Application EFSA-GMO-NL-2011-93 (soybean MON 87708)
Comments and opinions submitted by Member States during the three-months consultation period

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
Austria	Federal Ministry of Health	General comments	Genetically modified (GM) soybean MON 87708 contains a gene derived from Stenotrophomonas maltophilia that expresses the DMO protein. This trait confers tolerance to dicamba because it demethylates dicamba rendering it inactive. The present application shows a trend for a group of applications for GM plants with tolerance against selective herbicides. This trend is mainly caused by a rapid evolution of weed resistance against glyphosate due to repeated use of glyphosate without diversity (Powles 2010). It is very likely that cultivation of GM soybean MON 87708 causes chances in application management of dicamba. Therefore, even though the scope of this application excludes cultivation in the European Union, possible future scenarios such as import of MON 87708 derived food/feed with elevated dicamba herbicide residue pattern needs to be considered. Besides pesticide regulation these changes could, above all, effect nutritional or toxicological issues. It has to be stressed that the current application and the presented risk assessment data do not take this aspect into account. There is a particular need to focus on the investigation of long-term impacts of GMHT plants on humans, animals and the environment. It also shows the necessity to put more emphasis on the sustainable development in agricultural	The risk assessment of plant protection products is not within the remit of the EFSA GMO Panel. The comments raised in this comment box are further explained in the following sections. The EFSA GMO Panel therefore provides its responses to the specific comments in the respective sections shown below. The EFSA GMO Panel comments on the scientific content of the monitoring plan. EFSA has published guidance and scientific opinion on post-market environmental monitoring (PMEM) (EFSA, 2011). The EFSA GMO Panel is of the opinion that the information supplied by the applicant is in line with the guidance on PMEM. Please refer also to Section 6.1.2. of the Scientific Opinion on application EFSA-GMO-NL-2011-93.

Country	Organization	Reference	Comment	GMO Panel response
			production and food processing. Apart from the abovementioned point, the main deficits of the present notification are: * Consistent significant differences for 24 of 42 endpoints between MON 87708 and the conventional comparator which have not resulted in additional studies. * Migration differences in Southern blots due to inappropriate purification steps. * The lack of repeated dose study in toxicological assessment of the DMO enzyme. * The monitoring plan as presented by the applicant fails to address relevant questions for the monitoring of accidental spillage of MON 87708. Formal issues: Some of the study reports were presented as mere scans making word searches and copy and paste action impossible, and document reviewing even more time consuming. We appeal once more to EFSA not to accept scanned study reports in GMO applications. The concerned reports are: Beyene 2010a, Laufer and Bommireddy 2010a, RAR-10-030 2010. [Powles, S. B. (2010). Gene amplification delivers glyphosate-resistant weed evolution. Proc Natl Acad Sci U S A 107(3): 955-956.]	

Application EFSA-GMO-NL-2011-93 (soybean MON 87708)
Comments and opinions submitted by Member States during the three-months consultation period

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
Austria	Federal Ministry of Health	D, 02 Information on the sequences actually inserted or deleted	The molecular description provided by the notifier for the transgene insert present in GM Soybean MON 87708 is based on an analysis by Southern Blot to determine the size and copy number of detectable inserts (FROM CBI: Song et al. 2011). The analysis demonstrates the insertion of a single transgenic element in GM soybean MON 87708 and the absence of other sequences (T-DNA II and plasmid backbone sequences).	
			The sensitivity of the experiments to detect transgenic partial sequences other than the main insert was not assessed systematically. The utilisation of positive control sequences at a concentration of 0.1 genomic equivalents provides some indication that target sequences present at a lower than single copy ratio are detectable in the experiments. However the notifier should corroborate that also partial transgenic inserts can be reliably detected by the used methods.	The GMO Panel is of the opinion that the Southern analyses have been carried out properly. Sequencing of the flanking regions indicates that no partial transgene sequences are linked to the functional insert. Fragments that are not genetically linked can be eliminated during the subsequent breeding process. Furthermore, there are no indications from comparative agronomic performance and compositional analyses of any adverse effect caused by partial insertions.
			The notifier does not sufficiently discuss the potential effects of a 0.9 kb deletion which is identified in the 5' genomic sequence flanking the transgenic insert. This deletion which is presumably associated with the mechanism of Agrobacterium mediated transformation as well as an insertion of 128 bp at the 5' flank and a 35 bp insertion in the 3' flanking region are not further assessed. The notifier should better describe the rationale to disregard negative effects resulting from this rearrangement and to conclude that no relevant functions are associated with the abovementioned	Updated bioinformatic analyses were carried out on the pre-insertion site (3101 nucleotides, including the 899-nucleotide deletion), junctions and the whole insert (RAR-2012-0065). None of the analyses indicated a safety issue. In addition, there are no indications from comparative agronomic performance and compositional analyses of any adverse effects.

Country	Organization	Reference	Comment	GMO Panel response
			elements.	
Austria	Federal Ministry of Health	D, 03 Information on the expression of the insert	For the assessment of the developmental expression of the transgenic insert in dicamba-treated GM soybean MON 87708 during the life cycle of the plant, a field trial was conducted in the US in 2009 (Technical Dossier, p. 67). Dicamba mono-oxygenase (DMO) levels were tested for seven different plant tissues at various development stages: leaf (V3-V4, V6-V8, V10-V12 and V14-V16), root, forage as well as mature seed. Means, standard deviations and ranges were presented for each tissue type across sites (FROM CBI: Beyene and Niemeyer 2010a) and for individual sites (FROM CBI: Beyene and Niemeyer 2010b). The design of the presented study does not include a near-isogenic non-transgenic line as negative control as recommended by EFSA (2006) and Dolezel et al. (2009). The study also does not include a comparison between the expression levels of dicamba-treated and untreated GM soybean MON 87708. In addition further information important to assess transgene expression under different environmental conditions is not provided by the notifier. The notifier fails to provide a rationale for the selection of the different test sites as well as evidence for their representativeness for geographic regions, where soybean is commercially grown. The notifier should also indicate whether the agricultural procedures correspond to those usually applied for soybean crops in the respective	The ELISA method was validated and no non-specific binding (matrix effect) was noted in the experimental conditions used. Therefore the use of negative control plant samples is not critical as they would give zero as the result. Dicamba herbicide treatment was applied; this is in line with the agricultural practice for which the plants were specifically developed. The EFSA GMO Panel considers that the eight field sites, located in six clearly indicated states in USA are representative of regions where soybean is grown commercially.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			regions. Furthermore no indication is provided on whether the climatic conditions in 2009 were representative for the respective sites. In addition to seed and forage, which are certainly relevant for the environmental risk assessment, also pollen should be included in the analysis of the expression of the insert.	Considering the scope of the application and based on all the available information for this application, analysis of pollen is not considered necessary by the GMO Panel.
			We request that the notifier provides further information on the above-mentioned aspects. If no sufficient justification can be provided for the representativeness of the geographic regions and the range of receiving environments, additional data for more than one growing season at the same locations should be provided to account for variation of environmental conditions. Furthermore the between-site variation should be analysed to account for "gene x environment" interactions.	All raw data are provided in MSL0022723-RAW DATA. The mean values and ranges from the eight sites are considered sufficient to address relevant gene-environment interactions. No safety issues were raised.
			As described by the notifier, GM soybean MON 87708 expresses DMO protein as well as DMO+27 protein. Since the antibody used in the study recognises both DMO and DMO+27 protein, the data presented by the notifier do not differentiate between both forms of the protein. Furthermore the differential composition of the protein trimer, which is acting as the functional unit, cannot be assessed based on the data submitted by the notifier.	Since none of the two forms of DMO present in soybean MON 87708 are known to be toxic or allergenic, their proportion in the functional DMO trimers is not relevant from risk assessment point of view.
			As reference standard DMO protein produced in E. coli was used for analysis of the DMO levels. However, it remains unclear whether this protein is suitable as reference material for the quantification	Validation of the method included test of parallelism, which showed that the plant-produced DMO protein was immunologically equivalent to the *E. coli*-DMO protein standard. Quantity of the total DMO protein (all forms included) was

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			of both DMO and DMO+27. Clarification on these aspects should be provided by the notifier. [Beyene, A. and Niemeyer, K. (2010a). Assessment of DMO protein levels in soybean tissues collected from MON 87708 produced in United States field trials during 2009. Dossier EFSA/GMO/NL/2011/93. Beyene, A. and Niemeyer, K. (2010b). Assessment of DMO protein levels in soybean tissues collected from MON 87708 produced in United States field trials during 2009 - Raw data. Dossier EFSA/GMO/NL/2011/93. Dolezel, M., Miklau, M., Eckerstorfer, M., Hilbeck, A., Heissenberger, A. and Gaugitsch, H. (2009). Standardising the environmental risk assessment of genetically modified plants in the EU - BfN Skripten 259. Vienna, Umweltbundesamt: 1-295. EFSA (2006). Guidance document of the Scientific Panel on Genetically Modified Organisms for the risk assessment of genetically modified plants and derived food and feed. The EFSA Journal 99: 1-100.]	analysed, not its activity. The functionality (activity) of the DMO protein is assessed from the herbicide tolerance trait it confers. This is normal practice with herbicide tolerant GM crops, and allows the assessment of the allergenic and toxic potential of the protein as present in the plant.

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) Comments and opinions submitted by Member States during the three-months consultation period				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
Austria	Federal Ministry of Health	D, 04 Information on how the GM plant differs from the recipient plant in:	For the assessment of differences in reproduction, dissemination and survivability plant growth, development and yield characteristics as well as environmental interactions including plant response to abiotic stressors, disease damage and arthropod damage were evaluated in a field trial in the US in 2009 for GM soybean MON 87708 (Technical Dossier, p. 76). The notifier concluded that GM soybean MON 87708 has no altered phenotypic and agronomic characteristics compared to conventional soybean (Technical Dossier, p. 86). However, no comparison was provided for dicamba treated GM soybean MON 87708 vs. GM soybean MON 87708 not treated with this herbicide. In addition further information important to assess transgene expression under different environmental conditions is not provided by the notifier. The notifier fails to provide a rationale for the selection of the different test sites as well as evidence for their representativeness for geographic regions, where soybean is commercially grown. The notifier should also indicate whether the agricultural procedures correspond to those usually applied for soybean crops in the respective regions. Furthermore no indication is provided on whether the climatic conditions in 2009 were representative for the respective sites. We request that the notifier provides further information on the above-mentioned aspects. If no sufficient justification can be provided for the representativeness of the geographic regions and the range of receiving environments, additional	The field trial was designed according to suggestions supplied by the EFSA GMO Panel in its Guidance Document (EFSA, 2011), which partly is based on the information in the Scientific Opinion on statistical considerations for the safety evaluation of GMOs published in 2010. The EFSA GMO Panel accepted the description of agronomic characteristics of reference soybeans as presented in the outcome of the field trial. All the reference soybeans were non-GM soybeans that consumers have been exposed to and are suitable to be grown in the area of the field trial. However, as the applicant did not analyse their data according to the suggestions of the EFSA GMO Panel in the initial application, an additional statistical analysis was requested by the EFSA GMO Panel. The applicant supplied this information in October 2011. More information on the assessment performed by the EFSA GMO Panel can be found in Section 4 of the Scientific Opinion on application EFSA-GMO-NL-2011-93. Total DMO protein expression levels were analysed by enzyme-linked immunosorbent assay (ELISA) using leaf, root, forage and mature seed materials, from replicated field trial across eight major soybean-growing regions in the USA in 2009. These plants were treated with dicamba. The EFSA GMO Panel is of the opinion that no further expression data is required. Referring to the study report on the agronomic field trial, treatments included soybean MON 87708 unsprayed and soybean MON 87708 sprayed with dicamba. Considering the intended uses of soybean MON 87708 excluding cultivation, the EFSA GMO Panel considers that the field trial design and the information provided relating to the assessment of

Country	Organization	Reference	Comment	GMO Panel response
			data for more than one growing season at the same locations should be provided to account for variation of environmental conditions. Furthermore the between-site variation should be analysed to account for interactions with the respective environment ("gene x environment interactions"). Furthermore we request that the notifier provides additional information for the explanation of the rationale for the selection of the phenotypic and agronomic characteristics and whether these characteristics are relevant to assess persistence/invasiveness. In addition to the field study discussed above, seed dormancy and germination characteristics were evaluated in a separate laboratory study. In that study GM soybean MON 87708 was compared to a conventional non-GM control and eight commercial reference substances (two of them glyphosate-tolerant GM soybean) to establish a range of variation for comparison. The material was produced in 2008 in the US at three field sites (Technical Dossier, p. 87). In addition pollen morphology and viability was assessed for material from one of these sites comparing GM soybean MON 87708 with a conventional control and four commercial varieties, one of them being a different GM soybean line. The notifier should provide a rationale for the small number of test sites (three and one) compared to the assessment of agronomic and phenotypic characteristics. In addition the data from the GM	agronomic traits are sufficient to carry out the environmental risk assessment of soybean MON 87708. From the data presented in the application, there is no indication of an increased persistence and invasiveness potential of soybean MON 87708 compared to conventional soybean and it can be considered that soybean MON 87708 has no altered survival, multiplication or dissemination characteristics compared to its conventional counterpart, except under application of dicamba-based herbicides (see Section 6.1.1.1 of the Scientific Opinion).

Country	Organization	Reference	Comment	GMO Panel response
			reference varieties should be excluded from the calculation of the range for variation in unmodified varieties. In addition only untreated GM soybean MON 87708 was included in the assessment and no comparison has been provided between dicamba-treated and untreated GM soybean MON 87708. In addition further information important for the assessment in a range of conditions is not provided by the notifier. The notifier fails to provide a rationale for the selection of the different test sites as well as evidence for their representativeness for geographic regions, where soybean is commercially grown. The notifier should also indicate, whether the agricultural procedures correspond to those usually applied for soybean crops in the respective regions. We request that the notifier provides further information on the abovementioned aspects.	

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) Comments and opinions submitted by Member States during the three-months consultation period				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
Austria	Federal Ministry of Health	D, 04 Information on how the GM plant differs from the recipient plant in:	Specific comments on the phenotypic and agronomic evaluation (FROM CBI: Laufer and Bommireddy 2010a; Laufer and Bommireddy 2010b): The Lead Scientist and the report authors of the study assessing the phenotypic characteristics and ecological interactions of MON 87708 compared to the conventional soybean control were staff members of the applicant. Trial substances (test, control and reference substances): A description of control and reference substances in their phenotypic characteristics, so far as already known, and of the criteria for the choice of the reference substances should be given. From the reference varieties listed in Table 2 (p. 27) three were cropped on each trial site respectively. The way of distributing the reference varieties to the different sites is not reported, but may have an influence on the expectable reference range. So the composition of the reference assortments beside the test and control substances is to be commented. Laufer and Bommireddy (FROM CBI, 2010a) say, "Two additional experimental substances were detected at low levels in the A3525 control seed produced in Puerto Rico". We request more details on the detected	The post-market field trial referred to are legally required and have to be performed by the applicant or staff contracted by the applicant. The field trial was designed according to suggestions supplied by the EFSA GMO Panel in its Guidance Document (EFSA, 2011). The EFSA GMO Panel accepted the description of phenotypic characteristics of reference soybeans as presented in the outcome of the field trial. The field trials described for studying the event MON 87708 were not only used to study this event but also another unspecified event. For that reason it is necessary to control that that event does not influence the outcome of the trial with soybean MON 87708. Thus, the EFSA GMO Panel finds it appropriate not to include data from the contaminated control material in the comparative analysis. Considering the intended uses of soybean MON 87708 excluding cultivation, the EFSA GMO Panel considers that the field trial design and the information provided relating to the assessment of agronomic traits are sufficient to carry out the risk assessment of soybean MON 87708. The field trial design is in line with the requirements of the Guidance document of the EFSA GMO Panel for rsik assessment of food and feed from genetically modified plants (EFSA, 2011).

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			substances confirming the conclusions that they did not negatively affect the interpretation of the results. Trial design (p. 14): The field trial design with four replicates as Randomised Complete Block Design is adequate. Plots with eight rows with additional border rows between the plots are good standard. Trial series: The field experiments were planned for ten and carried out on eight sites for only one year (2009), as two of the trail sites - ILHI and ARSH - were lost during the testing period (p. 13 and Tab.5, p. 30f.). So the database for conclusions as given on p 86, part I, of the Technical Dossier remains rather small. A second growing season or more sites covering a broader environmental range within one year would give a more solid dataset. A detailed description of the climate characteristics on the trial sites is quoted (p. 15) but not added. Phenotypic characteristics: The phenotypic characteristics recorded in the study are useful, however observations for maturity and nodulation are lacking. Maturity and nodulation are considered to be critical traits in soybean, important for variety grouping to maturity classes and assessing performance in N2-assimilation capacity.	

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) Comments and opinions submitted by Member States during the three-months consultation period				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
			Results: The complete information about single plot data and randomisation of all trial sites is laudable (FROM CBI: Laufer and Bommireddy 2010c). [Laufer, T. C. and Bommireddy, P. L. (2010a). Amended report for MSL0023136: Phenotypic evaluation and environmental interactions of dicamba-tolerant soybean MON 87708 when treated and not treated with dicamba in U.S. field trials during 2009. Dossier EFSA/GMO/NL/2011/93. Laufer, T. C. and Bommireddy, P. L. (2010b). Amended report for MSL0023136: Phenotypic evaluation and environmental interactions of dicamba-tolerant soybean MON 87708 when treated and not treated with dicamba in U.S. field trials during 2009 - Ranges. Dossier EFSA/GMO/NL/2011/93. Laufer, T. C. and Bommireddy, P. L. (2010c). Amended report for MSL0023136: Phenotypic evaluation and environmental interactions of dicamba-tolerant soybean MON 87708 when treated and not treated with dicamba in U.S. field trials during 2009 - Raw data. Dossier EFSA/GMO/NL/2011/93.]	

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) **Comments and opinions submitted by Member States during the three-months consultation period**				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
Austria	Federal Ministry of Health	D, 04 Information on how the GM plant differs from the recipient plant in:	Specific comments on the phenotypic and agronomic evaluation (FROM CBI: Laufer and Bommireddy 2010a; Laufer and Bommireddy 2010b) (cont.): Significant differences: Significantly statistical differences were detected for "100 seed weight" in both test groups, treated and non-treated GM soybean MON 87708. The difference was consistent in both groups (lower than the control line) and the mean values were outside the overall reference ranges of the conventional varieties for both groups (see Chapters 4.1, 4.2). The individual-site analyses for treated MON 87708 resulted in lower 100 seed weights at all 8 sites and significant differences ($p < 0.05$) at 4 sites (see Table 8). The individual-site analyses for non-treated MON 87708 resulted in lower 100 seed weights at all 8 sites and significant differences ($p < 0.05$) at 5 sites (see Table 10). These results give indication of an unintended effect caused by the genetic modification of MON 87708. The applicant does not provide an adequate discussion but argues, "the assessed phenotypic values were within the range of values expected for commercial soybean" referring to conventional cultivars seed weight ranges of 0.12 to 0.18g/seed. Apart from referring to literature data, the	For more information, please refer to Section 6.1.1 of the Scientific Opinion of the EFSA GMO Panel on application EFSA-GMO-NL-2011-93: "*The observed difference in 100 seed weight is unlikely to be biologically significant in terms of increased weed potential.* *From the data presented in the application, there is no indication of an increased weed potential of MON 87708 compared to conventional soybean and it can be considered that soybean MON 87708 has no altered survival, multiplication or dissemination characteristics compared to its conventional counterpart except in the presence of dicamba herbicides"*.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			applicant is requested to discuss the consistent difference in more detail (e.g. regarding potential alterations in plant metabolism of MON 87708) and possibly to provide additional experimental data. Maturity: To some extent this information can be deduced from the growth stage observations. The character "date of maturity", however, would give more exact information about maturity performance of the trial substances. [Laufer, T. C. and Bommireddy, P. L. (2010a). Amended report for MSL0023136: Phenotypic evaluation and environmental interactions of dicamba-tolerant soybean MON 87708 when treated and not treated with dicamba in U.S. field trials during 2009. Dossier EFSA/GMO/NL/2011/93. Laufer, T. C. and Bommireddy, P. L. (2010b). Amended report for MSL0023136: Phenotypic evaluation and environmental interactions of dicamba-tolerant soybean MON 87708 when treated and not treated with dicamba in U.S. field trials during 2009 - Ranges. Dossier EFSA/GMO/NL/2011/93.]	

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) Comments and opinions submitted by Member States during the three-months consultation period				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
Austria	Federal Ministry of Health	D, 04 Information on how the GM plant differs from the recipient plant in:	Ad "Conclusion", Technical Dossier (p. 86): At least the variation of the reference varieties in the characters investigated is the basis for the interpretation of phenoptypic, agronomic and environmental interaction data: * The choice of these reference varieties should be founded and a description of the agronomic traits of the chosen varieties should be given, because the reference assortment is a critical point for the final result of the study. * The system of allocating the reference substances to the trials sites should be explained. * Eight trial sites from only one year are hardly sufficient for solid conclusions.	The field trial was designed according to suggestions supplied by the EFSA GMO Panel in its Guidance Document (EFSA, 2011), which partly is based on the information in the Scientific Opinion on statistical considerations for the safety evaluation of GMOs published in 2010. The EFSA GMO Panel accepted the description of agronomic characteristics of reference soybeans as presented in the outcome of the field trial. All the reference soybeans were non-GM soybeans that consumers have been exposed to and are suitable to be grown in the area of the field trial.
Austria	Federal Ministry of Health	D, 04 Information on how the GM plant differs from the recipient plant in:	Specific comments on evaluation of seed and pollen characteristics (FROM CBI: Laufer and Kendrick 2010a, Laufer and Kendrick 2010b): Evaluation of seed dormancy and germination (Tech. Doss., p. 87ff.): Seed of MON 87708 was tested with its conventional control variety (A3525) on germination and seed dormancy. AOSA (Association of Official Seed Analysis) methods of testing were used, but additionally other temperature regimes for germination. Methods are described in both reports (FROM CBI: Laufer and Kendrick 2010b; Laufer and Kendrick	Considering the intended uses of soybean MON 87708 excluding cultivation, the EFSA GMO Panel considers that the field trial design and the information provided relating to the assessment of agronomic traits are sufficient to carry out the risk assessment of soybean MON 87708. For more information, please refer to Section 6.1.1. of the Scientific Opinion of the EFSA GMO Panel on application EFSA-GMO-NL-2011-93: "*Germination and dormancy of seeds from soybean MON 87708, control and non-GM reference varieties, produced under different environmental conditions, were evaluated in growth chambers experiments through international protocols. Pollen characteristics were also assessed. Although some differences were observed under specific environmental conditions, they were not consistent and do not indicate a consistent plant response associated with the trait or any change*

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			2010a) in details. The methods are international standardised methods. However, it is not clear if the basis of analyses were pure seed. This needs to be clarified. Evaluation of pollen morphology and viability (FROM CBI: Phillips and Kendrick 2010; Tech. Doss. p.93ff.): MON 87708 was put in a field trial with its conventional control variety (A3525) and 4 listed reference varieties for producing flowers and pollen. Pollen was collected, stained with Alexanders's starch and tested on viability, additionally the diameter of pollen was measured. The field trial took place only for one year and on one site. On Page 14, Phillips and Kendrick (FROM CBI, 2010) describe that "the original pollen viability data and the details of the experimental methods were lost". The authors say that this loss did not cause any problem on finishing the study. However, a replication or follow up of the trial would have been useful. 20 flowers from each plot were collected, the plot size is not described, neither how many plants were sown per plot. The missing information needs to be forwarded.	*in fitness".*

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) Comments and opinions submitted by Member States during the three-months consultation period				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
			The fact that in both trials, germination and pollen viability, MON 87708 was statistically analysed only with its conventional control variety could be discussed. [Laufer, T. C. and Kendrick, D. L. (2010a). Amended report for MSL0022071: Dormancy and germination evaluation of dicamba-tolerant soybean MON 87708 using seed produced at three U.S. sites in 2008. Dossier EFSA/GMO/NL/2011/93. Laufer, T. C. and Kendrick, D. L. (2010b). Amended report for MSL0022071: Dormancy and germination evaluation of dicamba-tolerant soybean MON 87708 using seed produced at three U.S. sites in 2008 - Ranges. Dossier EFSA/GMO/NL/2011/93. Phillips, S. L. and Kendrick, D. L. (2010). Viability and morphology evaluation of pollen from dicamba-tolerant soybean MON 87708 produced in a U.S. field trial during 2008. Dossier EFSA/GMO/NL/2011/93.]	
Austria	Federal Ministry of Health	D, 05 Genetic stability of the insert and phenotypic stability of the GM plant	Genetic stability was assessed by analysing samples of 5 generations by Southern blot, however the number of individual plants analysed for each generation is not indicated (FROM CBI: Song et al. 2011). To demonstrate the stability of the insert in a conclusive way an adequate number of individual plants needs to be analysed. The notifier should submit additional data for an adequate number of individuals and include the rationale for the chosen number of samples in the presentation of the	Genetic stability of the inserted DNA was studied over five generations of the soybean by Southern analysis. The restriction enzyme/probe combinations used were sufficient to conclude that all of the generations tested retained the single copy insert together with its flanking regions. The insert is therefore stably inherited. Supporting evidence for the stability was obtained by Invader® DNA assay over three generations in approx. 3200 plants. This analysis also provided information on the zygosity of the plants which was consistent with a single genetic locus segregating according to Mendelian principles. The EFSA GMO Panel is of the opinion that, should instability leading to loss of the trait occur, no safety issue would arise.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			results. The Technical Dossier (p. 95) argues: "Any instability associated with the T-DNA I insert would be detected as novel bands within the fingerprint on the Southern blot". This statement is only valid for the part of the construct covered by probe 9 and/or if large parts of the insert were rearranged. The Southern blots presented in the dossier, however, are not suitable to show the stability of the insert as minor rearrangement cannot be detected through the experimental setup chosen. [Song, Z., Lawry, K. D., Rice, J. F. and Tian, Q. (2011). Amended report for MSL0022670: Molecular analysis of dicamba-tolerant soybean MON 87708,. Dossier EFSA/GMO/NL/2011/93.]	
Austria	Federal Ministry of Health	D, 05 Genetic stability of the insert and phenotypic stability of the GM plant	Evaluation of genetic stability of the insert (FROM CBI: Song et al. 2011) Specific comments: Page 19f.: "In most of the Southern blots, the migration of the genomic DNA is slightly different when compared to the migration of the molecular weight markers and, in some instances, there are slight migration differences between different DNA preparations. These altered migrations are likely the result of a difference in salt concentrations between the genomic DNA samples and the	Southern analysis has its advantages, limitations and sources of error which should be understood when designing experiments and interpreting the results (E Southern, 2006, Nature Protocols 1, 518-525). Overall, the Southern analyses presented in the dossier are fit for purpose and properly performed.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			molecular weight marker (Sambrook and Russell, 2001)". The notifier should overcome this problem by using appropriate purification steps during the preparation of DNA. This is important as the Southern blots should prove the integrity of the insert, which cannot be assessed when fragments show different migration due to the experimental setup. Furthermore, the notifier should explain why this phenomenon is only observed in some cases (e.g. deviations from the SOP?). Figure 3, page 36: Please note that the expected fragment sizes cannot be detected on the Southern blot presented. In particular, the short run lanes display deviations of expected vs. observed fragment sizes; "differences in salt concentrations" are likely not the reason as fragment sizes in the long run are not affected and – according to the methods – the same DNA was used for loading the gel. Please clarify! Figure 9, page 37: Both in the long and the short run the combination of MWM and migration of fragments does not allow for the exact determination of fragment sizes. In addition, there are clear deviations of fragment sizes in the long vs. the short run (see also Fig. 4, p. 37), the cause of which should be explained by the notifier. Evaluation of phenotypic stability (FROM CBI:	It is not clear which Figure is being referred to as there is no Figure 9 on page 37 either in MSL0023278 or in Technical dossier. The analysis (Figure 4 in Song 2011; Figure 7 in Technical dossier) was carried out to determine insert and copy number, not the exact size of the fragments. The result was clear. The fragment sizes are as expected, taking into consideration the general limitations of Southern analysis.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			Phillips et al. 2010) Specific comments: Generational stability analysis should include a cross between R5 (the generation used for commercial development according to the technical dossier, p. 49) and another soybean variety to show stability of the insert under conditions resembling the practical application. Although such a hybrid was used to generate segregation data, this hybrid was obtained taking plants from the generation before the one intended for later use (R4). The notifier should explain why this approach was chosen. The statement that the variety "did not contain the dmo expression cassette" should be defined more precisely, i.e. whether a conventional or a gm-variety has been used for the cross. The "segregation" analysis demonstrating the "fixed homozygosity" of plants (p. 3) should be displayed. [Phillips, S. L., Rinehart, J., Knox, A. and Kendrick, D. L. (2010). Revised summary: Heritability and stability of the dmo expression cassette in dicamba-tolerant soybean MON 87708 across multiple generations Dossier EFSA/GMO/NL/2011/93. Song, Z., Lawry, K. D., Rice, J. F. and Tian, Q. (2011). Amended report for MSL0022670: Molecular analysis of dicamba-tolerant soybean	 Stability of the trait has been demonstrated; thus the analysis on R5 segregation would be redundant as analysis on R4 segregation was already provided. For the purpose of this study, the essential information is that the variety with which the R4 (homozygous positive) plant was crossed did not contain the *dmo* expression cassette. Whether the variety was conventional soybean or another GM variety should not influence the outcome of the study. The GMO Panel does not consider this necessary for the safety assessment.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			MON 87708,.Dossier EFSA/GMO/NL/2011/93.]	
Austria	Federal Ministry of Health	D, 06 Any change to the ability of the GM plant to transfer genetic material to	D.6 (b) Plant to plant gene transfer: Even though "the scope of the current application does not include the cultivation of MON 87708 varieties in the EU", it should be noted that unintended spillage could occur during transportation (see also Tech. Doss. 9.3, p. 260ff.).	The EFSA GMO Panel shares this view: "*Considering the intended uses of soybean MON 87708, the environmental risk assessment is concerned with the indirect exposure mainly through manure and faeces from animals fed grain produced by soybean MON 87708 and with the accidental release into the environment of viable grains produced by soybean MON 87708 during transport and processing*".
Austria	Federal Ministry of Health	D, 07.01 Comparative assessment	For the comparative assessment GM soybean MON 87708 was compared to a non-transgenic control variety. In addition 14 different non-transgenic commercial varieties were grown in the same field trial in the US in 2009 as reference substances (Technical Dossier, p. 104). The analysis was conducted on forage and seed and included nutrients (proximate, ADF, NDF, amino acids, fatty acids, vitamin E for seed and proximate, ADF, NDF for forage) as well as anti-nutrients (raffinose, stachyose, lectin, phytic acid, trypsin inhibitors, isoflavones for seed). The analysis was conducted across-site and for the individual sites (FROM CBI: Harrigan et al. 2010a; Harrigan et al. 2010b). Significant differences were found for several compounds during the comparative assessment. However the notifier concludes that seed and forage produced from GM soybean MON 87708 are compositionally equivalent to that of the conventional soybean, since the magnitude of the differences were considered small and within the calculated range of the commercial varieties and the literature range (Technical Dossier, p. 117). However, no statistical comparison was provided	The field trial were designed according to suggestions supplied by the EFSA GMO Panel in its Guidance Document (EFSA, 2011), which partly is based on the information in the Scientific Opinion on statistical considerations for the safety evaluation of GMOs published in 2010. The EFSA GMO Panel accepted the description of agronomic characteristics of reference soybeans as presented in the outcome of the field trial. All the reference soybeans were non-GM soybeans that consumers have been exposed to and are suitable to be grown in the area of the field trial. However, as the applicant did not analyse their data according to the suggestions of the EFSA GMO Panel in the initial application, an additional statistical analysis was requested by the EFSA GMO Panel. The applicant supplied this information in October 2011. More information on the assessment performed by the EFSA GMO Panel can be found in Section 4 of the Scientific Opinion on application EFSA-GMO-NL-2011-93. The risk assessment of plant protection products is not within the remit of the EFSA GMO Panel. However, comparing the composition of soybean MON 87708 sprayed with dicamba with the composition of soybean MON 87708 not sprayed with dicamba, allowed the Panel to conclude that there was no indication of the dicamba treatment leading to differences in plant

Country	Organization	Reference	Comment	GMO Panel response
			for dicamba treated GM soybean MON 87708 vs. untreated GM soybean MON 87708. In addition further information important to assess to composition in a range of conditions is not provided by the notifier. The notifier fails to provide a rationale for the selection of the different test sites as well as evidence for their representativeness for geographic regions, where soybean is commercially grown. The notifier should also indicate, whether the agricultural procedures correspond to those usually applied for soybean crops in the respective regions. Furthermore no indication is provided on whether the climatic conditions in 2009 were representative for the respective sites. In addition, the scope of the comparative analysis is too narrow with a view to the characteristics of the application in question. The assessment does neither address the residual amounts of the herbicide nor the amounts of metabolites. One of these compounds, DCSA, which is generated by the action of the transgenic DMO-enzyme present in GM soybean MON 87708 is of particular relevance since its ADI is considerably lower than that of the precursor molecule, the herbicide dicamba (0.01 mg/kg bw * day versus 0.3 mg/kg bw * day) (EFSA 2011). We request that the notifier provides further information on the abovementioned aspects. If no sufficient justification can be provided for the representativeness of the geographic regions and the range of receiving environments, additional	metabolism that would influence the compositon of the soybean seed and forage. A suitable use of the reference varieties grown in the field trial have been suggested in the document: EFSA (2010) Scientic Opinion of the GMO Panel on statistical considerations for the safety evaluation of GMOs. The EFSA Journal 1250:1-59.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			data for more than one growing season at the same locations should be provided to account for variation of environmental conditions. Furthermore the between-site variation should be analysed to account for interactions with the respective environment (gene x environment interactions). In that respect, the reference range for each site should be calculated from the three commercial varieties grown at a specific site. [EFSA (2011). Conclusion on the peer review of the pesticide risk assessment of the active substance dicamba. 9(1): 1-52. Harrigan, G. G., Miller, K. D. and Sorbet, R. (2010a). Compositional analyses of soybean forage and seed collected from MON 87708 (herbicide untreated) grown in the United States during the 2009 season. Dossier EFSA/GMO/NL/2011/93. Harrigan, G. G., Miller, K. D. and Sorbet, R. (2010b). Compositional analyses of soybean forage and seed collected from MON 87708 (herbicide treated) grown in the United States during the 2009 season. Dossier EFSA/GMO/NL/2011/93.]	
Austria	Federal Ministry of Health	D, 07.01 Comparative assessment	The notifier should discuss the identified differences in more detail and further explain why they were not considered to be biologically meaningful. Differences for compounds, e.g. two fatty acids, which did not fall within the range of variation reported in literature, should be further assessed for relevance. Furthermore it remains unclear, why some	The applicant has discussed all statistically significant differences between soybean MON 87708 and soybean A3525. For more information please see Section 4 of the Scientific Opinion of the EFSA GMO Panel on application EFSA-GMO-NL-2011-93. Regarding compounds analysed in forage and seed, the applicant has largely followed the suggestion of OECD. Regarding allergens, please see Section 5.1.3. of the Scientific Opinion on application EFSA-GMO-NL-2011-93.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			nutrients were not measured for forage and anti-nutrients only assessed for seed. As soybean contains also a number of known food allergens it remains unclear, why only trypsin inhibitors were assessed. Other soybean allergens as described in Houston et al. (2010) should be considered as well. Because GM soybean MON 87708 represents a totally new GM soybean event with no authorisation status worldwide (see Part II, Summary, Chapter A.7), it would be valuable if data from at least two seasons/field trials are risk assessed. [Houston, N. L., Lee, D. G., Stevenson, S. E., Ladics, G. S., Bannon, G. A., McClain, S., Privalle, L., Stagg, N., Herouet-Guicheney, C., MacIntosh, S. C. and Thelen, J. J. (2010). Quantitation of soybean allergens using tandem mass spectrometry. J Proteome Res 10(2): 763-773.]	The scope of the present application is food, feed, import and processing. Cultivation is excluded from the scope. The data provided in the application is in line with the Guidance Document of the EFSA GMO Panel (EFSA, 2011).
Austria	Federal Ministry of Health	D, 07.01 Comparative assessment	Statistically significant differences in the combined-site analysis Consistent statistically significant differences in seed (i.e. similar results for untreated and treated soybean MON 87708) were detected for the following 12 components: carbohydrates, protein, arginine, aspartic acid, glutamic acid, histidine, phenylalanine, proline, palmitic acid, oleic acid, eicosenoic acid and behenic acid. Overall, significant differences were observed for:	The EFSA GMO Panel performed a comprehensive analysis of the data provided. A detailed explanation of the analysis of the comparative compositional, phenotypic and agronomic is provided in the Scientific Opinion of application EFSA-GMO-NL-2011-93.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			* 19 of the 34 seed nutrient levels: Carbohydrates, moisture, protein, arginine, aspartic acid, glutamic acid, histidine, isoleucine, leucine, phenylalanine, proline, valine, palmitic acid, oleic acid, linoleic acid, linolenic acid, eicosenoic acid, behenic acid, and vitamin E; ** 5 of the 8 anti-nutrient levels:* *Phytic acid, trypsin inhibitors, stachyose, genistein, and glycitein.* *The high number in significant differences (24) and consistent results (12), and the fact that proximates like carbohydrates and protein were concerned, make additional compositional studies necessary.* *Regarding the comparison with reference data it would be helpful if literature data on the natural compositional variation of the used reference lines is provided, if available.*	

Application EFSA-GMO-NL-2011-93 (soybean MON 87708)
Comments and opinions submitted by Member States during the three-months consultation period

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
Austria	Federal Ministry of Health	D, 07.01 Comparative assessment	Substance characterisation and field trial description: The study report (FROM CBI: Harrigan et al. 2010a, Chapter 4.4) mentions that "All results were as expected although one replicate (forage and seed) of the control at the INRC site was excluded from compositional analysis due to the presence of adventitious levels of the trait from a separate test substance…". The applicant is requested to define more exactly the term "adventitious levels". Information is also requested on what thresholds were established for the exclusion of contaminated seeds. Additional information also needs to be forwarded on what causes 8 (!) missing replicates: "Site NEYO had two missing replicates of reference forage and seed data. Sites INRC and KSLA each had one missing replicate of control forage and seed data. There was also one missing replicate each of MON 87708 (untreated) and Test 2 forage and seed data at sites IARL and ILCY, respectively" (FROM CBI: Harrigan et al. 2010a, p. 183 of 295). According to Chapter "1. Data Description" of both study reports (FROM CBI: Harrigan et al. 2010b; Harrigan et al. 2010a), "the field studies contained another test substance not further characterised but designated as Test 2". A schematic picture of the randomised allocation of	The applicant assessed the presence/absence of test substance in the various samples, and did not to include contaminated samples in the statistical analysis of the composition. The data provided are in line with the Guidance Document (EFSA, 2011). The EFSA GMO Panel considers that there is no need for experimental design information with regard to test substance 2 for the present application since an appropriate design of plots with soybeans MON 87708, A3525 and reference lines was provided. The data are in line with the Guidance Document (EFSA, 2011). Regarding the statistical analysis of the field trial data, the EFSA GMO Panel requested the applicant to perform additional statistical analysis according to the methodology described in its Guidance Document (EFSA, 2011). This information was delivered by the applicant in October 2011.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			the test, control and reference lines to the plots, including test substance "Test 2", is therefore requested. Statistical methodology: The applicant is requested to give for each endpoint the means and standard errors of means of the test line, and not the "least-square means". Please see EFSA recommendations: "Applicants should provide a table or graph, giving, for each (transformed) endpoint, the means and standard errors of means of the GM and conventional counterpart(s) for each site" (EFSA 2010, Chapter 4.2). The Technical Dossier (p. 105) says, "Compositional data from commercial conventional soybean varieties […] were combined across all sites and used to calculate a 99% tolerance interval for each component to define the natural variability in soybean varieties that have a history of safe consumption". A 99% tolerance interval is a very large statistical interval. Comparison of mean values with 99% tolerance intervals is a doubtful statistical approach, as this provides very low power. The applicant is asked to give a rationale on how this approach can both "provide a comprehensive comparative assessment of the levels of key nutrients and anti-nutrients in seed and forage of	

Country	Organization	Reference	Comment	GMO Panel response
			MON 87708" (Tech. Doss., p. 106) and be used for "reliable estimation of natural variability" (EFSA 2010,abstract). It is requested that a new statistical analysis is performed using confidence limits. [EFSA (2010). Scientific opinion of the GMO Panel on statistical considerations for the safety evaluation of GMOs. The EFSA Journal 1250: 1-59. Harrigan, G. G., Miller, K. D. and Sorbet, R. (2010a). Compositional analyses of soybean forage and seed collected from MON 87708 (herbicide untreated) grown in the United States during the 2009 season. Dossier EFSA/GMO/NL/2011/93. Harrigan, G. G., Miller, K. D. and Sorbet, R. (2010b). Compositional analyses of soybean forage and seed collected from MON 87708 (herbicide treated) grown in the United States during the 2009 season. Dossier EFSA/GMO/NL/2011/93.]	
Austria	Federal Ministry of Health	D, 07.08 Toxicology	Because the GM plant is designated to provide resistance against dicamba (3,6 dichloro 2 methoxybenzoic acid) herbicide, it is necessary to provide a detailed discussion regarding elevated residues of active/inert ingredients of dicamba containing herbicides in imported food and feed. The applicant is requested to submit the missing information and discussion, and thus completing the risk assessment of MON 87708. The Technical Dossier (p. 217) remarks: "A	The risk assessment of plant protection products is not within the remit of the EFSA GMO Panel. The EFSA GMO Panel agrees with the Competent Authority that it is not appropriate to calculate a MOE from an acute toxicity study.

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) Comments and opinions submitted by Member States during the three-months consultation period				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
			common approach used to assess potential health risks from chemicals or other potentially toxic products is to calculate a MOE between the lowest NOAEL from an appropriate animal toxicity study and an estimate of human exposure". However, an acute oral toxicity study cannot be regarded an appropriate animal toxicity study in this context. We ask for not using the term "margin of exposure" in relation to the outcome of acute animal studies as it is misleading. Uncertainty factors are normally increased in relation to the available data used: 100 for chronic studies, and higher if there is lack of data and only shorter toxicity studies are available. Therefore, compared to the NOAEL in an acute gavage study on mice, the mentioned values (500-1000) do not represent large margins as argued in the Technical Dossier (p. 217).	

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) Comments and opinions submitted by Member States during the three-months consultation period				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
Austria	Federal Ministry of Health	D, 07.08 Toxicology	D.7.8.1 Safety assessment of newly expressed proteins Characterisation of the donor organisms: The scientific paper cited by the applicant (Ryan et al. 2009) characterises the donor organisms S. maltophilia as a hospital-acquired pathogen which has been associated with bacteraemic infections and pneumonia, both with a high rate of mortality, in immunocompromised patients. In Austria, S. maltophilia is classified as "class 2 micro-organism", which may cause disease in humans ("http://bmg.gv.at/home/Schwerpunkte/Gentechnik/Rechtsvorschriften_in_Oesterreich/Gentechnikbuch_gemaess_99_GTG", Drittes Kapitel des Gentechnikbuches - Teil 1 (Risikogruppen Bacteria)). The argument that S. maltophilia is widespread in the home environment and that DMO proteins are present in salads, vegetables, frozen fish, milk, and poultry (see Tech. Dossier, p. 211) can hardly be seen as scientific proof of safety as long as its mode of action in human and animal organisms is not clarified. Differences in the amino acid sequence between the wild type DMO protein and the MON 87708 DMO protein (Tech. Doss., p. 188ff.) add another element of uncertainty.	The information supplied by the applicant for the safety assessment of the protein is in line with the EFSA Guidance Document. For more information on the toxicology assessment performed by the EFSA GMO Panel please see Section 5.1.2 of the Scientific Opinion on application EFSA-GMO-NL-2011-93. Please also note that on request from the EFSA GMO Panel, the applicant on 13 March 2012 supplied a 28-day oral toxicity study with a mixture of the MON 87708 DMO protein and MON 87708 DMO+27 proteins supplied in the diet in approximately the same ratio they occur in soybean MON 87708 (*i.e.*, 2:3). To allow the use of *Escherichia coli*-produced DMO proteins as substitute for those expressed in soybean MON 87708 in the 28-day toxicity study, the equivalence of the *E. coli*- and MON 87708-produced DMO proteins was shown by comparing their N-terminal sequences, immunoreactivity with anti-DMO antibodies, and apparent molecular weights. The highest dose administered in this study, i.e. 174 mg/kg bw per day in males and 179.7 mg/kg bw per day in females, is considered the no observed adverse effect level (NOAEL). Assuming an intake of 200 g of soybean per 70 kg adult per day in the EU and that all soybean consumed is derived from MON 87708, the daily intake of DMO proteins would be in the region of 110 g/kg bw. The highest estimated intake of DMO proteins in adults is about 1000- fold lower that the NOAEL from the 28-day mice feeding study. In addition, application EFSA-GMO-NL-2011-93 includes a 90-day feeding study in rats with diets containing processed meal of soybean MON 87708 (test groups fed diets containing soybean MON 87708 treated with the intended herbicide dicamba). In conclusion, the information provided by the applicant in the

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			Bioinformatic analysis: The Technical Dossier mentions that "higher order structures are a relevant measure of homology since structure is more conserved than amino acid sequence". To strengthen the conclusions that DMO shows no similarity to known toxins, it is thus important that also searches in 3-D structure databanks are carried out. Please see EFSA (2011): "A search for homology to proteins exerting a normal metabolic or structural function may also contribute valuable information" (Chapter 3.1.4.2.). As such tools are available it is unclear why they are not applied in the safety assessment process to strengthen the conclusions that DMO has no similarity to known toxins. We also refer that testing structural similarities is regarded a first step in risk assessment of newly expressed proteins that cannot replace fundamental toxicological testing of the whole GM food/feed aiming at identifying changes in metabolism/degradation/effect pathways possibly influencing other components. Digestibility of MON 87708 DMO in simulated gastric fluids: The applicant argues: "Rapid degradation of MON 87708 DMO in simulated gastric fluids makes it	original dossier and as additional information allows the EFSA GMO Panel to drawn conclusions on the food and feed safety of the newly expressed proteins.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			highly unlikely to be absorbed by the epithelial cells of the small intestine in a biologically active form" (Tech. Doss., p. 217). We agree that in vitro test results may be indicative of toxic effects. However, test systems relying on reconstituted purified protein or cell components, or immortalised laboratory cultures of cell lines are not representative of the functioning of such cell components or cells in living organisms (König et al. 2004). Conducting of appropriate toxicological studies is therefore recommended. [EFSA (2011). Guidance of the GMO Panel for risk assessment of food and feed from genetically modified plants. The EFSA Journal 9(5)(2150): 1-37. König, A., Cockburn, A., Crevel, R. W. R., Debruyne, E., Grafstroem, R., Hammerling, U., Kimber, I., Knudsen, I., Kuiper, H. A., Peijnenburg, A. A. C. M., Penninks, A. H., Poulsen, M., Schauzu, M. and Wal, J. M. (2004). Assessment of the safety of foods derived from genetically modified (GM) crops. Food and Chemical Toxicology 42(7): 1047-1088. Ryan, R. P., Monchy, S., Cardinale, M., Taghavi, S., Crossman, L., Avison, M. B., Berg, G., van der Lelie, D. and Dow, J. M. (2009). The versatility and adaptation of bacteria from the genus Stenotrophomonas. Nat Rev Microbiol 7(7): 514-525.]	

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
Austria	Federal Ministry of Health	D, 07.08 Toxicology	D.7.8.1 Safety assessment of newly expressed proteins (cont.) In vivo test systems: The applicant conducted an acute oral toxicity study with the DMO protein concluding "there were no adverse effects of the DMO enzyme when administered by oral gavage at a dose of 140 mg/kg in male and female mice" (FROM CBI: MSL0022527 2010). As regards acute toxicity tests, potential effects resulting from continuous additional loading of metabolic or effector systems which can lead to pathologic mechanisms are not detected. We concur with EFSA that "acute studies are of little additional value for the risk assessment of the repeated human and animal consumption of GM food/feed" (EFSA 2008). Thus, it is advisable to carry out investigations for predicting intermediate and long-term toxicity. This is strengthened by the fact that no evidence of the modes of action of the DMO protein as regards effects on the human and animal organism is presented. Please compare EFSA (2006) recommendations, "Repeated dose toxicity studies should be performed, unless reliable information can be provided which demonstrates the safety of the newly expressed protein (including its mode of action)…".	On request from the EFSA GMO Panel, the applicant on 13 March 2012 supplied a 28-day oral toxicity study with a mixture of the MON 87708 DMO protein and MON 87708 DMO+27 proteins supplied in the diet in approximately the same ratio they occur in soybean MON 87708 (*i.e.*, 2:3). To allow the use of *Escherichia coli*-produced DMO proteins as substitute for those expressed in soybean MON 87708 in the 28-day toxicity study, the equivalence of the *E. coli*- and MON 87708-produced DMO proteins was shown by comparing their N-terminal sequences, immunoreactivity with anti-DMO antibodies, and apparent molecular weights. The highest dose administered in this study, i.e. 174 mg/kg bw per day in males and 179.7 mg/kg bw per day in females, is considered the no observed adverse effect level (NOAEL). Assuming an intake of 200 g of soybean per 70 kg adult per day in the EU and that all soybean consumed is derived from MON 87708, the daily intake of DMO proteins would be in the region of 110 g/kg bw. The highest estimated intake of DMO proteins in adults is about 1000- fold lower that the NOAEL from the 28-day mice feeding study.

Country	Organization	Reference	Comment	GMO Panel response
			[EFSA (2006). Guidance document of the Scientific Panel on Genetically Modified Organisms for the risk assessment of genetically modified plants and derived food and feed. The EFSA Journal 99: 1-100. EFSA (2008). Updated guidance document for the risk assessment of genetically modified plants and derived food and feed - draft document adopted in May 2008. The EFSA Journal 727: 1-135. MSL0022527 (2010). An acute toxicity study of dicamba mono-oxygenase (DMO) enzyme from MON 87708 administered by oral gavage to mice. Dossier EFSA/GMO/NL/2011/93.]	
Austria	Federal Ministry of Health	D, 07.08 Toxicology	D.7.8.4 Testing of the whole GM food/feed: A 90-day feeding study in rats was conducted with processed soybean meal from GM soybean MON 87708. An additional study with unprocessed (ground) soybeans could be considered to strengthen the safety assessment. (For example, such study was submitted for toxicological assessment of GM soybean MON 40-3-2 and reviewed by EFSA (2010)). Looking at the results of the study, it is noticeable that with two verum groups, the 30% test group males and the 15% test group females, various parameters differed substantially from those of the corresponding control groups, so body weight gain, some hematology parameters, amino transferases, specific gravity of urine, absolute and relative weight of spleen. Even though these effects were,	Although a 90-day feeding study was not required in the case of application EFSA-GMO-NL-2011-93, the applicant provided the study in its application. The EFSA GMO Panel evaluated the assessment of the sub-chronic study in rats and concluded that there is no indication that administration of diets containing 15% or 30% processed soybean meal from soybean MON 87708 (test groups fed diets containing soybean MON 87708 treated with the intended herbicide dicamba) are any more hazardous than diets containing the corresponding amounts of soybean A3525, the conventional counterpart.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			at least for the female verum group, not dose-related, there is strong indication that something happened with these groups. To exclude or have a closer look at GMO-dependent effects, nearer elucidations would be necessary. (FROM CBI: MSL0022868 2010) Moreover, from the given studies and data, potential negative effects only revealed in times of reproduction or health stress or long-term influences cannot be excluded. Therefore, results of respective studies should be given, or it should be otherwise demonstrated that the product does not possess detrimental effects on reproduction or development. [EFSA (2010). Scientific Opinion of the GMO Panel on applications (EFSA-GMO-RX-40-3-2 [8-1a/20-1a], EFSA-GMO-RX-40-3-2 [8-1b/20-1b]) for renewal of authorisation for the continued marketing of (1) food containing, consisting of, or produced from genetically modified soybean 40-3-2; (2) feed containing, consisting of, or produced from soybean 40-3-2; (3) other products containing or consisting of soybean 40-3-2 with the exception of cultivation, all under Regulation (EC) No 1829/2003 from Monsanto. The EFSA Journal 8(12)(1908): 1-38. MSL0022868 (2010). A 90-day feeding study in rats with processed soybean meal from MON 87708. Dossier EFSA/GMO/NL/2011/93.]	
Austria	Federal Ministry of Health	D, 07.09 Allergenicity	D.7.9.1 Assessment of allergenicity of the newly expressed protein:	Regarding general issues of the risk assessment of newly expressed proteins in genetically modified organisms for

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			The assessment of the potential allergenicity of the newly expressed protein (DMO) was based on the food standard (Codex Alimentarius Commission 2003) which requires comparisons of amino acid sequences as well as digestibility assays. However, new methods combining structural information with analysis of conservation of primary structure could offer a sounder basis for assessing potential IgE cross-reactivity in novel proteins (Jenkins et al. 2005). Concerning the characterisation of the donor organism and the in vitro and in silico test systems conducted by the applicant, please see Austrian Comments on Chapter D.7.8. Since homology searches and digestibility assays are not in itself satisfactory to determine the potential allergenicity of the DMO protein, it is recommended carrying out further studies (e.g. target serum screening). This recommendation is consistent with considerations laid down in Chapter "Assessment of Possible Allergenicity", Section 5 (17) of the Codex Alimentarius Commission (2003). 7.9.2 Assessment of allergenicity of the whole GM plant or crop: According to the Technical Dossier, "IgE binding values obtained for the 17 reference soybean extracts were used to calculate a 99% tolerance interval for each subject's serum".	allergenicity, and the potential allergenicity of the GMO itself, the EFSA GMO Panel refers to the document on allergenicity assessment (EFSA, 2010) and to its Guidelines for risk assessment of GM Plants (EFSA, 2006; 2011). According to the EFSA GMO Panel Guidance Document, when the recipient of the introduced gene is know to be allergenic, the applicant should test any potential change in the allergenicity of the whole food derived from the GM plant. The applicant provided different studies for the allergenicity assessment of the endogenous allergenicity: i) two-dimensional (2D) electrophoresis of extracts of soybean MON 87708 and its conventional counterpart followed by Western blotting with individual human sera from allergic individuals containing IgE antibodies; and ii) a quantification of the IgE-binding of soybean proteins to human sera using an ELISA method. In these studies, the GM soybean MON 87708 was compared with its conventional counterpart. Based on this information, EFSA GMO Panel concluded that there are no indications that the genetic modification might significantly change the overall allergenicity of soybean MON 87708 when compared with that of its conventional counterpart.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			Since 99% tolerance intervals are very large intervals providing low statistical power, we would like the applicant to provide an adequate scientific explanation regarding this statistical approach. New results based on comparisons with confidence intervals calculated from reference soybean extracts shall be submitted and discussed. The applicant is also requested to explain why quantitative assessment of main soybean allergens (except trypsin inhibitors) as described in Houston et al. (2010) was not carried out. [Codex Alimentarius Commission (2003). Guideline for the conduct of food safety assessment of foods derived from recombinant-DNA plants. Rome. CAC/GL 45-2003: 1-13. Houston, N. L., Lee, D. G., Stevenson, S. E., Ladics, G. S., Bannon, G. A., McClain, S., Privalle, L., Stagg, N., Herouet-Guicheney, C., MacIntosh, S. C. and Thelen, J. J. (2010). Quantitation of soybean allergens using tandem mass spectrometry. J Proteome Res 10(2): 763-773. Jenkins, J. A., Griffiths-Jones, S., Shewry, P. R., Breiteneder, H. and Mills, E. N. (2005). Structural relatedness of plant food allergens with specific reference to cross-reactive allergens: an in silico analysis. J Allergy Clin Immunol 115(1): 163-170.]	

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) **Comments and opinions submitted by Member States during the three-months consultation period**				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
Austria	Federal Ministry of Health	D, 12.03 General Surveillance of the impact of the GM plant	D.11.4. General surveillance for unanticipated adverse effects: According to the submitted Monitoring plan General Surveillance will involve trade associations representing relevant operators, dealing with the import, handling and processing of viable GM soybean MON 87708 at EU level (COCERAL, UNISTOCK and FEDIOL). However it should be clear which existing national organisations will be involved in individual Member States in order to ensure that different import volumes of GM soybean into individual Member States can be taken into consideration. The conduct of General Surveillance will be substantially influenced by the availability, extent and composition of existing networks in the individual EU Member States. The active involvement of these organisations and their assistance to the notifier are essential elements in order to ensure a meaningful monitoring. As the main use of GM soybean MON 87708 will be in feed products, national veterinary networks and services should be involved in the General Surveillance of unanticipated effects on animal health of GM soybean MON 87708. In the proposed monitoring plan these institutions are not involved in the suggested monitoring network. Thus the monitoring plan at hands fails to address relevant questions with regard to surveillance of animal health. The proposed surveillance plan makes reference to the HACCP principles (Technical Dossier, p. 275).	Please refer to Section 5.1.7. of the scientific opinion where it is concluded that that no data have emerged to indicate that soybean MON 87708 is any less safe than its conventional counterpart. In addition, soybean MON 87708 is considered as nutritious as conventional soybeans. Therefore, and in line with the guidance document, the EFSA GMO Panel is of the opinion that post-market monitoring of the GM food/feed is not necessary. The EFSA GMO Panel comments on the scientific quality of the monitoring plan. The final agreement on the monitoring is made at authorisation. EFSA has published guidance and scientific opinion on post-market environmental monitoring (PMEM) (EFSA, 2011). The EFSA GMO Panel is of the opinion that the information supplied by the applicant is in line with the guidance on PMEM. Please refer also to the overall conclusions of the scientific opinion: "*In addition the EFSA GMO Panel acknowledges the approach proposed by the applicant to put in place appropriate management systems to restrict environmental exposure in case of accidental release of viable seeds of soybean MON 87708".*

Country	Organization	Reference	Comment	GMO Panel response
			However the notifier is requested to outline how the HACCP principles are specifically implemented to match with the requirements of an environmental monitoring plan addressing GM food and feed safety issues. The notifier states that "the baseline and controls for general surveillance will rely on the historical knowledge and experience with non-GM soybean as comparable reference where necessary" (Technical Dossier, p. 274). We request that the notifier provides more information with regard to this baseline. Furthermore it is not clear how the monitoring will address unintended release to the environment via accidental spillage of viable material during transport. Additionally the various tasks assigned to the consent holder as well as selected trade associations, e.g. distribution of information about the GMO (provided by the consent holder to operators via the website of EuropaBio) and the conduct of monitoring and reporting, are not appropriately specified in detail. No specification is given regarding the kind of data which ought to be collected. The proposed surveillance primarily relies on passively collecting information of unspecified nature. The notifier is requested to apply a more proactive approach of General Surveillance including specific activities for monitoring grain loss at different locations (e.g. ports, silos, processing facilities) and provides additional information with	

Country	Organization	Reference	Comment	GMO Panel response
			regard to the parameters that are going to be monitored, as well as on the methodological approaches implemented for monitoring. The notifier states that "exposure to the receiving environment will be limited ... and can easily be controlled by ….manual or mechanical removal and the application of herbicides other that dicamba" (Technical Dossier, p. 274). As no clear responsibilities are assigned in this respect, it remains unclear who actually will be responsible for instance for clean up measures in the case of accidental spillage during loading and unloading. In conclusion the proposed monitoring plan falls short of providing a detailed monitoring methodology laying down responsibilities and assigning concrete tasks to each party involved as well as addressing relevant questions for the monitoring of accidental spillage of GM soybean MON 87708.	
Belgium	BAC	D, 07.01 Comparative assessment	Comment1. As for anti-nutrient levels, stachyose was increased and phytic acid was decreased in Mon 87708 compared to the conventional control, whether dicamba treated or dicamba-untreated Mon 87708 was compared with conventional soybean. However, trypsin inhibitors were increased when dicamba-untreated Mon 87708 was compared with its conventional counterpart, and genistein and glycitein were increased when dicamba-treated Mon 87708 was compared with its conventional counterpart, but not the trypsin-inhibitors anymore.	Regarding the statistical analysis of the field trial data, the EFSA GMO Panel requested the applicant to perform additional statistical analysis according to the methodology described in its updated Guidance Document (EFSA, 2011). For more information on the assessment performed by the EFSA GMO Panel, please see Section 4 of the Scientific Opinion on application EFSA-GMO-NL-2011-93. Risk assessment of plant protection products is not within the remit of the EFSA GMO Panel. The EFSA GMO Panel noted a consistent reduction in 100 seeds weight. However, considering the magnitude of the difference in 100 seeds weight, its inherent variability and lack of impact on other parameters investigated,

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			Since the same control is used as comparator for both Mon 87708-treated and untreated soybean, it may be asked if this is due to "interacting" effects of the dicamba treatment with Mon 87708. Comment2. The enzymatic breakdown of dicamba by DMO results in the formation of formaldehyde. Even though also naturally produced in plants, formaldehyde is a toxic compound. It may therefore be relevant to measure the amount of formaldehyde in dicamba-treated and dicamba untreated soybeans, and compare this with data on naturally occurring amounts of formaldehyde in plants. Comment3. Only ADF and NDF fibers have been analysed. This makes sense for feed but for food it lacks the analysis on dietary fibre. In its previous advices the Biosafety Advisory Council has recommended the analysis on dietary fibre since this concept is widely accepted in human food studies and recommends the adaptation of the OECD consensus document accordingly. The carbohydrates were assessed by calculation. There are now a range of methods available for the direct assessment of carbohydrates which give more accurate information about the carbohydrate content. In its previous advices the Biosafety Advisory Council recommended therefore the adaptation of the OECD consensus document	including yield, the EFSA GMO Panel concludes that this difference does not pose safety concerns in the context of the scope of this application. The EFSA GMO Panel noted comment 3. In the EFSA GMO Panel Guidance Document, it is stated that the compounds for the anlysis should be selected in accordance with the OECD consensus documents.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			accordingly. The applicant only provided data for vitamin E. It is generally recognized that soybean is an important source of vitamins in the human diet, in particular vitamin E and vitamin K. In its previous advices the Biosafety Advisory Council underlined that in the revised version of the OECD Consensus Document on Compositional Considerations for New Varieties of soybean (still under discussion at OECD level), Vitamin K is also listed as suggested constituent to be analysed related to food use. The Biosafety Advisory Council is of the opinion that data provided by the applicants should comply with the latest scientific standards.	
Belgium	BAC	D, 07.06 Effect of the production and processing	The applicant reviews processes applied during transformation into different products. Attention is given to dehulling and flaking, oil extraction, solvent removal, production of crude oil and meal, oil refining, lecithin production, production of soy protein isolate. This brief review covers the most significant processes. Some processes are not further discussed although mentioned in fig 20. Production of soy drinks is also missing.	Please see Section 5.1.1 on effects of processing of the Scientific Opinion on application EFSA-GMO-NL-2011-93.
Belgium	BAC	D, 07.07 Anticipated intake/extent of use	- Desmethyltocopherols such as γ-tocopherol have been reported to possess anti-inflammatory, antineoplastic and natriuretic functions. Has the level of these tocopherols and isoflavones been compared in Mon 87708, treated and untreated with dicamba, with conventional counterpart? - Has urease activity been compared?	The compounds analysed in seeds and forage of the studied soybean materials are those suggested by the OECD Consensus Document on Compositional Considerations for New Varieties of Soybean: Key Food and Feed Nutrients and Anti-Nutrients published in 2001. This document advices the analysis of vitamin E (alpha tocopherol) and isoflavones. The isoflavones analysed in this study were daidzein, glycitein and genistein.

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) **Comments and opinions submitted by Member States during the three-months consultation period**				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
Belgium	BAC	D, 07.08 Toxicology	Clinical Pathology - Hematology And Coagulation: Monocytes in female animals in the 15% group seem to be rather low, whereas eosinophil count in male test subjects in both the 15% and 30% group is increased (only statistically significant for the 30% feeding group). The monocyte count seems to be of no concern as no dose-response relationship is observed. The number of eosinophils is elevated only in male rats, both compared to the control and the references. What about the amount of formaldehyde in the soybean meal? Can this exert an effect on granulocytes? Why only in male subjects? This has to be further investigated. Clinical Pathology - Serum Chemistry: The alanine aminotransferase (ALT) activities are higher compared to the control as well as the references and statistically significant for the 30% feeding group. As for the eosinophil count, only male rats are affected. Further investigation is needed.	The EFSA GMO Panel assessed the 90-day toxicity study and concluded that the outcome of the study in rats with diets containing toasted deffated soybean meal from soybean MON 87708, its conventional counterpart or any of two non-GM soybean varieties did not raise saety concerns. For more information on the evalution performed by the EFSA GMO Panel please see the Scientific Opinion (Section 5.1.3.4.) on application EFSA-GMO-NL-2011-93.

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) Comments and opinions submitted by Member States during the three-months consultation period				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
Belgium	BAC	D, 07.09 Allergenicity	Comment 1. The applicant insufficiently addressed the likelihood that due to DMO enzymatic activity, new (protein) derivatives are generated in the GM plant with potential allergenicity. The applicant effectively tested several potential non-protein endogenous substrates (Section 7.8.1.iii) but omitted potential protein substrates from this analysis. With regard to allergenicity, a convincing experimental approach to this end would consist of immunization of rats with MON 87708 water soluble extract, followed by comparative 2D Western blot analysis of GM and parental plant extracts using the rat antiserum for immunodetection. Such approach would provide more firm evidence for the absence or not of novel protein derivatives generated in the GM plant as a result of DMO enzymatic activity. Comment 2. Soy is very well known as an allergenic plant especially in children. There are different soy allergen with possible cross reactivity. This is acknowledged by Monsanto and the allergenicity to the modified plant was demonstrated with sera of known allergic patients. However, little data are given on these sera (total serum IgE, level of soya allergen specific IgE – to which allergen? – mono- or polysensitised patients? Age of the patients? Disappearance of binding after heating sera? In addition, recently a basophil activation technique has been described which is much more sensitive than the techniques applied hitherto (Sabato et al.,	The data provided in the application for both the assessment of allergenicity of the newly expressed protein and the overall allergenicity of the shole plant are in line with the Guidance Document of the EFSA GMO Panel. The Member State suggests a possible role of the enzymatic activity of the DMO on endogenous proteins. This issue has been taken into account by the GMO Panel in the assessment of the possible impact of the genetic modification on the overall allergenicity of the whole plant. The applicant provided different studies for the allergenicity assessment of the endogenous allergenicity: i) two-dimensional (2D) electrophoresis of extracts of soybean MON 87708 and its conventional counterpart followed by Western blotting with individual sera from allergic humans; and ii) a quantification of the IgE-binding capacity of protein extracts from GM vs non GM soybeans to human allergic sera using an ELISA method. In these studies, the GM soybean MON 87708 was compared with its conventional counterpart. Based on this information, the EFSA GMO Panel concluded that there are no indications that the genetic modification might significantly change the overall allergenicity of soybean MON 87708.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			2011). It might be worthwhile to apply this technique to the modified protein in order to be able to pick up very low amounts of cross reacting IgE. Sabato V, van Hengel AJ, De Knop KJ, Verweij MM, Hagendorens MM, Bridts CH, De Clerck LS, Schiavino D, Stevens WJ, Ebo DG (2011) Human basophils: a unique biological instrument to detect the allergenicity of food. J Investig Allergol Clin Immunol, 21(3):179-84.	

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) **Comments and opinions submitted by Member States during the three-months consultation period**				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
France	Ministère de l'Economie (Consommation)	General comments	CONCLUSION Conclusions du Comité d'Experts spécialisés « Biotechnologie » Au regard des résultats moléculaires présentés, l'événement de transformation intégré dans le génome des sojas MON87705 correspond à l'insertion d'une copie stable en un seul locus de la cassette d'expression du gène dmo. Le site d'intégration et les régions flanquant l'insert ont été caractérisés et leur analyse ne soulève pas de question de sécurité sanitaire concernant ces sojas. Le soja MON 87708 exprime le produit attendu ainsi qu'une forme tronquée de la séquence fusionnée de RuBisCO. Le CES considère que des éléments permettant de mieux comprendre la genèse de cette deuxième forme aurait dû être apportée. De même, la stratégie de construction basée sur l'introduction de deux ADN-T et sur l'élimination du caractère de résistance au glyphosate n'est pas expliquée. L'analyse comparée de composition chimique des graines et du fourrage de soja montre que la composition chimique des sojas MON 87708 n'est pas différente de celle du soja témoin et des variétés commerciales pour la plupart des composés analysés. Cependant, les résultats obtenus avec les activités d'inhibiteurs trypsiques auraient dû inciter le pétitionnaire à démontrer l'équivalence par des tests statistiques appropriés. En cas de non équivalence, les différences	Please find below the comments of the EFSA GMO Panel to the specific issues raised by the Competent Authority.

Country	Organization	Reference	Comment	GMO Panel response
			observées devraient être discutées. L'analyse des résultats de l'étude d'alimentarité chez le poulet durant 42 jours à partir des tourteaux de sojas MON 87708 permet de conclure que ces tourteaux ne présentent pas de propriétés nutritionnelles différentes de celles des tourteaux de soja témoin. L'analyse des résultats de l'étude de toxicité sub-chronique de 90 jours ne révèle pas d'effet toxique lié à la consommation de tourteaux de sojas MON 87708, cependant étant donné la nature de la modification génétique, il paraît indispensable de tester dans cette étude des sojas traités par le dicamba. Or cette information n'a pas été précisée. De plus, il est fait remarquer que cette étude ne documente pas la sécurité de l'huile destinée à la consommation. En l'absence de ces éléments, le CES estime qu'il ne peut se prononcer sur la sécurité sanitaire des sojas MON 87708 et de leurs produits dérivés. L'Agence nationale de la sécurité sanitaire de l'alimentation, de l'environnement et du travail endosse les conclusions du Comité d'Experts spécialisés « Biotechnologie ». **ENGLISH TRANSLATION** CONCLUDING POINTS Concluding points from the *Comité d'Experts spécialisés 'Biotechnologie' - CES* [Biotechnology	The two T-DNAs transformation strategy is described in detail in: *Komari T, Hiei Y, Saito Y, Murai N, Kumashiro T. (1996) Vectors carrying two separate T-DNAs for co-transformation of higher*

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			expert committee] With regard to the 'molecular' results presented, the transformation event of inclusion in the genome of MON87705 soya plants involves inserting a stable copy of the *dmo* gene into a single locus of the expression cassette. The site of inclusion and the adjoining regions were characterised and the investigation did not raise any questions of health-related safety regarding the soya plants. Soya variety MON 87708 expresses the expected product, together with a shortened form of the inserted sequence of RuBisCO. The CES considers that aspects allowing a better understanding of how this second form is produced should be provided. Similarly, the construction strategy based on introducing two transfer DNA (T-DNA) regions and removing the characteristic of resistance to glyphosate has not been explained. Comparative analysis of the chemical composition of soya beans and soya-bean forage has shown that the composition of MON 87708 soya plants does not differ from that of the control soya plants or from commercial varieties for most of the compounds investigated. However, the results obtained with trypsin-inhibition activity should have led the applicant to demonstrate the equivalence by appropriate statistical tests. In cases of non-equivalence, the differences observed should be discussed.	*plants mediated by Agrobacterium tumefaciens and segregation of transformants free from selection markers. Plant J. 10:165-74.* For more information on the evaluation performed by the EFSA GMO Panel, please see Section 4 of the Scientific Opinion on application EFSA-GMO-NL-2011-93. In relation to the trypsin inhibitor, the test of equivalence could not be performed because of the lack of variation among the non-GM soybean reference varieties. The EFSA GMO Panel evaluated the parameters for which equivalence could not be demonstrated and concluded that no further assessment was needed as their biochemical role is well known and the magnitude of the reported levels lack relevance from a food and feed safety and nutritional point of view (including trypsin inhibitor).

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) Comments and opinions submitted by Member States during the three-months consultation period				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
			Analysis of the results from the feed study in chickens over 42 days using MON 87708 soya cakes enabled the conclusion to be drawn that the nutritional properties of such cakes did not differ from those of the control soya cakes. Analysis of the results from the 90-day study of sub-chronic toxicity did not reveal any toxic effect associated with the consumption of MON 87708 soya cakes. However, given the nature of the genetic modification, it seems essential in this study to test soya plants treated with dicamba. This information was in fact not specified. It has also been noticed that the study does not provide documentary evidence of safety of the oil intended for consumption. In the absence of those items of information, the CES considers that it cannot give a judgement on the health-related safety of MON 87708 soya plants or products derived from them. ANSES, the French Agency for Food, Environmental and Occupational Health & Safety, endorses the conclusions of the CES.	On request of the EFSA GMO Panel, the applicant specified that the test diets in the 90-day and 42-day animal studies were treated with the intended herbicide (additional information received in June 2013).

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) Comments and opinions submitted by Member States during the three-months consultation period				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
France	Ministère de l'Economie (Consommation)	A. General information	(A) Information générale La demande est une première demande d'autorisation de mise sur le marché pour l'alimentation humaine et animale du soja génétiquement modifié MON 87708 et de ses produits dérivés. Elle ne concerne pas sa mise en culture. MON 87708 contient le gène codant l'enzyme DMO (dicamba O-déméthylase), une mono-oxygénase provenant de la bactérie Stenotrophomonas maltophilia (S.maltophilia) qui déméthyle la molécule de l'herbicide dicamba pour former le 3,6 DCSA (3,6-dichloro salicylique acide) et le formaldéhyde. L'enzyme rend ainsi le soja résistant à cet herbicide. Il conviendrait donc également d'évaluer dans le cadre du règlement (CE) N°1107/2009, le métabolisme de ces herbicides quand ils sont appliqués au soja MON 87708. Le dicamba est un herbicide sélectif systémique de la famille des acides benzoïques, qui agit par analogie avec les auxines végétales. Le DCSA est un des métabolites du dicamba chez les végétaux. L'intérêt de la modification génétique est de permettre une lutte plus facile contre les adventices du soja. ENGLISH TRANSLATION (A) General information The request was an initial application for a marketing authorisation for genetically modified	The EFSA GMO Panel takes note of this comment.

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) Comments and opinions submitted by Member States during the three-months consultation period				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
			MON 87708 soya and products derived from it for human food and animal feed. It does not relate to cultivation of the MON 87708 variety. MON 87708 contains a gene coding for the DMO (dicamba O-demethylase) enzyme, a mono-oxygenase from the bacterium *Stenotrophomonas maltophilia* (*S. maltophilia*), which demethylates the herbicidal compound dicamba, to give 3,6-DCSA (3,6-dichloro salicylic acid) and formaldehyde. The enzyme thus makes the soya plant resistant to that herbicide. The metabolism of these herbicides when applied to MON 87708 soya plants should therefore also be assessed in the context of Regulation (EC) No 1107/2009. . Dicamba is a selective systemic herbicide in the benzoic acid family and it acts analogously to plant auxins. DCSA is one of the metabolites from dicamba in plants. The advantage of the genetic modification is that it allows easier control of weeds competing with soya plants.	

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
France	Ministère de l'Economie (Consommation)	D, 01 Description of the trait(s) and characteristics which have been introduced	(D) Informations relatives à la plante génétiquement modifiée (1) La séquence de localisation aux chloroplastes ou CTP (Chloroplast Transit Peptide) est clivée au moment de l'adressage, ce qui conduit à la formation d'une protéine de 367 acides aminés (cette forme est dénommée DMO+27). Cependant, une forme protéique de 339 acides aminés est également produite. Cette forme correspond à l'élimination du CTP, des 27 acides aminés suivant et de la méthionine (elle est dénommée DMO). Le soja génétiquement modifié MON 87708 produit donc deux formes de la protéine DMO qui coexistent (MON 87708 DMO et MON 87708 DMO+27). Considérant que la forme active de l'enzyme est constitué de 3 monomères de DMO, il est fait l'hypothèse que dans le soja MON 87708, le trimère se forme à partir de MON 87708 DMO, de MON 87708 DMO+27 ou d'une combinaison des 2. Aucune expérience ne vient soutenir cette hypothèse et la genèse de la forme MON 87708 DMO n'est pas explicitée dans le dossier du pétitionnaire. ENGLISH TRANSLATION (D) Information about the genetically modified plant. (1) The localisation sequence for translocation into the chloroplasts ('chloroplast transit peptide' or CTP) is cleaved on arrival at that destination, leading to the formation of a protein with 367 amino acids (a form called DMO+27). A form of the	Quantity of the total DMO protein (all forms included) was analysed. This allows the assessment of the allergenic and toxic potential of the protein as present in the plant.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			protein (called DMO) with 339 amino acids is, however, also produced, the latter corresponding to removal of the CTP, the next 27 amino acids and methionine. Genetically modified MON 87708 soya plants therefore produce two forms of the DMO protein (MON 87708 DMO and MON 87708 DMO+27), which coexist. Considering that the active form of the enzyme is composed of three DMO monomers, the hypothesis is made that in MON 87708 soya plants, the trimer is formed from MON 87708 DMO, from MON 87708 DMO+27, or from a combination of the two. No experimental evidence is available to support this hypothesis and formation of the form MON 87708 DMO is not explained in the applicant's dossier.	Soybean MON 87708 expresses two versions of the monomer dicamba mono-oxygenase (DMO) protein, DMO and DMO+27. In relation to the protein used for the safety assessment, please see Section 5.1.2.1 of the Scientific Opinion on application EFSA-GMO-NL-2011-93. The studies provided by the applicant confirmed the structural and functional equivalence of the DMO proteins expressed in soybean MON 87708 with the corresponding proteins expressed in *E. coli*.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
France	Ministère de l'Economie (Consommation)	D, 07.01 Comparative assessment	(7.1-3) Analyse comparative de la composition chimique Dans l'étude présentée, les sojas ont été cultivés sur 8 sites répartis dans différents Etats des Etats-Unis au cours de l'année 2009, selon un plan d'expérience en blocs randomisés avec 4 blocs par site. La variété MON 87708 traitée ou non traitée par le dicamba a été comparée à la variété A3525 dont elle est issue. Les mesures ont également été effectuées sur 14 variétés commerciales cultivées conjointement à la lignée MON 87708 et à son comparateur à raison de 3 de ces variétés par site. Les choix des nutriments et des substances anti-nutritionnelles sont ceux recommandés par l'OCDE*1. L'analyse de composition des échantillons a porté: - pour la plante entière (fourrage), sur sept paramètres proximaux (protéines totales, hydrates de carbones totaux, fibres ADF et NDF, humidité, cendres et lipides) ; - pour la graine, sur les 7 paramètres proximaux précédents, 18 acides aminés, 8 acides gras (C8-C22), la vitamine E, 5 facteurs antinutritionnels (lectine, acide phytique, inhibiteur de trypsine, raffinose et stachyose) et 3 isoflavones (daidzéine, génistéine et glycitéine). Les valeurs en dessous de la LOQ (14 dans les graines) n'ont pas été prises en compte dans l'analyse. Deux types d'analyse de variance basés	

Country	Organization	Reference	Comment	GMO Panel response
			sur des modèles mixtes ont été réalisés successivement pour le soja génétiquement modifié (GM) non traité et pour le soja GM traité avec l'herbicide site par site et tous sites confondus. Ces ANOVA ont pour objectif d'identifier les différences de composition entre la plante GM et le comparateur. Lorsque l'ANOVA « tous sites confondus » révèle une différence significative (erreur de type 1 de 5%), la moyenne mesurée sur la plante GM est comparée à un intervalle de tolérance contenant 99% des valeurs issues de variétés commerciales (avec une confiance de 95%). Les résultats des substances qui présentent une différence significative avec l'ANOVA « tous sites confondus », sont examinés sur chacun des 8 sites. L'approche suivie par le pétitionnaire ne tient pas compte de l'incertitude associée à l'estimation des compositions moyennes de la variété GM ne permettant pas de réaliser un test d'équivalence selon les recommandations de l'EFSA (EFSA, 2010*2). Des différences de concentration de certains composés ont été observés entre les sojas MON 87708 et A3525. Ces différences sont de faible amplitude et sont comprises dans l'intervalle de tolérance établi à partir des variétés commerciales. Elles ne sont pas observées sur plusieurs sites pour les mêmes substances. Des différences significatives sont observées entre la variété GM et témoin pour quelques facteurs	

Country	Organization	Reference	Comment	GMO Panel response
			antinutritionnels (stachyose, acide phytique et inhibiteurs trypsiques). En particulier, les valeurs des activités d'inhibiteurs trypsiques sont augmentés (de 10 à 30%) dans la plante GM par rapport au témoin et les gammes de valeurs sortent des intervalles de tolérance établis à partir des variétés commerciales à la fois pour l'analyse de la combinaison des 8 sites, pour deux sites individuels non traités et pour un site traité. Pour de tels résultats, il serait pertinent de démontrer l'équivalence par un test statistique tel que proposé par l'EFSA. En cas de non équivalence, les différences observées devraient être discutées. Par ailleurs, aucun effet du traitement par le dicamba n'est observé sur les résultats. *1 Consensus document on compositional considerations for new varieties of soybean : Key food and feed nutrients and anti-nutrients, ENV/JM/MONO(2001)15, 30 November 2001. http://www.oecd.org/dataoecd/15/60/46815135.pdf *2 : Statistical considerations for GMOs safety EFSA Journal 2010; 8(1):1250 http://www.efsa.europa.eu/en/efsajournal/doc/1250.pdf **ENGLISH TRANSLATION** (7.1-3) Comparative investigation of chemical	Regarding the statistical analysis of the field trial data, the EFSA GMO Panel requested the applicant to perform additional

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			composition In the study presented, the soya plants are described as grown in 2009 at eight sites in different states of the United States, according to an experimental plan of random blocks (four on each site). The MON 87708 variety, whether or not treated with dicamba, was compared to the A3525 variety from which it is derived. Measurements were also carried out on 14 commercial varieties grown jointly with the MON 87708 variety and its comparator, with three of these varieties on each site. The nutrients and antinutrients chosen were those recommended by the OECD*1. Analysis of the samples' composition related to: - in the case of whole plants (forage), seven basic parameters: total protein, total carbohydrates, fibre (ADF and NDF), moisture content, ash, and lipids. - in the case of soya beans, the seven parameters mentioned above, 18 amino acids, eight fatty acids (C_8-C_{22}), vitamin E, five antinutrients (lectin, phytic acid, trypsin inhibitor, raffinose and stachyose), and three isoflavones (daidzein, genistein and glycitein). The analysis ignored values below the limit of quantification (LOQ: 14 for the soya beans). Two types of variance analysis (both based on mixed models) were carried out successively for the untreated genetically modified (GM) soya and for the GM soya treated with the herbicide, firstly at each site and then with all sites combined. The aim of these analyses of variance (ANOVA) was to identify differences in composition between the GM	statistical analysis according to the methodology described in EFSA (2011). Based on the information available, it is concluded that no differences were identified in the compositional data of forage and seeds obtained from soybean MON 87708 or in its agronomic and phenotypic characteristics that would require further assessment with regard to safety by the EFSA GMO Panel. For more information please see Section 4.1.2. of the Scientific Opinion on application EFSA-GMO-NL-2011-93.

Country	Organization	Reference	Comment	GMO Panel response
			plants and the comparator. Where ANOVA for all the sites combined revealed a significant difference (type 1 error of 5 %), the mean measurement for the GM plants was compared to a tolerance interval containing 99 % of the values from commercial varieties (with a confidence level of 95 %). The results from substances showing a significant difference from the ANOVA for all sites combined were examined for each of the eight sites. The approach followed by the applicant did not take account of the uncertainty associated with estimating the mean composition for the GM variety, making it impossible to carry out an equivalence test in accordance with EFSA's recommendations EFSA, 2010*2). Differences were observed between the soya varieties MON 87708 and A3525 in the concentrations of certain compounds. These differences were small, and were within the tolerance interval found for the commercial varieties. They were not observed, in respect of a given substance, at more than one site. Significant differences were observed between the GM and control varieties in respect of some antinutrients (stachyose, phytic acid and trypsin inhibitors). In particular, the values for trypsin-inhibitor activity were raised (by 10-30 %) in the GM plants, compared with the controls, and the ranges of values found when analysing the combined results for all eight sites, for two untreated sites and for one treated site were	

Country	Organization	Reference	Comment	GMO Panel response
			outside the tolerance intervals that had been established based on commercial varieties. For such results, it would be relevant to demonstrate equivalence by a statistical test, as suggested by EFSA. If found not to be equivalent, the differences observed should be discussed. In addition, the results did not show any effect resulting from the treatment with dicamba. *1 Consensus document on compositional considerations for new varieties of soybean: Key food and feed nutrients and anti-nutrients, ENV/JM/MONO(2001)15, 30 November 2001. http://www.oecd.org/dataoecd/15/60/46815135.pdf *2 : Statistical considerations for GMOs safety EFSA Journal 2010; 8(1):1250 http://www.efsa.europa.eu/en/efsajournal/doc/1250.pdf	
France	Ministère de l'Economie (Consommation)	D, 07.08 Toxicology	(7.8)Toxicologie Un essai de toxicité par administration unique de la protéine extraite du soja a été réalisé chez la souris albinos CD-1. Aucune anomalie clinique, baisse de croissance ou de consommation alimentaire, lésion macro ou microscopique n'ont été relevée après 14 jours d'observation quotidienne. Cette étude permet de conclure qu'à la dose de 140 mg/kg poids corporel, aucun effet néfaste n'est observé chez l'animal. Toutefois pour cette étude, le choix	

Country	Organization	Reference	Comment	GMO Panel response
			de la dose mise en œuvre aurait du être justifié. (7.8.4) Étude de toxicité sub-chronique Une étude pour évaluer la toxicité potentielle sub-chronique des tourteaux de soja a été réalisée, selon la ligne directrice OCDE 408, sur des groupes de 12 rats Sprague Dawley par type de traitement et par sexe. Le protocole comprend 8 groupes recevant chacun pendant 90 jours une alimentation contenant des tourteaux de soja incorporés à raison de 15 ou 30%. Les sojas testés sont le soja MON 87708, le soja A 3525 (comparateur) et deux lignées commerciales. Les rats ayant reçu le soja MON 87708 ont été comparés à ceux ayant reçu le soja témoin. Des examens cliniques ont été conduits durant l'essai. Des échantillons de sang et d'urine ont été prélevés au moment du sacrifice (semaine 13). L'analyse statistique des résultats des paramètres hématologiques et biochimiques repose sur des tests de différence paramétriques entre traitements. Seules les comparaisons entre les lots test MON 87708 et témoin A3525 ont été réalisées. La procédure exacte, en particulier le modèle statistique utilisé, n'est pas précisée. Aucune mortalité n'a été observée. Aucune différence significative n'a été relevée dans la croissance pondérale, la consommation alimentaire et les observations cliniques. Parmi les paramètres biochimiques et hématologiques, quelques différences	

Country	Organization	Reference	Comment	GMO Panel response
			statistiquement significatives isolées et sans signification biologique sont observées. Les résultats des 4 groupes de références (animaux nourris avec les lignées commerciales) n'ont pas été intégrés dans l'analyse statistique, leur examen montre des valeurs moyennes proches de celles des groupes test et témoin. Les résultats de cette étude ne révèlent donc pas d'effet toxique lié à la consommation de soja MON 87708. Toutefois, considérant que le matériel testé doit être aussi proche que possible du produit final tel que consommé, il est souhaitable que les sojas testés soient traités au dicamba. Cette information n'est pas précisée. De plus, il est souligné que cette étude ne documente pas la sécurité de l'huile issue du soja MON 87708 destinée à l'alimentation humaine et que la mise en œuvre d'un faible nombre d'animaux (12 rats de chaque sexe par groupe), augmente le risque d'avoir une puissance insuffisante pour les tests statistiques. **ENGLISH TRANSLATION** (7.8) Toxicology A toxicity trial was carried out by a single administration to albino CD-1 mice of the protein extracted from soya. No clinical abnormalities, reduction in growth or in food consumption, or macro- or microscopic lesions had been noted by the end of 14 days' observation on a daily basis. That study enabled the conclusion to be drawn that at a dose of 140 mg/kg of body weight, no adverse effects were observed in the animals. Nevertheless,	On request of the EFSA GMO Panel, the applicant supplied (additional information March 2012) a 28-day oral toxicity study with a mixture of the MON 87708 DMO protein and MON 87708 DMO+27 proteins supplied in the diet in approximately the same ratio they occur in soybean MON 87708 (*i.e.*, 2:3). Administration of DMO proteins did not induce any deaths or clinically relevant findings at any of the dose levels. There were no relevant differences in mean body weight, body weight gain and food consumption. The only statistically significant difference in clinical

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			justification should have been given for the choice of dose used in that study. (7.8.4) of sub-chronic toxicity A study was carried out to assess the potential sub-chronic toxicity of soya cake, in accordance with the guidelines in OECD 408, using one group of 12 Sprague Dawley rats of each sex for each type of treatment. The protocol comprised eight groups, each given feed containing either 15 % or 30 % of soya cake, for 90 days. The soya plants tested were the MON 87708 variety, A3525 variety (the comparator) and two commercial varieties. The rats which had been given MON 87708 soya were compared with those which had been given the control soya. Clinical examinations were carried out during the trial. Samples of blood and urine were taken when the rats were killed (week 13). Statistical analysis of the results obtained for haematological and biochemical parameters relied on parametric difference tests comparing the treatments. The only comparisons were between test batches of MON 87708 and the control, A3525. The exact procedure, and in particular the statistical model used, was not specified. No mortality was observed, and no significant difference was noted in weight gain, food consumption or the clinical observations.	pathology parameters assessed was an incidental higher mean absolute neutrophil count in males of the high-dose group, which was mainly driven by an an unusual high-value in one animal showing incidental inflammation of the skin. A slightly significantly higher mean spleen weight (relative to body weight) was seen in in male group given the high dose in comparison to control group; this was not associated with histopathologic changes and considered the expression of biological variability. No macroscopic or microscopic findings were reported in the examined organs and tissues that could be attributed to the test material. The highest dose administered in this study, i.e. 174 mg/kg bw per day in males and 179.7 mg/kg bw per day in females, is considered the NOAEL. Assuming an intake of 200 g of soybean per 70 kg adult per day in the EU and that all soybean consumed is derived from soybean MON 87708, the daily intake of DMO proteins would be in the region of 110 μg/kg bw. The highest estimated intake of DMO proteins in adults is about 1000-fold lower than the NOAEL from the 28-day feeding study. The 90-day feeding study in rats was performed according to OECD standard procedures on toasted and defatted soybean meal. The Member State points out that the 90-day feeding study is not performed with full fat soybean and therefore do not supply safety on the modified soybean oil intended for human food purposes. However, the oil components have been characterised in the compositional studies and these studies revealed no biologically relevant changes in the composition of the soybean oil from MON 87708 as compared to A3525, not requiring therefore an animal feeding study supporting this assessment. Based on the chemical analysis of the oil in the soybean seeds the EFSA GMO Panel concluded that it is highly unlikely that oil from soybean MON 87708 would be any less safe

Country	Organization	Reference	Comment	GMO Panel response
			Among the biochemical and haematological parameters, a few isolated statistically significant differences were observed. The results from the four reference groups (animals fed the commercial varieties) were not included in the statistical analysis; examination of them showed their mean values to be close to those of the test and control groups. The results from this study thus did not reveal any toxic effect associated with consumption of MON 87708 soya. Nevertheless, considering that the substances tested should be as close as possible to the final product in the form that will be consumed, it is desirable for the forms of soya tested to be treated with dicamba. This information was not specified. In addition, it is emphasised that this study does not provide documentary evidence on the safety of MON 87708-derived oil intended for human food purposes, and that making use of a small number of animals (12 rats of each sex per group), increases the risk of having inadequate power for the statistical tests.	or nutritious than oil from soybean A3525. In relation to the statistical analysis performed by the applicant and the herbicide treatments of the diets tested, the applicant provided additional information in June 2013 upon request of the EFSA GMO Panel.
Germany	Federal Agency for Nature Conservation	General comments	The Federal Agency for Nature Conservation (BfN) considers that further information is required before the risk assessment of EFSA-GMO-NL-2011-93 can be finalised (see specific comments). In particular the environmental risk assessment (e.r.a.) and the monitoring plan should be amended. Information (data and data analyses) provided on phenotypic evaluation, composition, and toxicology	Considering the intended uses of soybean MON 87708 excluding cultivation, the EFSA GMO Panel considers that the information provided relating to the environmental risk assessment is sufficient. The EFSA GMO Panel comments on the scientific content of the monitoring plan. EFSA has published guidance and scientific opinion on post-market environmental monitoring (PMEM) (EFSA, 2011). The EFSA GMO Panel is of the opinion that the information supplied by the applicant is in line with the guidance on PMEM.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			is insufficient and conclusions of equivalence of MON 87708 soybean and conventional soybean and on food and feed safety based on this information are premature. The applicant's proposal for an environmental monitoring plan does not meet the objectives defined in Annex VII of Directive 2001/18/EC and the supplementing guidance notes (2002/811/EC) and therefore should be amended.	Please find below comments of the EFSA GMO Panel to the specific issues raised by the Competent Authority.
Germany	Federal Agency for Nature Conservation	D, 03 Information on the expression of the insert	Expression of the dicamba mono-oxygenase (DMO) protein was assessed in various tissues of MON 87708 soybean through ELISA from samples collected from eight locations in the USA in 2008 (CBI: Beyene and Niemeyer 2010a). Material was produced under the same production plan (PPN-09-061) as material for composition and phenotype analysis (seed D.4. and D.7.1.) and therefore principally the same comments apply here. Unlike with composition and most of the phenotypic characteristics the expression study of MON 87708 DMO did not assess the impact of the complementary herbicide as recommended by EFSA (2011). Since protein expression in plants can be affected by climatic conditions, soil fertility, agricultural practice or unknown gene-environment interactions, data from a single season give a rough estimate of expression levels only. A more robust and reliable data basis should, therefore, include data from more than one field season at the same location (with six locations representing different environmental conditions) to integrate	Dicamba herbicide treatment was applied; this is in line with the agricultural practice for which the plants were specifically developed. The promoter (PC1SV) controlling the expression of *dmo* is a strong constitutive promoter (Maiti and Shepherd, 1998) and is not expected to be influenced by dicamba treatment. Furthermore, there are no indications that the DMO protein is toxic or allergenic. The EFSA GMO Panel considers that the eight field sites, located in six clearly indicated states in USA, are representative of regions where soybean is grown commercially.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			possible differences in expression values triggered by differences in ecological conditions and include data from material grown with and without the complementary herbicide.	
Germany	Federal Office of Consumer Protection and Food Safety	D, 02 Information on the sequences actually inserted or deleted	For the sake of clearness, Figure 2 in Tu (2011b) should be complemented by a legend which assigns the position to each feature (e.g., 5' flanking region, junction I, transgenic sequence, etc.). Tu, H. (2011b) Updated bioinformatics evaluation of MON 87708 utilizing the AD_2011, TOX_2011, PRT_2011, EST_2011, NT_2011, and NR_2011 databases, Monsanto Technical Report, RAR-2011-0073, 1-326.	The legend in Figure 2 of RAR-2011-0073 could be misunderstood as it shows the nucleotide sequence of the pre-insertion site ("flanking sequences"), which was used to analyse possible disruption of known coding sequences or regulatory elements (see Appendix III in Technical dossier). There are thus no transgenic sequences in Figure 2, which is also evident from Appendices 28-30 of RAR-2011-0073. The nucleotide sequence of the inserted T-DNA and the DNA sequences at the 5' and 3' junctions of the MON 87708 are shown in Figure 11 of MSL0023278.
Germany	Federal Agency for Nature Conservation	D, 04 Information on how the GM plant differs from the recipient plant in:	PartI The conclusions regarding the phenotypic and ecological equivalence (reproduction, dissemination, and survivability) of herbicide resistant MON 87708 soybean with conventional soybean are based on an evaluation of agronomic parameters and environmental interactions during field studies in the USA in 2009 (CBI: Laufer and Bommireddy 2010a) and supplemented with laboratory experiments on dormancy and germination (CBI: Laufer and Kendrick 2010a) and pollen viability (Phillips and Kendrick 2010). Phenotypic and agronomic characteristics and ecological interaction data were collected from eight sites in 2009, dormancy and germination was assessed from seeds produced at three sites in 2008 and pollen viability was assessed from flowers at one site in 2008. At each site, three to four	The agronomic characteristics of soybean MON 87708 as compared to soybean A3525 is based on a comprehensive set of data and not on individual parameters. The EFSA GMO Panel agree with Federal Agency for Nature Conservation that the data obtained do not indicate a potential for differences in reproduction, dissemination, and survivability of the MON 87708 soybean. The EFSA GMO Panel also agrees that plot sizes in field trial cannot be as large as fields for commercial production of soybean. Maintenance pesticides were used at the various field trial sites but importantly, the same treatments were given to all materials. In addition additional blocks with soybean MON 87708 were sprayed with dicamba. All field trial sites were in the soybean-growing region of the USA. The EFSA GMO Panel considers that the eight field sites, located in six clearly indicated states in USA, are representative of regions where soybean is grown commercially.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			replicated plots of MON 87708, a conventional soybean variety with a similar genetic background to the test plant (A3525), and three commercial references of a pool of 14 (Laufer and Bommireddy 2010a), four references of a pool of eight (Laufer and Kendrick 2010a) or four references (Phillips and Kendrick 2010) were planted using a randomized complete block design. Further data and analysis are required before phenotypic and ecological equivalence can be concluded. This is for several reasons: I. Although the agronomic characteristics addressed do not indicate a potential for differences in reproduction, dissemination, and survivability of MON 87708 soybean, the selected parameters themselves cannot sufficiently indicate such changes. II. Data sets are based on a field design which is – because of the small plot size – not comparable to common agricultural practice. Pesticides were applied between once only and six times depending on the site (dossier Appendix I Table 3). It cannot be excluded that both aspects interfered with the collection of ecological interaction data (e.g. arthropod abundance). III. The representativeness of the trial sites was not demonstrated and their location was not indicated. The following points leave it open whether the trial sites cover a sufficiently broad range of environments for the various parameters:	The test of difference of phenotypic and agronomic characteristics identified statistically significant differences between soybean MON 87708 and its conventional counterpart for only one endpoint (100 seed weight). Both soybean MON 87708 sprayed and not sprayed with dicamba had a lower 100 seed weight than its conventional counterpart (in both cases 14.6 g vs. 15.6 g). The equivalence test indicated that all the analysed characteristics fell within the equivalence limits established from the non-GM soybean reference varieties, except for 100 seed weight (100 seed weight: 15.0-17.7 g). The starting materials were secured by chain of custody documentation, and the presence or absence of the MON 87708 event was checked with PCR methodology. The EFSA GMO Panel has not asked for additional PCR studies. Considering the intended uses of soybean MON 87708 excluding cultivation, the EFSA GMO Panel considers that the field trial design and the information provided relating to the assessment of agronomic traits are sufficient to carry out the environmental risk assessment of soybean MON 87708. From the data presented in the application, there is no indication of an increased persistence and invasiveness potential of soybean MON 87708 compared to conventional soybean and it can be considered that soybean MON 87708 has no altered survival, multiplication or dissemination characteristics compared to its conventional counterpart, except under application of dicamba-based herbicides (see Section 6.1.1.1 of the Scientific Opinion of application EFSA-GMO-NL-2011-93).

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			a) Historical weather data are missing; b) Raw data for abiotic and disease stress together with information on prevailing pest and disease pressure (baseline) are missing; c) Appendix I (eight sites) and Appendix II (four sites) of the dossier both claim that their set of trial sites is representative, although there are five sites in Appendix I not covered by Appendix II and one site in Appendix II not covered by Appendix I. IV. Plant height data were collected from five representative plants per plot only and pubescence - unlike in comparable studies - was not assessed. V. The identity of starting material was not sufficiently verified. Starting material was tested for MON 87708 and a second soybean event grown at the sites, but not for contamination with other gm soybean events (certificates of analysis are missing). VI. The complementary herbicide dicamba was not applied for the production of MON 87708 material that was assessed for dormancy and germination and pollen viability as suggested by EFSA (2011).	

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) Comments and opinions submitted by Member States during the three-months consultation period				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
Germany	Federal Agency for Nature Conservation	D, 04 Information on how the GM plant differs from the recipient plant in:	PartII With regard to a final assessment, further information is required, because the information provided is not considered sufficient to support the conclusion of a substantial equivalence of MON 87708 soybean to conventional soybean, which is the basis of further conclusions in application EFSA-GMO-NL-2011-93. The applicant should be asked to provide a robust and reliable data basis for reproduction, dissemination, and survivability to demonstrate substantial equivalence of MON 87708 and conventional soybean. Field studies with ecology-based parameters such as frost tolerance, seed dormancy, time span of pollen emittance or duration of pollen viability of MON 87708 soybean tested under field conditions should be included in the application. Relevant data should be collected for MON 87708 treated with and without the complementary herbicide. Data should account for several locations and growing season, e.g. a minimum of three growing seasons and six locations representing different environmental conditions. The environmental conditions should be documented and provided with the application to assess their possible effects on the considered parameters. Differences between test and control should be assessed relative to non-gm references and in case of individual-site analyses relative to site-specific reference ranges to account for site by genotype interactions. A summarising statistical analysis should address the between-site variation	The EFSA GMO Panel notes that the scope of application EFSA-GMO-NL-2011-93 is for food and feed, import and processing. Regarding the extent of field trial and their design, the applicant has followed the guidance given by the EFSA GMO Panel (EFSA, 2011). On request from the Panel the applicant provided further statistical analysis as described in the Guidance for risk assessment of food and feed from genetically modified plants (EFSA, 2011). Considering the intended uses of soybean MON 87708 excluding cultivation, the EFSA GMO Panel considers that the field trial design and the information provided relating to the assessment of agronomic traits are sufficient to carry out the environmental risk assessment of soybean MON 87708. From the data presented in the application, there is no indication of an increased persistence and invasiveness potential of soybean MON 87708 compared to conventional soybean and it can be considered that soybean MON 87708 has no altered survival, multiplication or dissemination characteristics compared to its conventional counterpart, except under application of dicamba-based herbicides (see Section 6.1.2.1 of the scientific opinion).

Country	Organization	Reference	Comment	GMO Panel response
			of the data. We recommend including data on the occurrence of volunteers during cultivation of MON 87708 soybean at all sites and following the statistical approach of EFSA in its Scientific Opinion on statistical considerations for the safety evaluation of GMOs (EFSA 2010). In agreement with the 'step by step' principle field results including post-monitoring reports from the several releases of MON 87708 in the USA, Argentina, Chile, and Canada between 2005 and 2008 shall be provided.	
Germany	Federal Agency for Nature Conservation	D, 07.01 Comparative assessment	The compositional analysis of MON 87708 is based on forage and seed material from eight sites in the USA in 2009 grown without and with dicamba (CBI: Harrigan et al. 2010a; Harrigan et al. 2010b). At each site, four replicated plots of MON 87708, the conventional soybean variety A3525, and three commercial references (of a pool of 14 references) were planted using a randomized complete block design. According to the applicant, the results support a conclusion that MON 87708 soybean is compositionally equivalent to conventional soybean. Since both compositional studies share the same production plan as for phenotype evaluation (CBI: Laufer and Bommireddy 2010a) some of the deficits listed under D.4. also apply here, namely (i) to demonstrate the representativeness of the selected trial sites and to indicate their location; and (ii) to verify the starting material and test for contamination with other gm soybean events. Further deficits are (iii) that minerals and vitamins (apart from vitamin E) were not analysed although	The EFSA GMO Panel is of the view that the field trial sites choosen by the applicant are representative for sites where soybeans are commercially produced in the USA. The seed materials planted were guaranteed by chain of custody documentation. The applicant analysed the harvested material for the presence/absence of the MON 87708 event and also analysed for constituents recommended by OECD (supplemented with compounds linked to the genetic modification). The analytical data for each replicate of each compound and each material (MON 87708, A3525 and fourteen reference varieties) is available. The EFSA GMO Panel is of the opinion that the information provided by the applicant is in line with the data required in the EFSA Guidance (EFSA, 2011). Regarding the extent of field trial and its design, the applicant has followed the guidance given by the EFSA GMO Panel (EFSA, 2011). On request from the Panel the applicant provided further statistical analysis as described in the Guidance for risk assessment of food and feed from genetically modified plants (EFSa, 2011). On request of the EFSA GMO Panel, the applicant supplied the Production Plan PPN-09-061 for the field trial in the USA in 2009,

Country	Organization	Reference	Comment	GMO Panel response
			soybean is considered a significant source of e.g. potassium and magnesium, of bioavailable iron and water-soluble vitamins in the animal feed diet (Baker, 2000); and (iv) that site by genotype interactions were not adequately considered in individual-site analyses because tolerance intervals used were calculated using reference data from all eight sites rather than the three references from the respective sites only. With regard to a final assessment, further information is required, because the information provided is not considered sufficient to support the conclusion of a compositional equivalence of MON 87708 soybean and conventional soybean, which is the basis of further conclusions in application EFSA-GMO-NL-2011-93. The applicant should be asked to provide a more robust and reliable data basis for composition to demonstrate equivalence of MON 87708 soybean and conventional soybean. Plant material should be sampled from several locations and growing seasons, e.g. a minimum of three growing seasons and six locations representing different environmental conditions and the herbicide resistant MON 87708 should be grown with and without dicamba. Site-specific tolerance intervals should be used in the individual-site analyses to account for site by genotype interactions. Criteria on which the representativeness of locations has been established should be given and the environmental conditions should be documented and provided with the application to assess their	which were used to grow the materials for the comparative compositional and phenotypic/agronomic studies.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			possible effects on the considered parameters. Compositional analyses of samples shall include minerals and further vitamins. A summarising statistical analysis should address the between-site variation of all parameters. We recommend following the statistical approach of EFSA in its Scientific Opinion on Statistical considerations for the safety evaluation of GMOs (EFSA 2010). Baker, D.H. (2000): Nutritional constraints to use of soy products by animals. Pp. 1-12. In Soy in animal nutrition. J. K. Drackley (ed.) Federation of Animal Science Societies, Savoy, IL.	
Germany	Federal Agency for Nature Conservation	D, 07.08 Toxicology	D.7.8.1. Safety assessment of newly expressed protein DMO isolated from MON 87708 seed was used for protein characterization (CBI: Wang et al. 2010) and applied in further studies (CBI: MSL22527, Burge et al. 2010), but not for testing substrate specificity which used DMO isolated from E. coli (CBI: Burzio and McCann 2010). Some experimental details and further information is requested from the applicant: (i) The SOP BR-ME-1244 for the DMO assay and in particular information about the source of the ferredoxin and reductase component is missing; (ii) A representative table is missing for the isolation of DMO from MON 87708 seed with readings for specific activity, enrichment factor and yield after each purification step; (iii) Specific activities reported for various DMO preparations from MON 87708 and E. coli should be compared to check and confirm the quality of the material used in the	Comments to paragraph 1 and 2 is required In relation to the protein used for the safety assessment please see Section 5.1.2.1 of the Scientific Opinion on application EFSA-GMO-NL-2011-93. The studies provided confirmed the structural and functional equivalence of the DMO proteins expressed in soybean MON 87708 with the corresponding proteins expressed in *E. coli*. With regard to the enzymatic activity studies and in addition to the information included in the original applicantion, please note that additional information on the topic were provided in July 2012 and November 2012. Regarding the acute toxicity study with the DMO proteins, the EFSA GMO Panel considers that acute toxicity testing of newly expressed proteins is of little additional value to the risk assessment of the repeated human and animal consumption of food and feed derived from GM plants. On request from the EFSA GMO Panel, the applican supplied (add information received in March 2012) a 28-day oral toxicity study with a mixture of the

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			respective studies. Substrate specificity of DMO was tested with five aromatic compounds which occur in soybean and dicamba as control (CBI: Burzio and McCann 2010). Comparing dicamba and o-anisic acid in a separate experiment it was concluded that the two chlorine atoms in dicamba are required for substrate binding. Because chlorinated compounds similar to dicamba are limited in plants and other eukaryotes the applicant considers it unlikely for MON 87708 DMO to catalyze the conversion of endogenous substrates. Some experimental details are missing and further experiments and evaluation is required to complement the assessment on the capability of the newly expressed enzyme to convert alternative substrates: (i) The study does not provide the specific activity (units/mg protein) of the used DMO preparation with dicamba as substrate. This is required to compare values reported for different DMO preparations (see comments on Wang et al. 2010) and to verify the quality of the protein material used in the experiment; (ii) Since specific activities reported for the DMO enzyme are relatively low a prolonged incubation period for possible conversion of compounds of about 1 hour rather than 15 minutes is preferred; (iii) Compounds applied for pest management in soybean cultivation should be considered as possible substrates as well; (iv) Also, the range of naturally occurring compounds as possible substrates for DMO should be reconsidered. None of the compounds tested are similar to dicamba with respect to the two chloride	MON 87708 DMO protein and MON 87708 DMO+27 proteins supplied in the diet in approximately the same ratio they occur in soybean MON 87708 (*i.e.*, 2:3). Administration of DMO proteins did not induce any deaths or clinically relevant findings at any of the dose levels. There were no relevant differences in mean body weight, body weight gain and food consumption. The only statistically significant difference in clinical pathology parameters assessed was an incidental higher mean absolute neutrophil count in males of the high-dose group, which was mainly driven by an an unusual high-value in one animal showing incidental inflammation of the skin. A slightly significantly higher mean spleen weight (relative to body weight) was seen in in male group given the high dose in comparison to control group; this was not associated with histopathologic changes and considered the expression of biological variability. No macroscopic or microscopic findings were reported in the examined organs and tissues that could be attributed to the test material. The highest dose administered in this study, i.e. 174 mg/kg bw per day in males and 179.7 mg/kg bw per day in females, was considered the NOAEL. Assuming an intake of 200 g of soybean per 70 kg adult per day in the EU and that all soybean consumed is derived from soybean MON 87708, the daily intake of DMO proteins would be in the region of 110 μg/kg bw. The highest estimated intake of DMO proteins in adults is about 1000-fold lower than the NOAEL from the 28-day feeding study.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			groups which are bonded to the aromatic ring in para position and important for catalysis. However, the chloride groups might be replaced by hydroxyl-groups, and respective natural compounds should be tested. Acute toxicity of DMO isolated from MON 87708 was tested by oral administration of a single dose to a group of five male and five female mice using bovine serum albumin as control followed by observation for 14 days and subsequent gross necropsy (CBI: MSL22527, 2010). According to the study there were no treatment-related effects on survival, clinical observations, body weight, body weight gain, food consumption or gross pathology. Some further information is requested from the applicant: (i) The pre-dose activity of the DMO from MON 87708 should be compared with other reported values or values reported for other DMO preparations to check and confirm the full activity of the used material; (ii) Composition and source of main ingredients of the standard rodent diet #5002 are not specified and results of the analysis for environmental contaminants are missing. If main ingredients were from transgenic crops this could have masked effects of the tested substance; (iii) Two clinical findings with individual males (DMO-treatment) and a significant mean weight increase of the male DMO-treatment group were not regarded treatment-related amongst others because similar findings were not observed within the female group. Since toxic effects can be sex-related the applicant is requested to reconsider the study's conclusion.	

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) Comments and opinions submitted by Member States during the three-months consultation period				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
Germany	Federal Agency for Nature Conservation	D, 07.08 Toxicology	D.7.8.4. Testing of the whole GM food/feed The 90-day feeding study in rats (CBI: MSL22868, 2010) has got a couple of weak points: (i) The study did not test and compare soybean meal from MON 87708 grown with and without the complementary herbicide although MON 87708 is herbicide resistant; (ii) Test and control and reference varieties were produced at different locations. Following the specifications for phenotype and compositional studies the test material for feeding studies should be derived from the same location; (iii) Results of the molecular identification of test and control substances are missing. None of the substances (soybean meals of MON 87708, A3525, and reference varieties) or the prepared diets were analysed for contamination with other gm soybean varieties; (iv) Composition and source of main ingredients of the standard rodent diet #5002 are not specified. If they were from transgenic crops this could have masked effects of the tested soybean meal; (v) Based on the analysis of their composition all of the formulated diets were accepted for the study. However, the study ignores that test, control and reference-1 diets with 30% soybean meal – although within standard certification limits – contained less cadmium and lead and considerable less arsenic and malathion (pesticide) than the respective diets with only 15% soybean meal (Appendix C). Differences could be due to one of the main ingredients of the rodent diet #5002 which was substituted to a larger extent in the diets with 30% soybean meal. The differing	The EFSA GMO Panel notes that the molecular characterisation of soybean MON 87708 provided no indications of unintended effects of the genetic modification, and that no differences were identified in the compositional data of forage and seeds obtained from soybean MON 87708 or in its agronomic and phenotypic characteristics that would require further assessment with regard to safety by the EFSA GMO Panel. Nevertheless, the applicant presented a 90-day and a 42-day animal feeding studies that were assessed by the EFSA GMO Panel. As indicated in the Scientifi Opinion, the result of a 90-day feeding study in rats with diets containing toasted defatted soybean meal from soybean MON 87708, its conventional counterpart or any of two non-GM soybean varieties did not raise safety concerns. The compositional data indicating nutritional equivalence was corroborated by the chicken study. For more information on the 90-day and 42-day animal studies, please see Sections 5.1.2.3a and 5.1.2.3b of the Scientific Opinion on application EFSA-GMO-NL-2011-93. In relation to the treatments of the diets fed to the animals please see additional information received in June 2013. In relation to the comment revelant for the molecular characterisation of the MON 87708 and other GM events, a few materials were omitted from analysis because it was identified that they were contaminated by other GM events. Rodent diet #5002 is a commercial products and its composition is available at the website of the feed producer (as DMO-producing GM events were not on the market, any feed that contains GM material will not contain material that includes DMO).

Country	Organization	Reference	Comment	GMO Panel response
			composition of the diets might have interfered with MON 87707-related effects and therefore dismissing some of the significant findings on the ground of no dose-response relationship is not convincing. The applicant is requested to discuss this issue; (vi) Comparing data from the present study with historical control data derived from other studies is questionable since the exact experimental diet composition (in particular the origin of the remaining 70% or even 85% feed ingredients) presumably varies from batch to batch; this might influence the height of values and thereby artificially broad the range of control data when compiled. The applicant is asked to carry out another subchronic feeding which is devoid of the listed deficiencies. Because of shared sources for starting material and common aspects in design and analytics the 42-day broiler feeding study (CBI: MSL22551, 2010) has similar deficits: (i) The test substance was not grown with and without the complementary herbicide; (ii) Test and control and reference material was not produced at the same location; (iii) Neither starting material nor diets were tested for contamination with gm soybean varieties other than MON 87708. (iv) The identity and source of main ingredients is not specified. (v) Soybean meal but not the formulated diets were subjected to mycotoxin, microbiological, and pesticide analyses. Because of the mentioned deficiencies both feeding studies are not suited to support the conclusion that MON 87708 is as safe as conventional soybean	Risk assessment of plant protection products is not within the remit of the EFSA GMO Panel.

Country	Organization	Reference	Comment	GMO Panel response
			in terms of food and feed safety nor do they support the applicant's claim of the absence of any unanticipated or pleiotropic effects linked to the genetic modification.	
Germany	Federal Agency for Nature Conservation	D, 08 Post-market monitoring of GM food/feed	The data provided to show the human and animal safety of MON 87708 soybean on the basis of its equivalence to conventional soybean (except for the introduced trait) are not sufficient. Depending on further information requested above, a post-market monitoring of GM food/feed might be required. In this case, the applicant is further requested to explain how the post-market monitoring of MON 87708 soybean in mixed GMO commodities imported, processed or used for food/feed is realised. This is required because the monitoring of a GMO must be carried out on a case-by-case basis (Directive 2001/18/EC) with regard to species characteristics, modified traits, the intended use and the degree of exposition. Specific GM product quantities should be provided to estimate the degree of exposition. In case of mixed commodities, according to the precautionary principle, each imported and processed commodity must be assumed to contain any in EU approved GM soybean and consequently all parameters identified for the different GM soybean products should then be monitored.	The risk assessment concluded that no data have emerged to indicate that soybean MON 87708 is any less safe than its conventional counterpart. In addition, soybean MON 87708 is as nutritious as non-GM soybeans. Therefore, and in line with the Guidance Documents (EFSA, 2006a, 2011a), the EFSA GMO Panel is of the opinion that post-market monitoring of the GM food/feed is not necessary.
Germany	Federal Agency for Nature Conservation	D, 12.01 General	PartI The scope of this application is for import, processing, and all uses for food and feed. The	The EFSA GMO Panel comments on the scientific content of the monitoring plan. EFSA has published guidance and scientific opinion on post-market environmental monitoring (PMEM) (EFSA, 2011). The EFSA GMO Panel is of the opinion that the information

Country	Organization	Reference	Comment	GMO Panel response
			appli-cant provides an environmental monitoring plan, which remains very general and only covers adverse effects that may occur during handling and processing but fails to address areas such as effects resulting from loss and spillage of viable MON 87708 soybean. As indicated in D.7.11. the monitoring of MON 87708 soybean must be carried out on a case-by-case basis (Directive 2001/18/EC). Since traders may commingle MON 87708 soybean with other commercial GM soybean imported, processed or used for food/feed, the applicant is requested to explain how the monitoring will be designed to distinguish between potential adverse effects caused by MON 87708 soybean and those caused by other GM soybeans. For both general surveillance and case specific monitoring more details are requested with regard to the following issues: • Monitoring parameters: The notifier is requested to present for each parameter a detailed statement of the parameter definition, the observation methods (collection and analysis of samples with references), the frequencies of observations (time and number of visits to collect data) and the monitoring locations including number and size. Identification of relevant monitoring parameters should be based on potential risks (Hilbeck et al. 2008) and legal protection targets (Kowarik et al. 2008) that might be affected by the GM crop, for instance, species, habitats, particularly sensitive habitats, soil features and functions, biodiversity,	supplied by the applicant is in line with the guidance on PMEM. Please refer also to Section 6.1.2. of the scientific opinion.

Country	Organization	Reference	Comment	GMO Panel response
			ecosystem structures and functions, non-gm and organic farming. • Sampling methodologies: A basic prerequisite for comparing GMO monitoring data is the use of appropriate standard detection or analytical methods. Several standards specific for GMO monitoring are provided by the Association of German Engineers (VDI 2011). The implementation of these guidelines is recommended by the Commissions' Working Group on Monitoring. At present, the following VDI guidelines concerning monitoring methods to detect ecological effects of GMO are available: basic principles and strategies (VDI 4330, Part 1), pollen monitoring (VDI 4330, Part 3, 4), collection and preparation of plant samples for molecular biological analysis (VDI 4330, Part 5), PCR-methods for the detection of genetically modified nucleic acids (VDI 4330, Part 7), vegetation surveys (VDI 4330, Part 9), floristic mapping of genetically modified plants (GM plants), their crossing partners, and their hybrid offspring (VDI 4330, Part 10), immunochemical detection of insecticidal Bt proteins from genetically modified crops in soil samples and plant residues (VDI 4330, Part 11), monitoring of butterflies and moths (VDI 4330, Part 13). These VDI guidelines are available in German and English and can be applied, if appropriate. • Determination of the baseline status and/or reference areas (defined after 2002/811/EC) of the receiving environment.	

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) **Comments and opinions submitted by Member States during the three-months consultation period**				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
Germany	Federal Agency for Nature Conservation	D, 12.01 General	PartII • Spatial monitoring designs as to where the monitoring will be carried out and over what area. The monitoring should be run in regions, where MON 87708 soybean will be transported, processed or used. • In case of monitoring data being collected by external persons, institutions or networks other than the applicant, binding agreements/contracts with third parties are requested which clearly determine what data are provided and how these data are made available. • Methods of data analysis including statistical methods. • Application of the concept of adverse effects and environmental damages: The results of data analysis have to be assessed in order to determine whether observed changes may be classified as adverse effects impairing the environment or certain parts of the environment. For this purpose, a sound concept of environmental damages based on transparent operational criteria has to be applied. Adverse environmental effects can only be determined if they are related to certain relevant protection goals (e.g. protection of a natural resource such as a population of an endangered species). Damage occurs if the protection goal is significantly adversely affected. The identification of a significant adverse environmental effect should consider both effect intensity (e.g. extent of loss)	The EFSA GMO Panel comments on the scientific content of the monitoring plan. EFSA has published guidance and scientific opinion on post-market environmental monitoring (PMEM) (EFSA, 2011). The EFSA GMO Panel is of the opinion that the information supplied by the applicant is in line with the guidance on PMEM. Please refer also to Section 6.1.2. of the scientific opinion.

Country	Organization	Reference	Comment	GMO Panel response
			and the value of the impaired protection goal (e.g. protection of a certain rare species of high value) (Kowarik et al. 2008, Bartz et al. 2009). • The time-period of monitoring needs to be sufficient to detect delayed or long-term adverse effects. Therefore, it may be necessary to extend the monitoring of certain parameters beyond the period of the consent. The monitoring should serve as an early warning system. It should be "relevant to and suitable for a rapid assessment and implementation of measures to reduce any consequences to the environment" (Council Decision 2002/811/EC). The monitoring plan fails to meet this goal but only presents a general idea about how the monitoring might be carried out. Thus, the monitoring plan does not meet the objectives defined in Annex VII of Directive 2001/18/EC and the supplementing guidance notes (2002/811/EC). It requires further specification and amendment. The Federal Agency for Nature Conservation is of the opinion that a detailed monitoring plan has to be provided before consent can be given. There are gradual differences in the predictability among effects and therefore gradual transitions between case-specific monitoring and general surveillance. Hence, it is necessary to include the option of investigating similar parameters in case-specific monitoring, in general surveillance, or in	

Country	Organization	Reference	Comment	GMO Panel response
			both simultaneously. Consequently, the following monitoring issues are listed under both categories. Bartz, R., Heink, U. and Kowarik, I. (2009): Proposed Definition of Environmental Damage Illustrated by the Cases of Genetically Modified Crops and Invasive Species. Conservation Biology 24 (3): 675-681. DOI: 10.1111/j.1523-1739.2009.01385.x Hilbeck, A., Meier, M., Benzler, A. (2008): Identifying indicator species for post-release monitoring of genetically modified, herbicide resistant crops. Euphytica 164(3): 903-912. Kowarik, I., Bartz, R. and Heink, U. (2008): Bewertung „ökologischer Schäden" infolge des Anbaus gentechnisch veränderter Organismen (GVO) in der Landwirtschaft. Bonn - Bad Godesberg: 248 p. (Naturschutz und Biologische Vielfalt 56, with English Summary). VDI (2011): VDI Richtlinien zum Monitoring ökologischer Wirkungen gentechnisch veränderter Organismen [VDI Guidelines on monitoring ecological effects of genetically modified organisms]. http://www.vdi.de/42479.0.html	

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) Comments and opinions submitted by Member States during the three-months consultation period				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
Germany	Federal Agency for Nature Conservation	D, 12.01 General	PartIII Interplay between environmental risk assessment and monitoring: The information necessary to conclude on the ERA is partly missing. Thus, the safety of MON 87708 soybean cannot be fully assessed. Depending on those results the conclusions concerning case-specific monitoring may need to be revised.	The EFSA GMO Panel comments on the scientific content of the monitoring plan. EFSA has published guidance and scientific opinion on post-market environmental monitoring (PMEM) (EFSA, 2011). The EFSA GMO Panel is of the opinion that the information supplied by the applicant is in line with the guidance on PMEM. Please refer also to Section 6.1.2. of the scientific opinion.
Germany	Federal Agency for Nature Conservation	D, 12.02 Case-specific GM plant monitoring	Incidental spillage of viable MON 87708 soybean can occur during transport, storage, package, processing, and use. Furthermore, the exposure of viable MON 87708 soybean to the environment during or after the production process and during human or animal consumption is given. Therefore, case-specific monitoring has to focus on pathways where viable MON 87708 soybean enters the environment. It should comprise: i) exposure of viable MON 87708 soybean to the environment e.g. via spillage during transport, storage, packaging, processing, and use; ii) if spillage or loss during transport, storage, packaging, processing, and use occur, environmental effects such as spread and persistence of MON 87708 viable soybean have to be monitored; iii) if spread and persistence of MON 87708 viable soybean occur, further observations of impacts on organisms, food chains, and habitats are required.	The environmental risk assessment did not conclude on a potential risk of MON 87708; therefore case-specific monitoring is not required.

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) Comments and opinions submitted by Member States during the three-months consultation period				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
Germany	Federal Agency for Nature Conservation	D, 12.03 General Surveillance of the impact of the GM plant	According to Directive 2001/18/EC general surveillance is a compulsory part of the monitoring. The objective of general surveillance is to identify the occurrence of adverse effects of the GMO or its use on human health and the environment which were not anticipated in the environmental risk assessment. General surveillance is mainly focused on indirect, delayed and/or long term effects as well as cumulative effects. Additionally, it covers direct and immediate effects as far as they were not anticipated in the environmental risk assessment. The provided general surveillance plan is unspecific and does not meet the objectives defined in Annex VII of Directive 2001/18/EC and Council Decision 2002/811/EC. A revised plan is required that considers the following issues: The general surveillance plan has to focus on possible pathways how MON 87708 soybean can enter the environment and how unforeseen adverse effects on human and animal health and the environment can be linked to the consumption and dispersal of the GMO. Furthermore, It cannot be definitely excluded that spilled viable MON 87708 soybean becomes environmentally persistent or invasive. Therefore, the general surveillance plan has to comprise for viable soybeans at least: i) exposure of viable MON 87708 soybean to the environment e.g. via spillage during transport, storage, packaging, processing, and use;	The EFSA GMO Panel comments on the scientific content of the monitoring plan. EFSA has published guidance and scientific opinion on post-market environmental monitoring (PMEM) (EFSA, 2011). The EFSA GMO Panel is of the opinion that the information supplied by the applicant is in line with the guidance on PMEM. Please refer also to Section 6.1.2. of the scientific opinion.

Country	Organization	Reference	Comment	GMO Panel response
			ii) if spillage or loss during transport, storage, packaging, processing, and use occur, environmental effects such as spread and persistence of MON 87708 viable soybean have to be monitored; iii) if spread and persistence of MON 87708 viable soybean occur, further observations of impacts on organisms, food chains, and habitats are required. iv) MON 87708 soybean may enter the environment together with other approved GM soybean lines. Therefore a special focus should be on combined effects. The applicant's approach is to collect and coordinate information on adverse effects provided by the companies and existing European networks/associations (COCERAL, UNISTOCK, FEDIOL) involved in the production process. The monitoring activities and detailed information about these networks, however, remain unclear and thus have to be specified as well as how the monitoring data are made available. It is the applicants' task to define appropriate parameters and methodologies to detect potential adverse environmental effects. Therefore, the applicant is requested • to name the national and local organisations and factories involved in the monitoring, • to demonstrate the necessary representativeness of the selected factories and sampling sites,	

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			• to prove that a sufficient number of local operators agree to contribute to the general surveillance, • to explain how local operators will be instructed and trained for conducting the general surveillance, • to verify the necessary skills and expertise of local operators to detect adverse environmental impacts. In case the suggested operators are not suitable to cover all relevant observation objects, further monitoring systems have to be established. Because processed material may also be a cause of adverse effects, it is necessary, that the applicant involves operators further down the food chain in the process of monitoring.	
Germany	Federal Agency for Nature Conservation	D, 12.06 Reporting the results of monitoring	The applicant is required to report on the results of the monitoring including all issues of case-specific monitoring and general surveillance on an annual basis. Raw data have to be made available on request. The applicant is requested to use the reporting format specified by the Commission Decision 2009/770/EC. The monitoring report should also deliver detailed information on i) actual volumes of MON 87708 soybean imported into the EU, ii) the ports and silos where shipments of MON 87708 soybean were unloaded, iii) the processing plants where MON 87708 soybean was transferred to, iv) the amount of MON 87708 soybean used on farms for feed,	The publication of the monitoring results is not in the remit of the EFSA GMO Panel. In accordance with Regulation (EC) No 1829/2003, the authorisation holder "*shall submit reports to the European Commission in accordance with the terms of the authorisation. The monitoring reports referred to shall be made accessible to the public after deletion of any information identified as confidential in accordance with Article 30*" of Regulation (EC) No 1829/2003.

Country	Organization	Reference	Comment	GMO Panel response
			and v) transport routes of MON 87708 soybean.	
Germany	Federal Office of Consumer Protection and Food Safety	General comments	The scope of application EFSA-GMO-NL-2011-93 covers import and processing of soybean MON 87708 including all feed and food products containing, consisting of, or produced from the genetically modified soybean MON 87708. Cultivation is not covered by this application. The Federal Office of Consumer Protection and Food Safety (BVL) as German CA is of the opinion that the data so far provided by the applicant are not sufficient to complete the evaluation of the application. Thus, further information is required to conclude on the risk assessment of dossier EFSA-GMO-NL-2011-93 (see specific comments). In addition, the provided monitoring plan is incomplete at this stage and needs further elaboration for implementation.	Considering the intended uses of soybean MON 87708 excluding cultivation, the EFSA GMO Panel considers that the information provided relating to the environmental risk assessment is sufficient.

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) **Comments and opinions submitted by Member States during the three-months consultation period**				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
Germany	Federal Office of Consumer Protection and Food Safety	A, 07 Where appropriate, the conditions for placing on the market the food(s) or	The import documents should indicate that soybean MON 87708 has not been approved for cultivation by the EC. In addition to the intended GM labelling a clear labelling of MON 87708 indicating the tolerance to dicamba (3,6-dichloro-2-methoxybezoic acid) is recommended. Furthermore, appropriate measures have to be taken during transport, storage, and processing to avoid unintended release of viable soybean seed into the environment. In this context, the applicant should inform all parties involved in the handling and processing of soybean MON 87708 about avoidance and control of spillage.	Please see overall conclusions of the scientific opinion: "…. *the EFSA GMO Panel acknowledges the approach proposed by the applicant to put in place appropriate management systems to restrict environmental exposure in the case of accidental release of viable seeds of soybean MON 87708*."
Germany	Federal Office of Consumer Protection and Food Safety	D, 02 Information on the sequences actually inserted or deleted	For the sake of clearness, Figure 2 in Tu (2011b) should be complemented by a legend which assigns the position to each feature (e.g., 5' flanking region, junction I, transgenic sequence, etc.). Tu, H. (2011b) Updated bioinformatics evaluation of MON 87708 utilizing the AD_2011, TOX_2011, PRT_2011, EST_2011, NT_2011, and NR_2011 databases, Monsanto Technical Report, RAR-2011-0073, 1-326.	The legend in Figure 2 of RAR-2011-0073 could be misunderstood as it shows the nucleotide sequence of the pre-insertion site ("flanking sequences"), which was used to analyse possible disruption of known coding sequences or regulatory elements (see Appendix III in Technical dossier). There are thus no transgenic sequences in Figure 2, which is also evident from Appendices 28-30 of RAR-2011-0073. The nucleotide sequence of the inserted T-DNA and the DNA sequences at the 5' and 3' junctions of the MON 87708 are shown in Figure 11 of MSL0023278.
Germany	Federal Office of Consumer Protection and Food Safety	D, 04 Information on how the GM plant differs from the recipient plant in:	The applicant states that the agronomic and phenotypic assessment of MON 87708 included reference ranges determined from both GM and non-GM reference varieties. In this regard, the applicant should differentiate precisely between the conventional GM and the conventional non-GM varieties. In view of Table 2 in Laufer and Bommireddy (2010a) the applicant should apply identification to the GM and non-GM reference varieties, respectively. Moreover, it should be	The soybean varieties used as reference material in the statistical analysis performed by the applicant were non-GM soybeans. From the page 7 of the Table 2, it can be concluded that some reference lines have been removed and these are likely to be the GM reference lines.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			indicated which reference varieties were used to create the reference range. The applicants' statement that there is no substantial change in the range of values observed among the non-GM reference varieties, when the GM soybean varieties are removed from the population of the references, should be substantiated by showing the data. Laufer, T. C. and Bommireddy, P. L. (2010a) Amended Report for MSL0023136: Phenotypic Evaluation and Environmental Interactions of Dicamba-Tolerant Soybean MON 87708 When Treated and Not Treated with Dicamba in U.S. Field Trials During 2009, Monsanto technical report, MSL0023199, 1-119.	

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) Comments and opinions submitted by Member States during the three-months consultation period				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
Germany	Federal Office of Consumer Protection and Food Safety	D, 07.01 Comparative assessment	Production of material for comparative assessment was conducted at eight field sites in the U.S.A. during the 2009 field season. The sites were planted in a randomized complete block design with four replications. Samples were collected from MON 87708 (test) (dicamba-treated as well as dicamba-untreated) and the near isogenic control A3525. In addition, three different commercially available conventional non-GM soybean varieties were included at each site (with a total of 14 different reference varieties across all sites). According to the applicant, all plants were grown under normal agronomic field conditions for their respective geographic regions. In accordance with the recommendations of the EFSA Guidance Document (EFSA, 2011) the field sites should be chosen to be representative of the range of likely receiving environments where the plant will be grown, thereby reflecting relevant meteorological, soil and agronomic conditions. In the case under consideration, the eight field sites were located in typical soybean producing regions of the U.S.A. mainly belonging to the warm summer subtype of the humid continental climate. The choice of the eight field sites in the U.S.A. in different counties of six states should be explicitly justified regarding meteorological and other environmental conditions. The environmental influence on plant metabolism and composition should be sufficiently covered. Otherwise, it is recommended to replicate the trials over more than one year or to extend the trials to other representative field sites with differing	The EFSA GMO Panel is of the view that the field trial sites selected for the comparative studies on composition, phenotypic and agronomic characteristics have been described (see also information in Appendix I and to some extent Appendix II, as well as the Production Plan PPN-09-061 requested by the EFSA GMO Panel during the evaluation of the risk assessment). The design of the field trial follows the suggestions of the EFSA GMO Panel (EFSA, 2011). On request of the EFSA GMO Panel, the applicant provided a new statistical analysis according to the most recent EFSA GMO Panel Guidance Document for food and feed safety assessment (EFSA, 2011). Based on the information available, it is concluded that no differences were identified in the compositional data of forage and seeds obtained from soybean MON 87708 or in its agronomic and phenotypic characteristics that would require further assessment with regard to safety by the EFSA GMO Panel. The applicant has chosen field trial sites spread over several states of the USA where soybean is traditionally cultivated.

Country	Organization	Reference	Comment	GMO Panel response
			environmental conditions. In this regard, we would like to point out that the applicant had already performed further releases of MON 87708 in Argentina, Chile, and Canada (however, data are not presented in application EFSA-GMO-NL-2011-93). The statistical analysis of data is not fully in line with the statistical approach of the EFSA as outlined in its "Scientific Opinion on Statistical considerations for the safety evaluation of GMOs" (EFSA, 2010). However, the design of the performed statistical analysis does not give cause for concern. EFSA Panel on Genetically Modified Organisms (GMO); Scientific Opinion on Guidance for risk assessment of food and feed from genetically modified plants. EFSA Journal 2011; 9(5): 2150. [37 pp.] doi:10.2903/j.efsa.2011.2150. EFSA Panel on Genetically Modified Organisms (GMO); Scientific Opinion on Statistical considerations for the safety evaluation of GMOs. EFSA Journal 2010; 8(1):1250 [59 pp.] doi:10.2903/j.efsa.2010.1250.	
Germany	Federal Office of Consumer Protection and Food Safety	D, 07.07 Anticipated intake/extent of use	Soybean MON 87708 is to be used as any other soybean in the EU. The major soybean commodity products are defatted meal as feeding stuff as well as oil, lecithin, dietary fibre, and soy protein as starting material for the production of foods. The dietary intake of DMO protein is calculated based on the estimated dietary intake of feed/food derived from MON 87708 soybeans. However,	The EFSA GMO Panel notes the comment. Nearly all food and feed products derived from soybean are processed. The processing is likely to reduce the protein content or modify the proteins in the final product as compared to the proteins present in the growing soybean. Furthermore, proteins are degraded in the gastrointestinal system. As the applicant has used a worst-case scenario (all soybean products imported to the EU being derived from soybean MON 87708), the EFSA GMO Panel

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			adequate data about the nature and amount of soy ingredients in foodstuffs are missing.	considers that the exposure calculated is conservative and in this case useful for the risk assessment.
Germany	Federal Office of Consumer Protection and Food Safety	D, 07.08 Toxicology	D.7.8.1. Safety assessment of newly expressed protein According to the applicant, the safety of 3,6-dichlorosalicylic acid (DCSA) has been evaluated and deemed safe by the US EPA. However, the EPA website cited (see Technical Dossier page 184, footnote 45) does not contain the relevant information. Therefore, the applicant should be asked to provide the correct reference and/or deliver a document on the safety of DCSA. Plant-derived MON 87708 DMO was used for the bigger part of the molecular and biochemical characterization of the newly expressed protein. In consideration of this practice, the applicant states that equivalence evaluations between plant-produced and bacterial-derived DMO were not necessary. However, substrate specificity was mainly investigated using E. coli-produced wild-type DMO (only o-anisic acid was tested using plant-derived MON 87708 DMO). In consideration of the fact that DMO protein expressed in soybean MON 87707 is not 100% identical to wild-type DMO (due to two amino acid substitutions) and is further composed of the MON 87708 DMO protein as well as of the MON 87708 DMO + 27 protein and all forms of the trimer, the complete substrate specificity analysis should be performed using soybean MON 87708-derived material. Otherwise, equivalence between plant-produced and bacterial-derived DMO should be demonstrated.	The risk assessment of plant protection products is not within the remit of the EFSA GMO Panel. However, the EFSA GMO Panel agrees with the principle that all references given by the applicant should be correct. Information of the source requested could be available in: http://www.epa.gov/oppsrrd1/REDs/dicamba_red.pdf Crystallographic studies demonstrated the role of the carboxylic acid group of dicamba in binding to the active site of DMO and the chloride atoms in providing the correct orientation. The applicant identified a number of naturally occuring benzoic, phenolic and phenopropanoic acids which showed elements of structural similarities with dicamba and tested these in an assay positive for dicamba demethylation. No evidence of catabolism was seen with any other of the potential substrates tested indicating a high specificity of the DMO for dicamba. Please see also additional information of July 2012 and November 2012. In relation to the comments on the acute toxicity study, the EFSA GMO Panel considers that acute toxicity testing of newly expressed proteins is of little additional value to the risk assessment of the repeated human and animal consumption of food and feed derived from GM plants. On request of the EFSA GMO Panel the applicant supplied data on the thermal stability of aqueous solutions of the DMO enzyme purified from soybean MON 87708. For further information see additional information supplied in October 2011 and Section 5.1.2 of the Scientific Opinion on application EFSA-GMO-NL-2011-93. On request from the EFSA GMO Panel, the applicant supplied (March 2012) a 28-day oral toxicity study with a mixture of the MON 87708 DMO protein and MON 87708 DMO+27 proteins

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			According to the recommendations of the EFSA Guidance Document (EFSA, 2011) in the case of newly expressed enzymes, information on the enzyme activities including the temperature and pH range for optimum activity should be provided and, therefore, might be requested for MON 87708 DMO. The applicant performed an acute toxicity study of MON 87708 DMO administered by the oral route to mice. The results of this study indicate that there were no adverse effects of MON 87708 DMO when administered to mice by single oral gavage at a dose of 140 mg/kg body weight (MSL0022527, 2010). According to the applicant, this dose is several orders of magnitude higher than anticipated dietary exposure in the EU population. Nevertheless, we would like to point out that the administered dose of MON 87708 DMO is considerably smaller than recommended by the OECD (limit dose of 2000 mg/kg body weight). Referring to this, the applicant should be requested to explain in more detail the selected dose of 140 mg MON 87708 DMO per kg body weight. EFSA Panel on Genetically Modified Organisms (GMO); Scientific Opinion on Guidance for risk assessment of food and feed from genetically modified plants. EFSA Journal 2011; 9(5): 2150. [37 pp.] doi:10.2903/j.efsa.2011.2150. MSL0022527. (2010) An acute toxicity study of dicamba mono-oxygenase (DMO) enzyme from	supplied in the diet in approximately the same ratio they occur in soybean MON 87708 (*i.e.*, 2:3). Administration of DMO proteins did not induce any deaths or clinically relevant findings at any of the dose levels. There were no relevant differences in mean body weight, body weight gain and food consumption. The only statistically significant difference in clinical pathology parameters assessed was an incidental higher mean absolute neutrophil count in males of the high-dose group, which was mainly driven by an an unusual high-value in one animal showing incidental inflammation of the skin. A slightly significantly higher mean spleen weight (relative to body weight) was seen in in male group given the high dose in comparison to control group; this was not associated with histopathologic changes and considered the expression of biological variability. No macroscopic or microscopic findings were reported in the examined organs and tissues that could be attributed to the test material. The highest dose administered in this study, i.e. 174 mg/kg bw per day in males and 179.7 mg/kg bw per day in females, is considered the NOAEL. Assuming an intake of 200 g of soybean/70 kg adult per day in the EU and that all soybean consumed is derived from soybean MON 87708, the daily intake of DMO proteins would be in the region of 110 μg/kg bw. The highest estimated intake of DMO proteins in adults is about 1000-fold lower than the NOAEL from the 28-day feeding study.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			MON 87708 administered by oral gavage to mice, Monsanto Technical Report, CRO-09-419, 1-99.	
Germany	Federal Office of Consumer Protection and Food Safety	D, 07.08 Toxicology	D.7.8.4. Testing of the whole GM food/feed With regard to the soybean material providing the basis for the 90-day toxicity study in rats an analytical verification of the test material (presence of MON 87708) as well as of the control and reference material (absence of MON 87708) is not provided and should be requested from the applicant (basic validity criterion for acceptance of the study). Moreover, the description of the statistical analysis is not clear. The applicant should specify if the first ANOVA analysis exclusively compared the test group to the control group (data of the reference groups should not be included). Otherwise, an adequate analysis should be asked for from the applicant.	The EFSA GMO Panel notes that the molecular characterisation of soybean MON 87708 provided no indications of unintended effects of the genetic modification, and that no differences were identified in the compositional data of forage and seeds obtained from soybean MON 87708 or in its agronomic and phenotypic characteristics that would require further assessment with regard to safety by the EFSA GMO Panel. Nevertheless, the applicant presented a 90-day and a 42-day animal feeding studies that were assessed by the EFSA GMO Panel. As indicated in the Scientifi Opinion, the result of a 90-day feeding study in rats with diets containing toasted defatted soybean meal from soybean MON 87708, its conventional counterpart or any of two non-GM soybean varieties did not raise safety concerns. The compositional data indicating nutritional equivalence was corroborated by the chicken study. For more information on the 90-day and 42-day animal studies, please see Sections 5.1.2.3a and 5.1.2.3b of the Scientific Opinion on application EFSA-GMO-NL-2011-93. For more information on the the statistical analysis performed in the 90-day animal feeding study, please see Section 5.1.2.3 of the Scientific Opinion on application EFSA-GMO-NL-2011-93 and the additional information received in June 2013.
Germany	Federal Office of Consumer Protection and Food Safety	D, 08 Post-market monitoring of GM food/feed	The applicant states that there are no pleiotropic or unintended effects caused by the intended improved fatty acid profile (see Technical Dossier page 254). However, apart from that, soybean MON 87708 is characterised as a genetically modified plant modified for an agronomic input trait (tolerance to dicamba) and not for improved nutritional characteristics. The applicant should be	Based on the information available, it is concluded that no differences were identified in the compositional data of forage and seeds obtained from soybean MON 87708 or in its agronomic and phenotypic characteristics that would require further assessment with regard to safety by the EFSA GMO Panel. The reference to improved fatty acid profile in the context of application EFSA-GMO-NL-2011-93 is therefore incorrect.

Country	Organization	Reference	Comment	GMO Panel response
			requested to clarify his statement with respect to an intended improved fatty acid profile. Altogether, it is not feasible to decide on the necessity of measures for post-market monitoring of GM food/feed as the risk assessment of soybean MON 87708 cannot be finalised.	With regard to the post-market monitoring, the risk assessment concluded that no data have emerged to indicate that soybean MON 87708 is any less safe than its conventional counterpart. In addition, soybean MON 87708 is as nutritious as non-GM soybeans. Therefore, and in line with the Guidance Documents (EFSA, 2006, 2011), the EFSA GMO Panel is of the opinion that post-market monitoring of the GM food/feed is not necessary.
Germany	Federal Office of Consumer Protection and Food Safety	D, 12 Environmental Monitoring Plan	The monitoring plan is basically acceptable, but needs further elaboration for implementation. Therefore, the applicant is recommended to revise the monitoring plan during the initial implementation phase (after consent is given) and present this revised monitoring plan together with a first report one year after consent is given to be reassessed. The risk assessment of soybean MON 87708 cannot be finalized because of deficiencies of the application listed above. Therefore, the monitoring plan concerning the Case Specific Monitoring may need to be revised depending on the results of an updated risk assessment. The strategy of General Surveillance is mainly based on the involvement of importers, traders, silo operators, and processors coordinated by EuropaBio. The applicant will inform the selected networks of operators about market release of GM plant products und will remind them to report on 'any unanticipated adverse effect'. It is stated that these third parties have to follow legal obligations of food and feed hygiene (HACCP). Nevertheless, the role and interplay of all actors on behalf of recording, analysis, and evaluation of monitoring	The environmental risk assessment did not conclude on a potential risk of MON 87708; therefore case-specific monitoring is not required. The EFSA GMO Panel comments on the scientific content of the monitoring plan. EFSA has published guidance and scientific opinion on post-market environmental monitoring (PMEM) (EFSA, 2011). The EFSA GMO Panel is of the opinion that the information supplied by the applicant is in line with the guidance on PMEM. Please refer also to Section 6.1.2. of the scientific opinion.

Country	Organization	Reference	Comment	GMO Panel response
			data needs more transparency. In particular if GMO monitoring is based on implementation of such quality control mechanisms, it needs to be explained how audits and reports of the quality control mechanisms can be used as base for evaluation. Additionally, other sources of information, e.g. peer-reviewed publications, should be taken into account. The monitoring plan does not relate the monitoring activities to relevant protection goals. Even more, it is not described which routine observations (including parameters or monitoring characters) are carried out in relation to the protection goals. Only reporting on 'any unanticipated effect' is solely not an appropriate parameter, because it already anticipates an evaluation. This evaluation process should be based on a distinct set of parameters and a scientific sound data analysis. It is requested that the applicant specifies in detail, how and which information will be pro-actively queried, gathered and how they will be evaluated. In addition, it might be useful to integrate food and feed surveillance in coordination with the competent authorities. Information about the use of the product in food and feed could deliver supplementary helpful data (of exposure to consumers and animals) for general surveillance. Furthermore, the applicant should specify monitoring activities in the field of human and animal health. Therefore, it should be described in more detail how animal and human health surveillance is integrated in the monitoring plan.	

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) Comments and opinions submitted by Member States during the three-months consultation period				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
			A report on GS activities on an annual basis is sufficient. Reporting should refer to the requirements and format introduced by the Commission Decision 2009/770/EC. Joint reports considering different approved GM plant products are acceptable, but it has to be guaranteed that each specific event is evaluated per se.	
Italia	Ministero dell'Ambiente e della Tutela del Territorio e del Mare	A. General information	The compositional and nutritional analysis are complete in documents and bibliography presented by the applicant.	No comments required
Italia	Ministero dell'Ambiente e della Tutela del Territorio e del Mare	C. Information relating to the genetic modification	MOLECULAR ANALYSIS The description of the results of bioinformatic analysis is insufficient and for which an updating of data supported by an adequate bibliography is required, for a better understanding of the analysis. EFSA had already asked the applicant for more details. The applicant answered these requests in 29th march 2011, nevertheless the bioinformatic uptedate described in the report titled " Updated Bioinformatics Evaluation of MON 87708 Utilizing the AD_2011, TOX_2011, PRT_2011, EST_2011, NT_2011, and NR_2011 Databases" refers to previous reports (Tu e Silvanovich 2010 a, b, c, d), but they seem not to be reported in the appendix.	The updated report MSL0023308 replaces MSL0022498, and the report RAR-2011-0073 replaces MSL0022584, MSL0022679 and MSL0022682. Further updates were provided in February 2013. Therefore, to conclude about the bioinformatic analyses, MSL0023839 and RAR-2012-0065 are the relevant reports.
Italia	Ministero dell'Ambiente e della Tutela del Territorio e del	D, 07.02 Field trials	FIELD TRIAL Regarding field trial tests since results presented are for only one year, it would be appropriate to	The design of the field trial follows the most recent EFSA GMO Panel Guidance Document for food and feed safety assessment (EFSA, 2011).

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) Comments and opinions submitted by Member States during the three-months consultation period				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
	Mare		consider a longer period or several cycles of seeding. Moreover, control and reference varieties are not included in the OECD catalog and in the experimental design are considered only 3 of 14 reference varieties indicated that in each site are in turn used in different combinations. Consequently, the reference range so defined cannot be used in the statistical comparison between sites. It would be appropriate assessed statistically the difference between test and reference varieties and between treated and untreated.	Regarding the statistical analysis of the field trial data, the EFSA GMO Panel requested the applicant to perform additional statistical analysis according to the methodology described in its Guidance Document (EFSA, 2011).
Norway	Directorate for Nature Management	General comments	According to the Norwegian Gene Technology Act, possible contributions to a sustainable development and possible benefits to the society and ethical considerations through the use of a GMO shall be taken into consideration when evaluating a GMO notification in Norway. In the case of notification EFSA/GMO/NL/2011/93, we request the Notifier to provide more information relevant to these issues. Norway will through our national process also approach the Notifier directly to inform about the requirements in the Norwegian legislation, and to have a dialogue regarding information relevant to assess these issues. In more detail, Norway will invite the Notifier to provide more information on the event Mon 87708 compared to existing conventional soybean on issues such as; agricultural practise of relevance for farmers and the society, use of herbicides, benefit for the consumers and energy consumption.	This comment is on an issue outside the remit of the EFSA GMO Panel.
Norway	Directorate for Nature	D, 03 Information	The Notifier is asked to provide evidence that all isoforms of the newly expressed proteins are not	A portion of the newly expressed MON 87708 DMO+27 protein is post-translationally modified, resulting in MON 87708 DMO after

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) Comments and opinions submitted by Member States during the three-months consultation period				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
	Management	on the expression of the insert	post-translationally modified. In addition, the Notifier should provide evidence of the actual RNAs produced or absent at the integration junction and in the DNA surrounding the insert, preferably using high throughput transcriptome sequencing techniques.	proteolytic cleavage of the chloroplast targeting sequence. Neither MON 87708 DMO+27 nor MON 87708 DMO is glycosylated (Technical dossier, p. 208). As the bioinformatic analyses did not indicate a safety issue, and taking into account all available evidence, the GMO Panel considers that a request for comprehensive global RNA analysis is not reasonable or justified from the risk assessment point of view.
Norway	Directorate for Nature Management	D, 07.03 Selection of compounds for analysis	The DMO protein used in the specificity assays does not have the same amino acid sequence as DMO and DMO+27 expressed in MON 87708. The wildtype-DMO and DMO from 87708 differ in two positions: the latter contains an additional alanine at position 2 added for cloning purposes, and a Trp112Cys substitution was reported. The Notifier is asked to supply evidence about the substrate specificity of DMO either by using the in-planta produced DMO protein or by demonstrating the equivalence between the test protein and the in-planta produced form. In addition, the Notifier is requested to analyse substrate specificity by testing substances more relevant to the safety assessment.	Crystallographic studies demonstrated the role of the carboxylic acid group of dicamba in binding to the active site of DMO and the chloride atoms in providing the correct orientation. The applicant identified a number of naturally occuring benzoic, phenolic and phenopropanoic acids which showed elements of structural similarities with dicamba and tested these in an assay positive for dicamba demethylation. No evidence of catabolism was seen with any other of the potential substrates tested indicating a high specificity of the DMO for dicamba. Please see Section 5.1.2.2 of the Scientific Opinion on application EFSA-GMO-NL-2011-93.
Norway	Norwegian Scientific Committee for Food Safety	General comments	The GMO Panel of the Norwegian Scientific Committee for Food Safety has not found any analysis of the residues of the herbicide applied nor its metabolites as part of the compositional analysis. It is of importance to know the residues level, because the herbicide resistance provided by the genetic modification allows a more intensive use of the herbicide and it enables the plant to degrade the herbicide into metabolites which naturally would not occur in plants in the same concentrations. The metabolites, DCSA, DCGA and	The assessment of plant protection products is outside the remit of the EFSA GMO Panel.

Comments from National Competent Authorities under Directive 2001/18/EC **ANNEX G**

Country	Organization	Reference	Comment	GMO Panel response
			5-OH-dicamba should also been analysed. We recommend that the applicant provides a description of all herbicides which may be used in the cultivation of MON 87708 and their metabolites. Moreover an analysis of the soybean with regard to the herbicide applied and their metabolites is mandatory.	
Norway	Norwegian Scientific Committee for Food Safety	D, 07.08 Toxicology	The GMO Panel of the Norwegian Scientific Committee for Food Safety has evaluated soya MON 87708 as a food and feed ingredient. The acute toxicity study is performed using 140 mg protein/kg bw. This is a very low amount according to the OECD guidelines (OECD guidelines 420). If the acute study is performed with a fixed dose the exposure limit is 2000 mg test substance/kg bw. Moreover, a NOAEL is determined based on this acute study. According to the OECD guidelines it is not recommended to determine NOAEL based on acute oral toxicity studies since they limited to a 14 days observation period. The acute study is designed for determination of LD50. NOAEL should be determined based on the 90 days sub-chronic study (OECD 408). All animal experiments are performed using soya unexposed to Dicamba. Herbicide treated soya should have been included in the animal experiments, and the residue level of the herbicide and its metabolites should have been analysed. Fish meal and fish oil has to some extent been replaced by plant meal and plant oil. Soy meal and soy oil is today important ingredients in feed for	The EFSA GMO Panel agree with the GMO Panel of the Norwegian Scientific Committee that acute toxicity studies are designed for determining LD50 and dose finding purposes. On request from the EFSA GMO Panel, the applicant supplied (March 2012) a 28-day oral toxicity study with a mixture of the MON 87708 DMO protein and MON 87708 DMO+27 proteins supplied in the diet in approximately the same ratio they occur in soybean MON 87708 (*i.e.*, 2:3). Administration of DMO proteins did not induce any deaths or clinically relevant findings at any of the dose levels. There were no relevant differences in mean body weight, body weight gain and food consumption. The only statistically significant difference in clinical pathology parameters assessed was an incidental higher mean absolute neutrophil count in males of the high-dose group, which was mainly driven by an an unusual high-value in one animal showing incidental inflammation of the skin. A slightly significantly higher mean spleen weight (relative to body weight) was seen in in male group given the high dose in comparison to control group; this was not associated with histopathologic changes and considered the expression of biological variability. No macroscopic or microscopic findings were reported in the examined organs and tissues that could be attributed to the test material. The highest dose administered in this study, i.e. 174 mg/kg bw per day in males and 179.7 mg/kg bw per day in females, is considered the NOAEL.

Country	Organization	Reference	Comment	GMO Panel response
			marine fish. The Norwegian GMO Panel request that the applicant perform feeding studies on fish, e.g. salmonides.	Assuming an intake of 200 g of soybean/70 kg adult per day in the EU and that all soybean consumed is derived from soybean MON 87708, the daily intake of DMO proteins would be in the region of 110 μg/kg bw. The highest estimated intake of DMO proteins in adults is about 1000-fold lower than the NOAEL from the 28-day feeding study. According to Regulation (EC) No 1829/2003, the applicant should perform a risk assessment of the genetically modified organism. Risk assessment of the plant protection products is performed under another legislative framework (and assessed by another EFSA Panel). In relation to the comparative analysis and based on the information available, it is concluded that no differences were identified in the compositional data of forage and seeds obtained from soybean MON 87708 or in its agronomic and phenotypic characteristics that would require further assessment with regard to safety by the EFSA GMO Panel. The result of a 90-day feeding study in rats with diets containing toasted defatted soybean meal from soybean MON 87708, its conventional counterpart or any of two non-GM soybean varieties did not raise safety concerns. There are no indications that the genetic modification might significantly change the overall allergenicity of soybean MON 87708 when compared with that of its conventional counterpart. The compositional data indicating nutritional equivalence was corroborated by the chicken study.

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) Comments and opinions submitted by Member States during the three-months consultation period				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
The Netherlands	Ministry of Economic affairs, Agriculture and Innovation and Ministry of Health, Welfare and Sport	D, 03 Information on the expression of the insert	Data should be provided on the storage stability of DMO in tissue preparations prepared as in the study of Beyene and Niemeyer (2010a) for the purpose of measurement of (total) DMO levels in tissues.	The prepared tissue samples were stored at -80°C and transferred to the analytical facility on dry ice. This is the safest way to store protein samples.
The Netherlands	Ministry of Economic affairs, Agriculture and Innovation and Ministry of Health, Welfare and Sport	D, 07 Information on any toxic, allergenic or other harmful effects on human or	Data should be provided on the effects of soybean seed processing (e.g. heating) on levels, integrity and activity (functionality) of DMO and DMO+27.	On request of the EFSA GMO Panel the applicant supplied data on the thermal stability of aqueous solutions of the DMO enzyme purified from soybean MON 87708. For further information see additional information supplied in October 2011 and Section 5.1.2 of the Scientific Opinion on application EFSA-GMO-NL-2011-93.
The Netherlands	Ministry of Economic affairs, Agriculture and Innovation and Ministry of Health, Welfare and Sport	D, 07 Information on any toxic, allergenic or other harmful effects on human or	A description should be provided on the natural function and substrate of DMO in Stenotrophomonas maltophilia.	Crystallographic studies demonstrated the role of the carboxylic acid group of dicamba in binding to the active site of DMO and the chloride atoms in providing the correct orientation. The applicant identified a number of naturally occuring benzoic, phenolic and phenopropanoic acids which showed elements of structural similarities with dicamba and tested these in an assay positive for dicamba demethylation. No evidence of catabolism was seen with any other of the potential substrates tested indicating a high specificity of the DMO for dicamba. Please see also additional information of July 2012 and November 2012.
The Netherlands	Ministry of Economic affairs, Agriculture and Innovation and Ministry of	D, 07 Information on any toxic, allergenic or other harmful	In the study of Burzio and McCann it is mentioned that the tested substances were identified by 'chemical substructure searching for compounds related to dicamba followed by a literature search for the presence of these compounds in plants'. All details of these searches should be provided by the	Crystallographic studies demonstrated the role of the carboxylic acid group of dicamba in binding to the active site of DMO and the chloride atoms in providing the correct orientation. The applicant identified a number of naturally occuring benzoic, phenolic and phenopropanoic acids which showed elements of structural similarities with dicamba and tested these in an assay

Application EFSA-GMO-NL-2011-93 (soybean MON 87708) Comments and opinions submitted by Member States during the three-months consultation period				
Comments from National Competent Authorities under Directive 2001/18/EC				**ANNEX G**
Country	**Organization**	**Reference**	**Comment**	**GMO Panel response**
	Health, Welfare and Sport	effects on human or	applicant. The specificity of DMO was investigated in this study for just a limited number of substances present in a very limited number of crops (soybean, cotton and corn). It should be determined if there are other endogenous compounds in food that could serve as a substrate for this enzyme.	positive for dicamba demethylation. No evidence of catabolism was seen with any other of the potential substrates tested indicating a high specificity of the DMO for dicamba. Please see also additional information of July 2012 and November 2012.
The Netherlands	Ministry of Economic affairs, Agriculture and Innovation and Ministry of Health, Welfare and Sport	D, 07 Information on any toxic, allergenic or other harmful effects on human or	DMO is derived from a microorganism that is resistant to many antibiotics. With regard to substrate specificity, it should therefore also be investigated if DMO may play any role in the (chlorine-containing) antibiotic resistance of the source organism, as this may also compromise the effectivity of antibiotic treatments of consumers of products derived from MON 87708.	Crystallographic studies demonstrated the role of the carboxylic acid group of dicamba in binding to the active site of DMO and the chloride atoms in providing the correct orientation. The applicant identified a number of naturally occuring benzoic, phenolic and phenopropanoic acids which showed elements of structural similarities with dicamba and tested these in an assay positive for dicamba demethylation. No evidence of catabolism was seen with any other of the potential substrates tested indicating a high specificity of the DMO for dicamba. Please see also additional information of July 2012 and November 2012.

References to EFSA Guidance Documents and related Scientific Opinions cited in this document by EFSA:

- Guidance Document for the risk assessment of genetically modified plants and derived food and feed by the Scientific Panel on Genetically Modified Organisms (2006). EFSA Journal, 4, 99.
- Scientific Opinion of the Scientific Panel on genetically modified organisms on the Post Market Environmental Monitoring (PMEM) of genetically modified plants (2006). EFSA Journal, 4, 319.
- Statistical considerations for the safety evaluation of GMOs (2010). EFSA Journal, 8, 1250.
- Guidance Document for risk assessment of food and feed from genetically modified plants (2011). EFSA Journal 2150:1–37.
- Guidance Document on the post-market environmental monitoring (PMEM) of genetically modified plants (2011). EFSA Journal, 2316, 1–40.