Application (EFSA-GMO-NL-2016-135 (soybean MON87708 × MON89788 × A5547-127)
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Country	Organization	Reference	Comment	GMO Panel responses
Austria	Fed.Ministry_Health/Women's Aff.	II.1.2.2 Information relating to the genetically modified plant	2.2.1 General description of the trait(s) and characteristics which have been introduced or modified Scientific Information, p. 22: We would like to indicate that the source organism for the DMO protein, Stenotrophomonas maltophilia, is an important - usually multi drug resistant - nosocomial pathogen (Brooke 2012). It has been identified as the causative agent for bacteraemia, meningitis, urinary tract infections, mastoiditis, epididymitis, conjunctivitis, endocarditis, peritonitis, bursitis, keratitis, endophthalmitis, cholangitis, and a wide range of mucocutaneous and soft tissue infections that may mimic disseminated fungal infections (Murray et al. 1999). Murray et al. point out that "infection is becoming more frequent and has been associated with substantial morbidity and mortality " (Murray et al. 1999). S. maltophilia is, therefore, not the innocuous ubiquitously present pathogen as presented by the applicant. We would like to ask the EFSA GMO Panel to take this into consideration for their evaluations. [Brooke JS, 2012. Stenotrophomonas maltophilia: an emerging global opportunistic pathogen. Clin Microbiol Rev 25(1): 2-41. Murray PR, Baron EJ, Pfaller MA, Tenover FC, Yolken RH, 1999. Manual of Clinical Microbiology. Washington, ASM Press.]	Event MON87708 contains only the coding region of the DMO protein from *Stenotrophomonas maltophilia*, which is characterised for its safety in the context of AP135. Event MON 87708 does not include other genes from *Stenotrophomonas maltophilia* likely responsible for its pathogenesis.

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Austria	Fed.Ministry_Health/Women's Aff.	II.1.2.2 Information relating to the genetically modified plant	2.2.2 Information on the sequences actually inserted or deleted The notifier presents sequence data to confirm that the transgenic inserts contained in GM soybean MON87708xMON98788xA5547-127 are identical to the inserts contained in the single event GM lines which were combined into GM soybean MON87708xMON98788xA5547-127 (FROM CBI: Study 15-RSNKS003; Study: MSL0027428). We acknowledge this approach to provide an assessment of overall identity of inserts present in GM soy MON87708xMON98788xA5547-127 in comparison with the inserts contained in the parental events. However, the notifier indicates that there is a likelihood for molecular interactions between the individual transgenic inserts based on sequence similarities between these elements and therefore a likelihood for changes to these inserts in GM soy MON87708xMON98788xA5547-127 upon propagation (Part II - Scientific Information, p. 22). This likelihood is considered to be low by the notifier. We note that the notifier does not specify the degree of likelihood of such changes and that the submitted data are not suitable to identify the frequency of such changes. The notifier therefore should provide adequate information to assess the frequency of changes due to interaction of the transgenic inserts contained in GM soy MON87708xMON98788xA5547-127. Additionally, the submitted data are not entirely sufficient to provide information with regard to the chromosomal locations of the MON 87708 and MON 89788 inserts and the different transgenes contained in GM soybean MON87708xMON98788xA5547-127. EFSA is requested to ask for conclusive data concerning these issues. The control line (ID 11406744) used for the molecular characterisation experiments (FROM CBI: Study MSL0027428) is not sufficiently described; only stating that it has a similar genetic background to the control	Based on all the data provided in the molecular characterisation of this stack, including the genetic stability and levels of all the newly expressed proteins in the three-event stack and the corresponding singles, the GMO Panel concludes that there is no indication of an interaction between the events in this stack, that would raise any safety concerns. Information on the chromosomal location of the inserts is not a required based on the applicable EFSA guidelines. The control soybean line used in the sequence analysis of the pre insertion locus was the same as the one

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			substance. EFSA is requested to ask for clarifying the identity of the control lines and to unambiguously reference them. Additional comment We would like to indicate that MON87708xMON89788xA5547-127 is carrier of two fragments of a ß-lactamase gene which mediates antibiotic resistance to penicillin and several other clinically relevant penicillin derivatives (Technical Dossier, Notification EFSA-GMO-NL-2008-52). The presence of antibiotic resistance gene fragments – especially from an antibiotic resistance gene of significant clinical relevance – is not reported in the application for the stack under evaluation. Although indeed no intact antibiotic resistance gene is present in the stack under evaluation, the fragments which comprise approx. 800 bp of bacterial DNA content in total (see Table 9, Technical Dossier, Notification EFSA-GMO-NL-2008-52 and FROM CBI: study: 15-RSNKS003) may interact with homologous elements in bacterial receptor strains (Woegerbauer et al. 2015). This may fuel the antibiotic resistance gene pool and may lead to the formation of mosaic ß-lactamase genes potentially coding for enzymes with expanded or alternate substrate specificities leading to the dissemination of new antibiotic resistance functions in bacterial populations. We would like to ask the EFSDA GMO Panel to take this observation into consideration for their evaluations. [Woegerbauer M, Kuffner M, Kopacka I, Domingues S, Steinwider J, Nielsen KM, Fuchs K, 2015. Impact of mosaic genes on the risk assessment of GMOs. Federal Ministry of Health: 1-268.]	employed to perform the agronomic and phenotypic and compositional analyses. The GMO Panel has assessed the information on the genetic similarity between GM soybean MON87708xMON98788xA5547-127 and its comparator (A3555) and considers that the produced comparator is the conventional counterpart.

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Austria	Fed.Ministry_Health/Women's Aff.	II.1.2.2 Information relating to the genetically modified plant	2.2.3 Information on the expression of the inserted/modified sequence For the assessment of developmental expression of the 3 transgenic proteins (CP4-EPSPS, DMO and PAT) data from a field trial conducted at 5 sites in the US in 2015 are presented (Scientific Information, p. 26ff.). Means, standard deviations and ranges were presented for each tissue type across sites for the stacked GM soybean as well as for the concurrently grown parental single events, which were all treated with the respective herbicides as applicable (glyphosate, dicamba and glufosinate). However, the statistical analysis is restricted to basic descriptive statistics, such as means, data ranges, and standard deviation and an appropriate analysis of variance is lacking. In addition no untreated plots seem to have been included in the field trial and no information on the herbicide amounts applied on the plots is provided. Thus any potential impact of environmental conditions or interactions with the applied herbicides (genotype x environment interactions) cannot be accounted for. Differences in expression however may also result from interactions between the stacked transgenic inserts. As epigenetic interactions between the 3 single events cannot be excluded, we ask the notifier to further assess the reliability of expression and possible effects on the metabolism of the soybean stack (Dietz-Pfeilstetter 2010). Furthermore, the notifier should be requested to provide the production plan for the field trial used for the expression analysis. [Dietz-Pfeilstetter A, 2010. Stability of transgene expression as a challenge for genetic engineering. Plant Sci 179(3): 164-167.]	In order to assess any changes in protein expression levels which may result from potential interactions between the events, protein levels were determined for the three-event stack and the corresponding single events in different parts of the plant. Protein expression analyses show that the levels of the newly expressed proteins are comparable in the three-event stack and in the single events. The data and analysis on the expression levels is in line with applicable EFSA guidelines and were considered sufficient by the GMO Panel to conclude that there is no indication for an interaction that would affect the levels of the newly expressed proteins due to the combination of the single events to produce soybean MON 87708 x MON 89788 x A5547-127.

Austria	Fed.Ministry_Health/Women's Aff.	II.1.2.2 Information relating to the genetically modified plant	2.2.4 Genetic stability of the inserted/modified sequence and phenotypic stability of the GM plant Regarding the genetic stability of the inserts combined in GM soybean MON87708xMON98788xA5547 127 the notifier states that "There are no known mechanisms by which two inserts at different locations on different chromosomes could stimulate recombination on each other (if they do not express proteins involved in recombination pathways)." (Part II - Scientific Information, p28). However, no sufficient information on the chromosomal location of the MON87708 and MON89788 inserts are provided to support this conclusion. EFSA is requested to ask for additional information underlining the conclusion about genetic stability of inserts. Scientific Information, p. 28: The applicant is of the opinion that "it is appropriate for the MON 87708 × MON 89788 × A5547-127 genetic and phenotypic stability to refer to the genetic and phenotypic stability of MON 87708, MON 89788, and A5547-127." Since MON87708xMON89788xA5547-127 comprises a new plant variety, it would be recommendable to provide evidence for the genetic stability by analysing several generations of this new organism instead of only comparing it to the respective single events for a single generation. Scientific Information, p. 29: The applicant states that the insertion of additional common sequence information would not introduce additional genomic instability that is not already present in the endogenous genome, mentioning the presence of repetitive DNA sequences. However, this justification seems not to be adequate as diverse functional characteristics of introduced sequences may be influenced by the location of the insert. The applicant clearly shows that the inserts are intact according to the sequence information, and thus using a very precise method. However, this approach concentrates on the insert location only, which has to be taken into consideration when concluding on the overall stability of the inserts.	Information on the chromosomal location of the inserts is not a required based on the applicable EFSA guidelines. The genetic stability of the inserted DNA over multiple generations in the single soybean events was demonstrated in the singles. The data provided is sufficient for the GMO panel to conclude on the integrity of the events in stack soybean MON 87708 x MON 98788 x A5547 127.

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Austria	Fed.Ministry_Health/Women's Aff.	II.1.2.2 Information relating to the genetically modified plant	2.2.5 Potential risk associated with horizontal gene transfer Scientific Information, p. 29: The applicant emphasises that "systemic barriers" (e.g. stomach acid, pancreatic nucleases, blood/systemic nucleases etc.) limit and/or eliminate the availability of exogenous DNA. We would like to indicate that there a many peer-reviewed publications available providing evidence that orally administered DNA is not completely degraded by gastrointestinal fluids for a certain period of time and survives - albeit reduced in length - the passage through the gastrointestinal tract (Schubbert et al. 1994; Schubbert et al. 1997; Schubbert et al. 1998; Martin-Orue et al. 2002; Netherwood et al. 2004; Wilcks et al. 2004; Sharma et al. 2006; Alexander et al. 2007) and that free extracellular DNA - in spite of blood nucleases - is present in the circulation and is used as valuable diagnostic marker (Anker and Stroun 2000). Plant DNA derived sequences especially from multi-copy (plastid) genes are detectable in blood and/or tissues after ingestion (Phipps et al. 2003; Deaville and Maddison 2005; Hanusová et al. 2007; Rehout et al. 2008; Bertheau et al. 2009; Spisák et al. 2013). Proteins and DNA are excellently protected against acidic conditions in the stomach and degradation by digestive enzymes if encapsulated by a plant cell wall (Kwon and Daniell 2016). The plant cell wall which is densely packed with lignin and cellulose provides natural protection against lysis because human enzymes are incapable to efficiently crack the glycosidic bonds of the plant cell wall carbohydrates (Cummings 1984). The content of a plant cell is therefore predominantly released only in the lower gastrointestinal tract where commensal bacteria provide the means to digest these plant cell walls (Sierk and Pearson 2004; Martens et al. 2011). This protective effect is exploited for the oral delivery of protein drugs which are "bioencapsulated" in plant cells and, thus, resistant to degradation in the upper gastrointestinal tract (Kwon and Daniell 2016).	In relation to the comments on the fate of the protein in the gastrointestinal tract, EFSA thanks the comments from the Austrian Authority. The EFSA GMO Panel (2017) has recently published an opinion on *in vitro* protein gastrointestinal digestion. The principles and limitations of such studies as well as their usefulness in the overall risk assessment process were discussed. Please note that an EFSA procurement is currently ongoing where different gastrointestinal digestion models are tested. Following the conclusion of the EFSA procurement, EFSA will assess whether the test adds value to the allergenicity and overall risk assessment and, if so, what further steps are needed for its final implementation in the form of guidance for applicants.

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			[Alexander TW, Reuter T, Aulrich K, Sharma R, Okine EK, Dixon WT, McAllister TA, 2007. A review of the detection and fate of novel plant molecules derived from biotechnology in livestock production. Anim Feed Sci Technol 133(1-2): 31-62. Anker P, Stroun M, 2000. Circulating DNA in plasma or serum. Medicina (B Aires) 60(5 Pt 2): 699-702. Bertheau Y, Helbling JC, Fortabat MN, Makhzami S, Sotinel I, Audeon C, Nignol AC, Kobilinsky A, Petit L, Fach P, Brunschwig P, Duhem K, Martin P, 2009. Persistence of plant DNA sequences in the blood of dairy cows fed with genetically modified (Bt176) and conventional corn silage. J Agric Food Chem 57(2): 509-516. Cummings JH, 1984. Cellulose and the human gut. Gut 25(8): 805-810. Deaville ER, Maddison BC, 2005. Detection of transgenic and endogenous plant DNA fragments in the blood, tissues, and digesta of broilers. J Agric Food Chem 53(26): 10268-10275. Hanusová L, Vrabcová P, Rehout V, 2007. Detection of DNA fragments from feed containing GM organisms in blood of broilers. Genetics and Animal Breeding, Brno, Mendel University of Agriculture and Forestry Brno. Kwon K-C, Daniell H, 2016. Oral Delivery of Protein Drugs Bioencapsulated in Plant Cells. Mol Ther. Martens EC, Lowe EC, Chiang H, Pudlo NA, Wu M, McNulty NP, Abbott DW, Henrissat B, Gilbert HJ, Bolam DN, Gordon JI, 2011. Recognition and degradation of plant cell wall polysaccharides by two human gut symbionts. PLoS Biol 9(12): e1001221.	

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			Martin-Orue SM, O'Donnell AG, Arino J, Netherwood T, Gilbert HJ, Mathers JC, 2002. Degradation of transgenic DNA from genetically modified soya and maize in human intestinal simulations. Br J Nutr 87(6): 533-542. Netherwood T, Martin-Orue SM, O'Donnell AG, Gockling S, Graham J, Mathers JC, Gilbert HJ, 2004. Assessing the survival of transgenic plant DNA in the human gastrointestinal tract. Nat Biotechnol 22(2): 204-209. Phipps RH, Deaville ER, Maddison BC, 2003. Detection of transgenic and endogenous plant DNA in rumen fluid, duodenal digesta, milk, blood, and feces of lactating dairy cows. J Dairy Sci 86(12): 4070-4078. Rehout V, Hanusová L, Čítek J, Kadlec J, Hosnedlová B, 2008. Detection of DNA fragments from Roundup Ready soya in blood of broilers. Journal of Agrobiology 25: 145-148. Schubbert R, Hohlweg U, Renz D, Doerfler W, 1998. On the fate of orally ingested foreign DNA in mice: chromosomal association and placental transmission to the fetus. Mol Gen Genet 259(6): 569-576. Schubbert R, Lettmann C, Doerfler W, 1994. Ingested foreign (phage M13) DNA survives transiently in the gastrointestinal tract and enters the bloodstream of mice. Mol Gen Genet 242(5): 495-504. Schubbert R, Renz D, Schmitz B, Doerfler W, 1997. Foreign (M13) DNA ingested by mice reaches peripheral leukocytes, spleen, and liver via the intestinal wall mucosa and can be covalently linked to mouse DNA. PNAS 94(3): 961-966. Sharma R, Damgaard D, Alexander TW, Dugan MER, Aalhus JL, Stanford K, McAllister TA, 2006. Detection of transgenic and endogenous plant DNA	

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Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
			in digesta and tissues of sheep and pigs fed Roundup Ready canola meal. J Agric Food Chem 54(5): 1699-1709. Sierk ML, Pearson WR, 2004. Sensitivity and selectivity in protein structure comparison. Protein Sci 13(3): 773-785. Spisák S, Solymosi N, Ittzés P, Bodor A, Kondor D, Vattay G, Barták BK, Sipos F, Galamb O, Tulassay Z, Szállási Z, Rasmussen S, Sicheritz-Ponten T, Brunak S, Molnár B, Csabai I, 2013. Complete Genes May Pass from Food to Human Blood. PLoS One 8(7): e69805. Wilcks A, van Hoek AH, Joosten RG, Jacobsen BB, Aarts HJ, 2004. Persistence of DNA studied in different ex vivo and in vivo rat models simulating the human gut situation. Food Chem Toxicol 42(3): 493-502.]	

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Austria	Fed.Ministry_Health/Women's Aff.	II.1.2.2 Information relating to the genetically modified plant	2.2.5 Potential risk associated with horizontal gene transfer Scientific Information, p. 30: The applicant maintains that "it is highly unlikely, if not impossible, for DNA sequences from plants to recombine with genomic DNA in human or animal cells " and that "there are no reports "on" plant genomic DNA integrating into the genome of a consuming human or animal." We would like to indicate that there are several peer-reviewed reports available describing exactly this phenomenon (i.e. integration of food/feed/plant-derived DNA into the mammalian genome) (Schubbert et al. 1998), (Mazza et al. 2005), (Deaville and Maddison 2005). The applicant emphasises that "no evidence was found to suggest gene transfer between GM soybean and intestinal micro-flora occurred during the feeding experiments " but forgets to mention that Netherwood et al. "showed evidence of low-frequency gene transfer from GM soya to the microflora of the small bowel" (i.e. transfer of the transgenic epsps gene to bacteria) before the experiment (Netherwood et al. 2004). We would like to ask the EFSA GMO Panel to insist on correct and complete references if the applicant cites from scientific literature. The applicant maintains that "there are no reports plant genomic DNA integrating into the genome of a consuming human or animal." This is not quite correct. Plant-derived DNA sequences especially from multi-copy (e.g. plastid) genes are detectable in blood and/or tissues after ingestion (Phipps et al. 2003; Deaville and Maddison 2005; Hanusová et al. 2007; Rehout et al. 2008; Bertheau et al. 2009; Spisák et al. 2013) and Schubbert et al. are reporting of orally ingested foreign DNA which was subsequently found associated with mammalian chromosomal DNA (Schubbert et al. 1998). The applicant describes a scenario of factors which in his opinion have to occur concomitantly before horizontal gene transfer from genetically enhanced plants to environmental micro-organisms gains any significance and, thus, insinuates that all these factors are highly unlikely to occur in	The GMO Panel took note of the comments raised by Austria and wishes to clarify that besides exposure it also considered the consequences of an unlikely but theoretically possible HGT. The bioinformatics analysis for potential of homologous recombination for events MON87708, MON89788 and A5547-127 has been conducted according to EFSA guidelines (2010, 2017). The GMO Panel concludes that the unlikely, but theoretically possible, horizontal transfer of recombinant genes from this three-event stack soybean to bacteria does not raise any environmental safety concern. As mentioned above, an updated bioinformatic analysis has been conducted by the applicant in line with the latest EFSA requirements. Some uncertainty in the HGT risk assessment remains, because of the theoretically possible involvement of shorter sequences for facilitating homologous recombination and also because the databases do not harbour all DNA sequences of all existing microorganisms. However, in addition to the consideration for the likelihood of recombination, the risk assessment also includes the identification of potential hazards caused by the transfer of the genetic elements of bacterial origin from the GM plants to environmental bacteria. In the case of stack soybean MON87708 × MON89788 × A5547-127 it is also unlikely that a theoretically possible HGT will confer a selective advantage to recipients.

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			natural environments. We refute this line of argumentation by discussing the relevance of each mentioned factor for HGT (please see below): 1) "The recipient bacteria must be competent and able to accept exogenous DNA." The applicant seems to imply that there are probably no competent bacteria available in environments exposed to plant-derived transgenic inserts of microbial origin. We would like to indicate that this is no question of whether competent bacteria are present at all but when and under which circumstances bacteria become competent for DNA uptake. Competence is conserved in at least six different phyla and an old pathway in evolutionary terms (Lorenz and Wackernagel 1994; Johnsborg et al. 2007; Zaccaria et al. 2014). Many bacterial genera and families are carriers for competence genes. For more than 80 bacterial species experimentally proven data for their transformability in natural environments are available (Johnston et al. 2014). A more recent survey collected experimental data for natural transformability of more than 130 bacterial species (Woegerbauer et al. 2015). It was demonstrated that for instance probably all members of the gamma-proteobacterial section of the domain bacteria contain the signature of genes involved in the development of competence and uptake of free extracellular DNA (Cameron and Redfield 2006). The genes for the DNA uptake machinery are therefore putatively present throughout the bacterial and archaebacterial domains of the tree of life (Claverys and Martin 2003; Woegerbauer et al. 2015). It is only a matter of time to establish the conditions which induce the activation of these respective competence genes in natural environments (conditions which may vary even from species to species (Seitz and Blokesch 2013; Johnston et al. 2014)). 2) "The recipient bacteria and donor plant must share DNA that is homologous." We would like to indicate that all transgenic inserts mediating the desired	

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			phenotype in the stacked event under present evaluation are of bacterial origin (see page 20; Scientific Information) and are per definitionem homologous to their counterparts present in naturally occurring plant-associated, soil and gut bacteria and, thus, do "share DNA that is homologous." The applicant perpetuates a definition for homologous sequences focusing on a threshold of "at least two 70 bp of DNA sequences having at least 67 identical nucleotides" between incoming and receiving (genomic) DNA. We would like to indicate that these numbers are arbitrarily chosen and it is questionable if these set boundaries are of any biological relevance. Analyses of bacterial sequence databases using these set of parameters for the query are most likely completely irrelevant concerning the potential of the transgenic inserts to be transferred to bacterial receptor strains in natural environments. In this respect we would like to mention that EFSA is also recommending a different - unfortunately also suboptimal - approach to check the potential of transgenic insert sequences for their potential to undergo homologous recombination with genomic sequences endogenously present in exposed bacterial populations. 3) "The sequence between the two homologous regions in the bacterial genome cannot contain essential genes that if lost due to recombination would be lethal or otherwise compromise the fitness of the recipient bacteria." The applicant appears to be fixed on a model of recombination which relies on a substitutive replacement of genomic sequences as the only possible result of the process. We are of the opinion that the applicant is describing the situation in a much to narrow fashion. It appears that he does not take into account the possibility of homology-directed/facilitated illegitimate recombination (HFIR) as mechanism which may support the dissemination of prokaryotic genes and gene fragments in bacterial populations.	

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			Although HFIR indeed may be an extremely rare event under naturally occurring conditions it nevertheless may be of decisive significance for the risk assessment of HGT in bacterial populations under strong selection pressure (Heinemann and Traavik 2004). Glyphosate is interfering with bacterial growth and is acting as antimicrobial agent under certain circumstances leading to shifts in bacterial community structures (Araujo et al. 2003; Shehata et al. 2013; Arango et al. 2014; Kurenbach et al. 2015). Glyphosate may therefore act as potent selector for the acquisition of plant-derived transgenic epsps homologs. The most outstanding feature of HFIR is that it is relying only on a single anchor sequence which should provide a homologous region of approx. 150 bp (Acinetobacter baylyi) or 180 bp (Streptococcus pneumoniae) with 100% sequence identity to the recombination target sequence and a short region of microhomology (3-10 bp) with relaxed requirements for sequence complementarity on the opposite end of the incoming DNA strand (de Vries and Wackernagel 2002; Prudhomme et al. 2002; de Vries and Wackernagel 2004). Both requirements are much less stringent compared to the thresholds as defined by the relevant scientific note delivered by EFSA on this topic (i.e. significant alignments should meet a threshold of 95% identity in alignments of at least 200bp in length and have at least two regions of similarity between the incoming DNA fragment and the receiving genomic or extrachromosomal microbial sequence (EFSA 2015). These limits reduce the sensitivity of the sequence alignment search for biologically relevant recombination partner molecules significantly. EFSA indicates that HFIR has not been observed under field conditions. However, the currently available tools for monitoring horizontal gene transfers in natural environments are inadequate to capture rare events (i.e. the sensitivity of the available methodology is too low) (Nielsen and Townsend 2004; Townsend et al. 2012; Nielsen et al. 2014). Assuming an already extremely rare recombination/HGT plant to bacterial DNA transmission frequency of 10E-15 under naturally occurring conditions	

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			each square meter of an ordinary agricultural field would harbour at least one recombinant cell. This would accumulate to a total number of 10E12 recombinants/field. Nevertheless, 3 tons of soil would have to be analysed to detect one recombinant cell with the available technology (Heinemann and Traavik 2004). Both numbers (transmission frequency, amount of soil to be tested) currently exceed any detection limit and laboratory capacity by several orders of magnitude (Nielsen et al. 2014). Additionally, it must be stressed that frequency estimates for horizontal gene transfer are not predictive for long-term effects (Pettersen et al. 2005). In summary we would like to indicate that complete replacement of an endogenous gene or an essential part of it (and thereby destroying its function) by recombination is not the only possible outcome of homologous recombination. Gene transfer and exchange processes relying on HFIR provide a means for genetic variability allowing bacteria to easily adapt to changing environmental conditions (de Vries and Wackernagel 2002; Prudhomme et al. 2002; Woegerbauer et al. 2015) 4) "Assuming recombination has occurred, the gene transferred from the plant genome must provide an advantage to the recipient bacteria in the environment over its untransformed neighbors." The applicant is insinuating that there would be no selection pressure in natural environments and the transgenic inserts of prokaryotic origin would not provide any selective advantage if take up by a bacterial recipient. In the case of epsps quite the opposite is true on agricultural fields where soil- and plant-associated bacterial are under strong selection pressure by glyphosate. This may facilitate the selection, survival and establishment of rare gene transfer events in exposed bacterial populations which may then be affected by shifts in their community structure (Busse et al. 2001; Araujo et al. 2003; Kremer et al. 2005; Kuklinsky-Sobral et al. 2005; Ratcliff et al. 2006; Kremer and Means 2009; Barriuso et al. 2010; Lancaster et al. 2010; Barriuso et al. 2011a; Barriuso et al. 2011b; Zobiole et al. 2011; Lane et al. 2012; Krüger et al. 2013;	

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			Shehata et al. 2013; Arango et al. 2014; Karki and Ham 2014; Allegrini et al. 2015; Kurenbach et al. 2015). The applicant is referring to "FASTA searches of databases containing bacterial and archaea genomes, naturally occurring plasmids and viral (including bacteriophage sequence) DNA sequences." We would like to indicate that according to Hileman and Silvanovich (FROM CBI: Study: MSL0027378) only 4905 bacterial genomes were available in the respective database which was used for the analysis of potential recombination partner molecules. Considering the fact that it was estimated that 1 g of soil may contain 10,000 (Torsvik et al. 2002) to more than 10 million of different bacterial species (Gans et al. 2005), this bioinformatic approach covered only a negligible fraction of bacterial genomes which may serve as potential recombination partners. The relevance of this bioinformatic approach for assessing the risk of horizontal gene transfers via transformation is therefore highly questionable. The applicant concludes that "it is highly unlikely, if not impossible, for DNA sequences from plants to recombine with genomic DNA in cells of […] microorganisms." We would like to indicate that this conclusion is most likely correct considering endogenous plant DNA sequences, but it is most likely irrelevant considering transgenic inserts of microbial origin, because these prokaryotic sequences of constitute optimal recombination partners with bacterial chromosomes. We would like to ask the EFSA GMO Panel to take note of these observations. [Allegrini M, Zabaloy MC, Gomez ED, 2015. Ecotoxicological assessment of soil microbial community tolerance to glyphosate. Sci Total Environ 533: 60-68. Arango L, Buddrus-Schiemann K, Opelt K, Lueders T, Haesler F, Schmid	

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Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
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Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
Austria	Fed.Ministry_Health/Women's Aff.	II.1.2.3 Additional information relating to the genetically modified plant required for the environmental safety aspects	2.3.2 Any change to the ability of the genetically modified plant to transfer genetic material to other organisms Scientific Information, p. 31: In this section the applicant neglects any relevance of the transgenic inserts of microbial origin for horizontal plant to bacteria gene transfer and explains his no-risk-hypothesis by the absence of genetic elements with "a genetic transfer function". The inserted gene cassettes may indeed lack conventional genetic elements coding for proteins typically involved actively in horizontal gene transfer processes (like tra or vir operons). However, this section is clearly headed by the title "Any change to the ability of the genetically modified plant to transfer genetic material to other organisms." Concerning plant to bacteria gene transfer natural genetic transformation is a core mechanism for horizontal gene transfer (Stewart 1992; Lorenz and Wackernagel 1994; Chen and Dubnau 2004; Johnsborg et al. 2007). Bacterial transformation in general is relying on the presence of 2 crucial elements: 1) Free extracellular (donor-) DNA and 2) Competent bacterial (receptor-) cells (Dubnau 1999; Chen et al. 2005; Thomas and Nielsen 2005). The presence of genes coding for "genetic transfer functions" on the donor-DNA strand is absolutely no requirement for successfully transforming bacteria (and, thus, spreading genetic information from the transgenic plant to other organisms). In contrast to the initial statement of the applicant quite the opposite is true: Even the mere presence of bacterial sequence context in the transformed plant genome increases significantly the ability of the genetically modified plant to exchange the respective information with bacterial recipients compared to its non-modified conventional counterpart. We would like to ask the EFSA GMO Panel to take note of these observations. [Chen I, Christie PJ, Dubnau D, 2005. The ins and outs of DNA transfer in bacteria. Science 310(5753): 1456-1460.	The GMO Panel thanks Austria for these comments and took note of these observations.

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			Chen I, Dubnau D, 2004. DNA uptake during bacterial transformation. Nature Reviews Microbiology 2(3): 241-249. Dubnau D, 1999. DNA uptake in bacteria. Annual Rev Microbiol 53: 217-244. Johnsborg O, Eldholm V, Havarstein LS, 2007. Natural genetic transformation: prevalence, mechanisms and function. Res Microbiol 158(10): 767-778. Lorenz MG, Wackernagel W, 1994. Bacterial gene transfer by natural transformation in the environment. Microbiol Mol Biol Rev 58: 5563-5602. Stewart GJ, 1992. Gene transfer in the environment: transformation. Release of genetically engineered and other micro-organisms. Fry, J. C., Day, M. J., Martin, M. J. Cambridge University Press, Cambridge: 82–93. Thomas CM, Nielsen KM, 2005. Mechanisms of, and barriers to, horizontal gene transfer between bacteria. Nature Reviews Microbiology 3(9): 711-721.]	

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Austria	Fed.Ministry_Health/Women's Aff.	II.1.3.2 Experimental design and statistical analysis of data from field trials for comparative analysis	For the comparative assessment of composition as well as agronomic and phenotypic characteristics a field trial was conducted in 2015 in the US at 8 trial sites (see Scientific Information, p. 32ff.) including GM soybean MON87708xMON98788xA5547-127 untreated and treated with the complementary herbicides (glyphosate, dicamba and glufosinate). However the study design shows the following shortcomings: • The notifier states that the trial sites "are representative of commercial soybean growing areas and distributed to reflect a variety of agronomic practice, soils and climatic factors " (Scientific Information, p. 34). However, little information other than basic data on climatic conditions, soil type and use of maintenance chemicals are presented to characterise the test sites. However such data are considered insufficient to establish that the trials are representative as regards agronomic practices or abiotic (e.g. soil moisture, soil fertility) and biotic factors (e.g. prevailing pest and disease pressure, weed profiles). • The notifier states that the non-transgenic control (comparator) used in the food and feed safety assessment contains the same genetic background as MON87708xMON98788xA5547 127 (i.e. A3555). However, according to the breeding tree all single events originate from other genetic backgrounds (e.g. A3525, A3244). The stacked GM soybean was crossed twice with Inbred line 3555 later in the breeding process, but no further explanation for this breeding step is provided by the notifier. • The three complementary herbicides seem to have been applied in addition to other maintenance chemicals, in particular additional herbicides (but also glyphosate based herbicides) applied in the field trials (Postin and Werk 2016c), but no rationale for this approach is presented by the notifier. In addition, information on the amount and frequency of applications of the 3 complementary herbicides in the field trial is missing. The EFSA guidance documents (EFSA 2010; EFSA 2015) as well as Implementing Regulation (EU) No 503/2013 (EC 2013) state that a justification shall be provided that the sites and conditions are	The field trials were conducted in typical soybean growing areas of the USA, representing regions of diverse agronomic practices and environmental conditions, which is supported by the geographic map indicating the locations, the information provided on the variety of agronomic practice, soils and meteorological factors. In order to improve the representativeness of the selected field trials, EFSA published a guidance document on the agronomic and phenotypic characterisation of genetically modified plants (EFSA GMO Panel, 2015). Application EFSA-GMO-NL-2016-135 was submitted during the transitional period of the GMO Panel guidance (2015). Therefore, the requirements of the guidance document were not fully applicable for this application. Additional information to further described soil characteristics and agronomic management practices were provided on 21/4/2017 and 28/8/2017. The GMO Panel concludes that the geographical locations, soil characteristics, meteorological conditions and management practices of the field trials are typical for receiving environments where the test materials could be grown. Following questions from the GMO Panel, the applicant provided additional information on 21/4/2017 to provide an estimation of the genetic similarity between the GM soybean stack and the selected comparator. The GMO Panel concludes that the comparator used in

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			representative of the range of receiving environments, where the crop will be commercially grown, explicitly justifying the choice of sites (EFSA 2010). Additionally, an assessment is required whether the expected agricultural practices influence the expression of the transgenes. Thus, we request that the notifier provides further information concerning the selection of sites, evidence for the similarity of the genetic background of the GM soybean stack and the conventional counterpart as well as a clarification regarding the application of herbicides during the field trials. [EC, 2013. Commission Implementing Regulation (EU) No 503/2013 of 3 April 2013 on applications for authorisation of genetically modified food and feed in accordance with Regulation (EC) No 1829/2003 of the European Parliament and of the Council and amending Commission Regulations (EC) No 641/2004 and (EC) No 1981/2006. Official Journal of the European Union. L 157/1: 1-48. EFSA, 2010. Guidance of the GMO Panel on the environmental risk assessment of genetically modified plants. The EFSA Journal 8(11):1879: 1-111. EFSA, 2015. Guidance on the agronomic and phenotypic characterisation of genetically modified plants. The EFSA Journal 13(6):4128: 1-44.]	the field trials has a genetic background similar to that of soybean MON 87708 × MON 89788 × A5547-127 (as documented by the pedigree and by the additional information), and is therefore considered the conventional counterpart. Information on the amount of the three intended herbicides applied in addition to other maintenance chemicals at the corresponding soybean growth stages were reported in MSL0027659. The GMO Panel concludes that the management practices including the application of plant protection products were appropriate for the field trials.
Austria	Fed.Ministry_Health/Women's Aff.	II.1.3.4 Comparative analysis of composition	Besides the general comments on comparative analysis (see comments under 1.3) the compositional analysis contains several weak points: • Although for some of the assessed parameters, e.g. behenic acid, total fat and ADF, statistically significant differences and a lack of equivalence were identified (Scientific Information, Tab. 5 & 6), no analysis was conducted to test for potential genotype x environment interactions. According to Implementing Regulation (EU) No 503/2013 (EC 2013)	The genotype-by-enviroment interaction analysis provided by the applicant followed the recommendations of EFSA GMO Panel (2010, 2011). Per-site summary statistics was provided to aid the

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			however "in the case of significant differences and/or lack of equivalences for any particular endpoint, further statistical analysis shall be carried out to assess whether there are interactions between any of the test materials and site." • Although the stacked GM soybean is intended to be used in combination with the complementary herbicides glyphosate, dicamba and glufosinate the assessment does neither include residual levels of these herbicides nor residual levels of metabolites of the respective herbicide formulations. • The potential more frequent use of different herbicides and/or use of higher amounts in commercial cultures, may affect herbicide residue levels in crop material (Benbrook 2012; Cuhra 2015; Benbrook 2016; Myers et al. 2016). This has not been adequately considered in the field trials design used by the applicant (see comment to Chapter 1.3.2). Thus a per-site analysis should be conducted for those parameters, for which statistically significant differences were identified in the across-site analysis, in order to assess to what extent the environmental and agricultural conditions under which the stacked GM soybean may be grown affect any of the observed differences (EFSA 2010). The results of this analysis should be further considered as regards their relevance for potential adverse effects on human and animal health. Furthermore, we consider that the scope of the comparative analysis concerning food and feed risk assessment is too narrow with a view to the characteristics of GM soybean MON87708xMON98788xA5547-127 and that the presence of residual levels of herbicides as well as the levels of residual metabolites of the complementary herbicides in GM soybean grain material should be determined. The consequences of these findings for the conclusions of the assessment of effects on human and animal health should be considered by the applicant, specifically as regards sub-chronic, developmental and reproductive toxicity. In order to ensure that assessments are representative of commercial cultivation conditions, the potential increase in herbicide use (i.e. types of	interpretation of the results of the analysis. The GMO Panel was able to conclude based on the information provided by the applicant. The risk assessment of herbicide residues in GM plants is not in the remit of the GMO Panel, but is performed by EFSA's Pesticides Unit.

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			herbicides, application rates and frequencies) due to rising weed resistances, needs to be taken into account. Thus the applicant needs to justify, why the treatment regime used in the field trials is considered a realistic exposure scenario. [Benbrook C, 2012. Impacts of genetically engineered crops on pesticide use in the U.S. - the first sixteen years. Environmental Sciences Europe 24(1): 24. Benbrook CM, 2016. Trends in glyphosate herbicide use in the United States and globally. Environmental Sciences Europe 28(1): 1-15. Cuhra M, 2015. Review of GMO safety assessment studies: glyphosate residues in Roundup Ready crops is an ignored issue. Environmental Sciences Europe 27(1): 1-14. EC, 2013. Commission Implementing Regulation (EU) No 503/2013 of 3 April 2013 on applications for authorisation of genetically modified food and feed in accordance with Regulation (EC) No 1829/2003 of the European Parliament and of the Council and amending Commission Regulations (EC) No 641/2004 and (EC) No 1981/2006. Official Journal of the European Union. L 157/1: 1-48. EFSA, 2010. Scientific opinion of the GMO Panel on statistical considerations for the safety evaluation of GMOs. The EFSA Journal 8(1):1250: 1-59. Myers JP, Antoniou MN, Blumberg B, Carroll L, Colborn T, Everett LG, Hansen M, Landrigan PJ, Lanphear BP, Mesnage R, Vandenberg LN, Vom Saal FS, Welshons WV, Benbrook CM, 2016. Concerns over use of	

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			glyphosate-based herbicides and risks associated with exposures: a consensus statement. Environ Health 15(1): 19.]	
Austria	Fed.Ministry_Health/Women's Aff.	II.1.3.4 Comparative analysis of composition	Genotype by site analysis The applicant provides a table on the genotype x site analysis presenting p-values for each component (FROM CBI: Study: MSL0027449). For a comprehensive discussion of the genotype x site analysis, the applicant should present results of "significances per site" (e.g. p-values of the per-site comparisons). Without these data it is impossible to verify (in what samples) from which site the most significant results occurred, and if relevant genotype x site interactions exist. The applicant should provide this information to substantiate the argument raised that "no meaningful trends were found for any of the components in Tables 9a and 9b with significant interactions " (FROM CBI: Study: MSL0027449).	As recommended by EFSA guidance (EFSA GMO Panel, 2011), the applicant provided (a) the results of an analysis of genotype-by-site interaction and (b) descriptive statistics for each site, including mean and standard deviations for the GM, the conventional counterpart and the set of reference varieties. All this information was carefully scrutinised by the GMO Panel in the risk assessment. The GMO Panel was able to conclude on the risk assessment based on the information provided.

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Austria	Fed.Ministry_Health/Women's Aff.	II.1.3.4 Comparative analysis of composition	Results of the compositional analysis and statistically significant differences Compositional analysis was conducted using field trial data from the year 2015 in the United States. The field trials consisted of eight field sites where stacked GM soybean MON87708xMON98788xA5547 127, its near-isogenic control line (conventional counterpart variety A3555), and 16 different reference varieties were cultivated. Two different treatment regimes were included in the trial design and analysis: a) GM soybean treated with glyphosate (T), b) GM soybean not treated with glyphosate (NT). The compositional analysis consisted of difference and equivalence tests of 56 components in the forage and grain of the GM soybean stack: • For the GM soybean stack (T), 56 components in grain and forage were statistically assessed and 54% of the components (30 of 56) were significantly different in the Difference Test at 10% significance level. • For the GM soybean stack (NT), 56 components in grain and forage were statistically assessed and 45% of the components (25 of 56) were significantly different in the Difference Test at 10% significance level. Following a list of selected analytes that are statistically significant in the Difference Test with medium to high "relative differences of means" (data derived from study report FROM CBI: Study MSL0027449): 1) GM soybean stack (T): Behenic acid (grain) has a relative difference of -8.127%. NDF (forage) has a relative difference of 9.352%. ADF (forage) has a relative difference of 10.665%. Daidzein has a relative difference of -13.020%. Genistein has a relative difference of -7.599%. 2) GM soybean stack (NT): Behenic acid has a relative difference of -7.883%. Vitamin E has a relative difference of 7.525%. Trypsin inhibitor has a relative difference of	The GMO Panel assessed all significant differences between soybean MON 87708 × MON 89788 × A5547-127 and its conventional counterpart (difference test), taking into account the potential impact on plant metabolism and the natural variability observed for the set of non-GM reference varieties (equivalence test). For this particular three stack GM-soybean, the levels of acid detergent fibre (treated GM), total fat (treated GM) and behenic acid (treated and not-treated GM) in seeds were further assessed in terms of food & feed safety and their nutritional implications.

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			9.538%. Daidzein has a relative difference of -10.241%. The applicant in the study report (FROM CBI: Study MSL0027449) discusses the absolute differences in means and sets them in relation to the range of conventional counterpart values. However, the absolute differences are not meaningful. The applicant is requested to provide a discussion based on the relative differences of means which provide the more substantial data. Compare EFSA Guidance, "Differences are commonly expressed as a percent change, i.e. as relative differences (ratios) rather than absolute differences "(EFSA 2010) and the discussion presented on the example as shown in Chapter 5.2 "Results" in the same Guidance Document. It would be useful for each significant difference observed between the GM crop and its conventional counterpart to provide a discussion taking into account the (high) relative differences of means. It should be considered that highly significant differences give an indication that unexpected effects occurred in the metabolism of the plant potentially leading to shifts in minor plant compounds (e.g. secondary metabolites, precursors) that are not included in the compositional analysis. [EFSA, 2010. Scientific opinion of the GMO Panel on statistical considerations for the safety evaluation of GMOs. The EFSA Journal 8(1):1250: 1-59.]	
Austria	Fed.Ministry_Health/Women's Aff.	II.1.3.5 Comparative analysis of agronomic	The Non-GMO-variety A3555 used as backcross partner in the breeding history of MON87708xMON89788xA5547-127 and as conventional counterpart in the study below is not ident with any of the primal recipient varieties (A3525, A3244 and Benning inbred) of the single events stacked.	Following questions from the GMO Panel, the applicant provided additional information on 21/4/2017 to provide an estimation of the genetic similarity between the GM soybean stack and the selected comparator.

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		and phenotypic characteristics	The applicant is asked to explain, if and how A3555 is related to those varieties. The information about maturity range of the reference varieties is useful and according to EFSA Guidance on the environmental risk assessment of GM-plants (EFSA 2011). Conclusions concerning differences between test and control substances in agronomic and phenotypic characteristics are based on results of the agronomic study carried out by FROM CBI: Study: MSL0027659. Specific comments on the field trial study - FROM CBI: Study: MSL0027659. Trial sites and trial design: The distribution of the trial sites in USA is adequate for the maturity rage of the test materials including the reference varieties. The RCB-design with four replications, the number of eight trial sites and the number of four reference varieties on each site out of sixteen reference varieties in total are in accordance with the EFSA-opinion on statistical considerations for the safety evaluation of GMOs (EFSA 2010). Agronomic and phenotypic characteristics: The phenotypic characteristics recorded in the study are useful, however, the observations of days to maturity are lacking. Maturity behaviour of varieties is a crucial character in soybean cultivation. Following the EFSA Guidance on agronomic and phenotypic characterisation of genetically modified plants (EFSA 2015) recordings for the character pods per plant are lacking. [EFSA, 2010. Scientific opinion of the GMO Panel on statistical considerations for the safety evaluation of GMOs. The EFSA Journal 8(1):1250: 1-59. 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.	The GMO Panel concludes that the comparator used in the field trials has a genetic background similar to that of soybean MON 87708 × MON 89788 × A5547-127 (as documented by the pedigree and by the additional information), and is therefore considered the conventional counterpart. In order to improve the description of the field trials and to standardise the collection of the endpoints, EFSA published a guidance document on the agronomic and phenotypic characterisation of genetically modified plants (EFSA GMO Panel, 2015). Application EFSA-GMO-NL-2016-135 was submitted during the transitional period of the GMO Panel guidance on the agronomic and phenotypic characterisation of GM crops. Therefore, the requirements of the guidance document were not fully applicable for this application.

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			EFSA, 2015. Guidance on the agronomic and phenotypic characterisation of genetically modified plants. The EFSA Journal 13(6):4128: 1-44.]	
Austria	Fed.Ministry_Health/Women's Aff.	II.1.4 Toxicology	Results of the toxicological assessment and active principles DMO protein A repeated-dose feeding toxicity study in mice with a mixture of the DMO and DMO+27 proteins (actual doses: 0, 17.5, 52.4 and 174 mg/kg bw per day in males; 0, 15.5, 53 and 179.7 mg/kg bw per day in females; 28 days) resulted in the following outcomes (excerpt): Regarding the clinical pathology parameters there was a statistically significant difference in the mean absolute neutrophil count in males of the high-dose group (increase). A slightly significantly higher mean spleen weight (relative to body weight) was seen in a male group given the high dose than in the control group (EFSA 2013). In the 90-day whole food and feed study the following outcome was reported (excerpt): Body weight gain was transiently lower (up to 11%; statistically significant) in females given the diet containing 15 % soybean MON87708 (weeks 0-6) and in males given the diet containing 30% soybean MON87708 (weeks 0-3). No biologically relevant differences in feed intake were seen among groups. There were statistically significant differences in clinical pathology and urinalysis parameters between rats fed diets containing soybeanMON87708 and control animals (i.e. lower mean absolute monocytes counts in females fed the 15% MON87708 diet; higher mean percent eosinophils, higher alanine aminotransferase activity and serum chloride levels in male rats fed 30% MON87708; changes in urinary specific gravity, pH and volume in females fed 15% test diet; and lower spleen weight in female rats given diets containing 15% soybean MON87708) (EFSA 2013). PAT protein	The GMO Panel notes that these comments refer to toxicological studies assessed in the context of the single event applications.

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			WHO/FAO/JMPR states in its 1998 evaluation of Glufosinate-ammonium that information on the metabolism of glufosinate-ammonium and NAG (N-acetyl-L-glufosinate) in laboratory rats, lactating goats and laying hens was reported. In summary, most of the administered dose of both compounds is rapidly excreted. NAG may be partially metabolised back to glufosinate (WHO/FAO/JMPR 1998). Bremmer and Leist examined the possible conversion of NAG to glufosinate in rats. Up to 10% deacetylation occurred at a low dose of 3 mg/kg bw as shown by the occurrence of glufosinate in the faeces (Bremmer and Leist 1997). The authors concluded, however, that most of the conversion was caused by bacteria in the colon and rectum although toxicity findings indicate partial bioavailability (Bremmer and Leist 1998). Applicant's argumentation (Scientific Information, p. 47) "A comprehensive evaluation of the safety of the DMO, CP4 EPSPS and PAT proteins established that it is highly unlikely that they would cause any adverse effects on human or animal health." "Based on the above information and the weight of evidence, the consumption of MON 87708 × MON 89788 × A5547-127 and DMO, CP4 EPSPS and PAT proteins from MON 87708 × MON 89788 × A5547-127 should be considered safe for human and animal health and no further studies are necessary to confirm their safety. As expected, 90-day studies with the single events inherited in MON 87708 × MON 89788 × A5547-127 showed no biologically or toxicologically relevant effects and supports the conclusion that MON 87708 × MON 89788 × A5547-127 is as safe as conventional soybean from a food and feed perspective. The data presented in this application shows no indications of potential adverse effects of the stability of the inserts, the expression of the inserts or the potential synergistic or antagonistic effects resulting from the combination of the parental lines, therefore an additional 90-day feeding study with whole food and feed in rodents with MON 87708 × MON 89788 × A5547-127 is not scientifically justified, nor is it needed to assess the safety of	

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			MON 87708 × MON 89788 × A5547-127." Conclusions Some unresolved questions still remain regarding safety and possible toxicity which have not been addressed by the applicant yet. The applicant does not deem necessary to provide any additional data on toxicity for the whole GM food/feed. Regarding the 90-day whole food/feeding study, the main difference between testing chemicals and whole food/feed is that chemicals can be administered to the test animals at dose levels which are much higher than the likely human exposure levels, whereas such a testing approach is almost impossible with whole food or feed. In fact, administering high dose levels of whole food/feed is likely to result in satiation and/or unbalanced diets. Careful consideration should be given to effective ways in which the design, conduct and analysis of the OECD TG 408 are adapted to specific whole food/feed testing in order to increase the chance of detecting any toxicologically relevant effects. It is necessary to keep the test conditions and parameters within narrow boundaries, strictly to follow test protocols, and to minimise the intra-test variations. Increased attention has to be paid to even very slight deviations from control groups in different parameters because of the very small concentrations/dosages of the active principle(s), at least with whole GM food/feed, which can be used. Moreover, there may be findings which might have a pathological impact being the first step of detrimental effects for the time being only slightly apparent because of the relatively short duration and very low dosages. Nearly all of 90-day whole food/feed studies in rodents (Remark: And also with the given applications) reported statistically significant differences between GM and non-GM fed groups in at least some parameters tested (Domingo 2016). These differences - which in principle can be indeed statistical artefacts due to multiple testing - were argued away as biologically irrelevant or non-treatment related - usually without attempting to seek empirically for a causal relationship for	

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			the aberrations in follow-up studies. Chronic and subchronic trials which showed biologically relevant effects were usually discredited for shortcomings in the experimental design or the data evaluation, although several trials accepted as valid in the scientific community suffer from similar inconsistencies at a closer look (Snell et al. 2011). Taking into consideration the weaknesses and flaws in the assessment of the individual active principles, the testing of the combined traits (for instance by a 90-day toxicity study in rodents) becomes even more important, and should be done. Furthermore, a potential for increased toxicity and/or allergenicity to humans and animals or for modified nutritional value due to the stacked events may arise from additive, synergistic or interactions among the single events with regard to antagonistic effects of the gene products or by these produced metabolites. Hence, the safety of all newly expressed proteins in animal models applied simultaneously and combined should be assessed. In conclusion, several questions on the safety of the genetically modified products remain still unanswered and have to be clarified before final assessments can be made. Moreover, as already said elsewhere, with the given study batteries and designs, no final evidence is possible with reference to long-term (especially appropriate for foodstuffs), reproductive or developmental effects of the whole food and/or feed. This is even underlined by the EFSA GMO Panel, which states with regard to reproduction and developmental toxicity: „However, the subchronic, 90-day rodent feeding study is not designed to detect effects on reproduction or development, other than effects on adult reproductive organ weights and histopathology. Thus, in some cases, testing of the whole food and feed beyond a 90-day rodent feeding study may be needed" (EFSA 2008). [Bremmer JN, Leist K-H, 1997. Disodium-N-acetyl-L-glufosinate; AE F099730 - Hazard evaluation of L-glufosinate produced intestinally from	

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Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
			N-acetyl-L-glufosinate. Safety Evaluation Frankfurt. TOX97/014. A58659. Unpublished. Hoechst Schering AgrEvo GmbH. Bremmer JN, Leist K-H, 1998. Disodium-N-acetyl-L-glufosinate (AE F099730, substance technical) - Toxicity and metabolism studies summary and evaluation. Frankfurt. TOX98/027. A67420. Unpublished. Hoechst Schering AgrEvo GmbH. Domingo JL, 2016. Safety assessment of GM plants: An updated review of the scientific literature. Food Chem Toxicol 95: 12-18. 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. EFSA, 2013. Scientific Opinion of the EFSA GMO Panel on application EFSA-GMO-NL-2011-93 for the placing on the market of the herbicide-tolerant genetically modified soybean MON 87708 for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto. The EFSA Journal 11(10):3355: 1-30. Snell C, Bernheim A, Berge JB, Kuntz M, Pascal G, Paris A, Ricroch AE, 2011. Assessment of the health impact of GM plant diets in long-term and multigenerational animal feeding trials: A literature review. Food Chem Toxicol 50(3-4): 1134-1148. WHO/FAO/JMPR, 1998. Glufosinate-Ammonium (175); http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/Evaluation98/glufosi.pdf; (last accessed: 26/08/2015).]	

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Austria	Fed.Ministry_Health/Women's Aff.	II.5.3.2 Plant to micro-organisms gene transfer	5.3.2.1. Step 1: Problem formulation Scientific Information, p. 73: The applicant maintains that "MON 87708 × MON 89788 × A5547-127 does not contain antibiotic resistance marker genes and none of the genetic elements inserted into MON 87708, MON 89788 and A5547-127 and inherited in MON 87708 × MON 89788 × A5547-127 have a genetic transfer function." We would like to indicate that MON87708xMON89788xA5547-127 is carrier of two fragments of a ß lactamase gene which mediates antibiotic resistance to penicillin and several other clinically relevant penicillin derivatives (Technical Dossier, Notification EFSA-GMO-NL-2008-52). The presence of antibiotic resistance gene fragments - especially from an antibiotic resistance gene of significant clinical relevance - is not reported in the application for the stack under evaluation. We would like to ask the EFSA GMO Panel to take care that the applicant reports all information necessary for an informed decision making by risk managers. Although indeed no intact antibiotic resistance gene is present in the stack under evaluation, the fragments which comprise approx. 800 bp of bacterial DNA content in total (see Table 9, Technical Dossier, Notification EFSA-GMO-NL-2008-52 and FROM CBI: Study 15-RSNKS003) may interact with homologous elements in bacterial receptor strains (Woegerbauer et al. 2015b). This may fuel the antibiotic resistance gene pool and may lead to the formation of mosaic ß-lactamase genes potentially coding for enzymes with expanded or alternate substrate specificities leading to the dissemination of new antibiotic resistance functions in bacterial populations. Due to large data and knowledge gaps concerning selection pressure and the impact of resistance gene fragments on the development and dissemination of antibiotic resistance in natural environments it would be fair to acknowledge that risk assessments of plant to bacteria ARM gene HGT are currently affected	The GMO Panel took care of this aspect in the context of application EFSA-GMO-NL-2008-52 and EFSA-GMO-NL-2013-120 (EFSA GMO Panel, 2011 ;2017). Two fragments of the *bla* gene are present in event A5547-127 and are located at the 5' and 3' flanking regions. The two *bla* fragments do not constitute a functional gene. The assessment, based on updated bioinformatic analysis, confirmed that double homologous recombination could occur between the non-functional *bla* gene fragments of event A5547-127, with a chromosomally located *bla* gene, leading to a chromosomally inserted *pat* gene. Due to its plant codon optimisation, it is expected that the newly acquired *pat* gene would not provide a selective advantage to bacterial recipients. Confirming the previous conclusion of the GMO Panel, no risk was identified for HGT of the recombinant DNA derived from event A5547-127. The bioinformatics analysis for potential of homologous recombination for events has been conducted according to EFSA guidelines (2010, 2017). This analysis was conducted for event A5547-127 as well as for MON87708 and MON89788. Sequence homology with sequenced bacteria were identified with this analysis. The potential formation of mosaic genes is taken into account in the HGT assessment. The GMO Panel considers that non-homologous (illegitimate) recombination is possible but, in comparison with

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			with a high degree of uncertainty. We would like to ask the EFSDA GMO Panel to take this observation into consideration for their evaluations. The applicant refers to a "limited bacterially derived sequence content, the sequence source, the organization of those bacterially derived sequences in MON 87708 × MON 89788 × A5547-127 and the absolute requirement of the presence of a homologous sequence in the acceptor prokaryotic micro-organism" and insinuates that all these characteristics are inhibitive for horizontal gene transfer. We would like to reiterate and stress that: 1) the overwhelming part of the transgenic inserts in MON87708xMON89788xA5547 127 are of bacterial/prokaryotic origin and, thus, should constitute per definitionem optimal partner molecules for homologous recombination with bacterial receptor genomes, 2) the source of at least one insert is an important multi-drug resistant nosocomial pathogen, 3) the organisation of the elements on the transgenic insert are by no means more or less inhibitive as other prokaryotic DNA sequences involved in bacterial transformation, and 4) "absolute" homology in the sense of sequence identity between incoming and receptor DNA is no requirement for an effective bacterial transformation. The efficiency of recombination decreases in a log-linear relationship with increasing sequence diversity between donor and receptor DNA strands and drops below the limit of detection if sequence diversity surpasses 25-30% (Fraser et al. 2007; Woegerbauer et al. 2015b) The applicant is of the opinion that HGT of dmo, cp4 epsps and pat genes does not offer an evolutionary advantage, because "the genes would have been transferred to other microbes during evolution via HGT from microbes already possessing this gene." We would like to mention that this statement represents an utterly naïve	homologous recombination, does not contribute significantly to HGT events. In this case, natural variants of the bacterial genes exist in the environment and the likelihood of their HGT is much higher than for the transfer from GM plants to bacteria.

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			perception of bacterial evolution. Moreover, the applicant is ignoring the potential for creating genetic variability by the transfer of mutated dmo, cp4 epsps and pat gene variants or fragments thereof (Woegerbauer et al. 2015a). The transgenic genes in the insert are affected by the same intrinsically active mutation rate as any other plant gene. If released into the environment by plant decay or root exudates, the DNA is expected to get fragmented and suffer from lesions (Pontiroli et al. 2007; Pietramellara et al. 2009; Poté and Wildi 2012; Morrissey et al. 2015). Even DNA fragments and damaged DNA are taken up by competent bacteria leading to the formation of mosaic genes coding for proteins with new phenotypic properties (Woegerbauer et al. 2015b) or (if only short fragments are involved) are inducing mutations in the receiving genome (Overballe-Petersen et al. 2013). The applicant maintains that "current scientific evidence indicates that the transfer of genes derived from GM plants into bacteria and their stable integration, either does not occur or, unlikely, it has been below the limit of detection in all the studies performed." We would like to point to the fact that - quite to the contrary - it is highly likely that the studies which analysed the frequency of horizontal gene transfer from plant to bacteria and which retrieved negative results were affected by insufficient detection limits (Heinemann and Traavik 2004; Nielsen and Townsend 2004; Townsend et al. 2012; Nielsen et al. 2014). The word "unlikely" in this context is misleading and highly inappropriate according to recent literature. We would like to ask the EFSA GMO Panel to take note of it. The applicant refers to containment systems which should reduce environmental exposure with transgenic DNA: We would like to indicate that containment is not absolute. There are many report of feral plant growth alongside transport routes, at transportation hubs and at manufacturing plants (Pascher 2016; Pascher et al. 2016).	

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			[Fraser C, Hanage WP, Spratt BG, 2007. Recombination and the nature of bacterial speciation. Science 315(5811): 476-480. Heinemann JA, Traavik T, 2004. Problems in monitoring horizontal gene transfer in field trials of transgenic plants. Nat Biotechnol 22(9): 1105-1109. Morrissey EM, McHugh TA, Preteska L, Hayer M, Dijkstra P, Hungate BA, Schwartz E, 2015. Dynamics of extracellular DNA decomposition and bacterial community composition in soil. Soil Biol Biochem 86: 42-49. Nielsen KM, Bohn T, Townsend JP, 2014. Detecting rare gene transfer events in bacterial populations. Front Microbiol 4: 415. Nielsen KM, Townsend JP, 2004. Monitoring and modeling horizontal gene transfer. Nat Biotechnol 22(9): 1110-1114. Overballe-Petersen S, Harms K, Orlando LA, Mayar JV, Rasmussen S, Dahl TW, Rosing MT, Poole AM, Sicheritz-Ponten T, Brunak S, Inselmann S, de Vries J, Wackernagel W, Pybus OG, Nielsen R, Johnsen PJ, Nielsen KM, Willerslev E, 2013. Bacterial natural transformation by highly fragmented and damaged DNA. Proc Natl Acad Sci U S A 110(49): 19860-19865. Pascher K, 2016. Spread of volunteer and feral maize plants in Central Europe: recent data from Austria. Environmental Sciences Europe 28(1): 30. Pascher K, Hainz-Renetzeder C, Kneissl K, Gollmann G, Schneeweiss G, 2016. Unintended spillage of viable oilseed rape seeds along transportation routes in Austria: ecological risk assessment and management of feral plants.' Paper presented at, Lyon, France, 30/08/16	

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Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
			- 2/09/16, pp. 257. Pietramellara G, Ascher J, Borgogni F, Ceccherini M, Guerri G, Nannipieri P, 2009. Extracellular DNA in soil and sediment: fate and ecological relevance. Biol Fertility Soils 45(3): 219-235. Pontiroli A, Simonet P, Frostegard A, Vogel TM, Monier JM, 2007. Fate of transgenic plant DNA in the environment. Environ Biosafety Res 6(1-2): 15-35. Poté J, Wildi W, 2012. Plant leaf decomposition, DNA release, persistence and transfer into the environment. Transgenic Plants: Recent Developments. Zhu, S. Y., Hu, J. L., Nova Science. Townsend JP, Bohn T, Nielsen KM, 2012. Assessing the probability of detection of horizontal gene transfer events in bacterial populations. Front Microbiol 3: 27. Woegerbauer M, Kuffner M, Domingues S, Nielsen KM, 2015a. Involvement of aph(3‘)-IIa in the formation of mosaic aminoglycoside resistance genes in natural environments. Frontiers in Microbiology 6. Woegerbauer M, Kuffner M, Kopacka I, Domingues S, Steinwider J, Nielsen KM, Fuchs K, 2015b. Impact of mosaic genes on the risk assessment of GMOs. Federal Ministry of Health: 1-268.]	

Austria	Fed.Ministry_Health/Women's Aff.	II.5.3.2 Plant to micro-organisms gene transfer	5.3.2.2. Step 2: Hazard characterisation Scientific Information, p. 76: The applicant maintains that "there is negligible potential for recombination between genetic material inherited in MON 87708 × MON 89788 × A5547-127 and environmental prokaryotic micro-organisms due to limited bacterially derived sequence content, the sequence source, the organization of those bacterially derived sequences in MON 87708 × MON 89788 × A5547-127 and the absolute requirement of the presence of a homologous sequence in the acceptor prokaryotic micro-organism." We would like to indicate that transformation of bacteria with prokaryotic elements embedded in plant genomic DNA is observable and no argument against successful recombination (Gebhard and Smalla 1998; Gebhard and Smalla 1999). And postulating an "absolute" requirement for the presence of homologous sequences is misleading: the rate of homologous recombination is decreasing in a log linear relationship with increasing sequence divergence among the involved DNA molecules and fall below the level of detection at a sequence divergence above 25-30% (Fraser et al. 2007; Woegerbauer et al. 2015). We would like to ask the EFSA GMO Panel to take this into consideration. [Fraser C, Hanage WP, Spratt BG, 2007. Recombination and the nature of bacterial speciation. Science 315(5811): 476-480. Gebhard F, Smalla K, 1998. Transformation of Acinetobacter sp. strain BD413 by transgenic sugar beet DNA. Appl Environ Microbiol 64(4): 1550-1554. Gebhard F, Smalla K, 1999. Monitoring field releases of genetically modified sugar beets for persistence of transgenic plant DNA and horizontal gene transfer. FEMS Microbiol Ecol 28(3): 261-272. Woegerbauer M, Kuffner M, Kopacka I, Domingues S, Steinwider J, Nielsen KM, Fuchs K, 2015. Impact of mosaic genes on the risk assessment of GMOs. Federal Ministry of Health: 1-268.]	The GMO Panel took note of this comment. The GMO Panel concludes that the unlikely, but theoretically possible, horizontal transfer of recombinant genes from this three-event stack soybean to bacteria does not raise any environmental safety concern

Austria	Fed.Ministry_Health/Women's Aff.	II.5.3.2 Plant to micro-organisms gene transfer	5.3.2.3. Step 3: Exposure characterisation Scientific Information, p. 77: The applicant describes a study by Gulden et al. and points out that the study authors did not observe an accumulation of transgenic plant DNA in the tested soil but forgets to mention that several samples tested positive for transgenic CP4 epsps even two years after the last transgenic crop was planted in the respective plot (FROM CBI: (Gulden et al. 2008)). We would like to ask the EFSA GMO Panel to take care for a correct and full presentation of literature data by the applicants. The applicant maintains that "after duodenum passage, over 95% of DNA is hydrolyzed and bases are absorbed into the enterocytes." Considering a per capita uptake of transgenic inserts of 9 x 10E9 molecules per day of a genetically modified maize variety (FROM CBI: (Jonas et al. 2001)) a reduction by 95% would mean that still approximately 1 x 10E7 intact molecules would be available in the system for bacterial transformation. A reduction by 95% is irrelevant concerning the risk assessment of transgenic inserts in relation to bacterial transformation. We would like to ask the EFSA GMO Panel to take note of this calculation. [Gulden RH, Lerat S, Blackshaw RE, Powell JR, Levy-Booth DJ, Dunfield KE, Trevors JT, Pauls KP, Klironomos JN, Swanton CJ, 2008. Factors Affecting the Presence and Persistence of Plant DNA in the Soil Environment in Corn and Soybean Rotations. Weed Sci 56: 767-774. Jonas DA, Elmadfa I, Engel KH, Heller KJ, Kozianowski G, Konig A, Muller D, Narbonne JF, Wackernagel W, Kleiner J, 2001. Safety considerations of DNA in food. Ann Nutr Metab 45(6): 235-254.]	The GMO Panel took note of this comment and reminds that the scope of this application is for import/processing for food/feed uses, excluding cultivation. The GMO Panel also took note of the proposed calculation.

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Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
Austria	Fed.Ministry_Health/Women's Aff.	II.6 Post-Market Environmental Monitoring Plan (PMEM)	General remarks The proposed monitoring plan for GM soybean MON87708xMON98788xA5547-127 is basically identical to other monitoring plans for different products which were submitted earlier. A number of concerns have been raised towards these plans and numerous improvements have been requested by Austria with regard to these monitoring plans. The Austrian requests for improvement have been based on issues discussed in the scientific literature, in scientific reports of competent authorities from various member states (see e.g. (Züghart et al. 2011)) or on recommendations by EFSA derived from the review of monitoring approaches for GM maize lines (e.g. (EFSA 2011b; EFSA 2012). However, most of the recommendations are not taken into account in the monitoring plan at hands. Therefore it cannot be considered adequate. In particular, the monitoring plan for GM soybean MON87708xMON98788xA5547-127 is considered not adequate for the following reasons: The notifier does not specifically consider potential exposure of EU environments to GM soybean MON87708xMON98788xA5547-127 other than by unintended release of substantial volumes of viable GM soybean via losses during loading or unloading for processing into animal feed or human food products. Other exposure scenarios should be considered according to current EFSA guidance (EFSA 2011a), e.g. accidental spillage during transport, commingling with other grain lots and exposure via waste materials from processing or use. Since all exposure pathways should be taken into account in the monitoring plan appropriately, we consider the monitoring plan at hands to be insufficient to address the potential environmental effects of GM soybean MON87708xMON98788xA5547-127. We therefore suggest that the notifier considers the recommendations by EFSA derived from the evaluation of previous monitoring of other GM	The GMO Panel took note of this comment and reminds that the scope of this application is for import/processing for food/feed uses, excluding cultivation. The environmental risk assessment (ERA) of the three-event stack soybean is mainly concerned with: (1) the exposure of bacteria to recombinant DNA in the gastrointestinal tract of animals fed GM material and bacteria present in environments exposed to faecal material of these animals (manure and faeces); and (2) the accidental release into the environment of viable soybean MON87708 × MON89788 × A5547-127 seeds during transportation and/or processing. Moreover, monitoring and its practical implementation are related to risk management, and thus a final adoption of the post-market environmental monitoring plan falls outside the mandate of EFSA.

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			crops (among others (EFSA 2011b; EFSA 2012)) and implements suggestions, e.g. as regards the literature review, etc. Additional concerns regarding the monitoring plan proposed for GM soybean MON87708xMON98788xA5547-127 are reiterated in the following. [EFSA, 2011a. Guidance of the GMO Panel on the Post-Market Environmental Monitoring (PMEM) of genetically modified plants. The EFSA Journal 9(8):2316: 1-40. EFSA, 2011b. Scientific Opinion of the GMO Panel on the annual Post-Market Environmental Monitoring (PMEM) report from Monsanto Europe S.A. on the cultivation of genetically modified maize MON810 in 2009. The EFSA Journal 9(10):2376: 1-66. EFSA, 2012. Scientific Opinion of the GMO Panel on the annual Post-Market Environmental Monitoring (PMEM) report from Monsanto Europe S.A. on the cultivation of genetically modified maize MON 810 in 2010. The EFSA Journal 10(4):2610: 1-35. Züghart W, Raps A, Wust-Saucy A-G, Dolezel M, Eckerstorfer M, 2011. Monitoring of genetically modified organisms. A policy paper representing the view of the National Environment Agencies in Austria and Switzerland and the Federal Agency for Nature Conservation in Germany. Umweltbundesamt Wien, Reports, Volume 0305. Vienna: 1-56.]	

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Country	Organization	Reference	Comment	GMO Panel responses
Austria	Fed.Ministry_Health/Women's Aff.	II.6.3 General Surveillance (strategy, method)	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 MON87708xMON98788xA5547-127 at EU level (COCERAL, UNISTOCK and FEDIOL). However, it should be clear which existing national institutions 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 and that the monitoring is ensured to be proportionate to the extent of imports of GM soybean MON87708xMON98788xA5547-127 as indicated by the notifier. 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 MON87708xMON98788xA5547-127 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 MON87708xMON98788xA5547-127. 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 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 " (PMEM plan, Chapter 6.4.2, p. 3). 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. In this respect, we reiterate our request that appropriate measures are	Monitoring and its practical implementation are related to risk management, and thus a final adoption of the post-market environmental monitoring plan falls outside the mandate of EFSA.

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			implemented to determine the extent of exposure of the environment to GM soybean MON87708xMON98788xA5547-127 and the fate of transgenic material in the environment (c.f. (Züghart et al. 2011)). We note that the Finnish Board for Gene Technology has recommended that for general surveillance of stacked GM soybean applications appropriate management systems should be introduced for active monitoring of feral soybean plants in areas where soybean spillage and plant establishment are likely to occur and that appropriate management systems should also be used for restricting soybean seeds from entering cultivation. 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 regard to the parameters that are going to be monitored, as well as on the methodological approaches implemented for monitoring. The notifier only refers to substantial unintended losses of GM soybean MON87708xMON98788xA5547 127 during loading and unloading as a route for environmental exposure. Other routes of exposure of the environment by (waste) materials from processing or use of GM soybean MON87708xMON98788xA5547 127 are not assessed specifically. However the requirement that all potential routes of exposure should be addressed is one of the pillars of the EU approach to monitoring. The notifier states that "exposure to the environment will be limited ...	

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			Exposure can be controlled by clean up measures and the application of current practices used for the control of any adventitious soybean plants, such as manual or mechanical removal and the application of herbicides" (PMEM plan Chapter 6.4.1, p. 3f). As no clear responsibilities are assigned in this respect, it remains unclear who actually will be responsible e.g. 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 MON87708xMON98788xA5547-127. It should, therefore, be revised by the notifier to address the above noted issues and any other shortcomings compared with the current state of the art concerning PMEM approaches. [Züghart W, Raps A, Wust-Saucy A-G, Dolezel M, Eckerstorfer M, 2011. Monitoring of genetically modified organisms. A policy paper representing the view of the National Environment Agencies in Austria and Switzerland and the Federal Agency for Nature Conservation in Germany. Umweltbundesamt Wien, Reports, Volume 0305. Vienna: 1-56.]	

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Austria	Fed.Ministry_Health/Women's Aff.	Part I – General information	I. GENERAL REMARKS In the formal consultation of the Member States concerning the 3-month commenting period, EFSA has stated that "When reference is made to confidential business information, please highlight this in the following way: FROM CBI: Smith et al. 2003." In accordance to this announcement we point out that the whole Austrian statement (i.e. all comments submitted through the EFSA DMS System) refers to information and data provided in the "Part II - Scientific Information" which is considered as confidential business information by the applicant.	The GMO Panel took note of this comment

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Austria	Fed.Ministry_Health/Women's Aff.	Part V - Methods of detection, sampling and identification and reference material	Detection method The presented method describes the quantitative detection of GM soybean MON87708xMON98788xA5547-127. The detection method uses TaqMan technology and event specific primers, i.e. one primer resides within the transformed insert and one in the plant genome. Providing an event specific detection method for each parental line and a specific reference PCR system is not satisfactory. Generally, a validated event specific detection method for the stacked event should be presented before deciding about the placing on the market of this product. Furthermore, as long as no official (guidance) document on the interpretation of detection results, i.e. how to distinguish between a stacked event and its respective single events, of the described method for stacked events is available, no approval for placing on the market of this product should be given. The detection method for GM soybean MON87708xMON98788xA5547-127 was sent for validation to CRL. The current evaluation status of the method is "Step 2 (scientific assessment completed)" (http://gmo-crl.jrc.ec.europa.eu/StatusOfDossiers.aspx).	This issue is outside the remit of the GMO Panel.

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Belgium	Biosafety Advisory Council	II.1.2.1 Information relating to the genetic modification	In the bioinformatic searches for similarity of the newly expressed proteins with proteins of potential adverse biological activity using general protein databases (Study: RAR-2016-0188), the top alignments logically correspond to the intended proteins (here DMO and the chloroplast transit peptides). It does not make sense that the applicant comments on these (expected) top alignments only but he should comment on the best alignments after exclusion of the intended proteins. I tried to find the next best alignments in the Appendix 1 by myself but it seems that only the 50 best alignments are displayed (for 'frame 3' corresponding to the DMO encoding sequence) which all correspond to the intended protein. Conclusion: the applicant should be asked to remove the intended proteins from the displayed alignments in such analyses. It is not considered that there is a safety concern here but the suggestion aims at improving the quality of the assessment	The GMO Panel thanks Belgium for the comment. The methodology for the applicant's bioinformatics analyses was verified by EFSA's bioinformatics contractor and the GMO Panel concluded that there is not safety concern. However, the GMO Panel took note of this comment.
Belgium	Biosafety Advisory Council	II.1.3.4 Comparative analysis of composition	One allergen glycinin is not categorized due to a lack of variation in reference substance genotypes. No data are included to explain this conclusion. A further explanation is welcome	The EFSA GMO Panel took note of the comments. The lack of variation between reference varieties is a result of the statistical analysis done on the data for glycinin. It is noted, however, that the test of difference identified no significant differences between the GM and its conventional counterpart.

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Belgium	Biosafety Advisory Council	II.1.5.2 Assessment of allergenicity of the whole genetically modified plant	The applicant frequently refers in the dossier to "the history of safe use of the introduced proteins". However no reference to this statement is provided. The applicant should indicate on what data this statement is based on, such as scientific papers or health monitoring reports.	For the safety assessment of the newly expressed proteins the EFSA GMO Panel performed an assessment following considerations described in the relevant EFSA guidance documents and Codex Alimentarius guidelines. The single proteins have been assessed in accordance with such considerations in the single events and no indications of safety concerns were identified. The EFSA GMO Panel thank the comment by the Belgium Authority. In particular, EFSA is not aware of health monitoring reports on such products.
Belgium	Biosafety Advisory Council	II.5.3.4 Interactions of the GM plant with non-target organisms (NTOs)	"The two first paragraphs under "5.3.4.1. Step 1: Problem formulation" describe the potential toxicity of newly expressed Cry1.105, Cry2Ab2 and Cry1Ac proteins of MON 87751 × MON 87701 × MON 87708 × MON 89788 instead of MON87708 x MON89788 x A5547-127. It is supposed that this mistake reflects an inadequate copy and paste from another soybean dossier."	The GMO Panel thanks Belgium for spotting this mistake.

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France	DGCCRF - Min Conso	Part II – Scientific information	L'examen de la liste des pièces du dossier n° NL-2016-135 montre qu'il contient une étude de toxicité subchronique de 90 jours réalisée avec le soja A5547-127. Il est regrettable que cette étude menée en 2009 n'ait pas été fournie dans le cadre de l'évaluation du soja A5547-127 (dossier n°NL-2008-52) qui ne s'est terminée qu'en avril 2011. Le fait que la fourniture d'une telle étude ne soit à l'époque pas obligatoire n'est pas un élément suffisant justifiant que le pétitionnaire ne l'ait pas transmise plus tôt. Par ailleurs, le pétitionnaire aurait dû fournir cette étude lors du dépôt du dossier relatif au soja FG72 x A5547-127 (n° NL-2013-120) conformément aux exigences du règlement (CE) n°503/2013. L'article 6.1 du règlement précité devrait limiter ce type de situation en ce qu'il exige des pétitionnaires la fourniture de toutes les études publiées ou réalisées, y compris après la date de dépôt des dossiers d'autorisation. Pour les dossiers en cours d'instruction déposés avant l'application du règlement (CE) n°503/2013, l'AESA devrait inciter les pétitionnaires à transmettre toutes les études réalisées, y compris celles qui ne sont pas obligatoires au moment du dépôt du dossier. **ENGLISH TRANSLATION** A review of the list of the documents contained in dossier No NL-2016-135 shows a sub-chronic toxicity study (90 day) on soybean A5547 127. It is unfortunate that this study from 2009 was not submitted for the evaluation of soybean A5547 127 (dossier No NL 2016-135) that was completed only in April 2011. The fact that it was not compulsory at the time to provide this study is not sufficient to justify the applicant not having provided it earlier. The applicant should also have provided this study when submitting the file on soybean FG72 x A5547-127 (No NL 2013-120), in accordance with the requirements of Regulation (EU) No 503/2013.	The GMO Panel took note of the comment.

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			Article 6(1) of that Regulation should limit this kind of situation insofar as it requires applicants to provide any studies that have been published or carried out, including after the date of submission of the dossier for authorisation. For the dossiers under examination filed prior to the application of Regulation (EU) No 503/2013, EFSA should request all applicants to provide any studies carried out, including those that are not compulsory at the time of submission of the dossier.	

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Germany	BfN	II.1 Hazard identification and characterisation	Comments of the Federal Agency for Nature Conservation: The Federal Agency for Nature Conservation (BfN) considers that further information is required before the risk assessment of EFSA/GMO/NL/2016/135 can be finalised. Information provided on composition, phenotypic evaluation and toxicology is insufficient and con-clusions of equivalence of the GMO and conventional soybean and on food and feed safety based on this information are premature. Several of the deficits listed here are valid for the single events MON87708, MON89788, A5547-127 and the double stacked event MON87708 x MON89788 as well. Therefore, we refer to our previous comments on the corresponding applications EFSA-36, -52, -93 and EFSA-108. Most of them remain also valid after additional information has been provided by the applicant. The applicant's risk identification is largely focused on direct effects of the transgenic proteins (toxicity, allergenicity). Potential combinatorial effects due to the introduction of the two transgenes into the soybean genome and due to residues of the complementary herbicides or their metabolites were neither taken into consideration nor were they assessed. However, they cannot be excluded. In addition, the present monitoring plan has many shortcomings and thus need to be amended.	The assessment of this three-event stack soybean has been conducted in accordance to the GMO Panel Guidance documents, which establish the principle that "where all single events have been assessed, the risk assessment of stacked events focuses on issues related to: (a) stability of the events; (b) expression of the events; and (c) potential interactions between the events" (EFSA GMO Panel, 2011). Regarding the evaluation of combinatorial effects of transgenes in this three-event stack soybean, the toxicological assessment considers in first instance the safety profile of the individual proteins assessed in the single events, corroborated by up-to-date scientific data and updated bioinformatics. The potential for adverse effects relevant for humans and animals of new protein combinations is then evaluated. The GMO Panel based on the current knowledge on the biological characteristics of the newly expressed proteins, their mode of action (MoA) and the outcome of their toxicological assessment, considered that there is no expectation of interactions between the protein newly expressed in this triple-stack soybean relevant for food and feed safety Therefore no additional studies were considered necessary. The assessment of herbicides residues and metabolites is not in the remit of the GMO Panel.

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				It is worth noting that, in the context of the MIXTOX project, EFSA is developing a guidance on new approaches and tools for harmonising how to assess risks to humans and the environment from multiple chemicals in the food chain: "chemical mixtures" and their "cocktail effects". This document is intended to support all relevant areas within EFSA's remit, including human health and environmental aspects.

Germany	BfN	II.1.2 Molecular Characterisation	Comments of the Federal Agency for Nature Conservation: Expression analysis must be regarded as an important part of the GMO risk assessment because it allows reflecting on the stability of the genetic modification and indicates possible interactions be-tween the GMO, environmental factors and agricultural practice. Expression data should provide reliable estimates on the quantity of expression in different plant tissues with regard to biotic and abiotic factors. Expression data were submitted from five North American field locations for one growing season from material of the stacked event treated only with all three herbicides in combination and com-pared to material of the single events treated with the respective herbicide. The data presented in the dossier do not meet the above mentioned objective: I. It is stated, but not justified, that the locations are representative for commercial cotton pro-duction in the USA (cf. II.1.3.2). II. Expression of transgenic proteins should be measured in material of the stacked event treated with combinations of three herbicides and with each herbicide singly as well. This is (a) to compare the stacked event and the single events grown under the same agricultural practice, (b) to better reflect all possible growing conditions of the GM material that may en-ter the EU and (c) to test whether effects of the three herbicides point in opposite directions and annul each other. III. The starting material was not tested for contamination with other GM soybean varieties (cf. II.1.3.2). The expression analysis should be based on a field trial which is devoid of the above listed deficits and provide sufficient data in order to demonstrate that there are no interactions between the single events in the stacked event MON87708 x MON89788 x A5547-127.	I. The field trial was conducted in five locations that are considered typical soybean growing areas of the USA representing regions of diverse agronomic practices and environmental conditions. II. The data submitted on the levels of the newly expressed proteins are in line with the applicable GMO Panel guidelines and were considered adequate by the GMO Panel to conclude that there is no indication of interactions that may affect the levels of the newly expressed proteins in the three-event soybean stack. III. The guidelines read: "Expression data for specific treatments linked to the trait(s) (e.g. use of herbicides) are only necessary if data obtained from the GM plants containing the respective single events indicate a potential safety concern". There is no safety concern for these three herbicide resistance genes.

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Germany	BfN	II.1.3.2 Experimental design and statistical analysis of data from field trials for comparative analysis	Comments of the Federal Agency for Nature Conservation: Field trials for comparative assessment including agronomic and compositional analyses were conducted at eight locations in the USA in 2015 (From CBI: Study: MSL0027659). At each site, four replicated plots of the GMO, a conventional soybean variety with a similar genetic background to the test plant and four out of a pool of 16 non-GM references planted using a randomized com-plete block design. The experimental design has got several weak points: I. According to applicant the chosen field sites in the Midwest and East of the USA were repre-sentative of commercial soybean growing areas. However, this does not comply with Regula-tion 503/2013 (EC), which requires justification that the chosen sites reflect the different me-teorological and agronomic conditions under which the crop is to be grown. This is not demon-strated here, and there is no indication that growth of the GMO will be restricted to the Mid-west and East. Soybean is grown in other areas as well, as reflected by field trials in the North, in the South or the South East of the USA (such as Michigan, Minnesota, Wisconsin, Texas, Louisiana, Mississippi, Alabama, Florida and Georgia) which were considered as trial sites for other GM soybeans. II. The GMO was either treated or not treated with the three complementary herbicides in com-bination. As it cannot be excluded that effects of dicamba, glyphosate and glufosinate point in opposite directions and annul each other, studies for comparative assessment should also in-volve the GMO treated with each of the herbicides separately. III. The complementary herbicides were applied each solely at a uniform rate, not considering re-gional agronomic conditions. To our understanding rates of the complementary herbicides should also be case-specific and take into account the amount of active ingredients tolerated by a certain GMO. In this respect, data are missing and requested on the amount of the three herbicides tolerated by the GMO. IV. The trial site description contains relevant information, but historical	I. The field trials were conducted in typical soybean growing areas of the USA, representing regions of diverse agronomic practices and environmental conditions, which is supported by the geographic map indicating the locations, the information provided on the variety of agronomic practice, soils and meteorological factors and the additional information provided on 21/4/2017 and 28/8/2017. In order to improve the description of the field trials, EFSA published a guidance document on the agronomic and phenotypic characterisation of genetically modified plants (EFSA GMO Panel, 2015). Application EFSA-GMO-NL-2016-135 was submitted during the transitional period of the GMO Panel guidance on the agronomic and phenotypic characterisation of GM crops. Therefore, the requirements of the guidance document were not fully applicable for this application. However, the GMO Panel concludes that the geographical locations, soil characteristics, meteorological conditions and management practices of the field trials are typical for receiving environments where the test materials could be grown. II. The experimental design, including the application of the intended herbicides is in line with applicable requirements. III. Weeds control was guaranteed by the application of conventional herbicides in accordance with the

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			weather data and present pest and disease infestation is missing (cf. II. 1.3.5). V. The purity of starting material was not tested. Starting material of test and control was ana-lysed for identity only (results are missing), but putatively not for contamination with other GM soybean varieties. Starting material of commercial reference varieties was neither tested for purity nor identity. VI. Interactions between environmental factors (climate, soil or agricultural practices) and the GMO were not analysed. The experimental design of field trials should be devoid of the above listed deficits. We recommend including data from field experiments from several years for the analysis to include climatic varia-tion between years (cf. II.1.3.4). Study: MSL0027645	specific needs of each field trial site (see study M-497026-01-1). The application of the intended herbicides was conducted to satisfy legal requirements and in addition to the maintenance pesticide application and at a uniform rate representative of common practice. IV. Visually observable responses to naturally occurring diseases, abiotic stress and arthropod damage were recorded, in order to provide indications of altered stress responses of soybean MON87708 x MON89788 x A5547-127 as compared with its conventional counterpart. The data submitted for the field trials description are in line with the applicable GMO Panel guidelines and were considered adequate by the GMO Panel to conclude that the geographical locations, soil characteristics, meteorological conditions and management practices of the field trials are typical for receiving environments where the test materials could be grown. V. Following a request of the GMO Panel, the applicant provided further information to characterise the quality of the starting materials, including data on purity levels (additional information received on 28/8/2017). VI. The comparative assessment studies followed the recommendations of the GMO Panel (EFSA GMO Panel, 2010, 2011). The GMO Panel considered the field trial design and data analysis adequate for the risk assessment. Data from multiple growing seasons are

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				not among the requirements of the applicable EFSA guidance (EFSA GMO Panel, 2011).
Germany	BfN	II.1.3.4 Comparative analysis of composition	Comments of the Federal Agency for Nature Conservation: For general comments on field trial design and comparative assessment we refer to II.1.3.2. Herbicide resistance conferred by genetic modification allows for a more intensive use of the com-plementary herbicides and could result in metabolic alterations, thereby changing herbicide metabo-lism as shown for glyphosate by Vivancos et al. (2011). In consequence glyphosate resistant plants were reported to accumulate glyphosate residues at high levels (Cuhra 2015). In the EU, the risk assessment of active ingredients considers herbicide residues of GMO in general, but not case-by-case for each GM event, which is an important principle in the GMO risk assessment. We therefore suggest analysing herbicide residues in the GMO treated with and without intended herbicides as part of the	The risk assessment of herbicide residues in GM plants is not in the remit of the GMO Panel, but is performed by EFSA Pesticide residues unit.

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			compositional analysis and to compare the results with MRL set in EU pesticide regulation (EC 396/2005). Results could inform the pesticide risk assessment whether the event-specific modification in MON87708 x MON89788 x A5547-127 is likely to support herbicide accumulation at unacceptable levels when grown in different relevant receiving environments and with different agricultural practices. This suggestion complies with a request from the EU Commission to EFSA, to request information about glyphosate residues in GM feed from companies seeking approval of feed from GM crops on the EU market (EC 2016a). Toxicological impacts of combinatorial effects of glyphosate, glufosinate and dicamba residues in MON87708 x MON89788 x A5547-127 soybean were not addressed within the applicant's risk assessment, nor are they currently considered in the risk assessment of active ingredients, since appropriate methods are missing (EC 2016b). To account for combinatorial effects of glyphosate, glufosinate and dicamba residues in MON87708 x MON89788 x A5547-127 in the present situation we recommend a 90-day feeding study which compares GM material treated with and without glyphosate, glufosinate and dicamba and non-GM material (cf. II.1.4). Cuhra, M. (2015). Review of GMO safety assessment studies: glyphosate residues in Roundup Ready crops is an ignored issue. Environmental Sciences Europe, 27:20. DOI 10.1186/s12302-015-0052-7 EC (2016a) Ref. Ares(2016)970322-25/02/2016, https://www.testbiotech.org/sites/default/files/EU%20Commission_glyphosate_mandate_animal_health_2016.pdf EC (2016b) Ref Ares (2016)4031661-01/08/2016, https://www.testbiotech.org/sites/default/files/11_letter_from%20Commission_August_2016.pdf Vivancos et al. (2011). Perturbations of Amino Acid Metabolism Associated with Glyphosate-Dependent Inhibition of Shikimic Acid Metabolism Affect	

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			Cellular Redox Homeostasis and Alter the Abundance of Proteins Involved in Photosynthesis and Photorespiration. Plant Physiology, 157, 256-268	
Germany	BfN	II.1.3.5 Comparative analysis of agronomic and phenotypic characteristics	Comments of the Federal Agency for Nature Conservation: For general comments on comparative assessment and the production of material we refer to our comments under II.1.3.2. Results about volunteers from field releases performed in various countries are not provided. Further data and analysis are required before phenotypic and ecological equivalence can be concluded. Next to the weak points of the experimental design (cf. II.1.3.2) this is for the following reasons: I. The selected agronomic characteristics cannot sufficiently indicate differences in repro-duction, dissemination, and survivability of the GMO compared to conventional soy-bean. 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 rarely or frequent-ly depending on the site. It cannot be excluded that both aspects interfered with the col-lection of ecological interaction data (e.g. arthropod abundance). III. Ecological interaction data are insufficient and provide rather a snapshot than a sound basis for some stressors. This is because stressors	I. The agronomic and phenotypic endpoints evaluated in the field trials were: early stand count, days to 50% flowering, final stand count, plant height, plant lodging, pod shattering, seed moisture, seed weight and yield. Visually observable responses to naturally occurring diseases, abiotic stress and arthropod damage were also recorded, in order to provide indications of altered stress responses of soybean MON87708 x MON89788 x A5547-127 as compared with its conventional counterpart. Statistically significant differences between soybean MON 87708 × MON 89788 × A5547-127 treated with intended herbicides and its conventional counterpart were observed for early stand count, days to 50% flowering, plant height, seed moisture and seed weight. Statistically significant differences between

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			often varied between observations at a site and among sites. To enhance the basis, data should be collected from more than a single year, from trial sites in other areas and from greenhouse studies (cf. II.1.3.2). The applicant should be asked to provide a robust and reliable data basis for reproduction, dissemination, and survivability to demonstrate substantial equivalence of the GMO and conventional soybean, which is devoid of the above listed deficit and the ones listed under II.1.3.2. Field studies with ecology-based parameters such as frost tolerance, seed dormancy and time span of pollen emission or duration of pollen viability of the GMO tested under field conditions should be included in the application to comprehensively test for unintended effects. We recommend including data on the occurrence of volunteers during cultivation of the GMO at all sites. In agreement with the 'step by step' principle field results including post-monitoring reports from the releases of the GMO which have already taken place shall be provided. Field data should be supplemented by data from greenhouse studies, e.g. those already collected during breeding of the GMO, which allows simulation of well-defined abiotic and biotic conditions.	soybean MON 87708 × MON 89788 × A5547-127 not treated with intended herbicides and its conventional counterpart were observed for days to 50% flowering and seed moisture. The test of equivalence showed that all these endpoints were equivalent or more likely equivalent than non-equivalent to the non-GM soybean reference varieties (equivalence category I or II). II. The field trials design followed the recommendations of the GMO Panel (EFSA GMO Panel, 2011) and complied with Regulation (EU) No 503/2013 III. Given that the genetic modifications of the events combined in soybean MON87708 x MON89788 x A5547-127 are not designed to target specific seed characteristics, that soybean is not a persistent and invasive crop, and that the scope of the application EFSA-GMO-NL-2016-135 excludes cultivation, the GMO Panel did not consider additional data on e.g. seed dormancy, pollen emission or viability as essential for the risk assessment of soybean MON87708 x MON89788 x A5547-127.
Germany	BfN	II.1.4 Toxicology	Comments of the Federal Agency for Nature Conservation: Toxicology assessment of the GMO is mainly focused on the expression of the new proteins, but not on potential unintended effects deriving from alterations of plant metabolism and/or herbicide residues (cf. II.1.3.4). 90-day feeding studies in rats are available for the three single events of the GMO, but neither for the threefold stacked GMO nor for the double stacked event MON87708 x MON89788. Therefore, we refer to our previous comments on the corresponding applications EFSA-93	The GMO Panel took note of the comments. The studies submitted by the applicant for the single events were scrutinised with respect to their adherence to Reg (EU) 503/2013, and, whenever not in line with these, questions were asked to the applicant. Based on these, the applicant provided new 90-day studies on MON89788 and A55547-127 with details on the filed

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			(MON87708) and EFSA-108 (MON87708 x MON89788). The 90-day feeding studies in rats for the three single events have got several weak points which compromise the conclusions: I. The studies with MON87708, MON89788 and A55547-127 did not consider treatment with the complementary herbicide. II. The studies with MON87708, MON89788 and A55547-127 did not analyze test and control material for other GM soybean events. III. The studies with MON87708, MON89788 and A5547-127 did not assure the non-transgenic nature of main feed ingredients. It has recently been shown that charges of test diets contain considerably amounts of foreign GM material (Mesnage et al. 2015). The presence of further GMO in both test and control conditions may obscure the effect of the test GM material, because diet contamination enhance background effects and hide significant effects. IV. The study with A55547-127 did not provide a production plan, which includes information about the cultivation of the GM and non-GM test material. V. The study with MON87708 used start material from different locations. Because of these it remains open whether the 90-day feeding studies are suited to support the conclusion that MON87708 x MON89788 x A5547-127 is as safe as conventional soybean in terms of food and feed safety. Therefore, and to account for combinatorial effects (cf. II.1.3.4) the applicant is asked to submit a 90-day feeding study in rats for the stacked GMO. Mesnage, R., Defarge, N., Rocque, L.-M., Spiroux de Vendômois, J. and G.-E. Séralini (2015). Laboratory Rodent Diets Contain Toxic Levels of Environmental Contaminants: Implications for Regulatory Tests. PLoS ONE 10(7): e0128429. doi:10.1371/journal.pone.0128429	production plans; and clarification on the 90-day study on MON87708. The GMO Panel considered that no new studies on the three-event stack soybean is necessary.

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Comments from National Competent Authorities under Directive 2001/18/EC				
Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
Germany	BfN	II.4 Post-market monitoring on the genetically modified food or feed	Comments of the Federal Agency for Nature Conservation: The data provided to show the human and animal safety of MON87708 x MON89788 x A5547-127 soybean on the basis of its substantial equivalence to conventional soybean (except for the introduced trait) are not conclusive. Therefore, a post-market monitoring (PMM) for food and feed should be carried out. The applicant is further requested to explain how the PMM of MON87708 x MON89788 x A5547-127 soybean in mixed GMO commodities imported, processed or used for food/feed is realized. This is requested 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 GMO Panel concludes that MON87708 x MON89788 x A5547-127 soybean, as described in this application, is nutritionally equivalent to and as safe as the conventional counterpart and the non-GM reference varieties tested. Therefore, the GMO Panel considers that post-market monitoring of food and feed is not necessary.
Germany	BfN	II.5 Environmental risk assessment	Comments of the Federal Agency for Nature Conservation: The Federal Agency for Nature Conservation (BfN) considers that further information is required before the risk assessment of EFSA/GMO/NL/2016/135 can be finalised. The environmental risk assessment should be amended in accordance with the required further information.	The GMO Panel considered that the information submitted by the applicant on application EFSA-GMO-NL-2016-135 was sufficient to conclude on the environmental risk assessment (ERA) of soybean MON87708 x MON89788 x A5547-127.

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Comments from National Competent Authorities under Directive 2001/18/EC				
Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
Germany	BfN	II.6 Post-Market Environmental Monitoring Plan (PMEM)	Comments of the Federal Agency for Nature Conservation: The scope of this application is for import, processing, and all uses for food and feed. The applicant provides an environmental monitoring plan, which remains very general. The monitoring plan has to be elaborated in more detail in order to meet the following requirements: • Provision of a fully specified list of monitoring parameters. • Application of standardised 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). They are available under http://www.vdi.eu/engineering/vdi-standards/. • Elaboration of a sampling concept. • In case of monitoring data being collected by external persons or institutions 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. • Elaboration of the methods of data analysis including the statistical methods. • Application of the concept of adverse effects and environmental damages: Adverse environmental effects can only be determined if they are related to certain relevant subjects of protection (Bartz et al. 2009). The subject of protection is damaged if it is significantly adversely affected. The identification of a significant adverse effect should consider both its intensity (e.g. extent of loss) and the value of the impaired subject of protection (e.g. high value of protected species). The monitoring should be run in regions, where viable MON87708 x MON89788 x A5547-127 soybean will be transported, stored, packaged, processed or used for food/feed. In case of substantial losses and spread of MON87708 x MON89788 x A5547-127 soybean all receiving environ-	Monitoring and its practical implementation are related to risk management, and thus a final adoption of the post-market environmental monitoring plan falls outside the mandate of EFSA.

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Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
			ments need to be monitored. Since traders may commingle MON87708 x MON89788 x A5547-127 soybean with other com-mercial GM soybean imported, processed or used for food/feed, the applicant is requested to ex-plain how the monitoring will be designed to distinguish between potential adverse effects caused by MON87708 x MON89788 x A5547-127 soybean and those caused by other GM soybean. The Federal Agency for Nature Conservation is of the opinion that a detailed monitoring plan has to be provided before consent may be given. 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	
Germany	BfN	II.6.1 Interplay between Environmental Risk Assessment, Risk Management and PMEM	Comments of the Federal Agency for Nature Conservation: The information necessary to conclude on the ERA is partly missing. Thus, the safety of MON87708 x MON89788 x A5547-127 soybean cannot be fully assessed. Depending on those results the conclusions concerning case-specific monitoring may need to be revised.	The GMO Panel considered that the information submitted by the applicant on application EFSA-GMO-NL-2016-135 was sufficient to conclude on the environmental risk assessment (ERA) of soybean MON87708 x MON89788 x A5547-127. As the ERA did not identify potential adverse environmental effects from the three-event stack soybean, the GMO Panel did not require case-specific monitoring.

Germany	BfN	II.6.2 Case Specific Monitoring (strategy, method and analysis)	Comments of the Federal Agency for Nature Conservation: We do not share the opinion of the applicant that a case-specific monitoring is not necessary. Case-specific monitoring should be focused on pathways, where viable plant material of MON87708 x MON89788 x A5547-127 soybean enters the environment. Therefore the applicant is requested to provide an appropriate case-specific monitoring plan comprising at least the following elements: i.) spillage or loss of MON87708 x MON89788 x A5547-127 soybean during transport, storage, packaging, processing and use (feed and food), ii.) potential spread and persistence of MON87708 x MON89788 x A5547-127 soybean within all environments, where substantial amounts of viable MON87708 x MON89788 x A5547-127 soybean is spilled, if spillage or loss of viable MON87708 x MON89788 x A5547-127 soybean occurs. For parameters i.) – ii.), the use of the following methods is recommended (http://www.vdi.eu/engineering/vdi-standards/): o VDI-Guideline 4330 Part 10 "Floristic mapping of genetically modified plants their crossing partners and their hybrid offspring" o VDI-Guideline 4330 Part 5 "Guideline for the collection and preparation of plant samples for molecular biological analysis" If risk management measures are envisaged, e.g. to minimize incidental spillage during transport, storage, packaging, processing or feed and food use, their efficacy should be monitored during case-specific monitoring (EFSA 2011). EFSA (2011). Scientific opinion. Guidance on the Post-Market Environmental monitoring (PMEM) of genetically modified plants. EFSA Journal 9(8): 2316, 40 pp.	Considering the introduced traits and the outcome of the comparative analysis, the routes of exposure and limited exposure levels, the GMO Panel concluded that the three-event stack soybean would not raise safety concerns in case of accidental release of viable GM soybean seeds into the environment, irrespective of possible interactions between the individual events within this three-event stack soybean. There are no indications of an increased likelihood of spread and establishment of feral soybean MON87708 x MON89788 x A5547-127 plants, unless these plants are exposed to the intended herbicides. Moreover, in light of the scope of the application, data available for one of the sub-combinations, the GMO Panel is of the opinion that any sub-combinations of the individual events, including those not previously assessed by EFSA, would raise no environmental safety concerns. As the environmental risk assessment did not identify potential adverse environmental effects from the three-event stack soybean and the already assessed two-event stack soybean MON87708 x MON89788, the GMO Panel did not require case-specific monitoring.
Germany	BfN	II.6.3 General Surveillance (strategy, method)	Comments of the Federal Agency for Nature Conservation: The applicant states that the general surveillance will be based on information gathered from the existing networks of COCERAL, UNISTOCK and FEDIOL. Data shall be collected by operators handling and using viable MON87708 x MON89788 x A5547-127 soybean and reported to the authorisation holder, represented by EuropaBio. It remains unclear, how the authorisation holder/EuropaBio will inform operators about their surveillance function and how it will be assured that operators in duty for general surveillance show the necessary skills to detect environmental	Monitoring and its practical implementation are related to risk management, and thus a final adoption of the post-market environmental monitoring plan falls outside the mandate of EFSA.

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Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
			impacts of MON87708 x MON89788 x A5547-127 soybean. Therefore, the applicant is requested • to name the national and local organisations and factories involved in the monitoring, • to prove that a sufficient number of local operators agree to contribute to the general surveillance, to provide a schedule with all relevant observation objects to be monitored, • 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 capable to cover all relevant observation objects, further monitoring systems have to be established. The applicant does not suggest operators further down the food chain to be involved in the process of monitoring. We do not approve this, because processed material may also be a cause of adverse effects. Therefore, the applicant is requested to involve also operators further down the food chain in the process of monitoring. The general surveillance plan has to focus on possible pathways how MON87708 x MON89788 x A5547-127 soybean can get into the broader environment and how unforeseen adverse effects on human health and the environment can be linked to the dispersal and use of MON87708 x MON89788 x A5547-127 soybean in environmental media. Beside the implementation of management and safety standards, the applicant is requested to provide an appropriate general surveillance plan comprising at least the above mentioned monitoring elements. MON87708 x MON89788 x A5547-127 soybean may enter the environment together with other approved GM soybean lines. Therefore, a special focus should be on possible combined effects.	

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Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
Germany	BfN	II.6.4 Reporting the results of PMEM	Comments of the Federal Agency for Nature Conservation: 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 availa-ble. The monitoring report should also deliver detailed information on i) actual volumes of MON87708 x MON89788 x A5547-127 soybean imported into the EU, ii) the ports and silos where shipments of MON87708 x MON89788 x A5547-127 soybean were unloaded, iii) the processing plants and users where viable MON87708 x MON89788 x A5547-127 soybean was transferred to, iv) the amount of MON87708 x MON89788 x A5547-127 soybean used on farms for feed, and v) transport routes of MON87708 x MON89788 x A5547-127 soybean.	Monitoring and its practical implementation are related to risk management, and thus a final adoption of the post-market environmental monitoring plan falls outside the mandate of EFSA.

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Comments from National Competent Authorities under Directive 2001/18/EC				
Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
Germany	BVL	II.1 Hazard identification and characterisation	The scope of application EFSA-GMO-NL-2016-135 covers import and processing of soybean MON87708 × MON89788 x A5547-127 including all feed and food products containing, consisting of, or produced from the genetically modified soybean MON87708 × MON89788 x A5547-127. 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 entirety of available data supports the conclusion that soybean MON87708 × MON89788 x A5547-127 is unlikely to have adverse effects on human and animal health or on the environment in the context of its intended use. Nevertheless, completion and/or clarification on some points of the dossier are recommended.	The GMO Panel took note of this comment.
Germany	BVL	II.1.2.1 Information relating to the genetic modification	In the case of GM plants containing stacked events, applicants should assess the safety of potential interactions between any unintended modifications at each insertion site (EFSA, 2011). The applicants used PCR and subsequent sequencing to prove the intactness of the insertion site. The applicants should comment on how this approach can exclude a putative duplication of the event at the insertion site. However, given the data on expression and composition, the German CA does not see any risk related issue with the missing information. EFSA: Guidance for risk assessment of food and feed from genetically modified plants, EFSA Journal 2011; 9(5):2150, p.10	The GMO Panel thanks Germany and takes the comment into account. Insertion of duplicated region should have been detected during the PCR since the applicant used 5' and 3' anchored primers and overlapping PRC amplicons were used for sequencing.

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Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
Germany	BVL	II.1.3.2 Experimental design and statistical analysis of data from field trials for comparative analysis	Study MSL0027659 reported on analyses to confirm identities of the test and conventional counterpart starting seed. However, no data are available on methods, results and raw data. Furthermore, the applicant should comment on why he considered it unnecessary to perform event-specific analyses for the presence of soybean MON87708 × MON 89788 x A5547-127 in conventional commercial reference material starting seed. Study: MSL0027645	The GMO Panel requested clarifications on the purity level of the starting materials used for the comparative analysis. Information were received on 21 April and 28 August 2017. The GMO Panel is of the opinion that the three-event stack soybean and its conventional counterpart were of adequate quality. Therefore, the test materials were considered suitable for the comparative analysis.
Germany	BVL	II.5.3.1 Persistence and invasiveness including plant-to-plant gene flow	The import documents should indicate that soybean MON87708 ×MON89788 x A5547-127 has not been approved for cultivation by the EC. In addition to the intended GM labelling, a clear labelling of seed MON87708 × MON89788 x A5547-127 indicating the tolerance to dicamba, glyphosate and glufosinate 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 about avoidance and control of soybean MON87708 × MON89788 x A5547-127 spillage.	The GMO Panel is aware that, owing to the physical characteristics of soybean seeds and methods of transportation, accidental spillage cannot be excluded. Hence, it is important that appropriate management systems are in place to restrict seeds of soybean MON 87708 × MON 89788 x A5547-127 entering cultivation as this would require specific approval under Directive 2001/18/EC or Regulation (EC) No 1829/2003.

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Comments from National Competent Authorities under Directive 2001/18/EC				
Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
Germany	BVL	II.6 Post-Market Environmental Monitoring Plan (PMEM)	The monitoring plan is 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.	Monitoring and its practical implementation are related to risk management, and thus a final adoption of the post-market environmental monitoring plan falls outside the mandate of EFSA
Germany	BVL	II.6.2 Case Specific Monitoring (strategy, method and analysis)	According to the risk assessment, no adverse effects on the environment or human health were identified or were expected. Therefore, there is no necessity for a case-specific monitoring.	The GMO Panel took note of this comment.
Germany	BVL	II.6.3 General Surveillance (strategy, method)	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. Therefore, the applicant should specify monitoring activities in the field of human and animal health. He should describe in detail how animal and human health surveillance is integrated in the monitoring plan. The strategy of General Surveillance is mainly based on the involvement	The GMO Panel took note of this comment and reminds that the scope of this application is for import/processing for food/feed uses, excluding cultivation. Moreover, monitoring and its practical implementation are related to risk management, and thus a final adoption of the post-market environmental monitoring plan falls outside the mandate of EFSA. Similarly, food and feed monitoring and its practical implementation are related to risk management and therefore outside the mandate of EFSA.

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Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
			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 and will remind them to report on 'any unanticipated adverse effect'. He 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 data needs more transparency. Existing systems The applicant should consider whether other existing monitoring networks might be used in particular in the field of human and animal health. In such a case, the selection and evaluation process should be described in detail. In general, other sources of information e.g. peer-reviewed publications or on going research should be taken into account. However, the applicant should describe in detail how he would consider this information within General Surveillance.	
Germany	BVL	II.6.4 Reporting the results of PMEM	A report on GS activities on an annual basis is sufficient. Reporting should refer to the format introduced by the Commission Decision 2009/770/EC. The applicant is requested to state how the monitoring results will be published.	Monitoring and its practical implementation are related to risk management, and thus a final adoption of the post-market environmental monitoring plan falls outside the mandate of EFSA
Hungary	Ministry of Agriculture	II.1.1 Information relating to the recipient or (where appropriate) parental plants	1.1.4 Although soybean might have a history of safe use, GM soy has not. 20 years is not considered to be history.	The GMO Panel took note of this comment.

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Country	Organization	Reference	Comment	GMO Panel responses
Hungary	Ministry of Agriculture	II.1.2.1 Information relating to the genetic modification	1.2.1 It is true that the stack MON 87708 × MON 89788 × A5547-127 soybean has been created by traditional crossing of MON 87708, MON 89788 and A5547-127, but all "parents" are GM soy events. 1.2.1.3 (b) There is no history of safe use of the donor organisms. MON 87708 × MON 89788 × A5547-127 expresses the dicamba mono-oxygenase (DMO) protein from MON 87708, the CP4 5-enolpyruvylshikimate-3-phosphate (EPSPS) protein from MON 89788 and the phosphinothricin acetyltransferase (PAT) protein from A5547-127. Indeed, none of the donor organisms have ever been consumed as food or feed. All three proteins code for herbicide resistance. Consequently, a mixture of herbicides will be used on these crops. However, the safety of this herbicide mixture is not guaranteed. Indeed, the residues and metabolites of dicamba, glyphosate and glufozinate in combination have not been studied. In addition, there is evidence from literature that it is only an assumption that 'the dose makes the poison' in terms of chemicals causing detrimental health effects on organisms. Yet it has now been found that when organisms are exposed to two toxicants in sequence, the toxicity can differ if their order is reversed. This is due to the fact that some chemicals cause lingering damage to organisms' systems, causing a slow recovery time, resulting in 'carry over toxicity' which then compounds the effects of a second pollutant. It is well known now, that glyphosate lingers in the human body, and also in that of the animals. Toxicants are able to interact, even if exposure is days apart and the toxicants have a different chemical make-up, resulting in a build-up of toxicodynamic damage in organisms. The sequence effect and carry-over toxicity is currently not considered in health or environmental risk assessment, so this has wide-reaching implications. Guidelines for allowing chemicals such as pesticides to go on the market must be revised to look at mixtures over time, e.g. different sequences of pesticides	The GMO Panel took note of the comment. The risk assessment of herbicide residues in GM plants is not in the remit of the GMO Panel, but is performed by EFSA's Pesticides Unit.

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Comments from National Competent Authorities under Directive 2001/18/EC				
Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
			(Roman Ashauer , et al., (2017) Toxic Mixtures in Time—The Sequence Makes the Poison. Environ. Sci. Technol.,)	

Hungary	Ministry of Agriculture	II.1.2.2 Information relating to the genetically modified plant	1.2.2.3 (a) Which proteins were the antibodies developed against? The proteins from the GM plant, the bacterial recombinant version, or against the proteins purified from their natural hosts? Were the affinity of the antibody determined against all of these three kind of proteins, and what was the result? 1.2.2.5 There is evidence in the scientific literature that plant DNA does not degrade fully and passes through the intestinal epithelium. Plant genes can be detected in blood and other cell types, such as the mesenteric lymph nodes, kidney etc. Evidence show that not all of the plant genes consumed brake down in the GI tract (Spisak S, et al., (2013) Complete Genes May Pass from Food to Human Blood. PLoS ONE 8(7): e69805.; S. Calabrò et al., (2015) Genetically modified soybean in a goat diet: Influence on kid performance. Small Ruminant Research 126: 67–74). Mammals have been shown to take up dietary DNA from the gastrointestinal tract (Rizzi et al., 2012). Although DNA, transgenic or not, consists of the same building blocks, they do not necessarily degrade. Plant DNA was detected in Human blood. Transgenes have altered regulatory elements attached to them. They are presented to the intestine in a different million and environment, their fate concerning degradation is unpredictable. If 95% of it is degraded, the remaining 5% can alter intestinal/microbial function. The Netherwood study proved that the full transgenic DNA from GM soy can enter bacteria resident in the GI tract. The study, which was conducted on human subjects fed on genetically modified soybean has shown that a proportion of the full length of the plant transgene does survive passage through the human gastro- intestinal tracts, and evidence suggests that gene transfer actually occurred between GM soybean and intestinal micro-flora during the experiments (Netherwood et al., 2004).	The applicant provided information on the validation of the methodology followed for each protein-specific ELISA. Based on this information, the GMO Panel considered that the provided protein expression data were adequate for the risk assessment of the three-event soybean stack. The GMO Panel took note of the comment.

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Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
Hungary	Ministry of Agriculture	II.1.2.3 Additional information relating to the genetically modified plant required for the environmental safety aspects	1.2.3.2 The transgenes of a GM plant have different promoters and/or regulatory elements attached to them. They are in a different molecular environment; therefore their ability to transfer might have been altered.	The GMO Panel took note of the comment.

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Country	Organization	Reference	Comment	GMO Panel responses
Hungary	Ministry of Agriculture	II.1.3.4 Comparative analysis of composition	1.3.4.2 Statistically significant differences were found for soybean seeds treated with herbicides between MON 87708 × MON 89788 × A5547-127 soybean and its conventional counterpart for: • protein, arginine, aspartic acid, glutamic acid, glycine, histidine, leucine, lysine, phenylalanine, proline, serine, threonine, tyrosine, valine, stearic acid, oleic acid, linoleic acid, carbohydrates by calculation, moisture, vitamin E, vitamin K1,stachyose, daidzein, genistein, NDF, total fat and behenic acid. Statistically significant differences were found for soybean seeds non-treated with herbicides between MON 87708 × MON 89788 × A5547-127 soybean and its conventional counterpart for: • protein, arginine, aspartic acid, glutamic acid, glycine,histidine, leucine, lysine, proline, serine, threonine, valine, palmitic acid, stearic acid, oleic acid, linoleic acid, carbohydrates by calculation, vitamin E, vitamin K1, trypsin inhibitor, daidzein, genistein and behenic acid. The aim of these comparisons is to see unintended effects of the genetic modification and not to see if the new variety is, or is not in the range of conventional commercial (reference) lines of soybeans. The statistical differences or lack of equivalences in the nutrient composition observed between the stack and the control line cannot be explained away by not having any biological relevance to the food and feed safety.	The GMO Panel assessed all significant differences between soybean MON 87708 × MON 89788 × A5547-127 and its conventional counterpart (difference test), taking into account the potential impact on plant metabolism and the natural variability observed for the set of non-GM reference varieties (equivalence test). For this particular three stack GM-soybean, the levels of acid detergent fibre (treated GM), total fat (treated GM) and behenic acid (treated and not-treated GM) in seeds were further assessed in terms of food & feed safety and their nutritional implications.
			1.3.4.3 Based on the above differences Hungarian experts would not agree with conclusion that "based on the results of the equivalence and difference tests conducted according to the EFSA guidelines (EFSA, 2011), it can be concluded that MON 87708 × MON 89788 × A5547-127 (T and NT) is compositionally similar to the conventional soybean counterpart"	The GMO Panel acknowledges the comment from Hungarian experts. In fact, in the EFSA GMO Panel Scientific opinion it is not stated that soybean MON 87708 × MON 89788 × A5547-127 is compositionally similar to its conventional counterpart. The GMO Panel took into consideration the outcome of the comparative assessment and carried out a nutritional assessment of

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Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
				the changes in levels of acid detergent fibre, total fat and behenic acid in seeds. Based on the current knowledge on the biological role of these compounds, the magnitude and direction of the changes identified, and the relevance of soybean as contributor to the intake of these compounds, the GMO Panel concluded that the nutritional impact of foods and feeds from the three-event stack soybean is expected to be the same as those from its conventional counterpart and non-GM reference varieties.

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Comments from National Competent Authorities under Directive 2001/18/EC				
Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
Hungary	Ministry of Agriculture	II.1.3.5 Comparative analysis of agronomic and phenotypic characteristics	1.3.5.2 Statistically significant differences were found for soybean seeds treated with herbicides between MON 87708 × MON 89788 × A5547-127 soybean and its conventional counterpart for: •Early Stand Count (#/linear meter), •Days to 50% Flowering, •Plant Height (cm), • Grain Moisture (%), • 100 Seed Weight (g). Statistically significant differences were found for soybean seeds non-treated with herbicides between MON 87708 × MON 89788 × A5547-127 soybean and its conventional counterpart for: • Days to 50% Flowering, • Grain Moisture (%).	Statistically significant differences between soybean MON 87708 × MON 89788 × A5547-127 treated with intended herbicides and its conventional counterpart were observed for early stand count, days to 50% flowering, plant height, seed moisture and seed weight. Statistically significant differences between soybean MON 87708 × MON 89788 × A5547-127 not treated with intended herbicides and its conventional counterpart were observed for days to 50% flowering and seed moisture. The test of equivalence showed that all these endpoints were equivalent or more likely equivalent than non-equivalent to the non-GM soybean reference varieties (equivalence category I or II). Taking into account the natural variability observed for the set of non-GM reference varieties, the GMO Panel concludes that none of the differences identified in the agronomic and phenotypic characteristics tested between the three-event stack soybean and its conventional counterpart needs further assessment regarding their potential environmental impact.

Hungary	Ministry of Agriculture	II.1.4.1 Testing of newly expressed proteins	1.4.1 The testing ignores the fact that herbicide mixture and their residues and metabolites might have toxicological effects on the consumer. This fact is not examined by the applicant at all. However, impacts of the specific cultivation, management and harvesting techniques do not mention altered herbicide usage. Meyers et al. (2016. Environmental Health 15(1):1-13.) described the continuing increase in use of glyphosate in the United States from an annual usage of 2.72 to 3.62 million kg in 1987 (prior GE crop cultivation) to 81.6 to 83.9 million kg in 2007 (when glyphosate-resistant crops were widely planted), to about 108 million kg in 2014. This increase is responsible for spread of glyphosate to water, beer, wine and human urine. The increased use of herbicide on herbicide resistant transgenic crops resulted in the spread of glyphosate resistant weeds in the USA as well as other countries. 1.4.1.3 The applicant ignores the fact that herbicide mixture and their residues and metabolites might have toxicological effects on the consumer. 1.4.1.4 In the opinion of Hungary in vitro degradation studies are not suitable to establish true digestibility in the gut. 1.4.1.5 The source organisms of the transgenic proteins have no history of safe use. The transgenic proteins expressed have no history of safe consumption. Those transgenes and transgenic proteins have been modified and/or optimised to be expressed in plants and are different from the native proteins. They also have different regulatory elements attached to them. Neither the native nor the transgenic proteins were used as food or feed before; The fact that transgenic protein does not exert any acute toxicity to mammals does not mean that they do not exert any chronic toxicity. The in vivo digestibility of the transgenic proteins in planta is unknown. Protein degradation can be measured in vivo, but those measurements have not been performed. No data are provided on the effect of heat treatment on transgenic proteins. Therefore a 90 day repeat dose toxicological or feeding study is justified and should have been performed.	1.4.1 and 1.4.1.3: The risk assessment of herbicide residues in GM plants is not in the remit of the GMO Panel, but is performed by EFSA's Pesticides Unit. 1.4.1.4 The EFSA GMO Panel has recently published (2017) a guidance document on allergenicity providing additional considerations on the *in vitro* protein degradation studies. In Annex B of this document, the EFSA GMO Panel proposes a refined *in vitro* digestion test that extends the conditions currently used in the classical pepsin resistance test to better reflect the range of conditions found in vivo. This test proposed includes additional conditions more representative of the gastric environment with regard to pH and pepsin levels, together with an intestinal digestion phase. In addition, more informative read-outs of the test are laid out which define the extent to which either the intact protein or resistant fragments remain after *in vitro* digestion. However, the EFSA GMO Panel considers that additional investigation is needed before any additional recommendation in the form of guidance for applicants can be provided on the proposed *in vitro* protein digestibility tests. To this end, an interim phase period, which is currently ongoing, was considered necessary to evaluate the proposed revisions to the *in vitro* gastrointestinal digestion test. After this period, EFSA will assess whether the test adds value to the allergenicity risk assessment and, if so, what further steps are needed for its final implementation in the form of guidance for applicants. 1.4.1.5: the source organisms of the transgenic proteins have been considered in the safety assessment. Information on heat stability is also available and was considered in the assessment of the individual proteins in the single events.

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Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
Hungary	Ministry of Agriculture	II.1.4.4 Testing of the whole genetically modified food or feed	1.4.4.1 The equivalence of MON 87708 × MON 89788 × A5547-127 soybean and its conventional counterpart could not be proven, since statistically significant differences were found for soybean seeds not treated with herbicides between MON 87708 × MON 89788 × A5547-127 soybean and its conventional counterpart for: protein, arginine, aspartic acid, glutamic acid, glycine, histidine, leucine, lysine, proline, serine, threonine, valine, palmitic acid, stearic acid, oleic acid, linoleic acid, linolenic acid, carbohydrates by calculation, vitamin E, vitamin K1, trypsin inhibitor, daidzein, genistein and behenic acid; and for MON 87708 × MON 89788 × A5547-127 soybean and its conventional counterpart treated with herbicides between MON 87708 × MON 89788 × A5547-127 soybean and its conventional counterpart for: protein, arginine, aspartic acid, glutamic acid, glycine, histidine, leucine, lysine, phenylalanine, proline, serine, threonine, tyrosine, valine, stearic acid, oleic acid, linoleic acid, linolenic acid, carbohydrates by calculation, moisture, vitamin E, vitamin K1, stachyose, daidzein, genistein, NDF, total fat and behenic acid. Based on these statistically significant differences a 90 –day rodent feeding study should have been performed. In addition, the source organisms of the transgenic proteins have no history of safe use. The in vivo digestibility of the transgenic proteins is unknown. No data are provided on the effect of heat treatment on the transgenic proteins. 1.4.4.2, and 1.4.4.3 Based on the compositional differences, missing data and uncertainties performing reproductive, developmental, chronic experiment is justified according to the opinion of Hungarian expert.	The GMO Panel concluded that the nutritional impact of foods and feeds from the three-event stack soybean is expected to be the same as those from its conventional counterpart and non-GM reference varieties (see also reply to comment II.1.3.4). Information on the source organisms of the transgenic proteins have been considered in the safety assessment. Heat stability and *in vitro* protein degradation are also available information and it was considered in the assessment of the individual proteins in the single events. Overall, the safety assessment identified no indications of safety concern of this GM soybean as compared to its conventional counterpart and the reference varieties tested.

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Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
Hungary	Ministry of Agriculture	II.1.5.1 Assessment of allergenicity of the newly expressed protein	1.5.1.1, 1.5.1.2, and 1.5.1.3 The source organisms of the transgenic proteins have no history of safe use. The in vivo digestibility of the transgenic proteins is unknown. No data are provided on the effect of heat treatment on transgenic proteins.	The allergenicity assessment of this GM soybean has been performed following the relevant EFSA guidance documents and Codex Alimentarius guidelines. Information on the source organisms served to calibrate if and what additional studies were considered necessary. Information is also available on the in vitro degradation studies and on heat stability that was assessed in the dossiers considering the single events. Bioinformatic analysis searching for potential similarities to known allergens was also carried oat. Considering all the information available, the EFSA GMO Panel identified no indications of safety concern with this GM soybean when compared to its conventional counterpart and the references varieties tested.
Hungary	Ministry of Agriculture	II.1.5.2 Assessment of allergenicity of the whole genetically modified plant	5.2.2.2 The equivalence of MON 87708 × MON 89788 × A5547-127 soybean and its conventional counterpart could not be proven, since statistically significant differences were found for soybean seeds not treated with herbicides between MON 87708 × MON 89788 × A5547-127 soybean and its conventional counterpart (see above). 5.2.3, and 5.2.4 Hazard and exposure characterisation ignores the fact that transgene intake, especially in combination and considering also mixtures of herbicide and their residues might have toxic affect, and also that the intake is in pharmaceutical range.	5.2.2.2: The endogenous allergenicity of this GM soybean was assessed by the applicant. No changes in the levels of endogenous allergens raising concern are identified by the EFSA GMO Panel. Please see section 3.6.4.2 and 3.5.6 of the EFSA GMO Panel Scientific opinion on this GM soybean. 5.2.3 and 5.2.4: The allergenicity assessment of this GM soybean has been performed following the relevant EFSA guidance documents and Codex Alimentarius guidelines. Considering all the information available, the EFSA GMO Panel identified no indications of safety concern with this GM soybean when compared to its conventional counterpart and the references varieties tested.

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Hungary	Ministry of Agriculture	II.3 Risk characterisation	3 EPSPS catalyses the penultimate step of the shikimate pathway producing chorismate, a common precursor for the amino acids tryptophan, phenylalanine, tyrosine as well as leading to production of folate (vitamin B9), phylloquinone (vitamin K), and salicylate and glyphosate inhibits the action of this enzyme. Although this pathway is missing in human/animal cells, the pathway is important for gut microbes of Humans and their animals. Since the microbiota is responsible for producing all, or at least part of tryptophan, phenylalanine, tyrosine, folate (vitamin B9), phylloquinone (vitamin K), being essential for their hosts, any remaining glyphosate interferes with the function of the microbiome. Similarly, the herbicide glufosinate-ammonium inhibits glutamine synthetase, an enzyme again present in the microbiome. The risk characterisation performed by the applicant ignores the fact that herbicide mixture and their residues and metabolites might have toxicological effects on the consumer.	Substrate specificity of the enzyme was assessed in the dossier dealing with the single event. No indications of safety concerned were identified by the Panel. Similarly, the toxicological assessment was performed by the EFSA GMO Panel in line with its guidance documents and internationally agreed guidelines. The risk assessment of herbicide residues in GM plants is not in the remit of the GMO Panel, but is performed by EFSA's Pesticides Unit.
Hungary	Ministry of Agriculture	II.5.3 Specific areas of risks	5.3.2 Horizontal gene transfer between plants to microorganisms is well documented. A study conducted on human subjects fed on genetically modified soybean has shown that a proportion of the full length of the plant transgene does survive passage through the human gastro-intestinal tracts, and evidence suggests that gene transfer actually occurred between GM soybean and intestinal micro-flora during the experiments (Netherwood et al., 2004). Indeed, the study has shown that the full length of the transgene, although in small quantities, survived digestion and could be detected from samples of microbes taken from the ileostomy bag (from microbes resident in the gut). 5.3.2.3 There is also evidence that plant genes influence the metabolism of the consumers, although they do not integrate into their genomes (Chiara Pastrello et al., (2016) Circulating plant miRNAs can regulate	The GMO Panel took note of the comments. Genomic DNA can be a component of food/feed products derived from maize. It is well documented that such DNA becomes substantially degraded during processing and digestion in the human or animal gastrointestinal tract. However, bacteria in the digestive tract of humans and domesticated animals, and in other environments may be exposed to fragments of DNA, including the recombinant fraction of such DNA. Current scientific knowledge of recombination processes in bacteria suggests that horizontal transfer of non-mobile, chromosomally-located DNA fragments

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			human gene expression in vitro. Scientific Reports 6). Plant genes can be detected in blood and other cell types, such as the mesenteric lymph nodes, kidney etc. Evidence show that not all of the plant genes consumed brake down in the GI tract (Spisak S, et al., (2013) Complete Genes May Pass from Food to Human Blood. PLoS ONE 8(7):; and Calabrò, et al., (2015) Genetically modified soybean in a goat diet: Influence on kid performance. Small Ruminant Research 126: 67–74). Mammals have been shown to take up dietary DNA from the gastrointestinal tract (Rizzi et al., 2012). Although DNA, transgenic or not, consists of the same building blocks, they do not necessarily degrade. Plant DNA was detected in Human blood. Transgenes have altered regulatory elements attached to them. They are presented to the intestine in a different million and environment, their fate concerning degradation is unpredictable. If 95% of it is degraded, the remaining 5% can alter intestinal/microbial function. 5.3.4.1 Perhaps it is the result of cut and paste, but the Dossier includes the followings, although no Cry genes are expressed in this stack "Non-target organisms include all organisms, animals and plants, which may unintentionally be affected through a specific or non-specific mechanism, as a result of the newly expressed Cry1A.105, Cry2Ab2 and Cry1Ac proteins (page 80, para2). 5.3.5 and 5.3.7 This section ignores the fact that increased use of mixtures of herbicide and their residues might have toxic effect on the environment, on soil microorganisms, as well as on the consumers.	between unrelated organisms (such as from plants to bacteria) is not likely to occur at detectable frequencies under natural conditions (for further details, see EFSA, 2009). The only mechanism known to facilitate horizontal transfer of non-mobile, chromosomal DNA fragments to bacterial genomes is homologous recombination. This requires the presence of at least two stretches of DNA sequences that are similar in the recombining DNA molecules. In the case of sequence identity with the transgene itself, recombination would result in gene replacement. In the case of identity with two or more regions flanking recombinant DNA, recombination could result in the insertion of additional DNA sequences in bacteria and thus confer the potential for new properties. The bioinformatics analysis for potential of homologous recombination for events MON87708, MON89788 and A5547-127 has been conducted according to EFSA guidelines (2010, 2017). The GMO Panel concludes that the unlikely, but theoretically possible, horizontal transfer of recombinant genes from this three-event stack soybean to bacteria does not raise any environmental safety concern.

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				The scope of application EFSA-GMO-NL-2016-135 is for food and feed uses, import and processing of soybean MON 87708 × MON 89788 × A5547-127 in the EU, and excludes cultivation. Therefore, the point on the increased use of mixtures of herbicide and their residues might have toxic effect on the environment, on soil microorganisms is out of scope for this application. In addition the risk assessment of herbicide residues in GM plants is not in the remit of the GMO Panel, but is performed by EFSA's Pesticides Unit.
Hungary	Ministry of Agriculture	II.6.4 Reporting the results of PMEM	6.4.5 The existing monitoring system is not suitable to detect any adverse effect. Baseline data should have been collected already before releasing the very first GM plant into the environment. Because of long-term, and delayed effects the time period for monitoring should be much longer than the period for authorisation.	Monitoring and its practical implementation are related to risk management, and thus a final adoption of the post-market environmental monitoring plan falls outside the mandate of EFSA.
Hungary	Ministry of Agriculture	II.7 Additional information related to the safety of the genetically modified food or feed	7 The result of Systematic review depends on selection criteria, as it was proven by the GRACE Project. If one uses only the data gained with bacterial recombinant transgenic proteins, no negative effects on health could be found. Perhaps if data obtained with the GM plant would have been included, the outcome would have been different. As it is clear with step 3, all data on histology, clinical parameters, etc. have been excluded.	In the literature searches performed in the context of application EFSA-GMO-NL-2016-135, the applicant defined eligibility/inclusion criteria for assessing the relevance of publications for inclusion in the scoping review. These criteria were defined a priori following the recommendations outlined in the EFSA explanatory note on literature search (EFSA, 2017a). The GMO Panel assessed the methodology and outcome of the literature searches submitted by the applicant. As indicated in Section 3.1 of the Scientific Opinion, the GMO Panel considered that the overall quality of the performed literature searches is acceptable. However,

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				the GMO Panel made specific recommendations on how future searches on soybean MON 87708 × MON 89788 × A5547-127 should be improved.
Hungary	Ministry of Agriculture	Part II – Scientific information	General comment: 1./ Hungary has objected to the authorisations of the individual event in this stack. Hungary also objects to the authorisation of MON 87708 × MON 89788 × A5547-127 soybean in the European Union, based on strictly scientific reasons. The equivalence of MON 87708 × MON 89788 × A5547-127 soybean and its conventional counterpart could not be proven, since statistically significant differences were found for soybean seeds not treated with herbicides between MON 87708 × MON 89788 × A5547-127 soybean and its conventional counterpart for: protein, arginine, aspartic acid, glutamic acid, glycine, histidine, leucine, lysine, proline, serine, threonine, valine, palmitic acid, stearic acid, oleic acid, linoleic acid, linolenic acid, carbohydrates by calculation, vitamin E, vitamin K1, trypsin inhibitor, daidzein, genistein and behenic acid; and for MON 87708 × MON 89788 × A5547-127 soybean and its conventional counterpart treated with herbicides between MON 87708 × MON 89788 × A5547-127 soybean and its conventional counterpart for: protein, arginine, aspartic acid, glutamic acid, glycine, histidine, leucine, lysine, phenylalanine, proline, serine, threonine, tyrosine, valine, stearic acid, oleic acid, linoleic acid, linolenic acid, carbohydrates by calculation, moisture, vitamin E, vitamin K1,	The GMO Panel assessed all significant differences between soybean MON 87708 × MON 89788 × A5547-127 and its conventional counterpart (difference test), taking into account the potential impact on plant metabolism and the natural variability observed for the set of non-GM reference varieties (equivalence test). For this particular three stack GM-soybean, the levels of acid detergent fibre (treated GM), total fat (treated GM) and behenic acid (treated and not-treated GM) in seeds were further assessed in terms of food & feed safety and their nutritional implications.

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			stachyose, daidzein, genistein, NDF, total fat and behenic acid. 2./ Hungary still objects to the statistical approach used by the company and suggested by EFSA. The original question in the risk/safety assessment was if GM plants were different from the parent or not. At the present, the question appears to be if a GM plant would appear to be different from all existing varieties of the same plant species, a new approach, which is strongly opposed by the Hungarian authorities. 3./ It is acknowledged that there might not be any synergistic effects between the transgenes originating from the parents. However, an additive effect definitely might exist, since sometimes this is the goal of the novel stack. Therefore, the additive characteristic of the effect(s) must be checked experimentally, especially for toxicology, immunology/allergeneicity and nutrition. 4./ Nucleic acids are no GRAS 5./ All data should be given in the application. Giving references to earlier applications are not acceptable. Please provide ALL information relating to the authorisation request in the Dossiers. 6./ Using qualifications, such small, large, tiny for describing statistical differences is not acceptable. A statistical difference is either significant, or not.	The current statistical approach within the comparative frame of the RA of GM plants allow to identify first compositional changes as compared to its conventional counterpart, while the complementary use of reference varieties provides information on whether the changes fall under the natural variability of the plants. The GMO Panel took note of the comments.

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Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
Italy	Ministry of the Environment	II.1.3 Comparative analysis	Data and information, provided in comparative analysis paragraph, on pheno-agronomic characteristic of the soybean subject of the application (Study: MSL0027659), can be considered sufficient. Nevertheless, please note that information on agro-meteorological characteristic, of the selected fields in the USA, are missing. Moreover the applicant do not, slavishly, follow the EFSA "Guidance on the agronomic and phenotipic characterization of GM plants" (EFSA, 2015) indication, when providing the requested information.	In order to improve the representativeness of the selected field trials, EFSA published a guidance document on the agronomic and phenotypic characterisation of genetically modified plants (EFSA GMO Panel, 2015). Application EFSA-GMO-NL-2016-135 was submitted during the transitional period of the GMO Panel guidance (2015). Therefore, the requirements of the guidance document were not fully applicable for this application. Additional information to further described soil characteristics and agronomic management practices were provided on 21/4/2017 and 28/8/2017.

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Country	Organization	Reference	Comment	GMO Panel responses
Italy	Ministry of the Environment	II.5 Environmental risk assessment	We do not agree with the applicant when declaring that the GM soybean, that has been modified for the tolerance to three herbicide (glyphosate, glufosinate, dicambia) would not more persistant in agricultural habitats than the conventional soybean. The soybean MON 87708 × MON 89788 × A5547-127, for its characteristic of multiple herbicide tolerance can have a potential higher capacity to persist in cultivated fields, where the herbicide glyphosate and/or glufosinate and/or dicamba are used, in comparison to its conventional counterpart. Neverthelss, taking into account that the applicant, in the PMEM plan, has forseen a procedure to limit loss and spillage of viable soybean and to routinely eradicate adventitious population, and further treats, those population resisting to eradication procedures, as adverse effects; we can agree with applicant risk management proposed procedures. Finally, we agree with applicant environmental assessment when classifying as negligible the potential risks related with the commercial release of the soybean MON 87708 × MON 89788 × A5547-127, also taking into account that cultivation is excluded.	The GMO Panel took note of the comment. The GMO Panel considers it very unlikely that soybean MON 87708 × MON 89788 × A5547-127 will differ from conventional soybean varieties in its ability to survive until subsequent seasons, or to establish occasional feral plants under European environmental conditions in case of accidental release into the environment of viable seeds of the three-event stack soybean (for additional information see Section 3.7.1 of the EFSA Scientific Opinion).
Italy	Ministry of the Environment	II.6 Post-Market Environmental Monitoring Plan (PMEM)	• As described by the EFSA guidance on PMEM (EFSA Panel on Genetically Modified Organisms, 2011), "GS plans should include questionnaires to those involved in the handling and processing of the GMP and its products and be designed to monitor whether unanticipated levels of loss, spillage and establishment are occurring and/or if there are any adverse environmental consequences". Nowhere in the PMEM proposed by the applicant were described questionnaires to the operators involved, nor how these questionnaires are structured, which information collect and how this information will be analyzed: it is required to provide	Monitoring and its practical implementation are related to risk management, and thus a final adoption of the post-market environmental monitoring plan falls outside the mandate of EFSA.

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			this information. • 6.4.5 "Existing systems": the authorization holder is working together with other members of the plant biotechnology industry within the European Association of Bioindustries (EuropaBio) and trade associations representing the relevant operators in order to implement an harmonised monitoring methodology. Not all Member States are represented within these associations: therefore, it would be appropriate to provide explanations on the monitoring methodology adopted in the MS not represented. • 6.4.6 "Monitoring Methodology": the applicant states that the information collected will be evaluated and analyzed in order to assess the relevance: the method is not specified and then it is required to provide it. In the EFSA guidance on PMEM (EFSA Panel on Genetically Modified Organisms, 2011) is established that "In addition, applicants should provide raw data in order to allow different analyses and interrogation of the data and to allow scientific exchange and co-operation between applicants, Member States, the European Commission and EFSA": then, it would be appropriate that the applicant provides also the raw data, as well as the analyzes. Lastly, the notifier says that "Where information indicates the possibility of an unanticipated adverse effect, the authorisation holder will immediately investigate to determine and confirm whether a significant correlation between the effect and MON87705 x MON87708 x MON89788 can be established": we ask to specify the investigation method. • 6.5 "Reporting the results of monitoring": it would be useful include in the annual monitoring report for the MON87705 x MON87708 x MON89788 information on foreseen amount of imported soybean into the EU, ports, silos and processing facilities where the viable GM soybean will be loaded/unloaded and transferred, and transportation routes. In addition, it is advisable to specify in this paragraph if the annual report also contains the results of the screening of peer-reviewed publications	

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Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
			conducted by the notifier (referred to in par. 6.4.5). Referenze/References: - EFSA (European Food Safety Authority), 2008. Opinion of the Scientific Panel on Genetically Modified Organisms on application (reference EFSA-GMO-NL-2006-36) for the placing on the market of the glyphosate-tolerant genetically modified soybean MON89788, for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto. The EFSA Journal 2008, 758, 1–23; - EFSA GMO Panel (EFSA Panel on Genetically Modified Organisms), 2013. Scientific Opinion on application EFSA-GMO-NL-2011-93 for the placing on the market of the herbicide-tolerant genetically modified soybean MON 87708 for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto. EFSA Journal 2013;11(10):3355, 30 pp. doi:10.2903/j.efsa.2013.3355; EFSA GMO Panel (EFSA Panel on Genetically Modified Organisms), 2015. Scientific Opinion on application (EFSA-GMO-NL-2012-108) for the placing on the market of the herbicide-tolerant genetically modified soybean MON 87708 × MON 89788 for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto. EFSA Journal 2015;13(6):4136, 26 pp. doi:10.2903/j.efsa.2015.4136; - EFSA Panel on Genetically Modified Organisms (GMO); Scientific Opinion on application (EFSA-GMO-NL-2008-52) for the placing on the market of herbicide tolerant genetically modified soybean A5547-127 for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Bayer CropScience. The EFSA Journal (2011); 9(5):2147, 1-28. [27 pp.] doi:10.2903/j.efsa.2011.2147. - EFSA Panel on Genetically Modified Organisms (GMO). Guidance for risk assessment of food and feed from genetically modified plants. EFSA Journal 2011; 9(5):2150. - EFSA Panel on Genetically Modified Organisms, 2011. Guidance on the	

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Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
			Post-Market Environmental Monitoring (PMEM) of genetically modified plants. EFSA Journal 2011;9(8):2316. EFSA GMO Panel (EFSA Panel on Genetically Modified Organisms), 2015. Guidance on the agronomic and phenotypic characterisation of genetically modified plants. EFSA Journal 2015;13(6):4128, 44 pp. doi:10.2903/j.efsa.2015.4128 EFSA GMO Panel (EFSA Panel on Genetically Modified Organisms), 2015. Guidance on the agronomic and phenotypic characterisation of genetically modified plants. EFSA Journal 2015;13(6):4128, 44 pp. doi:10.2903/j.efsa.2015.4128 - EFSA GMO Panel (EFSA Panel on Genetically Modified Organisms), 2015. Guidance on the agronomicand phenotypic characterisation of genetically modified plants. EFSA Journal 2015;13(6):4128, 44 pp.doi:10.2903/j.efsa.2015.4128 - Study: MSL0027659.	

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Country	**Organization**	**Reference**	**Comment**	**GMO Panel responses**
Netherlands	Dutch GMO office	Part II – Scientific information	The applicant claims that the information in the application is confidential. The Aarhus Convention regularises the right of the public to access environmental information and has been implemented in the European legislation. According to Article 30 of Regulation (EC) No 1829/2003 information on amongst others the composition of a GMO, physico-chemical and biological characteristics, and effects on human and animal health and the environment cannot be declared confidential. The EFSA has informed the European Commission on the claim for confidentiality of the application and awaits its decision. Information which is crucial to assess potential risks of a GM crop should not be declared confidential, because a lack of transparency undermines public trust in the risk assessment.	EFSA and its GMO Panel based the scientific risk assessment of soybean MON 87708 x MON 89788 x A5547-127 on a comprehensive information package that was made of the valid application EFSA-GMO-NL-2016-135, additional information provided by the applicant during the risk assessment, relevant scientific comments submitted by the Member States and relevant peer-reviewed scientific publications. In parallel the European Commission is in charge to assess any confidentiality claims made by the applicant on elements of the application.
Netherlands	Dutch GMO office	Part II – Scientific information	The Dutch CA has assessed the dossier with respect to the food and feed safety of MON87708 x MON89788 x A5547-127 soybean and has no comments or requests for additional information in relation to the safety of this GM event.	The GMO Panel took note of the comment made by the Netherlands.
Norway	VKM	II.1.3.4 Comparative analysis of composition	The VKM GMO panel is of the opinion that data on residue levels of the intended herbicides dicamba, glyphosate and glufosinate should have been provided by the applicant.	The risk assessment of herbicide residues in GM plants is not in the remit of the GMO Panel, but is performed by EFSA's Pesticides Unit.

Note: For the full reference of the publications cited in the GMO Panel responses, please see the reference list of the Scientific Opinion. For the publications cited only in this document, a full reference is provided below.

EFSA (European Food Safety Authority), 2009. Statement of EFSA on the consolidated presentation of the joint Scientific Opinion of the GMO and BIOHAZ Panels on the "Use of Antibiotic Resistance Genes as Marker Genes in Genetically Modified Plants" and the Scientific Opinion of the GMO Panel on "Consequences of the Opinion on the Use of Antibiotic Resistance Genes as Marker Genes in Genetically Modified Plants on Previous EFSA Assessments of Individual GM Plants". EFSA Journal 2009;8(6):1108, 107 pp. https://doi.org/10.2903/j.efsa.2009.1108.

EFSA GMO Panel (EFSA Panel on Genetically Modified Organisms), 2017. Naegeli H, Birch AN, Casacuberta J, De Schrijver A, Gralak MA, Guerche P, Jones H, Manachini B, Messean A, Nielsen EE, Nogue F, Robaglia C, Rostoks N, Sweet J, Tebbe C, Visioli F, Wal J-M, Eigenmann P, Epstein M, Hoffmann-Sommergruber K, Koning F, Lovik M, Mills C, Moreno FJ, van Loveren H, Selb R and Fernandez Dumont A, 2017. Guidance on allergenicity assessment of genetically modified plants. EFSA Journal2017;15(5):4862, 49 pp