Bioveiligheidsraad
Conseil de Biosécurité

06-11-2009

Secretariaat
Secrétariat

O./ref.: WIV-ISP/BAC/2009_01493

Title: Advice of the Belgian Biosafety Advisory Council on the application EFSA/GMO/UK/2007/49 from Syngenta under Regulation (EC) No. 1829/2003

Context

The application EFSA/GMO/UK/2007/49 was submitted by Syngenta on 14 November 2007 for the marketing (import and processing) of the insect-resistant and glyphosate-tolerant genetically modified Bt11 x GA21 maize for food and feed uses under Regulation (EC) No. 1829/2003[1].

The application was officially acknowledged by EFSA on 19 February 2008. 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). Nine 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 19 May 2008.

The opinion of the EFSA Scientific Panel on GMOs was adopted on 15 September 2009 (The EFSA Journal, 2009, 7 (9):1320)[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 23 September 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_1211902910348.htm>

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In addition, the scientific evaluations of the single events, namely maize line Bt11 (application under Regulation (EC) No. 258/97) and maize line GA21 (EFSA/GMO/UK/2005/19), are taken into account in this advice. The Biosafety Advisory Council formulated positive advices for maize line Bt11[3] and for maize line GA21[4]. Both single events are already authorised for food and feed uses[5]. For maize Bt11 the procedure for renewal of authorisation is ongoing.

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 Bt11: BAC_2004_SC_116, BAC_2004_SC_165 and BAC_2009_904
[4] Advice of BAC on maize line GA21: BAC_2007_SC_614
[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/UK/2007/49 *and Comments submitted on the EFSAnet (ref: BAC_2008_758)*

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N./réf. : WIV-ISP/BAC/2008_758[1]
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26 May 2008

Compilation of comments of experts in charge of evaluating the application EFSA/GMO/UK/2007/49 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 04 March 2008
Coordinator: Prof. dr. ir. Dirk Reheul
Experts: Pascal Cadot (Consultant), Rony Geers (KUL), Jean-Claude Grégoire (ULB), André Huyghebaert (UGent), Jean-Pierre Maelfait (UGent), Peter Smet (Consultant), Wim Stevens (UIA), Frank Van Breusegem (VIB), Johan Van Waes (ILVO)
Domains of expertise of experts involved: Genetics, genome analysis, genetic engineering, analysis of food/feed, industrial processing, toxicology, immunology, alimentary allergology, animal nutrition, traceability of alimentary chain, agronomy, crop protection, crop production management, herbicide tolerance, ecology, plant-insect relations, effect on non-target species, risk analysis, monitoring, nature conservation, biosafety research, maize
Secretariat (SBB): Didier Breyer, Adinda De Schrijver, Martine Goossens, P. Herman

INTRODUCTION

Dossier **EFSA/GMO/UK/2007/49** concerns an application of the company **Syngenta** for the marketing of the genetically modified **maize Bt11 x GA21** for food and feed applications under Regulation (EC) 1829/2003.
The application has been officially acknowledged by EFSA on 19 February 2008.
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)

[1] revised version of document BAC_2008_751 completed with one additional comment received after EFSA deadline for comments

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

According to the dossier the scope of application does not include the authorization for the cultivation of Bt11 x GA21 maize seed products in the EU in the framework of the Directive 2001/18/EC. It can however be valuable to give some remarks on the different topics, dealing with cultivation and survivability of seeds, in the case that the applicant should ask in the near future for an extension for the scope of cultivation.
So as agronomical expert I will also give some comments in this questionnaire, related to the cultivation, the agronomical value and some environmental aspects.

Comment 2

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.

Comment 3

No comments/questions.

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

Comments/Questions of the expert(s)

Comment 1

No comments/questions

C. INFORMATION RELATING TO THE GENETIC MODIFICATION

Comments/Questions of the expert(s)

Comment 1

Table 1:
- The accession number indicated for the “Maize intervening intron sequence 6 from the maize *adh*1 gene (Entrez Accession Number X04090)” is incorrect. X04090 refers to a human catalase gene.

- Minor remark: it is irrelevant to indicate the lengthy urls that include accessed dates (NCBI http://www.ncbi.nlm.nih.gov/sites/entrez?db=Protein.%20Accessed%20August%2031%2C%202006). Simply http://www.ncbi.nlm.nih.gov/sites/entrez is OK.

D. INFORMATION RELATING TO THE GM PLANT

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

Comments/Questions of the expert(s)

Comment 1

No comments/questions

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

Comments/Questions of the expert(s)

Comment 1

No comments/questions

D.3. INFORMATION ON THE EXPRESSION OF THE INSERT

Comments/Questions of the expert(s)

Comment 1

No comments/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

Remarks concerning the survivability of seeds of maize. In the dossier it is mentioned that maize seed can only survive under a narrow range of climatic conditions. Volunteers are killed by frost. This is correct but from our experience maize seeds can survive in the soil during a not so severe winter. It can happen that out of full ears, fallen on the ground at harvest and after labouring of the land, covered with soil, some seeds survive and give plantlets during the next season. So here in the case of GMO-plants it will be necessary to have a follow up of the fields in the next year to detect for surviving

plants. This information is only relevant if at a certain moment the scope would be extended to cultivation in Northern and Western Europe with moderate to cold winter conditions.

Comment 2

The information received is satisfactory. In principle however, this question should be non relevant in the present application (provided there is no spillage), as the application only concerns food and feed uses for maize Bt11 x GA21.

Comment 3

No comments/questions

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

Comments/Questions of the expert(s)

Comment 1

No comments/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

No comments/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)

Comment 1

In this chapter it is mentioned that Bt11 x GA21 maize was compared with relevant control maize lines that had not been genetically modified. Commercial varieties were also included in the comparison where possible. What does it mean? The Bt11 x GA21 is tolerant to glyphosate and glufosinate-ammonium. So I think it is not possible to compare with commercial varieties, unless they are also tolerant to glyphosate and glufosinate-ammonium (= are also genetically modified).

Comment 2

Of the 56 analytes measured in grain, statistically significant differences were noted for levels of total dietary fiber (TDF) and fat, vitamin E (α-tocopherol), and linoleic fatty acid. The average values of all analytes measured for both the Bt11 x GA21 (measured in Bt11 x MIR604 x GA21) grain and the nontransgenic grain were within the ranges reported in the literature.

Comment 3

Bt11 x GA21 maize is further indicated as submitted maize.
Both Bt11 and GA21 have been previously compared to their respective near-isogenic conventional maize lines and found to be identical in terms of nutritional properties.
The submitted maize was compared with relevant non-GM control maize. Commercial varieties were included as well.

D.7.2 Production of material for comparative assessment

Comments/Questions of the expert(s)

Comment 1

The submitted maize and the controls were grown at six locations in the USA for forage and grain analysis. The comparative analysis was performed according to the OECD recommendations for maize.
Results were also compared with the range of data published in literature.

D.7.3 Selection of material and compounds for analysis

Comments/Questions of the expert(s)

Comment 1

A broad range of nutrients in grain were assessed: proximates (including carbohydrates), minerals (including all relevant constituents), vitamins (covering a range of important B vitamins including niacin, vit E and β- carotene) amino acids, fatty acids, secondary metabolites and anti-nutrients (like furfural, phytic acid, inositol, raffinose, trypsin inhibitor, ferulic acid and coumaric acid).

Comment: all nutrients and other relevant constituents are included.

For the majority of analytes no statistical differences were found. In a few cases, like total dietary fibre, vit E en linoleic acid a statistically significant difference was found. The values were however within the range of literature data.

Forage analysis includes mainly proximates, fibre constituents, calcium and phosphorous. No statically significant difference was found for any analyte.

The applicant concludes that the submitted maize is similar in nutrient composition to grain and forage from the control maize.

Conclusion: taking into account the in depth analysis and the broad range of nutrients covered I agree with this conclusion.

D.7.4 Agronomic traits

Comments/Questions of the expert(s)

Comment 1

First of all I agree with the important remark of the applicant that measurement and observation of agronomic characteristics can add to the assessment of unintended effects of the genetic modification.
The Bt11 x GA21 maize was tested in the USA during the 2005 growing season. The results of these trials suggest that there is no statistically significant difference in grain yield or agronomic performance between the Bt11 x GA21 maize hybrids and the corresponding near-isogenic hybrids.
So my remark: The results are only based on 1 year trials and the year effect can be given significant effects. And furthermore : were the trials treated against herbs with glufosinate ammonium or glyphosate so as to evaluate the real potential of the new hybrids?

Comment rephrased by the coordinator

The Bt11 x GA21 maize was tested in the USA during the 2005 growing season. The results of these trials suggest that there is no statistically significant difference in grain yield or agronomic performance between the Bt11 x GA21 maize hybrids and the corresponding near-isogenic hybrids.
These results are based on only 1 year of trials, excluding the potential year effect.

Comment 2

The information received is satisfactory. In principle however, this question should be non relevant in the present application (provided there is no spillage), as the application only concerns food and feed uses for maize Bt11 x GA21.

D.7.5 Product specification

Comments/Questions of the expert(s)

Comment 1

No further comment.

D.7.6 Effect of processing

Comments/Questions of the expert(s)

Comment 1

The submitted maize will be processed in the same way as conventional maize. The applicant concludes that there is no evidence that the expression of the proteins introduced in the maize will influence processing.
I agree with this conclusion.

D.7.7 Anticipated intake/extent of use

Comments/Questions of the expert(s)

Comment 1

The submitted maize will replace some of the maize in existing products. As there is no change in compositional parameters no nutritional changes are to be expected.
No further comment.

D.7.8 Toxicology

D. 7.8.1 Safety assessment of newly expressed proteins

Comments/Questions of the expert(s)

Comment 1

Mean concentrations of Cry1Ab and PAT proteins are indeed comparable in both Bt11 maize and Bt11 x GA21 maize.

a) Cry1Ab protein measured in Bt11 maize

Growth stage/ Tissue	**ng/mg Tissue Dry Weight Mean**	**Range**	**Standard deviation**
Leaves (V9-V12)	33.81	29.44-38.07	3.21
Leaves (Anthesis)	35.81	28.07-46.70	6.97
Leaves (Seed Maturity)	10.75	9.92-12.44	1.02
Roots (V9-V12)	13.90	11.90-15.81	1.51
Roots (Anthesis)	9.47	8.59-10.15	0.61
Roots (Seed Maturity)	4.66	4.27-5.20	0.37
Kernels (Seed Maturity)	1.24	0.84—1.60	0.32

Pollen (Anthesis)[1]	0.10

[1] One pooled sample analyzed in triplicate as received (air-dried overnight). Values represent the mean of three extractions.

Question concerning the concentrations of Cry1Ab protein measured in Bt11 maize. In dossier RX-Bt11 a range of 12 - 154 µg/g dry weight is mentioned. Is the 154 µg/g value correct?

b) Cry1Ab protein measured in Bt11 x GA21 maize

Growth stage/ Tissue	**ng/mg Tissue Dry Weight Mean**	**Range**	**Standard deviation**
Leaves (V9-V12)	36.96	30.99-49.10	7.56
Leaves (Anthesis)	34.09	30.61-37.43	2.60
Leaves (Seed Maturity)	10.48	9.11-11.82	1.29
Roots (V9-V12)	16.60	14.35-19.95	2.26
Roots (Anthesis)	11.67	9.46-12.97	1.50
Roots (Seed Maturity)	4.79	4.51-5.09	0.29
Kernels (Seed Maturity)	0.99	0.86-1.18	0.15
Pollen (Anthesis)	0.12		

c) PAT protein measured in Bt11 maize

Growth stage/ Tissue	**ng/mg Tissue Dry Weight Mean**	**Range**	**Standard deviation**
Leaves (V9-V12)	0.11	0.10-0.12	0.01
Leaves (Anthesis)	0.10	0.09-0.11	0.01
Leaves (Seed Maturity)	<0.041		
Roots (V9-V12)	0.11	0.09-0.13	0.02
Roots (Anthesis)	0.16	0.13-0.17	0.02
Roots (Seed Maturity)	0.13	0.12-0.14	0.01
Kernels (Seed Maturity)	<0.021		
Pollen (Anthesis)	<0.023		

d) PAT protein measured in Bt11 x GA21 maize

Growth stage/ Tissue	ng/mg Tissue Dry Weight Mean	Range	Standard deviation
Leaves (V9-V12)	0.13	0.11-0.14	0.02
Leaves (Anthesis)	0.11	0.10-0.14	0.01
Leaves (Seed Maturity)	<0.041		
Roots (V9-V12)	0.11	0.08-0.13	0.02
Roots (Anthesis)	0.16	0.13-0.22	0.04
Roots (Seed Maturity)	0.10	0.05-0.13	0.03
Kernels (Seed Maturity)	<0.021		
Pollen (Anthesis)	<0.023		

Mean concentrations of mEPSPS protein is indeed comparable in both GA21 maize and Bt11 x GA21 maize.

e) mEPSPS protein measured in GA21 maize

Growth stage/ Tissue	ng/mg Tissue Dry Weight Mean	Range	Standard deviation
Leaves (V9-V12)	82.94	75.85-91.21	6.01
Leaves (Anthesis)	92.96	75.63-103.55	12.73
Leaves (Seed Maturity)	24.75	20.16-31.93	5.12
Roots (V9-V12)	39.56	31.98-45.58	6.13
Roots (Anthesis)	39.04	34.93-42.71	3.37
Roots (Seed Maturity)	13.89	11.59-15.80	1.69
Kernels (Seed Maturity)	6.08	5.78-6.41	0.26
Pollen (Anthesis)	65.32		

f) mEPSPS protein measured in Bt11 x GA21 maize

Growth stage/ Tissue	ng/mg Tissue Dry Weight Mean	Range	Standard deviation
Leaves (V9-V12)	87.02	76.77-99.44	9.21
Leaves (Anthesis)	86.35	79.76-96.57	6.73
Leaves (Seed Maturity)	30.53	22.26-36.42	6.92
Roots (V9-V12)	36.38	24.80-42.39	7.04
Roots (Anthesis)	35.50	33.89-36.76	1.07
Roots (Seed Maturity)	12.61	11.32-13.13	0.87
Kernels (Seed Maturity)	5.3	4.77-5.98	0.50
Pollen (Anthesis)	80.53		

a) Degradation of the Cry1Ab protein in simulated gastric fluid (author).

Test was previously performed. Rapid digestion was demonstrated.

b) Degradation of the Cry1Ab protein in simulated intestinal fluid (author).

Not mentioned. Has this test been performed? If not, why isn't it performed?

c) Degradation of the PAT protein in simulated gastric fluid (author).

Test was previously performed. Rapid digestion was demonstrated.

d) Degradation of the PAT protein in simulated intestinal fluid (author).

Not mentioned. Has this test been performed? If not, why isn't it performed?

e) Degradation of the mEPSPS protein in simulated gastric fluid (author).

Test was previously performed. Rapid digestion was demonstrated.

f) Degradation of the mEPSPS protein in simulated intestinal fluid (author).

Test was previously performed. Rapid digestion was demonstrated.

g) Cry1Ab: Acute Oral Toxicity Study in Mice (author).

No toxic effects have been observed in acute toxicity studies done with test material derived from microbial cultures biochemically and insecticidally similar to the delta-endotoxin as produced by the Bt11 maize. **No further testing is needed.**

h) PAT: Acute Oral Toxicity Study in Mice (author).

Lack of acute toxicity was demonstrated earlier. **No further testing is needed.**

f) mEPSPS: Acute Oral Toxicity Study in Mice (author).

Lack of acute toxicity was demonstrated earlier. **No further testing is needed.**

Comment summarized by the coordinator

Mean concentrations of mEPSPS protein are comparable in both GA21 maize and Bt11 x GA21 maize.
Comparing mean concentrations of Cry1 Ab and PAT proteins, results from Bt11 are comparable with Bt11 x GA21.
In dossier RX-Bt11 a range of 12 - 154 µg/g dry weight is mentioned for Cry1 Ab. Is the 154 µg/g value correct?

b) Degradation of the Cry1Ab protein in simulated intestinal fluid (author).
Not mentioned. Has this test been performed? If not, why isn't it performed?

d) Degradation of the PAT protein in simulated intestinal fluid (author).
Not mentioned. Has this test been performed? If not, why isn't it performed?

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

a) 42-day poultry feeding study (Brake, 2006)

Poultry diets prepared with the Stacked Bt11 x GA21 Positive transgenic maize grain supported rapid broiler chicken growth at low mortality rates and very good feed conversion ratios without affecting carcass yield. There were no obvious deleterious effects associated with consumption of Stacked Bt11 x GA21 transgenic maize grain when compared to control (nontransgenic) maize grain.

b) 90-Day rat feeding study (author).

Not performed.
The composition of the genetically modified plant is not substancially modified, except for the inserted traits. So, at this time, **further testing is not recommended**.

D.7.9 Allergenicity

Comments/Questions of the expert(s)

Comment 1

Assessment of the allergenicity of the newly expressed proteins.
Cry1Ab, PAT and mEPSPS are unlikely to be allergenic.

Assessment of the allergenicity of the whole GM plant or crop.
The applicant did not assess the allergenicity of the whole GM plant. Conversely to what is stated by the applicant, maize allergy has been described, though it is not recognized as a major allergen source. Some maize allergens have already been described in the literature (Pastorello et al. 2003; Pasini et al. 2002, Weichel et al. 2006).
Due to the introduction of the three new traits described in the application, over-expression of endogenous proteins, among them the maize allergens, might occur. Therefore, it appears as relevant to analyze whether the expression levels of known maize allergens is increased in genetically modified Bt11 x GA21 maize grains. Patient IgE binding to maize grain extract or titration of known major allergens of maize should be carried out.

Comment 2 (received after EFSA deadline for comments)

The stacked Bt11 x GA21 product is a genetically modified (GM) maize that has been produced by a conventional breeding cross of two GM maize:
- Event Bt11 maize (hereafter referred to as 'Bt11 maize') which expresses a truncated Cry1Ab protein for control of certain lepidopteran pests and a phosphinothricin acetyltransferase (PAT) protein that confers tolerance to herbicide products containing glufosinate ammonium.
- Event GA21 maize (hereafter referred to as 'GA21 maize') which expresses a modified maize 5-enolpyruvylshikimate-3-phosphate synthase enzyme (mEPSPS) that confers tolerance to herbicide products containing glyphosate.

The assessments included an evaluation of the allergenic potential of each of the three proteins conducted according to recommendations of the Codex *ad hoc* Intergovernmental Task Force on Foods derived from Biotechnology (Codex, 2003), where an integrated stepwise approach is used for the assessment of potential allergenicity.
• The sources of the transgenes were considered. None of the three proteins expressed in Bt11 x GA21 come from donors with allergenic potential.
• An extensive bioinformatics search for sequence homologies and structural similarities between the expressed proteins and known allergens was performed. The results demonstrated that Cry1Ab, PAT and mEPSPS proteins show no homology to any known or putative allergenic proteins.

• The susceptibility of Cry1Ab, PAT and mEPSPS proteins to proteolytic degradation was evaluated in simulated mammalian gastric fluid (SGF) containing pepsin. All the proteins were readily degraded in SGF. No intact or immuno-reactive fragments were detected following digestion in SGF for 2 minutes. These data support the conclusion that Cry1Ab, PAT and mEPSPS expressed in transgenic plants will be readily digested as conventional dietary protein under typical mammalian gastric conditions.

Some remarks have to be made:

- allergenicity is an individual trait that cannot be predicted; any novel protein or polypeptide has potential allergenic properties which will only be discovered after meticullous follow up.
- the digestibility of proteins is only a relative capacity as far as allergenicity is concerned since proteins can as such induce allergic reactions before biotransformations as has been demonstrated for apple, carrot, potato and other allergens.

D.7.10 Nutritional assessment of GM food/feed

Comments/Questions of the expert(s)

Comment 1

The number of animals per treatment in the broiler trial were sufficient for testing with the right power.

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)

Comment 1

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

Provided information: sufficient.

Comment 2

I agree that the risks (should spillage occur) are extremely low, as maize appears not to reproduce outside of cultivation.
However, one sentence in § 9.1 raises concern (this again only if spillage occurs): "*Cultivation of Bt11 x GA21 maize in the EU is not within the scope of this application. In the unlikely event that small amounts of Bt11 x GA21 maize grain could accidentally find their way into the environment in the EU, most of the grain would not survive, for the reasons stated above, and any plants germinating from it could be easily controlled using any of the current agronomic measures taken to control other commercially available maize*". The reason for concern stems from the fact that Bt11 x GA21 maize is precisely resistant to products containing glufosinate ammonium and glyphosate and, therefore, "current agronomic measures" can not rely upon these tools.

Comment rephrased by the coordinator

The of germination and persistence of spilled kernels along transport ways is not probable. Hence invasiveness is not very probable neither. According to the precautionary principle, it is recommended to monitor transport routes in order to guarantee tracability. And of course, should transgenic plants survive, they can not be killed by the herbicides they are made resistant for, so the quote of the applicant "…could be easily controlled using any of the current agronomic measures…." is not true.

D.9.2 Selective advantage or disadvantage

Comments/Questions of the expert(s)

Comment 1

Provided information: sufficient.

Comment 2

I can see one risk, in case of accidental spillage. Should spillage occur in the proximity of conventional maize fields, then the arguments developed in the application do not hold true anymore. Reproduction becomes possible on the one hand and there are real selective advantages provided by

resistance to Lepidopteran pests and to products containing glufosinate ammonium and glyphosate, encouraging gene transfer in the field.

The concern regarding spillage is serious, particularly since the alledged discovery of living plants of canola GT73 along a road in Wallonia (RTBF1 - Info radio - 6 May 2008 12:31). Canola GT73 had been authorized for food and feed by the European Commission Decision of 22 June 2005 concerning the placing on the market, in accordance with Directive 2001/18/EC of the European Parliament and of the Council, of an oilseed rape product (*Brassica napus* L., GT73 line) genetically modified for tolerance to the herbicide glyphosate (notified under document number C(2005) 1838) (Only the Dutch text is authentic) (Text with EEA relevance) (2005/465/EC). *Official Journal of the European Union*, 24.6.2005 (EN): L 164/57.

Comment rephrased by the coordinator

It is very unlikely that spillage will occur within agriculture land. Should this occur, there are, anno 2008, no indications that the transgene would have a selective advantage in current Belgian agricultural practices. Nevertheless, according to the precautionary principle, it is recommended to monitor transport routes in order to guarantee traceability.

D.9.3 Potential for gene transfer

Comments/Questions of the expert(s)

Comment 1

Provided information: sufficient.

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 pollen. 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
More specific details are needed regarding the packing and other means of confinement during transportation and storage, as well as measures to be taken in case of accidental spillage.

This precaution is made compulsory since the alledged discovery of living plants of canola GT73 along a road in Wallonia (RTBF1 - Info radio - 6 May 2008 12:31).

Comment rephrased by the coordinator

The germination of spilled kernels along transport ways is not very probable (and hence the occurrence of flowering transgenic maize along the transport ways is very unlikely too). Therefore gene transfer via pollen is not very likely neither. Nevertheless, according to the precautionary

principle, it is recommended to monitor transport routes in order to guarantee traceability and clear prescriptions about packaging during transport and storage are needed.

D.9.4 Interactions between the GM plant and target organism

Comments/Questions of the expert(s)

Comment 1

Not applicable

Comment 2

Again, the question of spillage is central here.

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

Comments/Questions of the expert(s)

Comment 1

Provided information: sufficient.

Comment 2

The information is satisfactory.

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

In this paragraph it is mentioned again that the scope of application does not include cultivation of maize plants of Bt11 x GA21 maize in the EU. Nevertheless I give here some remarks in the case that the applicant should ask in the near future for an extension for the scope of cultivation. In the framework of the EU- regulation 2002/53 a new variety have to be submitted to DUS (Distinctness, Uniformity, Stability) and VCU (Value for Cultivation and Use) tests before the variety can be commercialised. The new variety has to be compared with the best existing standard varieties. So my question here is : can the GM- maize be incorporated in normal VCU trials, for example treated with specific herbicides for maize and will the agronomical value be the same as tested in trials, where herbicides for which the variety is tolerant were used?

Comment 2

Not applicable.

Comment 2

Irrelevant here

D.10. POTENTIAL INTERACTIONS WITH THE ABIOTIC ENVIRONMENT

Comments/Questions of the expert(s)

Comment 1

I agree with the comments given by the applicant

Comment 2

Provided information: sufficient.

D.11. ENVIRONMENTAL MONITORING PLAN

D.11.1 General

Comments/Questions of the expert(s)

Comment 1

If seeds were imported by train containers for making food and feed, some monitoring has to done to control if there are no maize plants along the railway roads. As already mentioned under a moderate winter seeds of maize can survive and can give plantlets in the next spring; so these plants have to destroyed.

Comment 2

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.
Monitoring and reporting on the possible establishment of feral populations, as indeed foreseen in Appendix 8 of the application at hand, should therefore be a point of particular interest in the report to be delivered annually to the Commission. More details on the organisation and implementation of that monitoring would be useful.

Comments rephrased by the coordinator

As already mentioned in D.9.1, D.9.2 and D.9.3, it is recommended to record all transport routes in order to guarantee traceability. So, 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.
Monitoring and reporting on the possible establishment of feral populations, as indeed foreseen in Appendix 8 of the application at hand, should therefore be a point of particular interest in the report to be delivered annually to the Commission. More details on the organisation and implementation of that monitoring would be useful.

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)

Comment 1

The proposed general surveillance of the impact of the GM plant and the provisions concerning traceability and labelling satisfy.

Comment 2

The application (p 49) states that "*Syngenta is committed to informing grain traders and maize processors with details on the safety of Bt11 x GA21 maize*". I understand from this that the monitoring will be done by the traders themselves. **I doubt that this is enough. I think that further information on package labelling and traceability is seriously needed. This is my most important comment on this dossier.**

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

Comment rephrased by the coordinator

The application (p 49) states that "*Syngenta is committed to informing grain traders and maize processors with details on the safety of Bt11 x GA21 maize*". This sentence makes one to presume that the monitoring will be overviewed by these traders and processors. A better and clear monitoring plan **on package labelling and traceability is needed.**

D.11.5 Reporting the results of monitoring

Comments/Questions of the expert(s)

References

Pasini et al. Allergy 2002; 57:98-106
Pastorello et al. J Allergy Clin Immunol 2003; 112:775-83
Weichel et al. Allergy 2006;61:128-35