive advice for each single event[4]. Maize MON810 is authorised for cultivation and food/feed uses[5] but the procedure to obtain renewal of this authorization is running. The authorization procedure for maize MON88017 is still running.

Scientific evaluation

1. Environmental risk assessment

According to the Biosafety Advisory Council no major risks were identified concerning the environment[6].

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

3.2. Assessment of toxicity
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
With regard to allergenicity, the Biosafety Advisory Council is of the opinion that the information provided is sufficient and does not raise safety concerns.

3.4. Nutritional value
The Biosafety Advisory Council is of the opinion that the information provided is sufficient and shows the nutritional equivalence of the GM maize with its non-GM counterpart and conventional maize varieties.

4. Monitoring

General surveillance is advised to follow-up unanticipated allergenicity aspects since the allergenicity of the whole GM maize has not been tested.

[3] Advice of BAC on maize line MON88017: BAC_2009_01045; Advice of BAC on maize line MON810: BAC_2009_01490
[4] Advice of BAC on maize line 59122: BAC_2007_SC_536; Scientific evaluation of SBB on mandate of BAC of maize line NK603: IPH/1520/GMCROPFF/2003-0767; Scientific evaluation of SBB on mandate of BAC of maize line 1507: IPH/1520/GMCROPFF/2006-0839.
[5] See Community Register <http://ec.europa.eu/food/dyna/gm_register/index_en.cfm>
[6] 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.

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 general surveillance to follow up unanticipated allergenicity aspects since the allergenicity of the whole GM maize has not been tested;

p.o.

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

Annexes:
- Full comments of experts in charge of evaluating application EFSA/GMO/CZ/2006/33 *(ref. BAC_2007_PT514)*
- Comments submitted on the EFSAnet (ref: BAC_2007_PT_515)

Bioveiligheidsraad
Conseil de Biosécurité

21 May 2007

Secretariaat
Secrétariat

N./réf. : WIV-ISP/BAC/2007/PT_515
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Application EFSA/GMO/CZ/2006/33
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 12 March 2007.
Coordinator: Prof. dr. ir. Dirk Reheul (UGent)
Experts: Jacques Dommes (ULg), Leo Fiems (ILVO), Jean-Claude Grégoire (ULB), Peter Smet (Consultant), Wim Stevens (UA), Hadewijch Vanhooren (KUL)
Domains of expertise of experts involved: genetics, genetic engineering, general biochemistry, immunology, animal nutrition, alimentary allergology, toxicology, ecology, plant-insect relations, biodiversity, entomology, insect resistance, phytopathology, risk analysis, consumers info
Secretariat: Didier Breyer, Adinda De Schrijver, Martine Goossens

INTRODUCTION

Dossier **EFSA/GMO/CZ/2006/33** concerns an application of the company **Monsanto** for the marketing of the genetically modified **maize MON88017 x MON810** for food and feed applications under Regulation (EC) 1829/2003.
The application has been officially acknowledged by EFSA on 21 February 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)

List of comments submitted on the EFSAnet

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).
When needed, comments from the experts have been summarized by the coordinator and for clarity some sentences have been rephrased.
For the full comments of the Belgian experts and the bibliographic references we refer to the document given in annex 2. It displays all the comments as there were transmitted by the experts (ref. BAC_2007_PT_514)

A. GENERAL INFORMATION

Comments submitted on the EFSAnet

Adequate information is provided.

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

Comments submitted on the EFSAnet

Information provided is sufficient.

C. INFORMATION RELATING TO THE GENETIC MODIFICATION

Comments submitted on the EFSAnet

Information provided is sufficient.

D. INFORMATION RELATING TO THE GM PLANT

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

Comments submitted on the EFSAnet

Information provided is sufficient.

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

Comments submitted on the EFSAnet

Information provided is sufficient. The presence and copy number of the insert from both parental lines was checked by hybridisation of specific probes on southern blots.

D.3. INFORMATION ON THE EXPRESSION OF THE INSERT

Comments submitted on the EFSAnet

Information provided is sufficient. The company provided data on expression level of the three proteins encoded by the genes present on both inserts in the MON 88017 x MON 810 hybrid, and also of the proteins encoded by the inserts present in both parental lines (3 field trials in USA during the 2002 growing season, 3 replicated plots per trial). CP4 EPSPS, Cry3Bb1 and Cry1Ab proteins were assayed in various tissues by ELISA. Expression levels were comparable in the MON 88017 x MON 810 hybrid and in the MON 88017 and MON 810 parental lines.

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

Comments submitted on the EFSAnet

Information provided is sufficient.

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

Comments submitted on the EFSAnet

Information provided is sufficient.

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

Comments submitted on the EFSAnet

Information provided is sufficient.

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 submitted on the EFSAnet

The safety of the Cry3Bb1, Cry1Ab, and CP4 EPSPS proteins has previously been assessed in the single events, for which positive opinions were issued (EFSA, 2005).

D.7.2 Production of material for comparative assessment

Comments submitted on the EFSAnet

None

D.7.3 Selection of material and compounds for analysis

Comments submitted on the EFSAnet

Analytical data dealing with the composition of forage maize and its use as a feed are not relevant (p.40-48 of Technical dossier), because it is not intended that maize will be used for crop production yielding forages within the EU, but the application is restricted to the import of maize grain into the EU. Cry3Bb1 and CP4 EPSPS proteins used for the analysis of the allergenic effects, were produced by E. coli (p.60-61 of Technical dossier). It has been mentioned that testing bacterial surrogate proteins should not substitute for testing the plant-expressed proteins (Freese & Schubert, 2004).

D.7.4 Agronomic traits

Comments submitted on the EFSAnet

None

D.7.5 Product specification

Comments submitted on the EFSAnet

None

D.7.6 Effect of processing

Comments/Questions of the expert(s)

None

D.7.7 Anticipated intake/extent of use

Comments submitted on the EFSAnet

None

D.7.8 Toxicology

Comments submitted on the EFSAnet

MON 88017 x MON 810 is produced by crossing MON 88017 and MON 810 using traditional breeding methods. So, no new genetic modifications are introduced. However, MON 88017 contains both the CP4 EPSPS and the Cry3Bb1 proteins, whereas MON 810 expresses the Cry1Ab protein.
All of these traits were introduced by genetic modification.
CP4 EPSPS, Cry3Bb1 proteins and Cry1Ab have previously been evaluated. No acute toxic effects were found in these studies. So it is not meaningful to test the individual proteins again.
Otherwise, it is necessary to test the whole food/feed, to look for possible combined effects (synergism).

D. 7.8.1 Safety assessment of newly expressed proteins

Comments submitted on the EFSAnet

Similar proteins to the three proteins present in MON 88017 X MON 810 maize have been assessed previously for safety (MON 863, NK603, MON 863 x NK603, MON 863 x MON 810, MON 863 x MON 810 x NK603). Additionally, a battery of tests designed to evaluate the Cry3Bb1 variant protein and the native CP4 EPSPS protein present in MON 88017 maize for characteristics associated with food allergens and toxins raised no concern. The mature CP4 EPSPS in MON 88017 is identical to the bacterial enzyme of 455 amino acids and is targeted to the plant chloroplast. The Cry3Bb1 in MON 88017 differs from the native Cry3Bb1 by 6 amino acid changes, and differs from the in MON 863 variant by only 1 amino acid.
The Cry1Ab, CryBb1, and CP4 EPSPS proteins do not share sequence homology with known toxins (other than B.t. proteins). There is a rapid digestion of the Cry3Bb1 and CP4 EPSPS proteins in *in vitro* simulated gastric fluids and the CryAb protein is rapidly degraded and its insecticidal activity lost under conditions simulating mammalian digestion. There is lack of toxicity for the Cry1Ab, CryBb1, and CP4 EPSPS proteins as determined by a mouse acute oral toxicity study. The proteins used for the *in vitro* digestibility testing and the acute oral toxicity testing in mice have been produced by E. coli and are considered to be equivalent to the MON 88017 x MON 810 proteins.

The introduced proteins are present at low levels in MON 88017 x MON 810 and were found comparable to the corresponding ranges in either MON 88017 or MON 810.

D.7.8.2 Testing of new constituents other than proteins

Comments submitted on the EFSAnet

No constituents other than the Cry1Ab, Cry3Bb1 and CP4 EPSPS proteins are novel. MON 88017 X MON 810 was shown to be compositionally equivalent to non-GM maize with comparable genetic background.

D.7.8.3 Information on natural food and feed constituents

Comments submitted on the EFSAnet

Compositional studies were conducted to establish the nutritional adequacy of MON 88017 X MON 810 maize compared with a conventional control maize with similar genetic background, as well as with other commercially available maize hybrids. In addition, MON 88017 X MON 810 maize was compared with MON 88017 and MON 810. All maize was grown at replicated field sites across the U.S. during the 2002 field season. A reduction in approx. 7.9% in 20:1 eicosenoic acid levels was observed in MON 88017 X MON 810 grain samples compared with the conventional control maize (20:1 eicosenoic acid was consistently lower at each of the field sites). However, the levels were well within the 99% tolerance interval and well within the literature and historical range for maize grain. Other differences were not indicative of an overall pattern of change that could be attributed to the modification [in forage: calcium (1 comparison); in grain: 16:1 palmitoleic acid, 18:1 oleic acid, 18:3 linolenic acid , glutamic acid, leucine, methionine, moisture, niacin, protein, vit B6, vit B1 (1 comparison); 20:0 arachidic acid, alanine, ferulic acid, potassium, vit B2 (2 comparisons); 18:2 linoleic acid, copper (3 comparisons)]. Nevertheless, greatest differences were observed for copper (24.3%) in grain and calcium (20.2%) in forage. (Copper content of the MON 863 x MON 810 was also found stat. sign. different: EFSA Journal (2004) 49, 1-25)
As concluded by the applicant: no particular natural constituents of maize are considered to be of significant concern to require additional information or further risk assessment.
Consideration: If the compositional studies would have been conducted on maize grown in different growing seasons and in different geographic regions, the origin of the current statistically significant differences would be much clearer. It is common knowledge that the expression of characteristics depends on environmental influences; it is common scientific practice to conduct field trials in different years and locations to study the importance of environmental influences.

D.7.8.4 Testing of the whole GM food/feed

Comments submitted on the EFSAnet

1. The applicant concluded that the safety assessment for the individual proteins is not changed when combined in MON 88017 x MON 810, since the proteins: 1° are unlikely to interact, 2° have very

different and well-documented modes of action, 3° are produced in very low quantities in MON 88017 x MON 810, and 4° were shown safe in their individual safety assessments.
It is important to check whether the protein levels in the hybrid line are comparable to the corresponding ranges in the parental lines.
These data are shown in tables 4, 5 and 6 of the technical dossier. As can be seen from these data, protein levels are indeed comparable.
Remark : Bhakhta *et al.*, 2003b does not provide raw data, only the mean values, which is scientifically not acceptable.

2. Poultry broilers feeding study with MON 88017 X MON 810 maize grain (42 days).

The study was undertaken to compare the wholesomeness of MON 88017 x MON 810 grain (treated with glyphosate herbicide? not mentioned in this study) to conventional control (LH59 x LH198) as well as to five commercial reference maize hybrids when fed to rapidly growing Ross x Ross 508 broilers (Taylor et al., 2005). Broilers were fed a starter diet (d0-21) and grower/finisher diet (d21-42) containing appr. 55% and 60% w/w maize, respectively, for all treatments. Treatments were randomly assigned to pens with five blocks for 16 pens (8 male, 8 female) with 10 broilers/pen for a total of 80 pens and 800 broilers. Broilers were weighed by pen on d0 and d42 and individually at study termination. Pen feed intake was determined at d42. At study termination, all surviving birds were processed to determine carcass yield and meat composition. Fat pad measurements were taken for each bird. One broiler/pen was randomly selected and sampled for breast and thigh meat quality assays.
Significant diet-by-gender interactions were noted for live weight, final live body weight, fat pad weight, and thigh weight. However, at the 5% level of significance, no differences were noted for males or females for any of these parameters. No differences were observed in the percentage of moisture, protein, and fat in thigh meat and breast meat of broilers. Comparison of the MON 88017 X MON 810 fed birds to the population of the other diets fed showed no differences on all performance parameters, carcass yields, or meat quality parameters measured. However, statistically significant differences ($p<0.05$) were noted for breast fat in the population comparison. The differences noted were within established literature ranges (but no own historical control data was made available by the testing company: also within these ranges?) for breast fat of broilers and no differences were observed in the pairwise comparisons between treatment diets for the breast meat measurements.
According to the applicant, the results of the broiler feeding study showed that there were no biologically significant differences on the parameters tested between broilers fed MON 88017 X MON 810 or the broilers fed control maize. Minor differences noted were consistent with literature values and within natural variability.

3. Rat feeding studies

3.1. Rat feeding studies with the parental lines

3.1.1. 90-days feeding study in rats with MON 88017 maize grain.

We refer to the remarks given in dossier EFSA/GMO/CZ/2005/27.

3.1.2. 90-days feeding study in rats with MON 810 maize grain.

In a sub-chronic (90-days) toxicity study in rats fed MON 810 maize (Lemen, 2001), no consistent differences in the measured clinical, biological and histological parameters were noted for rats fed on non-GM or MON 810 maize except for albumin/globulin count. For rats fed 33% MON 810 maize, a statistically significantly lower albumin/globulin count was observed compared with control and overall reference lines at study termination. It was accepted by EFSA that the differences found were considered not to be of biological significance.

According to the applicant, these studies confirm the absence of any toxic effects associated to the introduced proteins and the absence of any unanticipated or pleiotropic effects linked to the genetic modification. The significant difference for albumin/globulin count can however not be ignored.

3.2. Rat feeding studies with MON88017 x MON810

They are missing !

The applicant presents a poultry feeding study with the new hybrid, but does not present a rat feeding study. The applicant refers to rat tests with the parental lines (see 3.1). Simply postulating that any interaction seems unlikely is a scientific poor excuse for not conducting this feeding study.

D.7.9 Allergenicity

Comments submitted on the EFSAnet

Monsanto used simulated gastric and intestinal fluids to test the digestion of Cry3Bb1, Cry1Ab and CP4 EPSPS proteins (p. 73, p.91 and p.94 of Technical dossier). It has been shown that a rapid in vivo degradation of Cry proteins (Cry1Ab) does not always occur (Chowdhury et al., 2003). Furthermore, Spök et al (2005) have shown that digestibility studies can not be considered suitable tools to address the allergenic potential of a protein.

1. The possible allergenic effects of MON88017 were already dealt with in the application EFSA/GMO/CZ/2005/27. We refer to comments provided in this dossier.

2. As far as the MON 810 is concerned, there have been studies about the allergenicity of the Cry1Ab.

2.1. A study performed by Nakajima et al. (2007) could not find IgE antibodies to the protein:

" Enzyme-linked immunosorbent assay (ELISA) is the most convenient method of monitoring the occurrence of IgE antibodies specific for novel proteins in genetically modified (GM) foods. The levels of IgE specific for a recombinant protein, Cry1Ab, were determined using an ELISA method. A soluble form of the Cry1Ab protein purified from pCold1 vector-transformed Escherichia coli pTf16/BL21 was used as the ELISA coating antigen, and 1M NaCl was used as the washing buffer to remove IgE non-specifically bound to the coated antigen. Sera from 44 patients allergic to major food allergens were obtained, diluted 20-fold, tested, and found no identifiable IgE above background levels. We also
tested sera from patients with corn allergy against whole extracts of non-GM and GM-corn (MON 810) using immunoblotting. The staining patterns were similar for the two types of corn. These results indicate that significant levels of IgE antibodies specific to Cry1Ab were not found in the sera of Japanese patients with food allergies."

2.2. Sticker et al. (2003) employed epitope recognition by CD4 cells and found one major epitope in Cry1a (610 amino acids) and no major epitopes in Cry3Aa (644 amino acids). This was less than the know Brazil nut allergen (Sticker 2003). However MON810 contains Cry1Ab.

Based on the available information there is no major risk for sensitization with the proteins involved.

D.7.10 Nutritional assessment of GM food/feed

Comments submitted on the EFSAnet

The fact that there was no detrimental effect on performance, carcass yield and meat composition, and health in broiler chickens in comparison with conventional maize hybrids (Taylor et al., 2005) is an indication of its safety and nutritional equivalence. It is proposed that chickens can be used as target animal species for livestock feeding studies with a GM plant derived feed, to investigate possible effects of the new feed resource on animal performance, animal health and welfare, efficacy, and acceptability of the new feed ingredient (EFSA, 2006b). Although there are significant differences between MON88017 x MON810 and control varieties (p.40-48 of Technical Dossier) analyses are within the range of literature data.

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

Comments submitted on the EFSAnet

None

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

Comments submitted on the EFSAnet

None

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 submitted on the EFSAnet

In the dossier (p. 14): " *This maize was shown to be as safe and as nutritious as conventional maize. Therefore, MON 88017 x MON 810 and derived products from MON 88017 x MON 810 will be stored, packaged, transported, used, and handled in the same manner as current commercial maize varieties, and measures for waste disposal and treatment of MON 88017 x MON 810 products are the same as those for conventional maize*"
This lack of precautions might result in seed spillage and unwanted dissemination.

D.9.2 Selective advantage or disadvantage

Comments submitted on the EFSAnet

None

D.9.3 Potential for gene transfer

Comments submitted on the EFSAnet

The possibility of gene transfer seems to be very low to negligible.

The probability that (spillage + establishment + contamination) is limited at some parts of the itinerary (e g at ports), but not necessarily along the transportation routes. Even though it can not survive the winter, maize from spilled seeds can develop one generation on the sites of spilling, leading to potential dissemination of pollen.
More specific details are needed regarding the packing and other means of confinement during transportation and storage.

D.9.4 Interactions between the GM plant and target organism

Comments submitted on the EFSAnet

None

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

Comments submitted on the EFSAnet

None

D.9.6 Effects on human health

Comments submitted on the EFSAnet

None

D.9.7 Effects on animal health

Comments submitted on the EFSAnet

Studies of Taylor et al. (2005) indicated that broiler mortality based on diets containing MON88017 x MON810 was related to bacterial infection, dehydration, refusal of feed, or ascites during the first 7 d, and the causes of death between d 8 and 42 were primarily attributed to sudden death and ascites, which commonly occur in broilers. Remaining broilers in all treatments were in good health.

D.9.8 Effects on biogeochemical processes

Comments submitted on the EFSAnet

None

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

Comments submitted on the EFSAnet

None

D.10. POTENTIAL INTERACTIONS WITH THE ABIOTIC ENVIRONMENT

Comments submitted on the EFSAnet

None

D.11. ENVIRONMENTAL MONITORING PLAN

D.11.1 General

Comments submitted on the EFSAnet

None

D.11.2 Interplay between environmental risk assessment and monitoring

Comments submitted on the EFSAnet

None

D.11.3 Case-specific GM plant monitoring

Comments submitted on the EFSAnet

None

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

Comments submitted on the EFSAnet

None

D.11.5 Reporting the results of monitoring

Comments submitted on the EFSAnet

None

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Comments of experts in charge of evaluating the application EFSA/GMO/CZ/2006/33

Mandate for the Group of Experts: mandate of the Biosafety Advisory Council (BAC) of 12 March 2007.
Coordinator: Prof. dr. ir. Dirk Reheul (UGent)
Experts: Jacques Dommes (ULg), Leo Fiems (ILVO), Jean-Claude Grégoire (ULB), Peter Smet (Consultant), Wim Stevens (UA), Hadewijch Vanhooren (KUL)
Domains of expertise of experts involved: genetics, genetic engineering, general biochemistry, immunology, animal nutrition, alimentary allergology, toxicology, ecology, plant-insect relations, biodiversity, entomology, insect resistance, phytopathology, risk analysis, consumers info
Secretariat: Didier Breyer, Adinda De Schrijver, Martine Goossens

INTRODUCTION

Dossier **EFSA/GMO/CZ/2006/33** concerns an application of the company **Monsanto** for the marketing of the genetically modified **maize MON88017 x MON810** for food and feed applications under Regulation (EC) 1829/2003.
The application has been officially acknowledged by EFSA on 21 February 2007.
The scope of the application is:
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☒ 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).
The same experts already evaluated dossier EFSA/GMO/CZ/2005/27, an application of the same company for the marketing of the genetically modified maize MON 88017. Many comments already made for MON 88017 apply also for this new dossier and are therefore repeated here.

List of comments received from the experts

A. GENERAL INFORMATION

Comments/Questions of the expert(s)

Comment 1

Adequate information is provided.

Comment 2

The fact that:
- on the hand MON 88017 x MON 810 was obtained by traditional breeding of two inbred lines, one derived from MON 88017 and the other one derived from MON 810
- on the other hand:
  - consent was given by the competent authorities of France to place MON810 on the market (EC, 1998)
  - MON 810 has been approved (EFSA, 2006a), and that an approval of MON 88017 under Regulation (EC) No. 258/97 is pending

may be favorable with regard to the evaluation of the application of MON 88017 x MON 810.

Comment 3

NB – My competence is in the environmental effects of GM plants; therefore my contribution in this dossier will be limited. Every time I will feel that the question asked is out of my field, I will use this "No comment/question" reply.

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

Comments/Questions of the expert(s)

Comment 1

Information provided is sufficient.

Comment 2

Since MON 88017 × MON 810 is produced by crossing single-trait inbred plants of MON 88017 and MON 810, I like to refer to previous comments concerning each of these lines.

Note of the coordinator: MON810 is a single trait plant containing the *cry1Ab* gene. However MON 88017 is not a single trait plant but a double trait plant containing the *cp4epsps* and *cry3Bb1* gene

expression cassettes. In its dossier the applicant erroneously states that the hybrid was produced by crossing single-trait inbred plants.

C. INFORMATION RELATING TO THE GENETIC MODIFICATION

Comments/Questions of the expert(s)

Comment 1

Information provided is sufficient.

Comment 2

No comments or questions.

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

Information provided is sufficient.

Comment 2

No comments or questions.

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

Comments/Questions of the expert(s)

Comment 1

Information provided is sufficient. The presence and copy number of the insert from both parental lines was checked by hybridisation of specific probes on southern blots.

Comment 2

No comments or questions.

D.3. INFORMATION ON THE EXPRESSION OF THE INSERT

Comments/Questions of the expert(s)

Comment 1

Information provided is sufficient. The company provided data on expression level of the three proteins encoded by the genes present on both inserts in the MON 88017 x MON 810 hybrid, and also of the proteins encoded by the inserts present in both parental lines (3 field trials in USA during the 2002 growing season, 3 replicated plots per trial). CP4 EPSPS, Cry3Bb1 and Cry1Ab proteins were assayed in various tissues by ELISA. Expression levels were comparable in the MON 88017 x MON 810 hybrid and in the MON 88017 and MON 810 parental lines.

Comment 2

No comments or questions.

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

Information provided is sufficient.

Comment 2

No comments or questions.

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

Comments/Questions of the expert(s)

Comment 1

Information provided is sufficient.

Comment 2

No comments or questions.

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

Information provided is sufficient.

Comment 2

No comments or questions.

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)

According to EFSA (2005) the safety of the Cry3Bb1, Cry1Ab, and CP4 EPSPS proteins has previously been assessed in the single events, for which positive opinions were issued.

D.7.2 Production of material for comparative assessment

Comments/Questions of the expert(s)

No comments or questions.

D.7.3 Selection of material and compounds for analysis

Comments/Questions of the expert(s)

Analytical data dealing with the composition of forage maize and its use as a feed are not relevant (p.40-48 of Technical dossier), because it is not intended that maize will be used for crop production yielding forages within the EU, but the application is restricted to the import of maize grain into the EU. Cry3Bb1 and CP4 EPSPS proteins used for the analysis of the allergenic effects, were produced by E. coli (p.60-61 of Technical dossier). It has been mentioned that testing bacterial surrogate proteins should not substitute for testing the plant-expressed proteins (Freese & Schubert, 2004).

D.7.4 Agronomic traits

Comments/Questions of the expert(s)

No comments or questions.

D.7.5 Product specification

Comments/Questions of the expert(s)

No comments or questions.

D.7.6 Effect of processing

Comments/Questions of the expert(s)

No comments or questions.

D.7.7 Anticipated intake/extent of use

Comments/Questions of the expert(s)

No comments or questions.

D.7.8 Toxicology

Comments/Questions of the expert(s)

Comment 1

MON 88017 x MON 810 is produced by crossing MON 88017 and MON 810 using traditional breeding methods. So, no new genetic modifications are introduced. However, MON 88017 contains both the CP4 EPSPS and the Cry3Bb1 proteins, whereas MON 810 expresses the Cry1Ab protein.
All of these traits were introduced by genetic modification.
CP4 EPSPS, Cry3Bb1 proteins and Cry1Ab have previously been evaluated. No acute toxic effects were found in these studies. So it is not meaningful to test the individual proteins again.
Otherwise, it is necessary to test the whole food/feed, to look for possible combined effects (synergism).

Comment 2

No comments or questions.

D. 7.8.1 Safety assessment of newly expressed proteins

Comments/Questions of the expert(s)

Comment 1

Similar proteins to the three proteins present in MON 88017 X MON 810 maize have been assessed previously for safety (MON 863, NK603, MON 863 x NK603, MON 863 x MON 810, MON 863 x MON 810 x NK603). Additionally, a battery of tests designed to evaluate the Cry3Bb1 variant protein and the native CP4 EPSPS protein present in MON 88017 maize for characteristics associated with

food allergens and toxins raised no concern. The mature CP4 EPSPS in MON 88017 is identical to the bacterial enzyme of 455 amino acids and is targeted to the plant chloroplast. The Cry3Bb1 in MON 88017 differs from the native Cry3Bb1 by 6 amino acid changes, and differs from the in MON 863 variant by only 1 amino acid.
The Cry1Ab, CryBb1, and CP4 EPSPS proteins do not share sequence homology with known toxins (other than B.t. proteins). There is a rapid digestion of the Cry3Bb1 and CP4 EPSPS proteins in *in vitro* simulated gastric fluids and the CryAb protein is rapidly degraded and its insecticidal activity lost under conditions simulating mammalian digestion. There is lack of toxicity for the Cry1Ab, CryBb1, and CP4 EPSPS proteins as determined by a mouse acute oral toxicity study. The proteins used for the *in vitro* digestibility testing and the acute oral toxicity testing in mice have been produced by E. coli and are considered to be equivalent to the MON 88017 x MON 810 proteins.
The introduced proteins are present at low levels in MON 88017 x MON 810 and were found comparable to the corresponding ranges in either MON 88017 or MON 810.

Comment 2

Not meaningful, since this was done in earlier studies.

Comment 3

No comments or questions.

D.7.8.2 Testing of new constituents other than proteins

Comments/Questions of the expert(s)

Comment 1

No constituents other than the Cry1Ab, Cry3Bb1 and CP4 EPSPS proteins are novel. MON 88017 X MON 810 was shown to be compositionally equivalent to non-GM maize with comparable genetic background.

Comment 2

No comments or questions.

D.7.8.3 Information on natural food and feed constituents

Comments/Questions of the expert(s)

Comment 1

Compositional studies were conducted to establish the nutritional adequacy of MON 88017 X MON 810 maize compared with a conventional control maize with similar genetic background, as well as with other commercially available maize hybrids. In addition, MON 88017 X MON 810 maize was compared with MON 88017 and MON 810. All maize was grown at replicated field sites across the U.S. during the 2002 field season. A reduction in approx. 7.9% in 20:1 eicosenoic acid levels was observed in MON 88017 X MON 810 grain samples compared with the conventional control maize

(20:1 eicosenoic acid was consistently lower at each of the field sites). However, the levels were well within the 99% tolerance interval and well within the literature and historical range for maize grain. Other differences were not indicative of an overall pattern of change that could be attributed to the modification [in forage: calcium (1 comparison); in grain: 16:1 palmitoleic acid, 18:1 oleic acid, 18:3 linolenic acid , glutamic acid, leucine, methionine, moisture, niacin, protein, vit B6, vit B1 (1 comparison); 20:0 arachidic acid, alanine, ferulic acid, potassium, vit B2 (2 comparisons); 18:2 linoleic acid, copper (3 comparisons)]. Nevertheless, greatest differences were observed for copper (24.3%) in grain and calcium (20.2%) in forage. (Copper content of the MON 863 x MON 810 was also found stat. sign. different: EFSA Journal (2004) 49, 1-25)
As concluded by the applicant: no particular natural constituents of maize are considered to be of significant concern to require additional information or further risk assessment.
Consideration: If the compositional studies would have been conducted on maize grown over 2 field seasons and at 2 geographic regions, it would have been more clear if the statistically significant differences seen for some of the natural constituents of maize are to be considered of no significant concern or do require additional information and/or further risk assessment.

Comment 2

No comments or questions.

D.7.8.4 Testing of the whole GM food/feed

Comments/Questions of the expert(s)

Comment 1

The applicant concluded that the safety assessment for the individual proteins is not changed when combined in MON 88017 x MON 810, since the proteins: 1° are unlikely to interact, 2° have very different and well-documented modes of action, 3° are produced in very low quantities in MON 88017 x MON 810, and 4° were shown safe in their individual safety assessments.
A confirmatory animal feeding study was conducted using MON 88017 x MON 810 fed to broiler chickens.

<u>Poultry broilers feeding study with MON 88017 X MON 810 maize grain (42 days).</u>
The study was undertaken to compare the wholesomeness of MON 88017 x MON 810 grain (treated with glyphosate herbicide? not mentioned in this study) to conventional control (LH59 x LH198) as well as to five commercial reference maize hybrids when fed to rapidly growing Ross x Ross 508 broilers (Taylor et al., 2005). Broilers were fed a starter diet (d0-21) and grower/finisher diet (d21-42) containing appr. 55% and 60% w/w maize, respectively, for all treatments. Treatments were randomly assigned to pens with five blocks for 16 pens (8 male, 8 female) with 10 broilers/pen for a total of 80 pens and 800 broilers. Broilers were weighed by pen on d0 and d42 and individually at study termination. Pen feed intake was determined at d42. At study termination, all surviving birds were processed to determine carcass yield and meat composition. Fat pad measurements were taken for each bird. One broiler/pen was randomly selected and sampled for breast and thigh meat quality assays.
Significant diet-by-gender interactions were noted for live weight, final live body weight, fat pad weight, and thigh weight. However, at the 5% level of significance, no differences were noted for males or females for any of these parameters. No differences were observed in the percentage of

moisture, protein, and fat in thigh meat and breast meat of broilers. Comparison of the MON 88017 X MON 810 fed birds to the population of the other diets fed showed no differences on all performance parameters, carcass yields, or meat quality parameters measured. However, statistically significant differences ($p<0.05$) were noted for breast fat in the population comparison. The differences noted were within established literature ranges (but no own historical control data was made available by the testing company: also within these ranges?) for breast fat of broilers and no differences were observed in the pairwise comparisons between treatment diets for the breast meat measurements.
According to the applicant, the results of the broiler feeding study showed that there were no biologically significant differences on the parameters tested between broilers fed MON 88017 X MON 810 or the broilers fed control maize. Minor differences noted were consistent with literature values and within natural variability.

Rat feeding studies

90-days feeding study in rats with MON 88017 maize grain.

The objective of this study was to compare the responses of rats fed MON 88017 grain with the responses of rats fed the conventional control LH59 x LH198 that has background genetics similar to that of the MON 88017 grain (Kirkpatrick, 2005a), and compared with the responses of rats fed 6 commercial reference maize hybrids (Kirckpatrick, 2005b). All maize was grown in the same location at the same time (commercial reference hybrids on different fields). It is not mentioned in this study if MON 88017 maize was grown under glyphosate conditions. The study design included groups of Sprague-Dawley rats (20 rats/sex/group). One group was administered a diet containing 11% (w/w) MON 88017 supplemented with 22% (w/w) control grain. A second group was administered a diet containing 33% MON 88017. A third group was administered a diet containing 33% control grain. Another 6 groups were administered diets containing 33% reference maize varieties.
All animals survived, there were no test substance-related clinical observations. Body weights, food consumption and clinical pathology parameters were unaffected by the administration of MON 88017. No test-related effects were found on organ weights, and under macroscopic and microscopic examination. The few difference that were observed (higher mean food consumption and higher absolute neutrophil count in the 33% MON88017 females compared with the control group) fell within the range of responses of the six different groups fed conventional reference varieties of maize grain.

90-days feeding study in rats with MON 810 maize grain.

In a sub-chronic (90-days) toxicity study in rats fed MON 810 maize (Lemen, 2001), no consistent differences in the measured clinical, biological and histological parameters were noted for rats fed on non-GM or MON 810 maize except for albumin/globulin count. For rats fed 33% MON 810 maize, a statistically significantly lower albumin/globulin count was observed compared with control and overall reference lines at study termination. The slightly lower values for these parameters are not considered to be related to MON 810 maize feeding, given the small magnitude of the observed changes. It was accepted by EFSA that the differences found were considered not to be of biological significance.

According to the applicant, these studies confirm the absence of any toxic effects associated to the introduced proteins and the absence of any unanticipated or pleiotropic effects linked to the genetic modification. In conclusion, there was no evidence of any adverse effects on human or animal health.

Although broiler chickens are the livestock animal of choice for confirming nutritional equivalence, confirmatory data of the safety assessment of the hybrid MON 88017 x MON 810 is felt needed, in

particular, the need for an additional 90-day rat feeding study (including complete endpoints) with the hybrid MON 88017 x MON 810 to exclude any adverse effect on human health.

Comment 2

First, it is important to check whether the protein levels in the hybrid line are comparable to the corresponding ranges in the parental lines.
These data are shown in tables 4, 5 and 6 of the technical dossier. As can be seen from these data, protein levels are indeed comparable.
Remark : Bhakhta *et al.*, 2003b does not provide raw data, only the mean values.

A 42-day feeding study in broiler chickens showed no adverse effects **but, why is a 13-week feeding study in the rat missing? Simply postulating that any interaction seems unlikely, is not a sufficient criterion to by-pass such an important test.**

Comment 3

No comments or questions.

D.7.9 Allergenicity

Comments/Questions of the expert(s)

Comment 1

Monsanto used simulated gastric and intestinal fluids to test the digestion of Cry3Bb1, Cry1Ab and CP4 EPSPS proteins (p. 73, p.91 and p.94 of Technical dossier). It has been shown that a rapid in vivo degradation of Cry proteins (Cry1Ab) does not always occur (Chowdhury et al., 2003). Furthermore, Spök et al (2005) have shown that digestibility studies can not be considered suitable tools to address the allergenic potential of a protein.

Comment 2

As MON 88017 x MON 810 inherits the introduced traits from its parental single-trait maize inbreds, it is tolerant to glyphosate as well as protected from the targeted coleopteran and lepidopteran insect pests.

The possible allergenic effects of MON88017 were already dealt with in the application EFSA/GMO/CZ/2005/27 and are duplicated here:
Maize itself (Zea mais) rarely induces allergic reactions in man as a food nor as a pollination plant (heavy pollen)

The new proteins Cry3Bb1 and CP4 EPSPS were already evaluated for allergenicity in the context of MON 863 and NK603 maize.
The risk for allergenicity can be assessed by combining different approaches (Helm 2003):

- content of the protein(s) in the food/feed
- digestibility of the protein(s) and stability in acid proteases in the food/feed

- comparison of the amino acid structure of the protein(s) with known allergens
- testing with specific IgE from allergic patients
- testing in animal models

For three of these parameters the proteins Cry3Bb1 and CP4 EPSPS showed a good profile:
- low content of proteins Cry3Bb1 and CP4 EPSPS in the maize end product
- good digestibility in acid peptic digestion

It has to be mentioned nevertheless that not all allergens are stable proteins (eg Mal d 1 from apple) (Ebo et al. 2005)

As far as the comparison of the proteins Cry3Bb1 and CP4 EPSPS with known allergen structures is concerned:

- protein Cry3Bb1 showed some similarity with the Anisakis simplex tropomyosin Ani s3. The overlap of 120 aa contained four gaps and showed 27.5 % identity with an E score of 1.1. The longest stretch of continuous aa was 3; this was considered as non significant. Follow up of this situation is advised since tropomyosin are to be considered as pan-allergen in a high number of living animal, with possible cross reactivity (Ebo and Stevens 2001).

- protein CP4 EPSPS had an alignment of 30.5 % identity with Dermatophagoides farinae Der f 2over 82 aa with a high E score of 0.41. The longest stretch of contiguous aa was 5. This similarity was evaluated as insignificant. Follow up of this situation is advised since Dermatophagoides sp belong to the most frequently occurring inhalation allergens in moderate climate zones such as in important parts of the US and Europe.

Testing with specific IgE or animal studies were not done (not relevant at this moment).

The author also searched medical databases in order to find reports on allergenicity of the proteins Cry3Bb1 and CP4 EPSPS. No relevant data were found.
In conclusion, it can be stated that at present there is no evidence that the GM maize containing the proteins Cry3Bb1 and CP4 EPSPS will induce allergic reactions. Continuous surveillance is advised. It has also to be taken in consideration that other forms of allergic reactions than IgE mediated are possible (Bernstein et al. 2003)

As far as the MON 810 is concerned, there have also been studies about the allergenicity of the Cry1Ab, which were found negative.

A study performed by Nakajima et al. could not find IgE antibodies to the protein:

" Enzyme-linked immunosorbent assay (ELISA) is the most convenient method of monitoring the occurrence of IgE antibodies specific for novel proteins in genetically modified (GM) foods. The levels of IgE specific for a recombinant protein, Cry1Ab, were determined using an ELISA method. A soluble form of the Cry1Ab protein purified from pCold1 vector-transformed Escherichia coli pTf16/BL21 was used as the ELISA coating antigen, and 1M NaCl was used as the washing buffer to remove IgE non-specifically bound to the coated antigen. Sera from 44 patients allergic to major food allergens were obtained, diluted 20-fold, tested, and found no identifiable IgE above background levels. We also

tested sera from patients with corn allergy against whole extracts of non-GM and GM-corn (MON 810) using immunoblotting. The staining patterns were similar for the two types of corn. These results indicate that significant levels of IgE antibodies specific to Cry1Ab were not found in the sera of Japanese patients with food allergies."

Sticker et al. (2003) employed epitope recognition by CD4 cells and found one major epitope in Cry1a (610 amino acids) and no major epitopes in Cry3Aa (644 amino acids). This was less than the know Brazil nut allergen (Sticker 2003).

Based on the available information there is no major risk for sensitization with the proteins involved.

D.7.10 Nutritional assessment of GM food/feed

Comments/Questions of the expert(s)

The fact that there was no detrimental effect on performance, carcass yield and meat composition, and health in broiler chickens in comparison with conventional maize hybrids (Taylor et al., 2005) is an indication of its safety and nutritional equivalence. It is proposed that chickens can be used as target animal species for livestock feeding studies with a GM plant derived feed, to investigate possible effects of the new feed resource on animal performance, animal health and welfare, efficacy, and acceptability of the new feed ingredient (EFSA, 2006b). Furthermore, although there are significant differences between MON88017 x MON810 and control varieties (p.40-48 of Technical Dossier) analyses are within the range of literature data.

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

Comments/Questions of the expert(s)

No comments or questions.

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

Comments/Questions of the expert(s)

Comment 1

No comments or questions.

Comment 2

Adequately examined and described.

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

No comments or questions.

Comment 2

In the dossier (p. 14): " *This maize was shown to be as safe and as nutritious as conventional maize. Therefore, MON 88017 x MON 810 and derived products from MON 88017 x MON 810 will be stored, packaged, transported, used, and handled in the same manner as current commercial maize varieties, and measures for waste disposal and treatment of MON 88017 x MON 810 products are the same as those for conventional maize*"
This lack of precautions might result in seed spillage and unwanted dissemination.

D.9.2 Selective advantage or disadvantage

Comments/Questions of the expert(s)

Comment 1

No comments or questions.

Comment 2

Not relevant here.

D.9.3 Potential for gene transfer

Comments/Questions of the expert(s)

Comment 1

The possibility of gene transfer seems to be very low to negligible.

Comment 2

The probability that (spillage + establishment + contamination) is limited at some parts of the itinerary (e g at ports), but not necessarily along the transportation routes. Even though it can not survive the winter, maize from spilled seeds can develop one generation on the sites of spilling, leading to potential dissemination of spores. 1% of the pollen beyond 50 m (Sears and Stanley-Horn, 2000) does not seem negligible to me. If we do not know the routes, we do not know if maize is grown along the roads

I feel that more specific details are needed regarding the packing and other means of confinement during transportation and storage.

D.9.4 Interactions between the GM plant and target organism

Comments/Questions of the expert(s)

Comment 1

No comments or questions.

Comment 2

The documentation is satisfactory.

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

Comments/Questions of the expert(s)

Comment 1

No comments or questions.

Comment 2

The documentation is satisfactory.

D.9.6 Effects on human health

Comments/Questions of the expert(s)

No comments or questions.

D.9.7 Effects on animal health

Comments/Questions of the expert(s)

Studies of Taylor et al. (2005) indicated that broiler mortality based on diets containing MON88017 x MON810 was related to bacterial infection, dehydration, refusal of feed, or ascites during the first 7 d, and the causes of death between d 8 and 42 were primarily attributed to sudden death and ascites, which commonly occur in broilers. Remaining broilers in all treatments were in good health.

D.9.8 Effects on biogeochemical processes

Comments/Questions of the expert(s)

No comments or questions.

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

Comments/Questions of the expert(s)

Comment 1

This question is not relevant in view of the import of maize MON88017 x MON810 into the EU.

Comment 2

Irrelevant in this case.

D.10. POTENTIAL INTERACTIONS WITH THE ABIOTIC ENVIRONMENT

Comments/Questions of the expert(s)

No comments or questions.

D.11. ENVIRONMENTAL MONITORING PLAN

D.11.1 General

Comments/Questions of the expert(s)

No comments or questions.

D.11.2 Interplay between environmental risk assessment and monitoring

Comments/Questions of the expert(s)

No comments or questions.

D.11.3 Case-specific GM plant monitoring

Comments/Questions of the expert(s)

No comments or questions.

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

Comments/Questions of the expert(s)

Comment 1

No comments or questions.

Comment 2

I have not seen any risk assessment regarding changes in agricultural practices, even though it is of wide concern that GM spore dissemination might jeopardize organic agriculture. Since I am not totally convinced by the alleged low risk for genetic contamination, I cannot exclude this risk to other forms of agriculture.

Note of the coordinator: this comment is not relevant because out of the scope of the application.

D.11.5 Reporting the results of monitoring

Comments/Questions of the expert(s)

No comments or questions.

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