Bioveiligheidsraad
Conseil de Biosécurité

18-08-2011

Secretariaat
Secrétariat

O./ref.: WIV-ISP/41/BAC/2011_0745

Title: Advice of the Belgian Biosafety Advisory Council on the application EFSA/GMO/RX-40-3-2 (soybean 40-3-2) from Monsanto under Regulation (EC) No. 1829/2003

Context

The application EFSA/GMO/RX-40-3-2 was submitted by Monsanto on 29 June 2007 for the marketing within the framework of Regulation (EC) No. 1829/2003[1] of genetically modified (GM) soybean 40-3-2 for renewal of the authorisation of (1) food containing, consisting of, or produced from GM soybean 40-3-2; (2) feed containing, consisting of, or produced from GM soybean 40-3-2; and (3) other products containing or consisting of GM soybean 40-3-2 with the exception of cultivation, developed by Monsanto to provide tolerance to glyphosate herbicides. The scope of the renewal application covers the continued marketing of:
- existing food containing, consisting of, or produced from soybean 40-3-2 (including food additives) that have been placed on the market in accordance with Part C to the Directive 90/220/EC before the entry into force of Regulation (EC) No 258/97 and under Directive 89/107/EEC (Commission Decision 96/281/EC);
- existing feed containing, consisting of, or produced from soybean 40-3-2 that have been placed on the market in accordance with Part C to the Directive 90/220/EEC (Commission Decision 96/281/EC) and as feed materials and feed additives subject to Directive 70/524/EEC;
- other products containing or consisting of soybean 40-3-2 with the exception of cultivation (Commission Decision 96/281/EC).

Soybean 40-3-2 has been developed for tolerance to glyphosate herbicides by the introduction of a gene coding for 5-enolpyruvylshikimate-3-phosphate synthase from *Agrobacterium* sp. strain CP4 (CP4 EPSPS).

The application was officially acknowledged by EFSA on 12 March 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 being part of the products).

The Biosafety Advisory Council (BAC) did not took part in this consultation given the fact that comments concerning this GMO had already been sent to EFSA on 4 January 2007 in the frame of the consultation for application EFSA/GMO/NL/2005/24 (soybean 40-3-2, cultivation).

On 10 November 2010, the EFSA GMO Panel published its scientific opinion on application GMO-RX-40-3-2 (EFSA Journal 2010;8(12):1908)[2] including its response to the comments

[1] Regulation (EC) No 1829/2003 of the European Parliament and of the Council of 22 September 2003 on genetically modified food and feed (OJ L 268, 18.10.2003, p.1)
[2] See <http://www.efsa.europa.eu/en/efsajournal/pub/1908.htm>

Wetenschappelijk Instituut Volksgezondheid | Institut Scientifique de Santé Publique
Dienst Bioveiligheid en Biotechnologie | Service Biosécurité et Biotechnologie
Rue Juliette Wytsmanstraat 14 | B-1050 Brussels | Belgium
T + 32 2 642 52 11 | F + 32 2 642 52 92 | bac@wiv-isp.be | www.bio-council.be

and opinions submitted by Member States during the 3 months consultation period for this application.

In order to prepare its advice on application RX-40-3-2, the BAC checked whether information available in the scientific opinion of the EFSA GMO Panel on application GMO-RX-40-3-2 (including response to the comments and opinions submitted by Member States) allowed to answer the questions/comments of the BAC related to soybean 40-3-2. In addition, information available in BAC advices and comments related to other applications involving soybean and/or CP4 EPSPS protein were also checked.
As a result, a list of remaining questions/comments on application GMO-RX-40-3-2 was addressed to EFSA (through the Belgian Competent Authority) on the 3rd of March 2011.

The answers provided by EFSA to these questions/comments (received by the BAC on the 1st of July 2011) together with the opinion of EFSA form the basis of the advice of the Biosafety Advisory Council given below.

Scientific evaluation

1. Environmental risk assessment

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

2. Molecular characterisation

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

3. Assessment of food/feed safety and nutritional value

3.1. Assessment of compositional analysis

The Biosafety Advisory Council considers that even if the compositional analysis of the GM food/feed was performed according to the OECD consensus document[4], it lacks the analysis on dietary fibre. The Biosafety Advisory Council recommends the analysis on dietary fibre since this concept is widely accepted in human food studies and recommends the adaptation of the OECD consensus document accordingly.

The Biosafety Advisory Council also notes that carbohydrates were assessed by calculation. Even if many data regarding carbohydrate composition have been obtained by calculation, the Biosafety Advisory Council considers that there are now a range of methods available for the direct assessment of carbohydrates which give more accurate information about the carbohydrate content. The Biosafety Advisory Council recommends therefore the adaptation of the OECD consensus document accordingly.

Last but not least, the Biosafety Advisory Council notes that, as regards the compositional analysis of vitamins, the applicant only provided data for vitamin E. It is generally recognised

[3] As the application doesn't imply a cultivation of the GM crop in the EU, a full environmental assessment is not required in EFSA procedure and was not achieved.
[4] OECD, 2001. Consensus Document on Compositional Considerations for New Varieties of soybean: Key Food and Feed Nutrients and Anti-Nutrients. ENV/JM/MONO(2001)15. http://www.oecd.org/dataoecd/15/60/46815135.pdf

that soybean is an important source of vitamins in the human diet, in particular vitamin E and vitamin K. The Biosafety Advisory Council would like to underline that in the revised version of the OECD Consensus Document on Compositional Considerations for New Varieties of soybean (still under discussion at OECD level), Vitamin K is also listed as suggested constituent to be analysed related to food use. The Biosafety Advisory Council is of the opinion that data provided by the applicants should comply with the latest scientific standards.

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

The potential allergenicity of the newly expressed proteins has been assessed as well as the allergenicity of the whole GM soybean. 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

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

Conclusion

Taking into account the opinion of EFSA, on the basis on the answers of the EFSA GMO Panel to the questions raised by the Biosafety Advisory Council and considering the data presently available, the Biosafety Advisory Council,

Agrees with the GMO panel of EFSA that

"genetically modified soybean 40-3-2 is unlikely to have adverse effects on human and animal health and the environment, in the context of its intended uses".

p.o. Dr. Th. HERMAN

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

Annex I: Questions raised by the Biosafety Advisory Council in the context of application EFSA/GMO/RX-40-3-2 (ref. BAC_2011_0175)

Bioveiligheidsraad
Conseil de Biosécurité

03-03-2011

Secretariaat
Secrétariat

O./ref.: WIV-ISP/41/BAC_2011_0175

Title: Questions addressed by the Biosafety Advisory Council in the context of application EFSA/GMO/RX-40-3-2 (soybean 40-3-2)

Context

On 10 November 2010, the EFSA GMO Panel published its scientific opinion on application GMO-RX-40-3-2 (soybean 40-3-2, food and feed uses), including its response to the comments and opinions submitted by Member States during the 3 months consultation period for this application (who took place between 12 March and 12 June 2008).
The Biosafety Advisory Council (BAC) did not took part in this consultation because comments concerning this GMO had already been sent to EFSA on 4 January 2007 in the frame of the consultation for application EFSA/GMO/NL/2005/24 (soybean 40-3-2, cultivation). The opinion of the EFSA GMO Panel on this latter application has still to be published.

In order to prepare the advice of the BAC on application GMO-RX-40-3-2, the BAC checked whether information available in the scientific opinion of the EFSA GMO Panel on application GMO-RX-40-3-2 (including response to the comments and opinions submitted by Member States) allows to answer the questions/comments of the BAC related to soybean 40-3-2.
In addition, information available in BAC advices and comments related to other applications involving soybean and/or CP4 EPSPS protein was also checked.

The present document lists the questions/comments on application GMO-RX-40-3-2 that should be addressed to EFSA.
It also contains a few general questions about the use of Roundup Ready soybean that the BAC wants to address to the European Commission.

Questions/Comments to be addressed to EFSA

C. INFORMATION RELATING TO THE GENETIC MODIFICATION

What is the exact difference between the plant EPSPS and the EPSPS from *Agrobacterium* CP4 so that glyphosate does not block the latter but does so with the plants EPSPS ?

D. INFORMATION RELATED TO THE GM PLANT

D.7.1 Comparative assessment

In the proximate analysis the crude fibre method has been applied. This is the conventional approach for animal feed. For many years, the dietary fibre method is applied for foods. Is there material available to confirm the equivalence for an important group of constituents like dietary fibre?

In the same line of thinking carbohydrates were assessed by calculation. Nowadays there are however a range of methods available for the direct assessment of carbohydrates. These methods give more accurate information about the composition of the beans. Are further data available for individual carbohydrates ?

Anti-nutrients are studied in depth. However data are rather poor for a group of nutrients like vitamins. I found only data for vitamin E. This is an important vitamin. However other vitamins are important as well, particularly when soybeans are used as a food. Is there any additional information about the vitamin content ?

It is not clear what is meant by vitamin E expressed in mg/g. In soybean oil, there are several vitamin E vitamers with different biological activities. One way of expressing them together is as alpha-tocopherol equivalents (Eggermont, 2006). In order to judge compositional equivalence (and to calculate alpha-tocopherol equivalents), the tocopherol composition should be known. This may be of importance as different tocopherols exhibit different (patho)physiological properties (Morris et al., 2005).
Question: Is the vitamer E composition and alpha-tocopherol equivalents similar in the genetic modified soybean compared to non modified controls?

Soy sterols/stanols can be used for incorporation in foods or in food supplements (Spilburg et al., 2003).
Question: Is the stanol/sterol composition of the genetically modified soybean similar compared to non modified controls?

D. 7.8.1 Safety assessment of newly expressed proteins

Soybean protein isolate is the base of soy-based infant formula. The protein isolate of soy 40-3-2 is expected to contain the modified CP4 EPSPS protein.
Question: Is there a history of safe use of 40-3-20 soybean protein isolate as a base of baby food?

From the stained gel showing the gastric simulated digestion of purified CP4 EPSPS protein (Technical dossier, part 1, page 89) it appears that fragments of still considerable length (MW< 2.5 dalton) would not be detected. If such fragments would survive peptic digestion and enter the small intestine, it can not be excluded that they could exhibit physiological effects.
Question: Has the size range of the peptic digestion products been determined and its physio(pathological) implications considered? (Zaloga et al, 2004)

D.7.9 Allergenicity

Has the potential allergenicity (and toxicity) been considered in subgroups of the population such as patients with pancreatic insufficiency in whom postprandial gastric function is disturbed? (Reagen et al, 1979)

References

Eggermont E. Recent advances in vitamin E metabolism and deficiency (2006). Eur J Pediatr, 165: 429-434.

Morris MC, Evans DA, Tangny CC et al. (2005). Relation of the tocopherol forms to incident Alzheimer disease and to cognitive change. Am J Clin Nutr, 81: 508-514.

Spilburg CA, Goldberg AC, McGill JB et al. (2003). Fat-free foods supplemented with soy stanol-lecithin powder reduce cholesterol absorption and LDL cholesterol. J Am Diet Assoc, 103: 577-581.

Reagen PT, Malagelada JR, Dimagno EP, Go VL. (1979). Postprandial gastric function in pancreatic insufficiency. Gut , 20:249-254.

Zaloga GP, Siddiqui RA. (2004). Biologically active dietary peptides. Mini Rev Med Chem, 4: 815-821.

Additional questions that the BAC wants to address to the European Commission

In September 2010 GLS Bank and ARGE Gentechnik-frei published a report[1] mentioning potential toxic effects on health and the environment associated with cultivation of Roundup Ready soybean (40-3-2) in South America and in particular agricultural spraying of glyphosate herbicide.
Although these concerns fall *per se* outside the evaluation of application EFSA/GMO/RX-40-3-2, the BAC is of the opinion that they raise important safety and ethical issues related to the use of Roundup Ready soybean. The BAC would therefore appreciate that the European Commission addresses at its earliest convenience the following questions :

- How does the European Commission position this information within the large body of available scientific publications on Roundup Ready soybean and what is consequently the general opinion of the Commission on this report ?
- Should the health/environmental impact of the use of glyphosate in the country of cultivation been taken into account in the frame of the evaluation of a request for a food/feed application in the EU?
- What is the opinion of the European Commission regarding ethics of importers confronted with such delocalisation of health/environmental problems?

[1] See :<http://www.gmwatch.org/component/content/article/12479-reports-reports>