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Scientific Opinion on application (EFSA-GMO-NL-2012-108) for the placing on the market of the herbicide-tolerant genetically modified soybean MON 87708 × MON 89788 for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto

Arpaia, Salvatore ; Nicholas, Andrew ; Birch, Edmund ; Chesson, Andrew ; du Jardin, Patrick ; Gathmann, Achim ; Gropp, Jürgen ; Herman, Lieve ; Hoen-Sorteberg, Hilde-Gunn ; Jones, Huw ; Kiss, József ; Kleter, Gijs ; Lovik, Martinus ; Messéan, Antoine ; Naegeli, Hanspeter ; Nielsen, Kaare Magne ; Ovesna, Jaroslava ; Perry, Joe ; Rostoks, Nils ; Tebbe, Christoph

Abstract: Single events MON 87708 and MON 89788 were combined to produce the stack two-event soybean MON 87708 × MON 89788. The EFSA GMO Panel previously assessed the two single events and did not identify safety concerns in the context of their scope. No new data on single soybean events leading to a modification of the original conclusions on their safety were identified. Agronomic and phenotypic characteristics, as well as compositional data of soybean MON 87708 × MON 89788, did not give rise to food/feed and environmental safety concerns. The EFSA GMO Panel considers that there is no reason to expect interactions between the single events that could impact on the food and feed safety and the nutritional properties of soybean MON 87708 × MON 89788. There are no indications of an increased likelihood of establishment and spread of feral soybean plants. Considering the scope of application EFSA-GMO-NL-2012-108, potential interactions with the biotic and abiotic environment were not considered to be a relevant issue. The unlikely but theoretically possible transfer of the recombinant genes from soybean MON 87708 × MON 89788 to environmental bacteria does not give rise to any safety concern. The post-market environmental monitoring plan and reporting intervals are in line with the scope. In conclusion, the EFSA GMO Panel considers that the information available for soybean MON 87708 × MON 89788 addresses the scientific comments raised by Member States and that the soybean MON 87708 × MON 89788, as described in this application, is as safe as its non-GM comparator and non-GM soybean reference varieties with respect to potential effects on human and animal health and the environment in the context of its scope.

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SCIENTIFIC OPINION

Scientific Opinion on application (EFSA-GMO-NL-2012-108) for the placing on the market of the herbicide-tolerant genetically modified soybean MON 87708 × MON 89788 for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto[1]

EFSA Panel on Genetically Modified Organisms (GMO)[2,3]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

Single events MON 87708 and MON 89788 were combined to produce the stack two-event soybean MON 87708 × MON 89788. The EFSA GMO Panel previously assessed the two single events and did not identify safety concerns in the context of their scope. No new data on single soybean events leading to a modification of the original conclusions on their safety were identified. Agronomic and phenotypic characteristics, as well as compositional data of soybean MON 87708 × MON 89788, did not give rise to food/feed and environmental safety concerns. The EFSA GMO Panel considers that there is no reason to expect interactions between the single events that could impact on the food and feed safety and the nutritional properties of soybean MON 87708 × MON 89788. There are no indications of an increased likelihood of establishment and spread of feral soybean plants. Considering the scope of application EFSA-GMO-NL-2012-108, potential interactions with the biotic and abiotic environment were not considered to be a relevant issue. The unlikely but theoretically possible transfer of the recombinant genes from soybean MON 87708 × MON 89788 to environmental bacteria does not give rise to any safety concern. The post-market environmental monitoring plan and reporting intervals are in line with the scope. In conclusion, the EFSA GMO Panel considers that the information available for soybean MON 87708 × MON 89788 addresses the scientific comments raised by Member States and that the soybean MON 87708 × MON 89788, as described in this application, is as safe as its non-GM comparator and non-GM soybean reference varieties with respect to potential effects on human and animal health and the environment in the context of its scope.

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KEY WORDS

GMO, soybean (*Glycine max* (L.) Merr.), DMO, CP4 EPSPS, herbicide tolerant, stack

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[1] On request from the Competent Authority of the Netherlands on application (EFSA-GMO-NL-2012-108) submitted by Monsanto, Question No EFSA-Q-2012-00442, adopted on 27 May 2015.

[2] Panel members Salvatore Arpaia, Andrew Nicholas Edmund Birch, Andrew Chesson, Patrick du Jardin, Achim Gathmann, Jürgen Gropp, Lieve Herman, Hilde-Gunn Hoen-Sorteberg, Huw Jones, József Kiss, Gijs Kleter, Martinus Lovik, Antoine Messéan, Hanspeter Naegeli, Kaare Magne Nielsen, Jaroslava Ovesna, Joe Perry, Nils Rostoks and Christoph Tebbe. Correspondence: gmo@efsa.europa.eu

[3] Acknowledgement: The Panel wishes to thank the members of the Working Groups on: Molecular Characterisation; Food/Feed safety; and Environment on GMO applications for the preparatory work on this scientific opinion, and EFSA staff: Zoltán Divéki, Antonio Fernández Dumont, Anna Lanzoni and Sylvie Mestdagh, for the support provided to this scientific opinion.

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SUMMARY

Following the submission of application EFSA-GMO-NL-2012-108 under Regulation (EC) No 1829/2003 from Monsanto, the Panel on Genetically Modified Organisms of the European Food Safety Authority (EFSA GMO Panel) was asked to deliver a scientific opinion on the safety of herbicide-tolerant genetically modified (GM) soybean MON 87708 × MON 89788 (Unique Identifier MON-877Ø8-9 × MON-89788-1). The scope of application EFSA-GMO-NL-2012-108 is for food and feed uses, import and processing, but excludes cultivation within the European Union (EU).

Soybean containing the single events MON 87708 (expressing DMO) and MON 89788 (expressing CP4 EPSPS) were assessed previously and no concerns were identified for human and animal health or environmental safety. No safety issue was identified by updated bioinformatic analyses, nor reported by the applicant concerning the two single soybean events, since the publication of the respective scientific opinions. Consequently, the EFSA GMO Panel considers that its previous conclusions on the safety of the single soybean events remain valid.

The two-event stack soybean MON 87708 × MON 89788 was produced by conventional crossing to produce soybean tolerant to dicamba and glyphosate-based herbicides. The EFSA GMO Panel evaluated soybean MON 87708 × MON 89788 with reference to the scope and appropriate principles described in its guidelines for the risk assessment of GM plants and derived food and feed, the environmental risk assessment of GM plants and the post-market environmental monitoring of GM plants. The scientific evaluation of the risk assessment included molecular characterisation of the inserted DNA and analysis of the expression of the corresponding proteins. An evaluation of the comparative analyses of the compositional, agronomic and phenotypic characteristics was undertaken, and the safety of the newly expressed proteins and of the whole food/feed was evaluated with respect to potential toxicity, allergenicity and nutritional wholesomeness. An evaluation of environmental impacts and the post-market environmental monitoring plan was also undertaken. In accordance with the EFSA GMO Panel guidance document applicable to this application (EFSA GMO Panel, 2011a), "*For GM plants containing a combination of transformation events (stacked events) the primary concern for risk assessment is to establish that the combination of events is stable and that no interactions between the stacked events, that may raise safety concerns compared to the single events, occur. The risk assessment of GM plants containing stacked events focuses on issues related to: a) stability of the inserts, b) expression of the introduced genes and their products and c) potential synergistic or antagonistic effects resulting from the combination of the events*".

The molecular data establish that the transformation events stacked in soybean MON 87708 × MON 89788 have the same molecular properties and characteristics as the single transformation events. Comparison of the levels of the DMO and CP4 EPSPS proteins between the stack and the corresponding single events did not reveal an interaction that manifests at protein or trait expression level. From the molecular characterisation, no indications of interactions between the events based on the biological functions of the newly expressed proteins were identified.

Based on the agronomic and phenotypic characteristics of soybean MON 87708 × MON 89788 under the tested conditions (treated and not treated with both intended herbicides), some differences were observed in soybean MON 87708 × MON 89788 compared with its non-GM comparator. The significant differences observed in 100 seed weight were further assessed for their potential environmental impact. At the compositional analysis, differences in some fatty acids (equivalence category III and IV) and in trypsin inhibitor soybean (equivalence not established) were identified between MON 87708 × MON 89788 and its non-GM comparator. The EFSA GMO Panel concluded that none of the differences identified in the composition, agronomic and phenotypic characteristics of seed and forage obtained from soybean MON 87708 × MON 89788 is relevant to food and feed safety.

The safety assessment identified no concerns regarding the potential toxicity of the newly expressed proteins DMO and CP4 EPSPS in soybean MON 87708 × MON 89788. No reasons were identified that the presence of the two proteins in combination would result in interactions producing effects

different from those of the individual proteins. Similarly, the EFSA GMO Panel did not identify indications of safety concerns regarding allergenicity of the individual newly expressed proteins or their mixture in soybean MON 87708 × MON 89788, or regarding potential changes in its overall allergenicity. Soybean MON 87708 × MON 89788 is as nutritious as its non-GM comparator and non-GM soybean reference varieties.

Considering the scope of application EFSA-GMO-NL-2012-108, there is no requirement for scientific information on possible environmental effects associated with the cultivation of soybean MON 87708 × MON 89788 in Europe. There are no indications of an increased likelihood of establishment and spread of feral soybean MON 87708 × MON 89788 plants in case of accidental release into the environment of viable GM soybean seeds. Potential interactions of soybean MON 87708 × MON 89788 with the biotic and abiotic environment were not considered to be a relevant issue by the EFSA GMO Panel. The unlikely but theoretically possible transfer of the recombinant genes from soybean MON 87708 × MON 89788 to environmental bacteria does not give rise to safety concerns owing to the lack of a selective advantage in the context of the scope of this application. The post-market environmental monitoring plan provided by the applicant and the reporting intervals are in line with the scope of application EFSA-GMO-NL-2012-108.

In delivering its scientific opinion, the EFSA GMO Panel took into account application EFSA-GMO-NL-2012-108, additional information provided by the applicant, scientific comments submitted by the Member States and relevant scientific publications. In conclusion, the EFSA GMO Panel is of the opinion that the two-event stack soybean MON 87708 × MON 89788, as described in this application, is as safe as its non-GM comparator and non-GM soybean reference varieties with respect to potential effects on human and animal health and the environment in the context of its scope.

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BACKGROUND

On 29 March 2012, the European Food Safety Authority (EFSA) received from the Competent Authority of the Netherlands application EFSA-GMO-NL-2012-108, for authorisation of genetically modified (GM) soybean MON 87708 × MON 89788 submitted by Monsanto within the framework of Regulation (EC) No 1829/2003[4] for food and feed uses, import and processing.

After receiving the application EFSA-GMO-NL-2012-108 and in accordance with Articles 5(2)(b) and 17(2)(b) of Regulation (EC) No 1829/2003, EFSA informed Member States and the European Commission, and made the summary of the application available to the public on the EFSA website.[5] EFSA initiated a formal review of the application to check compliance with the requirements laid down in Articles 5(3) and 17(3) of Regulation (EC) No 1829/2003. On 29 June 2012 and on 19 July 2012 EFSA received additional information (requested on 24 May 2012 and 19 July 2012, respectively). On 20 July 2012, EFSA declared the application valid in accordance with Articles 6(1) and 18(1) of Regulation (EC) No 1829/2003.

EFSA made the valid application available to Member States and the European Commission, and consulted nominated risk assessment bodies of Member States, including national Competent Authorities within the meaning of Directive 2001/18/EC[6] following the requirements of Articles 6(4) and 18(4) of Regulation (EC) No 1829/2003 to request their scientific opinion. Member States had three months after the date of receipt of the valid application to make their opinion known (Member States three months period for application EFSA-GMO-NL-2012-108 was opened on 26 September 2013 following the finalisation of the risk assessment of the single events; the commenting period lasted till 8 January 2014).

The EFSA GMO Panel carried out an evaluation of the scientific risk assessment of soybean MON 87708 × MON 89788 for food and feed uses, import and processing in accordance with Articles 6(6) and 18(6) of Regulation (EC) No 1829/2003. The EFSA GMO Panel took into account the appropriate principles described in its guidelines for the risk assessment of GM plants and derived food and feed (EFSA GMO Panel, 2011a), the environmental risk assessment of GM plants (EFSA GMO Panel, 2010b) and on the post-market environmental monitoring of GM plants (EFSA GMO Panel, 2011b). Furthermore, the EFSA GMO Panel also took into consideration the scientific comments of Member States, the additional information provided by the applicant and relevant scientific publications.

On 13 August 2013, 6 December 2013, 10 February 2014, 5 June 2014 and 9 January 2015 the EFSA GMO Panel requested additional information from the applicant. The applicant provided the requested information on 2 September 2013, 20 December 2013, 19 February 2014, 20 June 2014 and on 27 January 2015. The applicant also spontaneously provided additional information on 28 March 2014, on 12 December 2014 and on 3 March 2015. The applicant requested clarifications on 13 October 2014 and 27 January 2015. EFSA provided clarifications to the applicant on 7 November 2014 and on 16 April 2015, respectively.

In giving its scientific opinion to the European Commission, the Member States and the applicant, and in accordance with Articles 6(1) and 18(1) of Regulation (EC) No 1829/2003, EFSA has endeavoured to respect a time limit of six months from the acknowledgement of the valid application. As additional information was requested by the EFSA GMO Panel, the time limit of six months was extended accordingly, in line with Articles 6(1), 6(2), 18(1), and 18(2) of Regulation (EC) No 1829/2003.

[4] 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. 1–23.
[5] Available online: http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2012-00442
[6] Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC. OJ L 106, 12.3.2001, p. 1–38.

According to Regulation (EC) No 1829/2003, this scientific opinion is to be seen as the report requested under Articles 6(6) and 18(6) of that Regulation and thus will be part of the EFSA overall opinion in accordance with Articles 6(5) and 18(5).

TERMS OF REFERENCE

The EFSA GMO Panel was requested to carry out a scientific assessment of soybean MON 87708 × MON 89788 for food and feed uses, import and processing in accordance with Articles 6(6) and 18(6) of Regulation (EC) No 1829/2003.

Where applicable, any conditions or restrictions which should be imposed on the placing on the market and/or specific conditions or restrictions for use and handling, including post-market monitoring requirements based on the outcome of the risk assessment and, in the case of GMOs or food/feed containing or consisting of GMOs, conditions for the protection of particular ecosystems/environment and/or geographical areas should be indicated in accordance with Articles 6(5)(e) and 18(5)(e) of Regulation (EC) No 1829/2003.

The EFSA GMO Panel was not requested to give an opinion on information required under Annex II to the Cartagena Protocol. Furthermore, the EFSA GMO Panel did not consider proposals for labelling and methods of detection (including sampling and the identification of the specific transformation event in the food/feed and/or food/feed produced from it), which are matters related to risk management.

ASSESSMENT

1. Introduction

Application EFSA-GMO-NL-2012-108 covers a two-event stack soybean MON 87708 × MON 89788 produced by conventional crossing. The scope of this application is for food and feed uses, import and processing, but excludes cultivation within the European Union (EU).

European Food Safety Authority (EFSA) guidance establishes the principle that "*For GM plants containing a combination of transformation events (stacked events) the primary concern for risk assessment is to establish that the combination of events is stable and that no interactions between the stacked events, that may raise safety concerns compared to the single events, occur. The risk assessment of GM plants containing stacked events focuses on issues related to: a) stability of the inserts, b) expression of the introduced genes and their products and c) potential synergistic or antagonistic effects resulting from the combination of the events*" (EFSA GMO Panel, 2011a).

Soybean MON 87708 × MON 89788 was developed to confer tolerance to dicamba (3,6-dichloro-2-methoxybenzoic acid) and glyphosate (*N*-(phosphonomethyl)glycine)-based herbicides. Dicamba tolerance is achieved by the expression of dicamba mono-oxygenase (DMO) protein, which demethylates dicamba, producing 3,6-dichlorosalicylic acid and formaldehyde. Tolerance to glyphosate is achieved by expression of the CP4 5-enolpyruvylshikimate-3-phosphate synthase (CP4 EPSPS). It should be noted that the assessment of herbicide residues in soybean tolerant crops relevant for this application has been investigated by the EFSA Pesticides Unit (EFSA, 2009, 2013).

The two single soybean events MON 87708 and MON 89788 have been previously assessed (see Table 1) on the basis of experimental data. No concerns for human and animal health or environmental safety were identified.

Table 1: Single soybean events already assessed by the EFSA GMO Panel

Events	Application or mandate	EFSA Scientific Opinions
MON 87708	EFSA-GMO-NL-2011-93	EFSA GMO Panel (2013)
MON 89788	EFSA-GMO-NL-2006-36	EFSA (2008)

2. Issues raised by Member States

Issues raised by Member States on soybean MON 87708 × MON 89788 were considered in this scientific opinion and are addressed in detail in Annex G of the EFSA overall opinion.[7]

3. Updated information on single events

Since the publication of the scientific opinions on the single soybean events by the EFSA GMO Panel (EFSA, 2008; EFSA GMO Panel, 2013), no safety issue pertaining to the two single events has been reported by the applicant.

Updated bioinformatic analyses[8] on the junction regions for events MON 87708 and MON 89788 confirmed that no known endogenous genes were disrupted by any of the inserts. Updated bioinformatic analyses[9] of the amino acid sequences of the newly expressed proteins and Open Reading Frames in the insert and spanning the junction regions revealed no significant similarities to known toxins or allergens. The search for similarity to allergens used the criterion of 35 % identity to the amino acid sequence of known allergens in a window of 80 amino acids. No matches of eight contiguous identical amino acid sequences between these sequences and known allergens were found.

[7] Available online: http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2012-00442
[8] Additional information: 03/03/2015.
[9] Additional information: 030/3/2015.

In order to conclude on the possibility of horizontal gene transfer by homologous recombination, a sequence identity analysis of the regions of bacterial origin of MON 87708 and MON 89788 was performed. In soybean MON 87708, the dicamba mono-oxygenase coding sequence (*dmo*) is derived from *Stenotrophomonas maltophilia*, with a total length of 1022 bp and with 99.9 % sequence identity to the donor organism. In addition, the left border sequence (246 bp) displays 100 % sequence identity with *Agrobacterium tumefaciens*. These two sequence identities are unlikely to represent double homologous recombination potential. In soybean MON 89788, no pairs of sequences with sufficient length of identity and correct orientation with bacterial genomes were found to facilitate the transfer of insert sequences to bacterial recipients by double homologous recombination.

Having assessed the updated information on soybean MON 87708 and MON 89788, the EFSA GMO Panel considers that its previous conclusions on the safety of the single soybean events remain valid.

4. Risk assessment of the two-event stack soybean MON 87708 × MON 89788

4.1. Molecular characterisation

Possible interactions between the known biological functions conferred by the individual inserts and interactions that would manifest at protein or trait expression level are considered.

4.1.1. Genetic elements and their biological functions

Soybean MON 87708 and MON 89788 are combined by conventional crossing to produce soybean MON 87708 × MON 89788. The structure of the inserts introduced into soybean MON 87708 × MON 89788 are described in detail in the EFSA GMO Panel scientific opinions, and no new genetic modifications were involved. Genetic elements in the expression cassettes of the single events are summarised in Table 2.

Table 2: Genetic elements in the expression cassettes of the events stacked in soybean MON 87708 × MON 89788

Event	Promoter	5′ UTR	Transit peptide	Coding region	Terminator
MON 87708	Full-length transcript promoter from Peanut chlorotic streak virus	5′ UTR from Tobacco etch virus	*RbcS* (*Pisum sativum*)	*dmo* (*S. maltophilia*)	3′ UTR of *RbcS2* (*P. sativum*)
MON 89788	35S promoter from Figwort mosaic virus and promoter from the *Tsf1* gene of *Arabidopsis thaliana*	5′ UTR and intron from *Tsf1* gene of *A. thaliana*	*ShkG* (*A. thaliana*)	CP4 *epsps* (*A. tumefaciens* strain CP4)	3′ UTR of *RbcS2* (*P. sativum*)

UTR, untranslated region.

There are two newly expressed proteins in soybean MON 87708 × MON 89788, both of which are enzymes. Biological functions conferred by these proteins are summarised in Table 3.

Table 3: Biological functions related to the events stacked in soybean MON 87708 × MON 89788

Event	Protein	Function in donor organism	Function in GM plant
MON 87708	DMO	Donor organism: *S. maltophilia* strain DI-6. DMO is an enzyme that catalyses the demethylation of dicamba to the non-herbicidal compound 3,6-dichlorosalicylic acid and formaldehyde (Herman et al., 2005)	DMO confers tolerance to dicamba-based herbicides
MON 89788	CP4 EPSPS	Donor organism: *A. tumefaciens* strain CP4. EPSPS is an enzyme involved in the shikimic acid pathway for aromatic amino acid biosynthesis in plants and microorganisms (Herrmann, 1995). Glyphosate is a competitive inhibitor of this enzyme	The bacterial CP4 EPSPS confers tolerance to glyphosate-based herbicides as it has a greatly reduced affinity towards glyphosate than the plant endogenous enzyme

GM, genetically modified.

4.1.2. Integrity of the events in soybean MON 87708 × MON 89788[10]

The genetic stability of the inserted DNA over multiple generations in the single soybean events MON 87708 and MON 89788 was demonstrated previously (EFSA, 2008; EFSA GMO Panel, 2013). Integrity of the events in soybean MON 87708 × MON 89788 was demonstrated by Southern analyses in the seventh self-pollinating generation after crossing the parental lines.

4.1.3. Information on the expression of the inserts[11]

Plants were grown at eight locations (four replicate blocks each) under field conditions in 2009 in the USA. The levels of DMO and CP4 EPSPS proteins in soybean MON 87708 × MON 89788 and the two single events were quantified by enzyme-linked immunosorbent assay. Proteins levels were determined in over-season leaf (OSL1 through OSL4 stages), root, forage and seed. The plants were treated with the intended herbicides (dicamba and/or glyphosate). Data on seed are reported and discussed below (Table 4). DMO and CP4 EPSPS protein levels in the two-event stack soybean were similar to the corresponding levels in the single-event soybean plants.

Table 4: Means and standard deviations (upper row) and ranges (lower row) of protein levels (µg/g dry weight) in seed from soybean MON 87708 × MON 89788 and from single soybean events MON 87708 and MON 89788

Protein	MON 87708 × MON 89788	MON 87708	MON 89788
DMO	41 (9.3) [(a)] 24–63	40 (11) [(b)] 21–65	NA
CP4 EPSPS	93 (17) [(a)] 67–140	NA	95 (18) [(a)] 64–130

(a): N = 32.
(b): N = 31.
NA, not applicable.

4.1.4. Conclusion

The molecular data establish that the transformation events stacked in soybean MON 87708 × MON 89788 have the same molecular properties and characteristics as the single transformation events.

[10] Dossier: Part II—Section A2.2.3.
[11] Dossier: Part II—Section A3.

Comparison of the levels of the DMO and CP4 EPSPS proteins between the stack and the single events did not reveal an interaction that manifests at protein or trait expression level. The molecular characterisation revealed no indications of interactions between the events based on the biological functions of the newly expressed proteins.

4.2. Comparative analysis

4.2.1. Evaluation of relevant scientific data

4.2.1.1. Choice of comparator and production of material for the comparative analysis[12]

In field trials carried out in the USA in 2009, soybean MON 87708 × MON 89788 was compared with the Asgrow variety A3525, and, in total, 14 commercial non-GM soybean reference varieties[13]. The latter set of soybean varieties was included in the study to describe natural variability among commercial soybean varieties. The commercial Asgrow variety, A3525, was the soybean variety originally transformed to establish transformation event MON 87708, and is the progeny of soybean variety A3244 crossed with the soybean variety A3469. A3244 was the soybean variety originally transformed to establish transformation event MON 89788. Therefore, the EFSA GMO Panel considered A3525 to have a comparable genetic background to the genetically modified soybean and to be a suitable non-GM comparator.

The field trials were performed at eight sites within the soybean cultivation areas in the USA (one each in Arkansas, Iowa, Kansas and Nebraska, and two each in Illinois and Indiana). At each site the following test materials were grown in a randomised complete block design with four replicates: soybean MON 87708 × MON 89788, the non-GM comparator (A3525) and three different non-GM soybean reference varieties, all treated with required maintenance pesticides; and soybean MON 87708 × MON 89788 treated with both dicamba and glyphosate on top of required maintenance pesticides (treatment called dicamba + glyphosate).

4.2.1.2. Statistical analysis of field trials data

The statistical analysis of the agronomic, phenotypic and compositional data followed the recommendations by the EFSA GMO Panel (EFSA GMO Panel, 2010a, 2011a). This includes a test of difference to determine whether the GM plant is different from its comparator/conventional counterpart, and a test of equivalence to determine whether the GM plant falls within the range of natural variation estimated from the non-GM soybean reference varieties. As described in EFSA GMO Panel (2011a), the result of the equivalence test is categorised into four possible outcomes to facilitate drawing conclusions with respect to the presence or absence of equivalence. These four categories are category I, indicating full equivalence; category II, indicating that equivalence is more likely than non-equivalence; category III, indicating that non-equivalence is more likely than equivalence; and category IV, indicating non-equivalence.

4.2.1.3. Agronomic and phenotypic characteristics[14]

The phenotypic and agronomic characteristics evaluated[15] were early stand count, seedling vigour, days to 50 % flowering, flower colour, plant height, lodging, pod shattering, final stand count, seed moisture, 100 seed weight, yield and plant growth stages.

In the analysis of soybean MON 87708 × MON 89788 not treated with dicamba + glyphosate, the test of difference of phenotypic and agronomic characteristics identified statistically significant differences

[12] Dossier: Part II—Sections A3.1, A3.2; additional information: 02/09/2013 and 20/06/2014.
[13] The commercial non-GM soybean reference varieties included in the field trials were Channel Bio 3461, Channel Bio 37002, Croplan HT3596STS, Crows C37003N, Crows C3908, FS 3591, Garst 3585N, Midland 363, NK S38-T8, NK 32Z3, Pioneer 93M52, Quality Plus 365C, Stewart SB3454 and Wilken 3316.
[14] Dossier: Part II—Section A3.4; additional information: 02/09/2013, 19/02/2014 and 20/06/2014.
[15] Flower colour and plant growth stages were not statistically analysed using the most recent EFSA methodology (EFSA, 2010a, 2011a).

between soybean MON 87708 × MON 89788 and its non-GM comparator for three endpoints (seed moisture, 100 seed weight and yield). The test of equivalence on soybean MON 87708 × MON 89788 (not treated with dicamba + glyphosate) showed that seed moisture and yield fell under equivalence category I, and 100 seed weight fell under equivalence category II. The test of equivalence could not be performed for seedling vigour (due to the small variation among the non-GM soybean reference varieties for this endpoint); however, no significant difference was identified for this endpoint. For seed moisture, for which a significant genotype × environment interaction had been detected, no consistent relationship to descriptive site characteristics was observed.

In the analysis of soybean MON 87708 × MON 89788 treated with dicamba + glyphosate, the test of difference identified statistically significant differences between soybean MON 87708 × MON 89788 and its non-GM comparator for six endpoints (early stand count, seedling vigour, days to 50 % flowering, plant height, 100 seed weight and yield). The equivalence test showed that five of these endpoints fell under equivalence category I, and the endpoint 100 seed weight fell under equivalence category II. The test of equivalence could not be performed for seedling vigour (due to the small variation among the non-GM soybean reference varieties); however, the difference in seedling vigour between the GM soybean and the non-GM comparator was small (3.4 vs. 3.0), and in all cases the vigour grading for this soybean remained normal to excellent. For 100 seed weight, for which a significant genotype × environment interaction had been detected, no consistent relationship to descriptive site characteristics was observed.

As for 100 seed weight, full equivalence with the range of non-GM reference varieties could not be demonstrated (for either of the two spraying regimens) and, because this endpoint is relevant for the assessment of possible changes in persistence and invasiveness of the GM soybean, the significant differences observed in 100 seed weight are further assessed for their potential environmental impact in Section 4.4.

Data on environmental interaction of soybean MON 87708 × MON 89788 compared with the non-GM comparator were obtained for materials that had received equivalent maintenance pesticide treatments, i.e. they were not treated with dicamba and glyphosate. The studies included plant response (damage) to three abiotic stressors, three diseases and three arthropods at each field trial site four times during the growing season. Comparable responses to abiotic stressors, such as cold, compaction, drought, flood, frost, hail, nutrient deficiency and wind, were observed. There were also no differences observed between soybean MON 87708 × MON 89788 and the non-GM comparator for any of the diseases on this legume crop. A few differences were observed for arthropod damage (see Section 4.4).

4.2.1.4. Compositional analysis[16]

The EFSA GMO Panel has already assessed data on the composition of soybean MON 87708 and MON 89788 (treated and untreated with target herbicides) as compared with their corresponding conventional counterparts (EFSA, 2008; EFSA GMO Panel, 2013). It was concluded that the composition of both soybean MON 87708 and soybean MON 89788 was comparable to that of their conventional counterparts (A3525 and A3244, respectively) and commercial soybean varieties.

Soybean MON 87708 × MON 89788 forage and seeds harvested from the field trials were analysed for 63 constituents (56 in seeds[17] and seven in forage[18]), including the key constituents recommended

[16] Dossier: Part II— Section A3.3; additional information: 02/09/2013, 20/6/2014 and 27/01/2015.

[17] Proximates (protein, fat, ash, moisture, and carbohydrates by calculation), fibre fractions (acid detergent fibre and neutral detergent fibre), amino acids (alanine, arginine, aspartic acid, cysteine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine and valine), fatty acids (caprylic acid (C8:0), capric acid (C10:0), lauric acid (C12:0), myristic acid (C14:0), myristoleic acid (C14:1), pentadecanoic acid (C15:0), pentadecenoic acid (C15:1), palmitic acid (C16:0), palmitoleic acid (C16:1), heptadecanoic acid (C17:0), heptadecenoic acid (C17:1), stearic acid (C18:0), oleic acid (C18:1), linoleic acid (C18:2), linolenic acid (C18:3), linolenic acid (C18:3), arachidic acid (C20:0), eicosenoic acid (C20:1), eicosadienoic acid (C20:2), eicosatrienoic acid (C20:3),

by OECD (2001). Seventeen seed constituents with more than 50 % of the observations below the limit of quantification were excluded from the statistical analysis[19].

The test of difference between compositional data of soybean MON 87708 × MON 89788 not sprayed with dicamba + glyphosate and the non-GM comparator (A3525) identified statistically significant differences for 17 constituents (15 in seeds[20] and two in forage[21]).

The test of equivalence between compositional data from soybean MON 87708 × MON 89788 (not sprayed with dicamba + glyphosate) and the non-GM soybean reference varieties indicated that the levels of 16 of the 17 constituents fell under equivalence category I or II, while the level of the seed constituent palmitic acid (% total fatty acid (FA)) fell under equivalence category III (Table 5). For 5 of the 17 significantly different endpoints[22], a significant genotype × environment interaction was identified.

For soybean MON 87708 × MON 89788 sprayed with dicamba + glyphosate, statistically significant differences were identified for 19 constituents (16 in seeds[23] and three in forage[24]).

The test of equivalence between compositional data on soybean MON 87708 × MON 89788 sprayed with dicamba + glyphosate and the non-GM soybean reference varieties indicated that the levels of 17 of the 19 constituents fell under equivalence category I or II. The level of the seed constituent palmitic acid (%FA) fell under equivalence category III, while for trypsin inhibitor the test of equivalence could not be performed because of the small variation among the non-GM soybean references varieties (Table 5). For 7 of the 19 significantly different endpoints[25], a significant genotype × environment interaction was identified.

Upon request from the EFSA GMO Panel, the applicant provided a statistical analysis of the fatty acid profile on a dry weight (% dw) basis[26]. In the outcome of the analysis, the level of palmitic acid in the GM soybean (both sprayed and not sprayed with dicamba + glyphosate) was significantly different and fell under equivalence category I. The levels of oleic acid (GM soybean not sprayed with dicamba + glyphosate) and behenic acid (GM soybean both sprayed and not sprayed with dicamba + glyphosate) measured in % dw were significantly different and fell under equivalence category IV (Table 5).

arachidonic acid (C20:4) and behenic acid (C22:0)), vitamin E, anti-nutrients (phytic acid, trypsin inhibitor, lectins, stachyose and raffinose) and other secondary metabolites (isoflavones: daidzein, genistein and glycitein).

[18] Proximates: protein, fat, ash, moisture, and carbohydrates by calculation; fibre fractions: acid detergent fibre and neutral detergent fibre.

[19] Caprylic acid (C8:0), capric acid (C10:0), lauric acid (C12:0), myristic acid (C14:0), myristoleic acid (C14:1), pentadecanoic acid (C15:0), pentadecenoic acid (C15:1), palmitoleic acid (C16:1), heptadecanoic acid (C17:0), heptadecenoic acid (C17:1), gamma-linolenic acid (C18:3), eicosadienoic acid (C20:2), eicosatrienoic acid (C20:3) and arachidonic acid (C20:4).

[20] Protein and moisture; the amino acids arginine, cystine and proline; the fatty acids palmitic acid (C16:0), stearic acid (C18:0), oleic acid (C18:1), linoleic acid (C18:2), arachidic acid (C20:0) and behenic acid (C22:0); the anti-nutrients raffinose and stachyose; and the isoflavones genistein and daidzein.

[21] Carbohydrates and fat.

[22] Seed levels of protein, palmitic acid (C16:0), oleic acid (C18:1), linoleic acid (C18:2) and stachyose.

[23] Protein, moisture and ash; the amino acids arginine, cystine and proline; the fatty acids palmitic acid (C16:0), stearic acid (C18:0), oleic acid (C18:1), linoleic acid (C18:2), arachidic acid (C20:0) and behenic acid (C22:0); the anti-nutrients raffinose and stachyose; and the isoflavones genistein and daidzein.

[24] Carbohydrates, protein and fat.

[25] Seed levels of protein, arginine, cystine, palmitic acid (C16:0), linoleic acid (C18:2), behenic acid (C22:0) and stachyose.

[26] Additional information: 27/01/2015.

Table 5: Compositional endpoints that are further discussed based on the results of the statistical analysis: means (for the non-GM comparator and the GM soybean) and equivalence limits (from the non-GM reference varieties) estimated from field trials data collected in 2009. Significantly different entries are marked with a star. The outcomes of the test of equivalence are differentiated by greyscale backgrounds: white (the test of equivalence could not be performed), light grey (equivalence category III) and dark grey (equivalence category IV)

Endpoint	Comparator (A3525, untreated)	Soybean MON 87708 × MON 89788		Equivalence limits from non-GM soybean reference varieties (untreated)
		Untreated [(a)]	Treated [(b)]	
Palmitic acid (16:0) (% FA) [(c)]	11.74	12.17*	12.12*	(9.48, 12.08)
Oleic acid (18:1) (% dw)	2.97	2.81*	2.87	(3.00, 4.32)
Behenic acid (22:0) (% dw)	0.045	0.048*	0.049*	(0.052, 0.060)
Trypsin inhibitor (TIU/mg dw)	35.32	35.08	38.71*	Not applied

(a): Untreated: soybean MON 87708 × MON 89788 not sprayed with the target herbicides (dicamba + glyphosate).
(b): Treated: soybean MON 87708 × MON 89788 sprayed with the target herbicides (dicamba + glyphosate).
(c): Fatty acid proportions are given as percentages of total fatty acids.
dw, dry weight; TIU, trypsin inhibitor unit.

The EFSA GMO Panel assessed all compositional differences between soybean MON 87708 × MON 89788 and its non-GM comparator. After considering the well-known chemical characteristics of the compounds concerned, the magnitudes of the changes observed (Table 5) and denaturation of trypsin inhibitor by heat during processing, the EFSA GMO Panel did not identify any need for further assessment with regard to food and feed safety.

For each of the parameters for which a significant genotype × environment interaction had been detected, no consistent relationship to descriptive site characteristics was observed.

4.2.2. Conclusion

Based on the agronomic and phenotypic characteristics of soybean MON 87708 × MON 89788 under the tested conditions (treated and not treated with both intended herbicides), some differences were observed in soybean MON 87708 × MON 89788 compared with its non-GM comparator. The significant differences observed in 100 seed weight are further assessed for their potential environmental impact in Section 4.4.

The EFSA GMO Panel concluded that none of the differences identified in the agronomic and phenotypic characteristics and in the composition of seed and forage obtained from soybean MON 87708 × MON 89788 required further assessment regarding food and feed safety.

4.3. Food and feed safety assessment

4.3.1. Effect of processing[27]

Soybean MON 87708 × MON 89788 will undergo existing methods of production and processing used for commercial soybean. No novel method of production and processing is envisaged.

[27] Dossier: Part II—Section A3.5.

4.3.2. Toxicology

4.3.2.1. Toxicological assessment of newly expressed proteins[28]

Two proteins (DMO and CP4 EPSPS) are newly expressed in various tissues of the two-event stack soybean MON 87708 × MON 89788. The EFSA GMO Panel assessed these proteins previously (see Table 1), and no safety concerns to humans or animals were identified. The CP4 EPSPS protein has also been previously assessed in other GM applications (e.g. EFSA GMO Panel, 2012, 2014). The EFSA GMO Panel is not aware of any new information that would change these conclusions.

The two proteins are enzymes which catalyse distinct biochemical reactions and act on unrelated substrates in the plant. No reasons were identified that the presence of the two proteins in combination would result in interactions producing effects different from those of the individual proteins (see Section 4.1.4). Since the individual proteins are considered safe for humans and animals (e.g. EFSA 2008, 2013), the same conclusion can be extended to the mixture.

4.3.2.2. Toxicological assessment of components other than newly expressed proteins[29]

The compositional analysis of soybean MON 87708 × MON 89788 did not identify changes (see Section 4.2) that would require further assessment.

4.3.3. Allergenicity

For allergenicity assessment, a weight-of-evidence approach is followed, taking into account all of the information obtained on the newly expressed proteins, since no single piece of information or experimental method yields evidence to predict allergenicity (EFSA, 2006; Codex Alimentarius, 2009; EFSA GMO Panel, 2011a). In addition, when known functional aspects of the newly expressed protein or structural similarity to known adjuvants may indicate an adjuvant activity, the possible role of these proteins as adjuvants is considered (EFSA GMO Panel, 2011a). When newly expressed proteins with a potential adjuvant activity are expressed together, possible interactions increasing adjuvanticity and impacting the allergenicity of the GM crop are assessed.

4.3.3.1. Assessment of allergenicity of the newly expressed proteins[30]

For allergenicity, the EFSA GMO Panel has previously evaluated the safety of the DMO and CP4 EPSPS proteins, and no concerns about allergenicity were identified in the context of the applications assessed (e.g. see Table 1; EFSA GMO Panel, 2012, 2014). No new information on allergenicity of the single events that might change the previous conclusions of the EFSA GMO Panel has become available. Based on current knowledge, and since none of the newly expressed proteins showed allergenicity, no reasons for concern regarding the mixture of these newly expressed proteins in this two-event stack soybean affecting allergenicity were identified.

As regards adjuvanticity, no information available on the structure or function of the newly expressed DMO and CP4 EPSPS proteins would suggest an adjuvant effect of the individual proteins or their mixture in soybean MON 87708 × MON 89788 resulting in or increasing an eventual IgE response to a bystander protein.

4.3.3.2. Assessment of allergenicity of the whole GM plant[31]

Soybean is considered to be a common allergenic food[32] (OECD, 2012). Therefore, any potential change in the endogenous allergenicity of the GM plant when compared with that of its comparator(s)

[28] Dossier: Part II—Section A4.2; additional information: 19/03/2013.
[29] Dossier: Part II—Section A4.3.
[30] Dossier: Part II—Section A5; additional information: 03/03/2015.
[31] Dossier: Part II—Section A5; additional information: 02/09/2013 and 20/12/2013.
[32] Directive 2007/68/EC of the European Parliament and of the Council of 27 November 2007 amending Annex IIIa to Directive 2000/13/EC of the European Parliament and of the Council as regards certain food ingredients. OJ L 310, 27.11.2007, p. 11–14.

should be assessed (EFSA GMO Panel, 2011a). Such assessments were performed for the single events soybean MON 87708 and soybean MON 89788, and no reasons for concern were identified by the EFSA GMO Panel (EFSA, 2008; EFSA GMO Panel, 2013).

At the request of the EFSA GMO Panel, the applicant provided an assessment of the endogenous allergenicity of protein extracts of soybean MON 87708 × MON 89788 and of its non-GM comparator (A3525) as determined by gel electrophoresis followed by mass spectrometry. The intensities of the bands corresponding to specific allergens were analysed. No relevant changes in the allergen content between the protein extracts of soybean MON 87708 × MON 89788 and of its non-GM comparator were identified.

The EFSA GMO Panel considers that there is no evidence that the genetic modification might significantly change the overall allergenicity of soybean MON 87708 × MON 89788 when compared with that of its non-GM comparator.

4.3.4. Nutritional assessment of GM food/feed

The intended trait of soybean MON 87708 × MON 89788 is herbicide tolerance, with no intention to alter the nutritional parameters. Comparison of the composition of soybean MON 87708 × MON 89788 with its conventional counterpart did not identify differences that would require a safety assessment (see Section 4.2). From these data, the nutritional characteristics of soybean MON 87708 × MON 89788-derived food and feed are not expected to differ from those of conventional soybean varieties.

4.3.5. Post-market monitoring of GM food/feed

The EFSA GMO Panel considers that post-market monitoring of GM food/feed is not necessary, given the absence of safety concerns identified for soybean MON 87708 × MON 89788.

4.3.6. Conclusion

The safety assessment identified no concerns regarding the potential toxicity of the newly expressed proteins DMO and CP4 EPSPS in soybean MON 87708 × MON 89788. No reasons were identified that the presence of the two proteins in combination would result in interactions producing effects different from those of the individual proteins. Similarly, the EFSA GMO Panel did not identify indications of safety concerns regarding allergenicity of the individual newly expressed proteins or their mixture in soybean MON 87708 × MON 89788, or regarding potential changes in overall allergenicity. Soybean MON 87708 × MON 89788 is as nutritious as its non-GM comparator and non-GM soybean reference varieties.

4.4. Environmental risk assessment and monitoring plan

4.4.1. Evaluation of relevant scientific data

Considering the scope of application EFSA-GMO-NL-2012-108, the environmental risk assessment (ERA) of soybean MON 87708 × MON 89788 is concerned mainly with (i) exposure of bacteria to recombinant DNA in the gastrointestinal tract of animals fed GM material and bacteria present in environments exposed to faecal material; and (ii) accidental release into the environment of viable seeds of soybean MON 87708 × MON 89788 during transportation and processing.

As the scope of application EFSA-GMO-NL-2012-108 excludes cultivation, environmental concerns in the EU related to the use of glyphosate-based and dicamba-based herbicides on the GM soybean do not apply.

4.4.2. Environmental risk assessment

4.4.2.1. Potential unintended effects on plant fitness due to the genetic modification[33]

Cultivated soybean (*Glycine max* (L.) Merr.) is a species in the subgenus *Soja* of the genus *Glycine*. The species originated from eastern Asia and is a highly domesticated crop (Lu, 2005). The major worldwide soybean producers are Argentina, Brazil, China, North Korea, South Korea and the USA. In the EU[34], soybean is mainly cultivated in Italy, Romania, France, Hungary, Austria, Slovakia and the Czech Republic (Dorokhov et al., 2004; Krumphuber, 2008). Cultivated soybean seeds rarely display any dormancy characteristics, and only under certain environmental conditions grow as volunteers in the year following cultivation. If volunteers occur, they do not compete well with the succeeding crop, and can easily be controlled mechanically or chemically (OECD, 2000). In soybean fields, seeds usually do not survive during the winter owing to herbivory, rotting and germination resulting in death, or owing to management practices prior to planting the subsequent crop (Owen, 2005).

The herbicide tolerance traits can be regarded as providing a potential agronomic and selective advantage to this GM soybean plant only where and when glyphosate-based and dicamba-based herbicides are applied. However, survival of soybean plants outside cultivation where glyphosate-based and dicamba-based herbicides are applied is limited mainly by a combination of low competitiveness, absence of a dormancy phase and susceptibility to plant pathogens and cold climatic conditions. Based in the inserted traits, the EFSA GMO Panel considers that these general characteristics are unchanged in soybean MON 87708 × MON 89788; herbicide tolerance is therefore unlikely to provide a selective advantage outside cultivation. Even if glyphosate-based and dicamba-based herbicides are applied to these plants, this will not change their ability to survive over seasons. Therefore, it is considered very unlikely that soybean MON 87708 × MON 89788 will differ from conventional soybean varieties in its ability to survive until subsequent seasons or to establish feral populations under European environmental conditions.

Laboratory tests and field studies have been carried out to assess the phenotypic and agronomic characteristics as well as environmental interactions of GM soybean as described in Section 4.2.1.3. Phenotypic and agronomic characteristics were evaluated in a field trial across eight locations in the USA in 2009. In addition, environmental interactions, such as soybean MON 87708 × MON 89788 responses to abiotic and biotic stressors, were evaluated in the same trials (i.e. they were not treated with dicamba-based and glyphosate-based herbicides) (for further details, see Section 4.2.1.3).

Considering the scope of application EFSA-GMO-NL-2012-108, special attention is paid to those agronomic characteristics which may affect the survival, establishment and fitness of soybean MON 87708 × MON 89788 seeds which could be accidentally released into the environment: e.g. early and final stand count, seedling vigour, 100 seed weight, plant height and yield. As described in Section 4.2.1.3, soybean MON 87708 × MON 89788 treated and not treated with dicamba-based and glyphosate-based herbicides had lower 100 seed weight than its non-GM comparator. Moreover, the equivalence test for the 100 seed weight endpoint indicates that equivalence with non-GM reference varieties is more likely than not. For this reason and because this endpoint is relevant for the assessment of possible changes in persistence and invasiveness of the GM soybean, the significant differences observed in 100 seed weight are further assessed below. For 100 seed weight for which a significant genotype × environment interaction had been detected, no consistent relationship to descriptive site characteristics was observed (see Section 4.2.1.3).

During the ERA of the single transformation event MON 87708 (EFSA GMO Panel, 2013), the EFSA GMO Panel also observed that "*dicamba-treated and non-treated soybean MON 87708 had lower 100 seed weight than its conventional counterpart and the non-GM reference varieties planted in these field trials.*" The observed differences in 100 seed weight might therefore be an indication of

[33] Dossier: Part II—Section E3.1 and Appendix D.
[34] http://epp.eurostat.ec.europa.eu/portal/page/portal/agriculture/data/database

unintended effects due to the genetic modification. Differences in seed lots quality could also explain such observations; however, the information included in the dossier does not indicate such an effect.

Specific data on pollen viability, seed germination and dormancy for soybean MON 87708 × MON 89788 were not provided by the applicant. Therefore, the EFSA GMO Panel asked the applicant to clarify the origin and production conditions of the test materials used, and to justify that the best materials allowed a proper comparative assessment. The applicant did not provide additional data but did provide a rationale[35] for relying on seed germination data for the two single soybean events[36] and data on the early stand count for soybean MON 87708 × MON 89788 compared with its non-GM comparator. The applicant concluded that "*the use of MON 87708 × MON 89788 and control materials that had similar genetic backgrounds except for the trait of interest, and the seed germination characteristics already provided, demonstrate the suitability of the test and control materials utilized in the comparative assessment*".

The EFSA GMO Panel therefore considered the data provided by the applicant on seed germination and dormancy of the single soybean events MON 89788 and MON 87708, their comparators and non-GM reference varieties, produced under different environmental conditions (see EFSA, 2008; EFSA GMO Panel, 2013). No differences in seed germination of soybean MON 89788 compared with its conventional counterpart were observed under any controlled environmental conditions. For soybean MON 87708, the two differences in seed germination observed under certain controlled environmental conditions (i.e. at constant temperature of approximately 10 °C and at alternating temperatures of approximately 10 °C and 30 °C) fell within the range of commercial reference varieties. The observed differences showed a lower seed germination percentage for soybean MON 87708 than for its non-GM comparator. Moreover, the observed differences were not consistent across sites and did not indicate a consistent plant response associated with the herbicide tolerance trait or any change in fitness.

Considering that available dataset on soybean MON 87708 × MON 89788, and in the light of the scope of application EFSA-GMO-NL-2012-108, the EFSA GMO Panel did not expect changes in the seed germination characteristics of soybean MON 87708 × MON 89788.

Although the differences observed in 100 seed weight might result from the genetic modification, they are unlikely to be biologically relevant in terms of increased weed potential of soybean MON 87708 × MON 89788 in the context of the scope of this application and considering that the other characteristics of soybean MON 87708 × MON 89788 relevant to persistence and invasiveness are not changed.

In addition to the data presented by the applicant, the EFSA GMO Panel is not aware of any scientific report of increased spread and establishment of existing GM soybeans and any change in survival capacity, including overwintering (Dorokhov et al., 2004; Owen 2005; Bagavathiannan and Van Acker, 2008; Lee et al., 2009).

Therefore, the EFSA GMO Panel is of the opinion that the likelihood of unintended environmental effects of the soybean MON 87708 × MON 89788 in Europe will not be different from that of conventional soybean varieties.

4.4.2.2. Potential for gene transfer[37]

A prerequisite for any gene transfer is the availability of pathways for the transfer of genetic material, either through horizontal gene transfer of DNA or through vertical gene flow via seed spillage followed by cross-pollination.

[35] Additional data, 18 February 2014.
[36] Section D.4 of EFSA/GMO/NL/2006/36 and Section D.4 of EFSA/GMO/NL/2011/93.
[37] Dossier: Part II—Sections E3.1, E3.2.

(a) Plant to bacteria gene transfer

The potential for horizontal gene transfer of the recombinant DNA of the single events has already been assessed in previous opinions (EFSA, 2008; EFSA GMO Panel, 2013) and no concern for an unlikely, but theoretically possible, horizontal gene transfer of the recombinant genes to bacteria in the gut or other receiving environments was identified.

Bioinformatic analyses revealed for MON 87708 two sequences with sequence identity of considerable length with bacterial genes in databases; the *dmo* coding sequence of DMO from *S. maltophilia*, with a total length of 1 022 bp and 99.9 % identity, and the left border sequence (246 bp) with 100 % identity to the *A. tumefaciens* Ti plasmid. Considering that these occur is in different bacterial species, there is no indication for facilitated horizontal gene transfer from plants to bacteria by double homologous recombination. Substitutive homologous recombination of the *dmo* gene and the left border sequence with natural variants of these sequences as they occur in *S. maltophilia*, *A. tumefaciens* or other environmental bacteria could be facilitated, but such events would not confer any novel traits on the recipients.

For the bioinformatic analyses of MON 89788, no sequence identity with bacterial DNA, including the CP4 *epsps* gene, which was plant codon optimised, were identified. Thus, there is no indication of facilitated gene transfer of recombinant DNA of MON 89788 to bacteria.

Synergistic effects of the recombinant genes in increasing the likelihood for horizontal gene transfer, for instance combinations of recombinogenic sequences, were not identified. Since soybean MON 87708 × MON 89788 is produced by conventional crossing, close linkage of the different events is extremely unlikely.

Therefore, in line with its previous assessments of MON 89788 and MON 87708, and considering the new, additional bioinformatic analyses provided by the applicant, the EFSA GMO Panel concludes that, considering the scope of application EFSA-GMO-NL-2012-108, the unlikely but theoretically possible transfer of the recombinant genes from soybean MON 87708 × MON 89788 to environmental bacteria does not raise a safety concern.

(b) Plant-to-plant gene transfer

Considering the scope of application EFSA-GMO-NL-2012-108 and the physical characteristics of soybean seeds, a possible pathway of gene dispersal is from seed spillage and pollen of occasional feral GM soybean plants originating from accidental seed spillage during transportation and/or processing.

The genus *Glycine* is divided into two distinct subgenera: *Glycine* and *Soja*. Soybean is in the subgenus *Soja*. The subgenus *Glycine* contains 16 perennial wild species, while the cultivated soybean, *G. max*, and its wild and semi-wild annual relatives, *Glycine soja* and *Glycine gracilis*, are classified in the subgenus *Soja* (OECD, 2000). Owing to the low level of genomic similarity among species of the genus *Glycine*, *G. max* can cross only with other members of *Glycine* subgenus *Soja* (Hymowitz et al., 1998; Lu, 2005). Hence, the three species of the subgenus *Soja* are capable of cross-pollination and the hybrid seed that is produced can germinate normally and produce plants with fertile pollen and seed (Abe et al., 1999; Nakayama and Yamaguchi, 2002). However, since *G. soja* and *G. gracilis* are indigenous to China, Taiwan, Korea, Japan, the far east region of Russia, Australia, the Philippines and the South Pacific, and since they have not been reported in other parts of the world where the cultivated soybean is grown (Dorokhov et al., 2004; Lu, 2005), the plant-to-plant gene transfer from soybean is restricted to cultivated areas and the occasional soybean plants resulting from seed spillage in the EU.

Soybean is an annual almost completely self-pollinating crop in the field, and its percentage of cross-pollination is usually lower than 1 % (Weber and Hanson, 1961; Caviness, 1966; Ray et al., 2003; Lu,

2005; Yoshimura et al., 2006; Abud et al., 2007). Soybean pollen dispersal is limited because the anthers mature in the bud and directly pollinate the stigma of the same flower (OECD, 2000).

However, cross-pollination rates as high as 6.3 % have been reported for closely spaced plants (Ray et al., 2003), suggesting the potential for some within-crop gene flow in soybean. These results indicate that natural cross-pollination rates can fluctuate significantly among different soybean varieties under particular environmental conditions, such as favourable climate for pollination and an abundance of pollinators (Gumisiriza and Rubaihayo, 1978; Kikuchi et al., 1993; Ahrent and Caviness, 1994; Ray et al., 2003; Lu, 2005).

Plant-to-plant gene flow could therefore occur under the following scenario: imports of soybean MON 87708 × MON 89788 seeds (although most MON 89788 × MON 87708 seeds will be processed in countries of production), processing outside importing ports, transport in regions of soybean production in Europe, spillage of GM seeds during transport, germination and development of spilled seeds within soybean fields or in the very close vicinity of cultivated soybean fields, overlap of flowering periods and particular environmental conditions favouring cross-pollination. The overall likelihood of cross-pollination between GM soybean plants and cultivated soybean is therefore extremely low. Except in seed production areas, such plants will not persist over time. Dispersal of soybean seeds by animals is not expected because of the characteristics of the seed, but accidental release into the environment of seeds may occur during transport and processing for food, feed and industrial uses. However, cultivated soybean seeds rarely display any dormancy characteristics and only under certain environmental conditions grow as volunteers in the year following cultivation (OECD, 2000). Even in soybean fields, seeds usually do not survive during the winter because of predation, rotting or germination resulting in death, or as a result of management practices prior to planting the subsequent crop (Owen, 2005).

The EFSA GMO Panel takes into account that this application does not include cultivation of the soybean within the EU so that the likelihood of cross-pollination between cultivated soybean and the occasional soybean plants resulting from seed spillage is considered extremely low. However, in countries cultivating this GM soybean and producing seed for export, there is a potential for admixture in seed production and thus the introduction of GM seeds through this route. Hence, it is important that appropriate management systems are in place to restrict seeds of soybean MON 87708 × MON 89788 entering cultivation as this would require specific approval under Directive 2001/18/EC or Regulation (EC) No 1829/2003.

In conclusion, as soybean MON 87708 × MON 89788 has no altered survival, multiplication or dissemination characteristics, the EFSA GMO Panel is of the opinion that the likelihood of unintended environmental effects as a consequence of spread of genes from this GM soybean in Europe will not differ from that of conventional soybean varieties.

4.4.2.3. Potential interactions of the GM plant with target organisms[38]

Considering the scope of application EFSA-GMO-NL-2012-108, and in the absence of target organisms, potential interactions of the GM plant with target organisms were not considered a relevant issue by the EFSA GMO Panel.

4.4.2.4. Potential interactions of the GM plant with non-target organisms[39]

Considering the scope of application EFSA-GMO-NL-2012-108, and the low level of exposure to the environment, potential interactions of the GM plant with non-target organisms were not considered a relevant issue by the EFSA GMO Panel.

[38] Dossier: Part II—Section E3.3.
[39] Dossier: Part II—Section E3.4.

4.4.2.5. Potential interactions with the abiotic environment and biogeochemical cycles[40]

Considering the scope of application EFSA-GMO-NL-2012-108, and the low level of exposure to the environment, potential interactions with the abiotic environment and biogeochemical cycles were not considered a relevant issue by the EFSA GMO Panel.

4.4.3. Post-market environmental monitoring[41]

The objectives of a post-market environmental monitoring plan according to Annex VII of Directive 2001/18/EC are (1) to confirm that any assumption regarding the occurrence and impact of potential adverse effects of the GMO, or its use, in the ERA are correct and (2) to identify the occurrence of adverse effects of the GMO, or its use, on human health or the environment that were not anticipated in the ERA.

Monitoring is related to risk management, and thus a final adoption of the post-market environmental monitoring plan falls outside the mandate of EFSA. However, the EFSA GMO Panel gives its opinion on the scientific content of the post-market environmental monitoring plan provided by the applicant (EFSA, 2006; EFSA GMO Panel, 2011b). The potential exposure to the environment of soybean MON 87708 × MON 89788 would be through faecal material from animals fed the GM soybean or through accidental release into the environment of GM soybean seeds during transportation and processing. The EFSA GMO Panel is aware that, owing to the physical characteristics of soybean seeds and methods of transportation, accidental spillage cannot be excluded. Hence, it is important that appropriate management systems are in place to restrict seeds of soybean MON 89788 × MON 87708 entering cultivation as this would require specific approval under Directive 2001/18/EC or Regulation (EC) No 1829/2003.

The post-market environmental monitoring plan proposed by the applicant includes (1) the description of an approach involving operators (federations involved in soybean import and processing) reporting to the applicant via a centralised system any observed adverse effect(s) of GMOs on human health and the environment; (2) a coordinating system established by EuropaBio for the collection of the information recorded by the various operators; and (3) the use of networks of existing surveillance systems (Lecoq et al. 2007; Windels et al., 2008). The applicant proposes to submit a post-market environmental monitoring report on an annual basis and a final report at the end of the consent.

The EFSA GMO Panel is of the opinion that the post-market environmental monitoring plan proposed by the applicant is in line with the scope of application EFSA-GMO-NL-2012-108 as the ERA did not cover cultivation and identified no potential adverse environmental effects. No case-specific monitoring is necessary. The EFSA GMO Panel agrees with the reporting intervals proposed by the applicant in its post-market environmental monitoring plan.

4.4.4. Conclusion

Considering the scope of application EFSA-GMO-NL-2012-108, there are no indications of an increased likelihood of establishment and spread of feral soybean MON 87708 × MON 89788 plants in the case of accidental release into the environment of viable GM soybean seeds. Potential interactions of soybean MON 87708 × MON 89788 with the biotic and abiotic environment were not considered a relevant issue by the EFSA GMO Panel. The unlikely but theoretically possible transfer of the recombinant genes from soybean MON 87708 × MON 89788 to environmental bacteria does not give rise to a safety concern owing to the lack of a selective advantage in the context of the scope of this application. The post-market environmental monitoring plan provided by the applicant and the reporting intervals are in line with the scope of application EFSA-GMO-NL-2012-108.

[40] Dossier: Part II—Section E3.6.
[41] Dossier: Part II—Section E4.

OVERALL CONCLUSIONS AND RECOMMENDATIONS

No new data on the single soybean events MON 89788 and MON 87708 that would lead to a modification of the original conclusions on their safety were identified.

The combination of soybean single events MON 89788 and MON 87708 in the two-event stack soybean MON 87708 × MON 89788 did not give rise to issues—relating to molecular, agronomic, phenotypic or compositional characteristics—regarding food and feed safety. The EFSA GMO Panel considers that there is no reason to expect interactions that could impact on the food and feed safety and nutritional properties. The compositional data indicate that soybean MON 87708 × MON 89788 would be expected to deliver the same nutrition as its non-GM comparator.

Considering the scope of application EFSA-GMO-NL-2012-108, there are no indications of an increased likelihood of establishment and spread of feral soybean MON 87708 × MON 89788 plants in the case of accidental release into the environment of viable GM soybean seeds. Potential interactions of soybean MON 87708 × MON 89788 with the biotic and abiotic environment were not considered a relevant issue by the EFSA GMO Panel. The unlikely but theoretically possible transfer of the recombinant genes from soybean MON 87708 × MON 89788 to environmental bacteria does not give rise to a safety concern owing to the lack of a selective advantage in the context of the scope of this application. The post-market environmental monitoring plan provided by the applicant and the reporting intervals are in line with the scope of application EFSA-GMO-NL-2012-108.

In conclusion, the EFSA GMO Panel considers that the information available for soybean MON 87708 × MON 89788 addresses the scientific comments raised by Member States and that the soybean MON 87708 × MON 89788, as described in this application, is as safe as its non-GM comparator and non-GM soybean reference varieties with respect to potential effects on human and animal health and the environment in the context of its scope.

CORRESPONDENCE

1. Letter from Competent Authority of the Netherlands received on 29 March 2012 concerning a request for authorisation for the placing on the market of soybean MON 87708 × MON 89788 (application EFSA-GMO-NL-2012-108) submitted in accordance with Regulation (EC) No 1829/2003 by Monsanto Europe S.A./N.V.

2. Acknowledgement letter dated 12 April 2012 from EFSA to the Competent Authority of the Netherlands.

3. Letter from EFSA to applicant dated 24 May 2012 requesting additional information under completeness check.

4. Letter from applicant to EFSA received on 29 June 2012 providing additional information under completeness check.

5. Email from APDESK to applicant sent on 19 July 2012 providing clarifications.

6. Email from applicant to APDESK received on 19 July 2012 providing clarifications.

7. Letter from EFSA to applicant dated 20 July 2012 delivering the 'Statement of Validity' of application EFSA-GMO-NL-2012-108 (soybean MON 87708 × MON 89788) submitted by Monsanto Europe S.A./N.V under Regulation (EC) No 1829/2003.

8. Letter from EFSA to applicant dated 24 July 2012 stopping the clock due to single event.

9. Letter from EFSA to applicant dated 13 August 2013 requesting additional information and maintaining the clock stopped.

10. Letter from applicant to EFSA received on 2 September 2012 providing additional information upon the request dated 13 August 2012.

11. Letter from applicant to EFSA received on 2 September 2013 providing additional information spontaneously.

12. Letter EFSA to applicant dated 23 September 2013 re-starting the clock due to single event but maintaining the clock stopped pending EFSA's questions.

13. Letter from EFSA to applicant dated 6 December 2013 requesting additional information and maintaining the clock stopped.

14. Letter from applicant to EFSA received on 20 December 2013 providing additional information.

15. Letter from EFSA to applicant dated 10 February 2014 requesting additional information and maintaining the clock stopped.

16. Letter from applicant to EFSA received on 19 February 2014 providing additional information.

17. Letter from applicant to EFSA received on 28 March 2014 providing additional information spontaneously.

18. Letter from EFSA to applicant dated 5 June 2014 requesting additional information and maintaining the clock stopped.

19. Letter from applicant to EFSA received on 20 June 2014 providing additional information.

20. Letter from applicant to EFSA received on 13 October 2014 asking clarifications on the progress of the application.

21. Letter from EFSA to applicant dated 15 October 2014 re-starting the clock.

22. Letter from EFSA to applicant dated 7 November 2014 providing clarifications on the progress of the application.

23. Letter from applicant to EFSA received on 12 December 2014 providing additional information spontaneously.

24. Letter from EFSA to applicant dated 9 January 2015 requesting additional information and stopping the clock.

25. Letter from applicant to EFSA received on 27 January 2015 providing additional information.

26. Letter from applicant to EFSA received on 27 January 2015 asking clarifications on the progress of the application.

27. Letter from applicant to EFSA received on 3 March 2015 providing additional information spontaneously.

28. Letter from EFSA to applicant dated 25 March 2014 re-starting the clock.

29. Letter from EFSA to applicant dated 16 April 2015 providing clarifications on the progress of the application.

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