Bioveiligheidsraad
Conseil de Biosécurité

14/09/2012

Secretariaat
Secrétariat

O./ref.: WIV-ISP/41/BAC/2012_0831

Title: Advice of the Belgian Biosafety Advisory Council on applications EFSA/GMO/UK/2005/09 and EFSA/GMO/RX-MON531xMON1445 from Monsanto under Regulation (EC) No. 1829/2003

Context

The application EFSA/GMO/UK/2005/09 was submitted by Monsanto on 6 January 2005 within the framework of Regulation (EC) No. 1829/2003[1] for marketing of genetically modified insect-resistant and herbicide-tolerant cotton MON 531 × MON 1445 for food and feed produced from it.
Cotton MON 531 × MON 1445 was produced by conventional crossing (no new genetic modification involved) between two single events:
- Cotton MON 531 expressing the Cry1Ac insecticidal protein conferring resistance to specific lepidopteran cotton pests, as well as genes coding for neomycin phosphotransferase type II (NPTII) and 3′(9)-O-nucleotidyltransferase (AAD, not expressed in MON 531), which were used as antibiotic resistance marker genes during product development, and
- Cotton MON 1445 expressing the CP4 EPSPS protein conferring tolerance to glyphosate, and also carries genes coding for neomycin phosphotransferase type II (NPTII) and 3′(9)-O-nucleotidyltransferase (AAD, not expressed in MON 1445), which were used as antibiotic resistance marker genes during product development.

The application was officially acknowledged by EFSA on 12 July 2005. 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).

The Belgian Biosafety Advisory Council (BAC) did not take part in this consultation. However, several experts chosen from the common list of experts drawn up by the BAC and the Biosafety and Biotechnology Unit (SBB) were contacted early 2006 to evaluate the dossier. Three experts answered positively to this request, and formulated a few comments (see Annex I for an overview of these comments).

On 29 June 2007, EFSA received application EFSA-GMO-RXMON531×MON1445 submitted under Regulation (EC) No 1829/2003 for renewal of the authorisation of food additives produced from cotton MON 531 × MON 1445 and feed produced from cotton MON 531 × MON 1445 (feed materials and feed additives). It was officially acknowledged by EFSA on 12 March 2008.

[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)

On the same date EFSA started the formal three-month consultation period of the Member States. Since all data provided in the renewal application were identical to those already provided in application EFSA/GMO/UK/2005/09, the BAC did not take part in this consultation.

Since both EFSA-GMO-UK-2005-09 and EFSA-GMO-RX-MON531×MON1445 cover products derived from cotton MON 531 × MON 1445 that do not contain viable plant parts, the EFSA GMO Panel adopted on 8 March 2012 a single scientific opinion, valid for both applications (EFSA Journal, 2012;10(3):2608)[2]. This opinion was published on 28 March 2012 together with the responses from the EFSA GMO Panel to comments submitted by the Member States during the three-month consultation periods.

In the same logic, the Biosafety Advisory Council issues below a single comprehensive advice covering both applications. This advice is drafted taking into account in particular the following set of information:
- The EFSA opinion on applications EFSA-GMO-UK-2005-09 and EFSA-GMO-RX-MON531×MON1445 including the answers of the EFSA GMO Panel to comments submitted by Member States;
- The comments formulated by the Belgian experts on application EFSA-GMO-UK-2005-09;
- Complementary information received on May 22, 2012 from EFSA following questions addressed by the BAC on specific issues related to the compositional analysis;
- The two advices already published by the BAC on the single events MON 531[3] and MON 1445[4].

Regarding this last point, the conclusions of the BAC were as follows:
- For GM cotton MON 531, the BAC was unable to give an advice on the health safety of the GMO because the applicant did not follow the OECD recommendation on the comparative compositional analysis regarding the content of Vitamin E in the seeds and did not argue why not. However, the BAC was of the opinion that the presented data formed a good basis to give a positive advice regarding the biosafety of the event in case the applicant could prove that the analysis of alfa tocoferol in the oil (which is the analysis the applicant performed) is a good proxy for the analysis required by the OECD.
- For GM cotton MON 1445, the BAC gave a negative advice regarding the health safety of this event given that (i) the applicant did not follow completely the OECD recommendation on the comparative compositional analysis and did not argue why not; (ii) relevant statistical differences were observed in the compositional analysis concerning the level of the natural toxicant gossypol, raising uncertainties as regards the toxicological safety of this GM cotton; and (iii) as the compositional analysis does not take away all concerns and according to EFSA guidance for risk assessment of food and feed from genetically modified plants, further nutritional and toxicological assessment should be performed to exclude any potential risk for human and animal health.

[2] See <http://www.efsa.europa.eu/en/efsajournal/pub/2608.htm>
[3] Advice of the Belgian Biosafety Advisory Council of 16 December 2011 on application EFSA/GMO/RX-MON531 from Monsanto under Regulation (EC) No. 1829/2003 (ref WIV-ISP/41/BAC/2012_0034)
[4] Advice of the Belgian Biosafety Advisory Council of 10 February 2012 on application EFSA/GMO/RX-MON1445 from Monsanto under Regulation (EC) No. 1829/2003 (ref WIV-ISP/41/BAC/2012_0217)

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Conclusion

The Biosafety Council gave previous advices on the two components of this stacked event. On the GM cotton MON 531, the BAC was unable to give an advice on the health safety. On the GM cotton MON 1445, the BAC gave a negative advice. In absence of new information on these two single events, and considering that a positive advice on the two single events is a prerequisite for the assessment of the stacked event, the BAC gives a negative advice for marketing of food and feed products from this stacked event.

p.o. D. Ph. Herman

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

Annex I: Full comments of experts in charge of evaluating application EFSA/GMO/UK/2005/09 (ref. WIV-ISP/BAC/2006/PT/335)

Bioveiligheidsraad
Conseil de Biosécurité

13 March 2006

Secretariaat
Secrétariat

N./réf. : WIV-ISP/BAC/2006/PT/335
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Expertise report for the EFSA dossier EFSA/GMO/UK/2005/09 - Compilation of all the comments received from the experts

Mandate for the Group of Experts: mandate of the Biosafety Advisory Council (BAC) of 12 december 2005
Coordinator: Prof. Philippe Baret
Experts: Jean-Luc Hofs (CIRA), Wim Stevens (UA), Nancy Terryn (UGent)
Domains of expertise of experts involved: genetics, genome analysis, genetic engineering, agronomy, plant-insect relation, biosafety research, immunology, alimentary allergology, cotton.
Secretariat: Adinda De Schrijver, Martine Goossens

INTRODUCTION

Dossier **EFSA/GMO/UK/2005/09** concerns a notification of the company **Monsanto** for the marketing of the genetically modified **cotton MON531 x MON1445** for food and feed applications under Regulation (EC) 1829/2003.
The notification has been officially acknowledged by EFSA on 12 July 2005.
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 notification on its 1) molecular, 2) allergenicity, 3) toxicity and/or 4) food and feed aspects. Its was expected that the expert should evaluate if the information provided in the notification 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 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.

List of comments received from the experts

A. GENERAL INFORMATION

Comments/Questions of the expert(s)

Comment 1

Information is satisfactory according to the scope of the application.

Comment 2)

This dossier is about the application of a breeding line between Mon513 and MON1445. It is not clear to me whether Mon513 and MON1445 separately have been approved for feed and food use in the EC. In the document it is mentioned "notified" and a number, but not the evaluation of the dossier. Maybe that information should have been more clearly added.

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

Comments/Questions of the expert(s)

Comment 1

Information is satisfactory according to the scope of the application.

Comment 2

None

C. INFORMATION RELATING TO THE GENETIC MODIFICATION

Comments/Questions of the expert(s)

Comment 1

No comment

Comment 2

This dossier is about the application of a breeding line between Mon513 and MON1445, therefore the only concerns would be interaction between the two inserts. As far as I can judge from the data presented, there is no evidence that this has caused any changes on the transgenes and their expression.

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 comment

Comment 2

None

D.2. Information on the sequences actually inserted or deleted

Comments/Questions of the expert(s)

Comment : for the additional 242 bp fragment that is present it is not clear whether this will actually also be present in the final commercial product. At some stage (Ref Reiser, 2001 P11) it is mentioned that not all MON513 commercial lines have this insert. Can for "cleanness" not all commercial lines be selected not to have this? Else for detection this might be good to be informed about.

D.3. Information on the expression of the insert

Comments/Questions of the expert(s)

None

D.4. Information on how the GM plant differs from the recipient plant in: reproduction, dissemination, survivabiliity

Comments/Questions of the expert(s)

Comment 1)

No comment (according to the scope of the application**)**

Comment 2

Not applicable

D5. Genetic stability of the insert and phenotypic stability of the GM plant

Comments/Questions of the expert(s)

related to comment D2

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)

No comment

D.7.2 Production of material for comparative assessment

Comments/Questions of the expert(s)

The number of sites is only four and only located in USA. What about results in Australia and South Africa?
Data are from 1999 trials only, aren't there more recent ones?

D.7.3 Selection of material and compounds for analysis

Comments/Questions of the expert(s)

No comment

D.7.4 Agronomic traits

Comments/Questions of the expert(s)

No comment

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)

D. 7.8.1 Safety assessment of newly expressed proteins

Comments/Questions of the expert(s)

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)

D.7.9 Allergenicity

Comments/Questions of the expert(s)

In this GM cotton two proteins (Cry1Ac and CP4 EPSPS) are added. Both proteins have been screened for homology with known allergens. For the CP4 EPSPS protein, a 30 % homology was found with the *Dermatophagoides farinae* 2 protein (Der f 2). Although this homology is under the limit of 35 %, it would be interesting to compare the 3d structures of Der p 2 and CP4 EPSPS and to test some sera of patients allergic to Der p 2. For the Cry1Ac protein no homology was found.

It is stated that "the scope of the current application covers cottonseed oil … and that it has been demonstrated that there is no detectable level of protein in refined cottonseed oil …" p55 part 1 technical dossier.
Nevertheless, allergic patients can react to very minute amounts of protein below the detection limit of a number of methods for determination of proteins. The two publications cited are Monsanto reports that can be found in the confidential business information.

Based on the available data and on a search of the literature I cannot state at the moment that the proposed protein FORMS an allergic threat**.**

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)

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)

NOT APPLICABLE

D.9.2 Selective advantage or disadvantage

Comments/Questions of the expert(s)

NOT APPLICABLE

D.9.3 Potential for gene transfer

Comments/Questions of the expert(s)

NOT APPLICABLE

D.9.4 Interactions between the GM plant and target organism

Comments/Questions of the expert(s)

NOT APPLICABLE

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)

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)

NOT APPLICABLE

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

Comments/Questions of the expert(s)

NOT APPLICABLE

D.10. POTENTIAL INTERACTIONS WITH THE ABIOTIC ENVIRONMENT

Comments/Questions of the expert(s)

NOT APPLICABLE

D.11. ENVIRONMENTAL MONITORING PLAN

D.11.1 General

Comments/Questions of the expert(s)

NOT APPLICABLE

D.11.2 Interplay between environmental risk assessment and monitoring

Comments/Questions of the expert(s)

NOT APPLICABLE

D.11.3 Case-specific GM plant monitoring

Comments/Questions of the expert(s)

NOT APPLICABLE

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

Comments/Questions of the expert(s)

NOT APPLICABLE

D.11.5 Reporting the results of monitoring

Comments/Questions of the expert(s)

NOT APPLICABLE

References

none