B EFBS CFSB
Eidgenössische Fachkommission für biologische Sicherheit
Commission fédérale d'experts pour la sécurité biologique
Commissione federale per la sicurezza biologica
Swiss Expert Commission for Biosafety

EFBS Statement on permit application C01006: Extension of permit for marketing genetically modified soya (strain 40-3-2) as food and feed

c/o Bundesamt für Umwelt, Wald und Landschaft, CH-3003 Bern / Office fédéral de l'environnement, des forêts et du paysage, CH-3003 Berne / Ufficio federale dell'ambiente, delle foreste e del paesaggio, CH-3003 Berna

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1 Starting point

In its letter of 19 December 2001, SAEFL asks the Swiss Expert Commission on Biosafety (EFBS) for a Statement on the permit application C01006, Extension of permit for marketing genetically modified soya (strain 40-3-2) as food and feed. According to its mandate the EFBS is active in the field of gene technology and biotechnology for the protection of humans and the environment[1] and among others issues Statements on permit applications for genetically modified organisms, according to the Release Ordinance[2] Art. 2, para. 2c. At its meeting of 22 January 2002 the EFBS discussed this application and issues the present Statement taking particular note of biological safety.

2 Permit application

2.1. Introduction

The genetically modified soya strain 40-3-2, from Monsanto, is a product that is resistant to the herbicide glyphosate.

The genetic modification was achieved by inserting a gene from the soil bacterium *Agrobacterium* sp. CP4. This gene codes for 5-enolpyruvilshikimate-3-phosphate synthase (EPSPS), an enzyme that plays an important role in the biosynthesis of aromatic amino acids. Since the synthesis of aromatic amino acids is limited to plants and micro-organisms, this synthetic pathway is a natural target for herbicides that are not toxic to animals. Glyphosate is such a herbicide. Glyphosate functions as a reversibly competitive inhibitor of phosphoenolpyruvate (PEP), one of the substrates of the enzyme EPSPS[3].

Unlike most of the plant EPSPS genes, the gene products of which are sensitive to glyphosate, expression of the bacterial EPSPS produces a natural tolerance to glyphosate. This means that the genetic modification leads to the soya plants becoming tolerant to glyphosate thanks to the inserted bacterial EPSPS gene, and thus despite the partial inhibition of the plant's own EPSPS can still produce sufficient aromatic amino acids in the presence of the herbicide (e.g. Roundup Ready®).

2.2. Objective of the application

The present application seeks an extension of the authorisation of the genetically modified soya (strain 40-3-2). The first authorisation by the competent office, the Swiss Federal Office of Public Health (SFOPH), took place on 20.12.1996[4], i.e. before the Release Ordinance[5] came into force and before the EFBS was established. The application has therefore not yet been evaluated by the EFBS. The application of 1996 encompasses the import of these soya beans into Switzerland as food and feed, but not the import as seed for sowing or reproduction.

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[1] Ordinance on the Swiss Expert Commission for Biosafety of 20 November 1996, SR 172.327.8
[2] Ordinance on the Release of Organisms into the Environment (Release Ordinance) of 25 August 1996, as of 23. November 1999, SR 814.911
[3] OECD Environmental Health and Safety Publications, 1999: Consensus Document on General Information Concerning the Genes and Their Enzymes that Confer Tolerance to Glyphosate Herbicide.
[4] http://www.bag.admin.ch/verbrau/lebensmi/gvo/d/entscheid%20_roundup_ready.pdf
[5] Release Ordinance of 25 August 1999, as of 23. November 1999, SR 814.911

After the introduction of a 1% declaration limit for genetically modified organisms in food in 1999[6] the proportion of imported genetically modified soya decreased sharply, and in 2001 was about 100 t for food, which is equivalent to 3-4 delivery batches (by comparison, in 1999 83,350 t soya were imported[7]). This decrease may at least partially be explained by the fact that before the introduction of a declaration limit, the sensitivity of the contamination detection methods for genetically modified soya meant that all deliveries of soya where a residual risk could not be ruled out were declared to be GM in order to err on the side of safety. Conversely, the small quantities of GM soya imported could also be explained by the market situation: in Switzerland no foods declared as GM are currently on the market[8]. The proportion of genetically modified feed imported is greater than that of food.

Soya for food is imported mostly in the form of beans[8] (total imported in 1999: 83,350 t, of which 78,000 t were in an unprocessed form), as well as in the form of soya oil or derivatives (such as lecithin).

3 Soya strain 40-3-2

3.1. Genetic modifications

The soybean (strain 40-3-2) contains the following genetic modifications:

- CP4 EPSPS gene: this gene originates from the bacterium *Agrobacterium* sp.CP4 and confers tolerance to glyphosate.
- Coding sequence of the chloroplast transit peptides (CTP): this gene segment is derived from *Petunia hybrida* and transports the EPSPS synthesised in the cytoplasm into the chloroplasts, where both the shikimate biosynthetic pathway and the action of glyphosate take place.
- The E35S promoter of cauliflower mosaic virus.
- The untranslated 3'-sequence of the NOS (nopaline synthetase) gene from *Agrobacterium tumefaciens* as a transcriptional terminator.

Subsequently discovered sequences (see also 3.2.):

- An additional 254 bp fragment of the CP4 EPSPS gene at the 3' end of the NOS fragment.
- An additional sequence of 534 bp at the end of the CP4 EPSPS fragment.
- A second insert with a length of 72 bp, which is also a fragment of the CP4 EPSPS gene, and which is located in a *Hind*III restriction fragment.

3.2. New gene sequences

The genetically modified variety of soya, strain 40-3-2, was analysed in 2000/2001 by an independent research team from Belgium. This group determined that the soya variety contained additional gene sequences that were not described in Monsanto's application[9, 10].

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[6] Ordinance on Foodstuffs of 1 March 1995, as of 23. November 1999, SR 817.02
[7] Warenflusstrennung von GVO in Lebensmitteln, http://www.bag.admin.ch/d/pdf.htm
[8] BAG-Bulletin No. 17, 23 April 2001
http://www.bag.admin.ch/dienste/publika/bulletin/2001/d/bu17_01d.pdf
[9] P. Windels et al., 2000: Characterisation of the 3'NOS junction of Roundup Ready soybean; Med. Fac. Landbouw Univ. Gent. 65/3b
[10] P. Windels et al., 2001: Characterisation of the Roundup Ready soybean insert; Eur Food Res Technol 213:107-112

Monsanto had however already carried out an additional molecular characterisation of the soybean strain 40-3-2[11]. It confirmed that there was an additional fragment of the CP4 EPSPS gene[11], and also soya sequences which were probably produced by a "rearrangement" during the transformation process[12]. Only the question of whether the additional sequences of the CP4 EPSPS gene are in fact unexpressed still remains to be clarified and is the object of investigations currently underway, which the SFOPH must follow.

All genetic modifications were, according to details from Monsanto, present in the original construct from 1993, which was approved in Switzerland in 1996[11, 12].

4 Environmental aspects

Since the soybean strain 40-3-2 must not be cultivated in Switzerland but only imported as food or feed, the EFBS limits its comments on this application to possible environmental impacts that may occur through a mix-up of seed and feed, or through an unintended loss of viable seed during transport.

4.1. The danger of mixing up seed and feed

There are two places in particular where a mix-up could take place: at the central distribution points and at the end-user. As far as the distributors are concerned, seed is subject to strict quality control before sale. This minimises the risk of unnoticed contamination. Furthermore, in practice measures are taken if contamination below the declaration limit of 0.5% of genetically modified organisms is detected, as laid down in the Ordinance on Seeds[13].

Mixing up of feed and seed by the end-user (farmer) can be almost entirely ruled out: for one thing, the costs of seed exceed those of feed, and for another seed is usually stained, so that the difference is easily visible.

4.2. Gene transfer

The possibility of vertical or horizontal gene transfer exists only in the case of an unintentional release following the loss of viable soybeans during transport. As a strongly autogamous variety with a cross-pollination rate of less than 1%[14], however, there is hardly any possibility of vertical gene transfer. Wild soya varieties are endemic in China, Korea, Japan, Taiwan and the former Soviet Union [14], but Switzerland has neither wild soya nor wild relatives of soya[15], so that outcrossing to other varieties is unlikely.

4.3. Persistence in the wild

The possibility of escape or of a population of transgenic soya establishing itself is strongly reduced by the climatic conditions, which are unfavourable for soya. In Switzerland a

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[11] Lirette P.R. et al., 2000: Further Molecular Characterisation of Roundup Ready Soybean Event 40-3-2; Monsanto
[12] Monsanto Comments on Windels et al. (2001) Publication Regarding Roundup Ready Soybeans
[13] Ordinance on Seeds of 7 December 1998, as of 20. February 2001), SR 916.151
[14] OECD Environmental Health and Safety Publications, 2000: Consensus Document on the Biology of *Glycine max* (L.) Merr. (Soybean)
[15] Hess H. – Landolt E. – Hirzel R. 1977, 2. Aufl. Bd. 2, p. 611, Flora der Schweiz und Landolt E. 2001 Flora der Stadt Zürich, p. 789

maximum of 30% of agricultural land could be considered suitable for soya[16] (in the Mittelland at altitudes below 550 metres, in parts of French-speaking Switzerland and the Ticino). Furthermore, soya is a warmth-loving annual the seeds of which do not germinate at soil temperatures of less than 10°C, and which rarely form dormancy structures.

4.4. Formation of resistance

Resistance of crops to glyphosate, which would have developed due to a high selection pressure in agriculture, has not been observed in the countries where these crops are cultivated. Conversely, glyphosate-resistant weeds are known (*Lolium rigidum*[17], *Eleusine indica*[18] and *Conyza canadensis*[19]). In several cases of resistant *Lolium rigidum*, the resistance, the precise mechanism of which is still unknown, may be attributed to the years and years of glyphosate use in farming and consequent strong selection pressure[20]. The same applies to glyphosate resistance in *Conyza canadensis*[20] and *Eleusine indica*[21].

5 Conclusions

The EFBS declares itself in agreement with the extension of the approval.

6 Critical comments

The Commission states that conventional soybeans worldwide are produced neither sustainably nor in an environmentally friendly fashion. The Roundup Ready® soybean awaiting permission is, from today's point of view, an improvement. The increased use of glyphosate is a shift towards a more environmentally tolerable herbicide, which is also less toxic to the user, although the application of this herbicide is not unproblematic (see Section 4.4) and does not reduce the total quantities of herbicide used. On the other hand, planting Roundup Ready® soya means that less has to be sown and thus better soil quality is achieved.

Despite these improvements, the agricultural strategy of large-scale cultivation of herbicide-resistant crops is problematic in the long term. To ensure sustainability in agriculture, alternative weed-combating methods should also be considered, and more emphasis placed on crop rotation and mixed cultivation.

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[16] www.schweizerbauer.ch/news/aktuell/Artikel/03261/artikel.html

[17] Hartzler, B. 1998. Roundup resistant rigid ryegrass. Iowa State University Weed Science Online, http://www.weeds.iastate.edu/weednews/rigidryegrass.htm

[18] Hartzler, B. 1998. Roundup resistant rigid ryegrass. Iowa State University Weed Science Online, http://www.weeds.iastate.edu/weednews/rigidryegrass.htm

[19] VanGessel M.J., 2001: Rapid Publication. Glyphosate-resistant horseweed from Delaware, Weed Science 49: 703-705

[20] Heap I.M. 2000: The occurrence of herbicide-resistant weeds worldwide. Pesticide Science 51, 235-243; Hin C.J.A. et al, 2001: Agronomic and environmental impacts of the commercial cultivation of Glyphosate-tolerant soybean in the USA. CLM Centre for Agriculture and Environment, Utrecht.

[21] www.botanischergarten.ch/debate/FelsotHerbTolGen3Environm.pdf