TONIO BORG

MEMBER OF THE EUROPEAN COMMISSION

Brussels, 08. 01. 2013

Dear Mr Then,

Thank you for your letter dated 6 August 2012 whereby you requested, on behalf of your organisation, the Commission to review its Decision 2012/347/EU of 28 June 2012, authorising the placing on the market of genetically modified soybean MON 87701 x MON 89788 under Regulation (EC) No 1829/2003 of the European Parliament and of the Council on genetically modified food and feed[1].

More specifically, you ask for *"the re-examination of the risk analysis by EFSA and the Commission and for the immediate withdrawal of the market authorisation of the genetically modified soybean MON 87701 X MON 89788"*[2].

The Commission considers that your organisation complies with the criteria set in Article 11 of Regulation (EC) 1367/2006 and is therefore entitled to make a request for internal review. Your request has been lodged on the basis of Title IV of Regulation (EC) No 1367/2006 of the European Parliament and of the Council of 6 September 2006 on the application of the provisions of the Aarhus Convention on Access to Information, Public Participation in Decision-making and Access to Justice in Environmental Matters to Community institutions and bodies[3].

You argue that the Commission Decision is unlawful because of the following reasons:

(1) Failures in EFSA's assumption that the soy is "substantially equivalent";
(2) Failure to consider synergistic/combinatorial effects;
(3) Insufficient assessment of immunological risks;
(4) Failure to request monitoring of health effects.

Against this background, you claim that both EFSA opinion and the Commission Decision for authorisation do not meet the requirements of Directive 2001/18/EC of the European Parliament and of the Council and Regulation 1829/2003, and Regulation (EC) 178/2002.

The Commission has consulted EFSA on the scientific aspects of the technical dossier on which you base your request for internal review. EFSA considers that there are no scientific arguments that would invalidate the conclusions of the GMO Panel on soybean MON 87701 X MON 89788 published in February 2012.

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1 OJ L 268, 18.10.2003, p. 1.
2 Last paragraph of page 4 of the l request for internal review.
3 OJ L 264, 25.9.2006, p. 13.

We can accept none of your legal and scientific allegations invoked to substantiate your request for internal review of the Commission Decision 2012/347/EU of 28 June 2012 authorising the placing on the market of genetically modified soybean MON 87701 x MON 89788 under Regulation (EC) No 1829/2003 of the European Parliament and of the Council on genetically modified food and feed.

The grounds of your request for internal review should be refuted as they fail to prove that the Commission Decision 2012/347/EU is in breach of Regulation (EC) No 1829/2003. The Commission considers that EFSA has duly performed its task of risk assessor in the sense of Articles 22 (3) and 23 of Regulation (EC) 178/2002, allowing the Commission to conclude on the safety of soybean MON 87701 x MON 89788. Both EFSA and the Commission have taken into account all relevant data.

EFSA has indeed appropriately reviewed the studies and the information submitted by the applicant, in line with its Guidance document of the Scientific Panel on Genetically Modified Organisms for the risk assessment of genetically modified plants and derived food and feed (EFSA 2006).

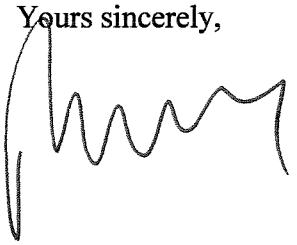
The Commission notes that in this context you have never contested the appropriateness of EFSA's Guidance documents to establish the safety of the products covered by Regulation (EC) 1829/2003, in accordance with the conditions foreseen by this Regulation. Indeeed, in most cases, you consider that EFSA has failed to demonstrate that the applicant has adequately fulfilled the requirements reflected in its Guidance documents.

To conclude, the Commission considers that its Decision 2012/347/EU is in compliance with Regulation (EC) 1829/2003, which is based on Article 168 of the Treaty on the Functioning of the European Union stating that "A high level of human health protection shall be ensured in the definition and implementation of all Union policies and activities", and on the precautionary principle.

Please find in annexes the Commission's reply to your claims.

Should you not agree with the present reply, you may bring the matter before the Ombudsman or before the Court of First Instance if you have a complaint which falls within the conditions laid down in Articles 228 and 263 respectively of the Treaty on the Functioning of the European Union.

Yours sincerely,



ANNEX I - GENERAL LEGAL FRAMEWORK

Section 1 of your request for internal review is dedicated to the "general legal framework" that aims at substantiating your claim that *"EFSA's opinion and the decision of the Commission do not fulfil the requirements of current EU Regulations"*[1].

Before entering into the substance of the "grounds for complaint", the Commission would like to comment on the interpretation provided on the GMO legal framework applicable to the placing on the market of food and feed containing, consisting of, or produced from genetically modified soybean MON 87701 X MON 89788.

Firstly, point (a) of section 1 refers to provisions of Directive 2001/18/EC which, in your opinion, would be applicable to the placing on the market of food and feed containing, consisting of, or produced from genetically modified soybean MON 87701 X MON 89788. In particular, you refer to Article 13 (which refers to the "notification procedure" under Part C of the Directive) and to Article 19 ("consent") of this Directive as the legal provisions to be complied with by the authorisation of the products covered by the Commission Decision 2012/347/EU.

The Commission would like to recall that the Commission Decision 2012/347/EU is based on Regulation (EC) 1829/2003 on genetically modified food and feed, and not on Directive 2001/18/EC.

In this context, Article 12(1) and (3) of Directive 2001/18/EC states that:

> *1. "Article 13 to 24 shall not apply to any GMO as or in products as far as they are authorised by Community legislation which provides for a specific environmental risk assessment carried out in accordance with the principles set out in Annex II and on the basis of information specified in Annex III without prejudice to additional requirements (...) at least equivalent to those laid down in this Directive.*
>
> *(...)*
>
> *3. Procedures ensuring that the risk assessment, requirements regarding risk management, labelling, monitoring as appropriate, information to the public and safeguard clause are equivalent to those laid down in this Directive shall be introduced, in a Regulation of the European Parliament and of the Council. Future sectorial legislation based on the provisions of that Regulation shall make a reference to this Directive (...)'.*

As recalled by the European Court of Justice in its judgment in joined cases C-58/10 to C-68/10[2], Regulation (EC) No 1829/2003 constitutes an implementation of Article 12(3) of Directive 2001/18/EC (see point 47 of the judgment).

In line with Article 12(1) of Directive 2001/18/EC, Articles 5(5) and 17(5) of Regulation (EC) No 1829/2003 are applicable to GMOs or food/feed containing or consisting of GMOs, explicitly refer to the Annexes of Directive 2001/18/EC. By application of Article 12(1) of

1 Page 3 of the request for internal review.
2 Judgement of the 8th September 2011 Monsanto SAS a.o, joined cases C-58/10 to C-68-10.

Directive 2001/18/EC, Regulation (EC) 1829/2002 foresees that *"in such case, Articles 13 to 24 of Directive 2001/18/EC shall not apply"* (Articles 5(5) and 17 (5)).

The non-application of Article 13 to 24 of Directive 2001/18/EC (Part C of this Directive) is also indirectly acknowledged by Articles 7(8) and 19(8) of Regulation (EC) 1829/2003, which provide the following:

> *"Reference made in Part A and D of Directive 2001/18/EC to GMOs authorised under Part C shall be considered as applying equally to GMOs authorised under this Regulation".*

It follows that Articles 13 and 19 of Directive 2001/18/EC mentioned in your request are not applicable to GM food and feed authorised under Regulation (EC) No 1829/2003. All references to these Articles of the Directive should therefore be considered as invalid.

Secondly, you claim that the environmental risk assessment (ERA) performed in the framework of the authorisation of MON87701xMON 89788 soybean and the environmental post-monitoring plan are not appropriate regarding the effects on human and animal health.

More specifically, you state that:

> *"the environmental risk assessment has to include all effects which the placing of a GMO on the market may have on human health, including any possible cumulative effects"* of GM plants on which herbicides have been sprayed and that *"this also includes the potential effects of the use of herbicides or pesticides on the GMO plant or product"*[3].

You also claim that:

> *"the Commission has to determine, whether the monitoring plan has to include the control of potential adverse effects of the genetically modified plant during the use and consumption stage. Even when EFSA, in any of its opinion, does not comment on the need for such a control, the Commission was obliged to decide on that issue"*[4].

In answer to these allegations, the Commission would like to make the following observations:

Risk assessment

- As mentioned above, Articles 13 to 24 of Directive 2001/18/EC do not apply to genetically modified food and feed, which must be authorised under the conditions and procedures of Regulation (EC) No 1829/2003.

Articles 5 and 6 and 16 and 17 of the Regulation require a thorough risk assessment procedure for food and feed containing or consisting of GMOs, and food and feed produced from or containing ingredients produced from GMOs. This includes data on toxicity and allergenicity effects.

3 Page 10 of the request for internal review. Underlined by us.
4 Page 15 of the request for internal review. Underlined by us.

Additional data on the environmental risk assessment are requested for food and feed containing or consisting of GMOs (which all consist or contain "live" GMOs") in Articles 5 (5) (a) and 17 (5) (a) of Regulation (EC) 1829/2003.

These articles refer to Annexes II, III and IV of Directive 2001/18/EC, with the objective to ensure that the health effects on persons handling the GMOs (workers), in contact with or in the vicinity of GMOs (e.g. allergicity issues) are properly assessed.

This is explicitly mentioned in Point D of Annex II (*"Conclusions on the potential environmental impact from the release or the placing on the market of GMOs"),* applicable both for GM higher plants or GMOs other than higher plants, which reads:

> *"possible immediate and/or delayed effects on human health resulting from potential direct and indirect interactions of the GMOs and persons working with, coming into contact with or in the vicinity of the GMO release(s)"*[5].

This is to ensure that an assessment of the environmental effects of the placing on the market of these GMOs is performed based on the same criteria than any other GMOs falling under Directive 2001/18/EC. This environmental risk assessment should not be confused with the safety assessment which is also carried out in accordance with Articles 5 to 7 and 16 to 19 of Regulation (EC) No 1829/2003, as it is clearly indicated in its recital 33, as follows:

> *"Where an application concerns products containing or consisting of a GMO, the applicant should have the choice of either supplying an authorisation for the deliberate release into the environment already obtained under Part C of Directive 2001/18/EC (...), or of applying for the environmental risk assessment to be carried out at the same time as the safety assessment under this Regulation. In the latter case, it is necessary for the evaluation of the environmental risk to comply with the requirements referred to in Directive 2001/18/EC (...).*[6]*"*

In view of the above, the Commission cannot agree with your interpretation that the obligation to carry out a risk assessment of the safety of consumption of GMOs by humans would come from Annex II of Directive 2001/18/EC.

- Along the same lines, the Commission cannot agree with your allegations that Annex II of Directive 2001/18/EC requires to assess the effects on health of the consumption by humans of GMOs combined with the applied herbicide. The assessment of the effects on human health of plant protection products, is not regulated by the GMO legislation, but under two specific EU legislations:

  - Regulation (EC) No 1107/2009 concerning the placing on the market of plant protection products and repealing Council Directives 79/117/EEC and 91/414/EC;

  - Regulation (EC) No 396/2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC.

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5 Point 6 of Points D.1 and D.2 of Annex II of Directive 2001/18/EC.
6 Underlined by us.

As its title indicates, Regulation (EC) No 1107/2009 concerns the placing on the EU market of plant protection products. Given that the products covered under Decision 2012/347/EU do not correspond to the products described in Article 2 "scope" of Regulation (EC) No 1107/2009, this Regulation is not applicable to the products covered under Decision 2012/347/EU.

However, Regulation (EC) No 396/2005 is fully applicable to the control of pesticides residues on food and feed imported from third country, including food and feed derived from GM plants. This Regulation provides for the risk assessment of pesticide residues in food and feed and sets maximum residue levels (MRL) applicable to all food and feed placed on the market, including GMOs. This MRL takes into account cumulative effects of regular consumption of food containing such residues.

The Commission concludes that there is no legal vacuum as regards the assessment of the effects on health of pesticide residues and rejects your allegation on this regard.

Monitoring obligations

- As regards the monitoring obligations to be imposed on GM food and feed authorised under Regulation (EC) No 1829/2003, you consider that the monitoring plan of Annex VII of Directive 2001/18/EC (to which Regulation (EC) No 1829/2003 refers in the case of GMOs or food/feed containing or consisting of GMOs) should include the potential effects of the GMO on human health during the use and consumption stages including the cumulative effects of herbicide residues and genetically modified plants[7]. You therefore consider that the authorisation should be amended in order to provide for such a surveillance[8].

- As a supplementary evidence, the Commission observes that Articles 5(5)(b) and 17(5)(b) of Regulation (EC) No 1829/2003 only refer to "environmental effects" which includes the monitoring of the effects on the health workers which could be exposed to potentially harmful effects during the transport, or handling of the product (taking into account the fact that cultivation is excluded from the scope of the Decision) or to other persons which have been in contact or in the vicinity of GMOs.

The effect of the consumption by humans of the GMO is not covered by the monitoring plan set out in accordance with Annex VII of the Directive but by Article 5(3)(k) of Regulation (EC) 1829/2003 which foresees that the application for authorisation shall be accompanied by, *"where appropriate, a proposal for post-market monitoring regarding the use of the food for human consumption"*[9].

The words "where appropriate" in this Article 5(3)(k) are mirrored by the words "where applicable" in Article 6(5)(e). This means that the Regulation foresees that a post-market monitoring regarding the use of the food for human consumption should be envisaged, only where necessary, on a case by case basis.

- In this context, the Commission considers that the monitoring obligations provided in the monitoring plan for soybean MON 87701 x MON 89788[10] required by Article 4 of

[7] Pages 13 and 53 of the request for internal review.
8 Page 53 of the request for internal review.
[9] Underlined by us.
10 Available at

Decision 2012/347/EU complies with Regulation (EC) 1829/2003 in light of the nature of the product and of the uses which are covered in the application for authorisation, and taking into account the outcome of the EFSA opinion following which no monitoring for the use of GM food/feed was deemed appropriate, and in so far that:

- It has the objective to confirm that any assumption regarding the occurrence and impact of potential adverse effects of the GMO or it use in the ERA are correct, and identify the occurrence of adverse effects of the GMO or its use on human health or the environment which were not anticipated in the ERA (point 2.1. of the monitoring plan);

- It is adapted to the uses which are authorised (not for cultivation) and proportionate to the extent of imports of food and feed containing, consisting of, or produced from genetically modified soybean MON 87701 X MON 89788 and to the use by Member States;

- It is to be undertaken for the duration of the authorisation (point 2.3. of the monitoring plan);

- As the authorisation holder cannot control the entire food and feed chains, it involves operators handling and using food and feed containing, consisting of, or produced from genetically modified soybean MON 87701 X MON 8978. The most important operators in this area are thus associated to the monitoring obligations. As indicated in point 2.5 of the monitoring plan, *"they are exposed to the import viable MON 87701 X MON 89788 soybean and are therefore the best placed to observe and report any unanticipated adverse effect in the framework of their routine surveillance of the commodities they handle and use. The routine surveillance is based on the HACCP principles"*;

- It obliges the authorisation holder to actively screen reports and peer reviewed publications.

In this context, the Commission rejects the interpretation on page 16 of your request implying that the Commission would not exercise its powers of risk manager by blindly relying to the EFSA's opinion. As you rightly indicate, the Commission is not obliged to follow an EFSA opinion. However, Regulation (EC) 1829/2003 foresees that in case it decides to disregard it, it should provide an explanation of the differences (Article 7(1) and 19(1)). In the present case, the Commission did not deem justified to propose a draft Decision for authorisation diverging from the EFSA opinion. It considers that EFSA has carried out the scientific assessment appropriately, in line with its Guidance of the Scientific Panel on the Genetically Modified Organisms for the risk assessment of genetically modified plants and derived food and feed (EFSA 2006).

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http://ec.europa.eu/food/dyna/gm_register/Monitoring%20plan%20for%20soybean%20MON87701xMON89788.pdf

ANNEX II - GROUNDS OF THE COMPLAINT

A. Failures in EFSA's assumption that the soy is "substantially equivalent"

A1. Weakness in assumptions concerning parental plants

You question EFSA's conclusion about the equivalence of the parental plants, MON87701 and MON89788, to their conventional comparators.

According to you, in comparison with their conventional counterparts, many significant differences in the compositional analysis and significant and unintended effects were found but these were not investigated further. Instead, references were made to the ILSI database, which you consider to be unreliable.

Both applications submitted for the parental plants, MON 87701 and MON 89788, included field trials in which the GM lines were tested together with their appropriate isogenic comparator and a set of non-GM reference soybean lines used to define the range of natural variation to which consumers would be normally exposed. In both cases the design of the field trials and the parameters analysed were in line with the requirement laid down in the EFSA Guidance Document (EFSA, 2006) and the OECD guidelines (OECD, 2001).

Contrary to your statement, EFSA has not identified scientific uncertainties. Rather, it concluded that no biologically relevant differences were identified when comparing the two GM lines with their respective isogenic comparators taking into account the natural variation estimated from non-GM soybean reference varieties grown in the same environmental conditions (i.e. same field trial). One parameter for MON 87701, namely the vitamin E content, was increased compared to its isogenic comparator, but the value observed was still within the range of the non-GM soybean reference varieties grown in the trial.

The Commission considers that EFSA provided a conclusive scientific rationale to consider that both MON 87701 and MON 89788 are as safe as their respective comparator in the context of their intended uses.

Therefore, the Commission cannot accept your claims in this regard.

A2. Missing comparators

You claim that, since there are justifiably severe doubts in the substantial equivalence of the parental plants, using only one conventional comparator in the test of difference of the stacked soybean is insufficient. In your opinion, EFSA's assumption of equivalence of the stacked soy is founded on a flawed assumption of equivalence of the parental plants and is not based on sufficient and reliable data from the appropriate comparators.

The comparator used in the field trials presented in the application for soybean MON 87701 x MON 89788 complies with the requirements laid down in the EFSA Guidance Document (EFSA, 2006). In fact, the non-GM comparator used in the field trial was the Asgrow variety A5547, which was the soybean variety originally transformed to produce soybean MON 87701. Therefore, the Asgrow variety A5547 can be considered an appropriate non-GM

comparator. Twenty non-GM commercial soybean varieties were also included in the study to provide an estimate of the range of natural variation.

EFSA's assessment of MON 89788 x MON 87701 adopted on 26/01/2012 (EFSA 2012a) was built on the assessment of both single events already performed by EFSA (MON 89788, opinion published on 02/07/2008 and MON 87701, opinion published on 06/07/2011), secondly by addressing that "the combination of events is stable and that no interactions between the stacked events".

The Guidance Document on stacked events (EFSA 2007) requires the parental lines in the field and do not require the completion of all the single events (in this case the parental lines). Since, in this case, both parental lines had been previously risk assessed, the inclusion of the conventional counterpart without the parental was considered sufficient. It is fully in line with the spirit of both the 2007 Guidance Document (parental must be risk assessed) and the EFSA Guidance document (EFSA 2011b) (singles are a pre-requisite).

Therefore, the Commission cannot accept your claims in this regard.

A3. Wrong references

You claim that instead of using appropriate comparator lines, many other soybean varieties were grown in parallel as reference lines, and that the ILSI data base was used as a reference for historical data. According to you, a large number of statistically significant differences were not sufficiently assessed, and EFSA's assessment of equivalence of the stacked soybean is not based on sufficient and reliable data.

As highlighted under A2 above, the Commission considers that the appropriate comparator has been used. The comparative approach followed is clearly defined in EFSA's guidance document (EFSA, 2006) and is in line with internationally agreed standards for risk assessment. The use of non-GM commercial reference varieties is a fundamental part of this comparative approach and is used to estimate under the same environmental conditions the range of natural variation to which consumers would be exposed by consuming a specific crop. Every statistically significant difference identified when comparing the GM plant with its comparator is then evaluated against the values derived from the set of non-GM commercial reference varieties planted in the same field trial to assess its biological relevance.

In the case of soybean MON 87701 x MON 89788, the only statistically significant differences consistently found between this GM crop and its comparator were changes in the level of some fatty acids and increased levels of daidzein and genistein. These differences fell within the range estimated from the non-GM commercial soybean varieties grown in the same field trials. This means that if the GM plant displays a statistically significant higher or lower content of a specific compound with respect to its comparator, such content is not higher or lower than that of commercial varieties grown under the same conditions. Therefore, consumers will not be over- or under-exposed to any component when consuming soybean MON 87701 x MON 89788 as compared to the consumption of conventional soybean. Conclusions on safety were based on these data, and not on the ILSI database.

Therefore, your allegation in this respect should be refuted.

A4. Wrong approach for interpretation of phenotypical data

You claim that data stemmed from field trials was not properly assessed by EFSA regarding the agronomic and phenotypical differences and their possible consequences on safety.

EFSA has assessed and interpreted the agronomic and phenotypical data in light of the scope of the application, which does not include cultivation.

The data from the field trials enabled EFSA to conclude that no consistent changes in phenotypic and agronomic characteristics could be observed between soybean MON 87701 x MON 89788 and its comparator, with the exception of a small increase in final stand count, which was not considered biologically relevant.

In conclusion, the agronomic and phenotypic characteristics did not indicate unintended effects. This is also supported by the outcome of the compositional analysis.

The Commission considers that EFSA has carried its assessment in compliance with its guidance document (EFSA, 2006).

Therefore, in view of the scope of the application and EFSA scientific opinion, the Commission cannot accept your claims.

A5. Missing data on impact from relevant geo-climatic regions

You claim that the risk assessment of the soybean did not take account any data from the relevant geo-climatic regions where the soybean will be grown because the field trials were conducted in US and Argentina but not in Brazil.

The field trials for compositional analysis and phenotypic characteristics of soybean MON 87701 x MON 89788 were conducted in locations characterised by geo-climatic conditions which are typical for soybean cultivation areas, in North America and in South America. The scope of the application covers import and processing of the GM plant into the European Union, independently of the country of origin. Therefore, the data are representative and meet the requirements of the EFSA GMO Guidance Document (EFSA, 2006).

Your allegation should therefore be rejected.

A6. and A7. Missing data on the impact of specific abiotic stressors and biotic stressors

You claim that no reliable data was available on the impact of abiotic stressors on the composition. You also stress that, on the basis of the data provided on biotic stressors, no conclusion can be drawn on the potential impact of environmental conditions and their consequences on the vulnerability of the soybean compared to its comparator.

The assessment of soybean MON 87701 x MON 89788 was carried out in the context of its intended uses, namely for import and processing. Considering these intended uses, which exclude cultivation, and the low level of exposure to the environment, potential interactions with the biotic and abiotic environmental cycles were not considered an issue by EFSA.

Nevertheless, the data provided by the applicant within its file on abiotic and biotic stressors has been assessed by EFSA. As regards abiotic stressors, the evaluation of 96 observations

did not reveal differences between the GM plant and its comparator. Therefore, there is no evidence that the possible effects of abiotic stressors will be different between the two plants. The references you provided with regard to abiotic stress on GM plants refers to crops different from soybean MON 87701 x MON 89788, and are thus not relevant in this context.

With respect to the data on biotic stressors, 9 out of 334 comparisons made on the effects of different biotic agents showed statistically significant differences not related to the intended effects of the genetic modification. However, these differences were not consistently observed in the analysis across sites, they were small and did not indicate that soybean MON 87701 x MON 89788 is neither more nor less affected than other commercial soybeans. The references you provided supporting potential effects of biotic stress on GM plants refer to crops different from soybean MON 87701 x MON 89788 and are thus not relevant in this context.

Therefore, your allegation on biotic and abiotic stressors is not pertinent and should therefore be refuted.

A8. Missing scientific standards

You claim that investigations concerning interaction with the environment, phenotypical characteristics and also some investigations concerning the plants composition were subject only to the internal quality standards of Monsanto and do not meet the basic standards of Good Laboratory Practice. You also claim that the Commission does acknowledge the lack of sufficient scientific standards in the presented dossiers.

Good laboratory practice (GLP), is a standard commonly used in the area of chemical toxicity laboratory testing and in the analysis of compounds. It is not a methodology implemented in other areas such as field trials to assess agronomic and phenotypic characteristics. With regard to studies other than toxicological studies, these should be conducted under ISO or GLP standards or other appropriate quality assurance.

All the experimental methodologies presented in the dossier were appropriately described, and the scientific standards were evaluated by EFSA and found appropriate.

Thus, the Commission considers that the requirements of Regulation (EC) No 1829/2003, which does not specifically refer to GLP, are complied with and therefore cannot accept your claims in this regard.

A9. Incomplete data check of Soybean sprayed with glyphosate

You claim that, as EFSA has identified increased levels of daidzein and genistein, known to exhibit hormonal activity and considered as the major phytoestrogens in soy, a more comprehensive risk assessment addressing these findings should have been carried out. You also state that there is no scientific basis for claiming substantial equivalence of the soy treated with glyphosate. According to you, EFSA's opinion is wrong with regards to its overall approach and conclusions.

The increased levels of daidzein and genistein identified when comparing soybean MON 87701 x MON 89788 sprayed with glyphosate with its comparator, were assessed and found to be within the range of natural variation defined by the non-GM commercial soybean varieties used in the study. This means that consumers will not be over-exposed to daidzein or genistein when consuming soybean MON 87701 x MON 89788 as compared to the

consumption of conventional soybean. Therefore, as stated in the scientific opinion (EFSA, 2012a), the differences observed were not considered to pose any safety concern.

The references you provided are not applicable to soybean MON 87701 x MON 89788, as no differences were observed in the compositional analysis between this GM plant, its comparator and different non-GM soybean commercial varieties treated with glyphosate.

The Commission considers that EFSA has undertaken its risk assessment in a comprehensive manner, which allows concluding on the safety of soybean in this regard.

Therefore, your allegation in this respect is not pertinent and should be refuted.

A10. Missing data on processed food and feed

You claim that no data have been provided to assess the equivalence and the safety of processed food and feed products. In your opinion, degradation of naturally occurring antinutrients could be affected by processing such as fermentation and heat treatment, with a particular concern for the production of soybean sprouts where an assessment of the metabolic profiling is needed.

In its scientific opinion, EFSA concludes that since the compositional analysis did not indicate relevant changes between the GM and its comparator (except for the expression the CP4 EPSPS and Cry 1 Ac proteins), the characteristics of soybean MON 87701 x MON 89788 and derived processed products, including soybean sprouts, would not be any different from those of the corresponding products derived from soybean MON 87701, soybean MON 89788 and conventional soybean varieties.

As a consequence of the equivalence of the grain to its conventional counterpart, no data on processed food and feed were considered necessary. Supporting evidences also demonstrated that the two newly expressed proteins are almost undetectable when soybean undergoes heat treatments simulating industrial processing: CP4 EPSPS is reduced by more than 97% when soybean is heated at 190 °C for 30 min, while Cry 1 Ac is reduced by more than 94% when soybean is heated at 190 °C for 15.5 min.

The Commission considers that you fail to provide evidence supporting the need for further data on processed food and feed and therefore rejects this allegation.

A11. Some comments from Member States

You claim that EFSA has not sufficiently taken into account Member States' concerns regarding the compositional equivalence of the soy with its conventional counterparts.

EFSA answers to all comments raised by Member States on the application and explains how they have been addressed. It publishes the comments as part of the overall opinion (annex G of EFSA's overall opinion). This has been the case for soybean MON 87701 x MON 89788.

After the publication, the Commission invited EFSA to present its scientific opinion to the SCFCAH meeting of 12 May 2012 and to address all the comments from Member States. Moreover, EFSA answered in writing to further comments from Member States received after the publication of the scientific opinion.

Therefore, the Commission considers that all comments received from Member States on the soybean MON 87701 x MON 89788 application were taken in account and that answers were provided.

Therefore, your allegation in this respect is not pertinent and should therefore be refuted.

B. Failure to consider synergistic/combinatorial effects

B1. False conclusion stemming from comparative approach

You contest the comparative approach followed by the applicant and agreed by EFSA in the risk assessment of soybean MON 87701xMON89788.

The comparative approach is a well-established and internationally recognised tool for the risk assessment of GMOs. The global community of risk assessors for food safety (OECD, Codex Alimentarius) values the principle of substantial equivalence as a key step in the safety assessment of food and feed derived from biotechnology. It is considered the most appropriate strategy for safety assessment of food and feed derived from GM plants.

The strategy is the following: a thorough comparison between a GMO and a conventional safe counterpart allows the identification of all the differences created by the genetic modification. This is in fact the starting point of the safety assessment. All these differences are then investigated in detail with respect to possible toxicological, allergenicity or nutritional aspects.

The Commission considers that EFSA applies the principle of substantial equivalence in a correct and scientifically solid manner as part of the framework for the risk assessment. In case of soybean MON 87701 x MON 89788, the experimental data provided in the dossier enabled EFSA to conclude that this GM crop as safe as its comparator, in the context of its intended uses.

The Commission considers that you do not confer any elements to prove that the risk assessment was not done in a reliable manner. Your allegation should therefore be rejected.

B2. Insufficient investigation of selection of the newly expressed toxin

You claim that the safety of the toxins belonging to Cry-classification such as Cry1AC was insufficiently addressed.

The Commission considers that you fail to provide any new scientific information that might change EFSA's conclusions on the toxicity assessment of soybean MON 87701 x MON 89788. In addition, you refer to the mode of action and selectivity of Cry proteins in target organisms which is not relevant in the context of food and feed safety assessment.

The Commission therefore considers that the safety of CryIAc has been appropriately addressed also on the basis of experimental evidence, in previous scientific opinions (EFSA, 2010a, 2011a and 2011c).

Your allegation in the respect to the scope of this application is not pertinent and should therefore be refuted.

B3. The Cry toxin lacks authorisation under pesticide regulation

You claim that Cry1Ac toxin in the GM plants was not assessed according to the Council Directive 91/414/EEC concerning the placing on the market of plant protection products.

This allegation is addressed in the comments on the general legal framework[1].

B4. Not assessing the interactivity of the BT toxin with plant constituents

You claim that possible interactions between the newly expressed proteins and enzymes ort other stressors, especially pesticides were not assessed.

As specified in the EFSA's scientific opinion on soybean MON 87701 x MON 89788 (EFSA, 2012a), interactions between the newly expressed proteins were considered. On the basis of the known functions and modes of action of the newly expressed proteins (CrylAc being one of them), EFSA considers it unlikely that interactions raising any safety concern between those proteins would occur. Furthermore, the compositional analyses provided by the applicant included data from plants sprayed with glyphosate and maintenance pesticides, and did not indicate unintended effects. Thus, a potential combined effect of the newly expressed proteins and the herbicide treatment was considered.

The publications you provide are taken out of context and do not provide any new information that might change the conclusions on the toxicity assessment of soybean MON 87701 x MON 89788.

The Commission considers that your allegation shall be refuted.

B5. Insufficient assessment of expression of the Bt toxin

You claim that the assessment of the expression of the newly expressed proteins under different environmental conditions is insufficient and that the stacked soybean has a substantially higher content of the newly expressed proteins than the parental plants.

The methodology applied to study protein expression is described in details in the application, and considered adequate by EFSA. Data were obtained from five field trials, under conditions similar to cultivation for commercial purposes, and covering different environmental conditions.

Considering the scope of the application (excluding cultivation) and the non-toxic nature of the newly expressed proteins to humans and animals, the data provided is considered adequate. Differences between the levels of expression of soybean MON 87701 x MON 89788 and its parental lines were either not consistent throughout the growing season or very small, and in no way show emerging genomic effects in the stack.

Therefore, your allegation in this respect is not pertinent and should be refuted.

[1] Pages 4 and 5.

B6 and B7. Failure to assess risks from residues of spraying and interactivity with residues from spraying

You claim that neither the interactivity of the herbicides with the plant constituents nor the residues from spraying were assessed.

The compositional analyses provided by the applicant included data from GM plants sprayed with glyphosate and maintenance pesticides. Thus, unintended effects on the composition of soybean MON 87701 x MON 89788 resulting from any hypothetical interactivity of the newly expressed proteins with these herbicides have been considered.

Your allegation in this respect is not pertinent and should therefore be refuted.

The other allegations invoked under B6 and B7 are addressed in the comments on the general legal framework[2].

B8. Insufficient assessment of exposure and effects of processing

You claim that, since there are no data on the effects from treatments other than baking that are commonly used to process soybeans, no conclusions can be drawn on the factual exposure of consumers and animals if the soy is used in food and feed.

As no biologically relevant differences were identified in the compositional, agronomic and phenotypic characteristics of soybean MON 87701 x MON 89788 (including the levels of antinutrients) with respect to its comparator (except that it expresses the Cry 1 Ac and CP4 EPSPS proteins), it is not expected that any effects of processing and cooking would be different among these two soybeans. In addition, the data provided by the applicant on the baking treatment of the soybean confirmed this. That is why EFSA has not requested additional data on the effects of processing to the applicant.

The Commission considers that you do not provide any evidence substantiating your allegation and that EFSA has carried out the scientific risk assessment in a comprehensive manner.

In view of the above, the Commission considers that your claim should be rejected.

B9. Further relevant issues: endocrinological studies

You claim that no assessment of the potential impact of Soybean MON87701xMON89788 on the reproductive system was performed despite the detected increase in the levels of daidzein and genistein.

As indicated in point A9 above, no biologically relevant differences were identified in the composition or agronomic and phenotypic characteristics of soybean MON 87701 x MON 89788 with respect to its comparator, except for the newly expressed proteins.

Based on these data and the toxicology, allergenicity and nutritional studies, EFSA considered that soybean MON 87701 x MON 89788 is as safe and as nutritious as its conventional counterpart. Hence, no specific endocrinological studies were considered

[2]Pages 4 and 5.

necessary.

The Commission considers that EFSA has followed the principle described in its guidance document regarding in particular the request for toxicological studies.

The Commission cannot therefore accept your claim.

B10. Further relevant issues: transfer of biologically active compounds

You claim that the possible transfer of plant DNA and RNA to animal tissues was not taken in account during the risk assessment.

The reference you provide on potential regulatory effects of micro RNAs (Zhang et al., 2012), was previously analysed in the context of a mandate posed to EFSA (EFSA 2012c, online). The molecular characterisation working group of the EFSA GMO Panel concluded that this is a first study of its kind and, whilst interesting, needs to be confirmed before its implications can be further evaluated. There is no scientific evidence in such study showing effects that would affect the safety of soybean MON 87701 x MON 89788.

The Commission has based its Decision on the fact that EFSA has demonstrated that the transgenic construct in soybean MON 87701 x MON 89788 has been fully characterised at the molecular level, including sequence information, and did not raise safety concern.

Therefore, your allegation in this respect is not pertinent and should be refuted.

C. Insufficient assessment of immunological risks

C1. Insufficient testing of allergic reactions

You claim that the potential allergenicity of the parental lines has not been sufficiently assessed as too few sera were used. You also consider that none of the studies submitted in the application on allergenicity fulfil the standards of Good Laboratory Practice (GLP).

With regard to the safety of the parental lines MON 87701 and MON 89788, their potential allergenicity was assessed by different methodologies including bioinformatic analyses, one- and two-dimensional gel electrophoresis of proteins from extracts of soybeans, simulated digestion, and IgE assays in human sera. As detailed in EFSA's scientific opinions (EFSA, 2011a, 2008), these data indicated that the overall allergenicity of soybeans MON 89788 and MON 87701 is unlikely to be different from that of their corresponding conventional counterparts and commercial soybean varieties.

For soybean MON 89788 x MON 89788, the applicant supplied additional data (one- and two- dimensional gel electrophoresis of proteins from extracts of soybeans, in which bands of major and also less abundant allergens were identified by mass spectrometry), to check whether the overall allergenicity of the GM crop was altered with respect to its comparator. Based on all the information provided, EFSA considered it unlikely that potential interactions that might change the allergenicity of the crop will occur in soybean MON 87701 x MON 89788.

EFSA issued a scientific opinion in 2010 on the assessment of allergenicity of GM plants and microorganisms and derived food and feed (EFSA, 2010b). You quote an EFSA document which is an "internal document of EFSA" that reflects preliminary discussions in a Working Group meeting that cannot be considered as a final outcome of the deliberations. Based on the discussions of that Working Group on the use of human sera, the following recommendation was included in that scientific opinion, and subsequently in the EFSA Guidance Document (EFSA, 2011b): *"in order to optimise the sensitivity of the test (serum screening), individual sera from well-characterised allergic individuals should be used rather than pooled sera".*

With respect to your claim on GLP, all the experimental methodologies presented in the dossier were appropriately described, and the scientific standards were evaluated by EFSA and found adequate.

The Commission considers that you do not provide any evidence substantiating your allegation and that EFSA has carried out the scientific risk assessment in a comprehensive manner.

Therefore, your allegations in this respect are not pertinent and should therefore be rejected.

C2. Missing investigations on the impact on infants

You claim that no assessment on the specific risks of potential allergenicity for infants was carried out.

Following international guidance (Codex Alimentarius, 2009), allergenicity assessment is based on a weight-of-evidence approach from various methodologies, as no single experimental method yields decisive evidence for allergenicity. Based on all the information available and following a weight-of-evidence approach, EFSA concluded that it is unlikely that the newly expressed proteins in soybean MON 87701 x MON 89788 are allergenic. Therefore, EFSA considered that no further studies were needed. The "internal document" to which you refer to corresponds to the discussions on the preparation of a scientific opinion on the assessment of allergenicity in GM food (EFSA, 2010b) and does not represent the final views of EFSA on that matter. Please see section C1 above for further details.

With respect to the publication you refer to (Finamore et al., 2008), this study, which was previously analysed by the EFSA GMO Panel (EFSA, 2012b), is not relevant as it is not related to soybean MON 87701 x MON 89788 and does not contain any evidence that would invalidate the conclusions on this GM crop.

Therefore, your allegations should be refuted.

C3. False assumption on the digestibility of Cry proteins

You claim that scientific data have shown that Cry1A proteins can show higher stability in monogastric species than predicted by current in vitro digestion experiments.

In line with international guidance (Codex Alimentarius, 2009), EFSA recommends the use of pepsin resistance test to add to the weight-of-evidence approach for the allergenicity assessment of the newly expressed protein. Thus, the outcome of the pepsin resistance test cannot be seen in isolation; only the sum of all evidence determines the outcome of the allergenicity assessment.

EFSA considers that the scientific publications you refer to contain no information that might change the conclusions on the allergenicity assessment of soybean MON 87701 x MON 89788.

The Commission considers that you failed to provide evidence substantiating your claim and that, therefore, your allegation should be rejected.

C4. Missing assessment of further immunological effects

You claim that EFSA should have asked for immunological studies in order to assess if Cry toxin can trigger an immune system reaction.

In line with internationally agreed documents (Codex Alimentarius, 2009), a weight-of-evidence approach is recommended when assessing the potential allergenicity of a newly expressed protein, taking into account all of the information obtained with various test methods, as no single experimental method yields decisive evidence for allergenicity. Based on all the information available and following a weight-of-evidence approach, EFSA concluded that it is unlikely that the newly expressed proteins in soybean MON 87701 x MON 89788 are allergenic. Therefore, no further studies were needed.

The scientific publications you mention do not refer to CrylAc and EFSA considers that they do not contain any new information which might change EFSA's conclusions on the allergenicity assessment of soybean MON 87701 x MON 89788.

The Commission considers that you failed to provide evidence substantiating your claim and that, therefore, your allegation should be rejected.

D. Failure to request monitoring of health effects

You claim that there is no plan for surveillance as required by European regulation that would allow identification of particular health impacts that might be related to the use of these genetically engineered plants in food and feed.

You further suggest that monitoring of health effects should include the risks associated with the spraying of glyphosate formulations and their residues in the plants.

These allegations are addressed in the comments on the general legal framework[3].

[3] Pages 5 and 6.

ANNEX III - REFERENCES

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