Comments from The Norwegian Scientific Committee for Food safety (VKM) GMO Panel on the application for stacked event soybean MON 87705 × MON 87708 × MON 89788 (EFSA-GMO-NL-2015-126)

A, 3.3 Compositional assessment

Worldwide, soybean oil is the second most produced oil after palm oil. Traditional soybean oil has high levels of unsaturated fatty acids, mainly 18:2n-6 (linoleic acid), making it unstable and prone to oxidation. The dietary shortcoming of soybean oil is its high n-6/n-3 ratio.

Compared to its conventional counterpart and other conventional soybean cultivars, soybean MON 87705 × MON 87708 × MON 89788 has a significantly modified fatty acid profile with the main modifications being an increased level of 18:1n-9 oleic acid and lower levels of saturated fats (16:0 palmitic acid and 18:0 stearic acid) and 18:2n-6 linoleic acid, the latter an essential fatty acid for humans and animals. The mean values (as percentage total fatty acids (TFAs)) of the main fatty acids were Palmitic acid 2.65%, Stearic acid 3.37%, Linoleic acid 16.46% and Oleic acid 67.73%. Thus the point of the genetic modification was to induce significant compositional differences compared to conventional comparators. Comparing the above values with fatty acid profiles of other vegetable oils, the profile of soybean MON 87705 × MON 87708 × MON 89788 is similar to the fatty acid profile of rapeseed oil and olive oil. The applicant thus claims that with these compositional changes, the oil from soybean MON 87705 × MON 87708 × MON 89788 may have health benefits. However, substituting conventional soybean oil with oil from soybean MON 87705 × MON 87708 × MON 89788 may lead to reduced intake of the essential fatty acid 18:2n-6 linoleic acid, as well as a changed intake pattern of other fatty acids and fat-soluble components (see below). Under certain circumstances this may introduce a possible safety risk for the consumers' nutritional status. However, if the applicant were to provide a thorough comparison of soybean MON 87705 × MON 87708 × MON 89788 with other commercial vegetable oils based on levels provided in the scientific literature, the risk may be partially mitigated. The Norwegian GMO panel therefore requests additional information that include a comparison of soybean MON 87705 × MON 87708 × MON 89788 with other commercial vegetable oils.

The major components of vegetable oils are TAGs (triacylglycerides). In traditional soybean seeds the most abundant triacyl combinations are 1) 18:2n-6 in all three positions 2) 18:1n-9 in sn-1 position and 18:2n-6 in sn2/3 and 3) 18:2n-6 in sn1/2 and 18:3n-3 in position sn-3 (Li, Butka and Wang 2014). The acyl combinations in soybean MON 87705 × MON 87708 × MON 89788 is not given by the applicant and we do not know if positional redistribution of fatty acids has occurred in soybean MON 87705 × MON 87708 × MON 89788. Fatty acid position on the TAG molecule may affect digestibility of the individual fatty acids and largely determines the physical behavior of dietary fats as a whole in food products (Karupaiah and Sundram 2007). Preferential hydrolysis by pancreatic and lipoprotein lipases target the fatty acids in the sn-1 and sn-3 positions resulting in free fatty acids (FFAs) and sn-2 monoacylglycerols (Nillson-Ehle et al 1973; Yang et al 1991). In order to assess the effect of soybean MON 87705 × MON 87708 × MON 89788 compared to traditional soybean on nutrition and health, it would be valuable to see the alteration in TAG structure.

This is also of importance in light of soybean as a major source of phospholipids. The soybean phospholipids represent a mixture of phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidylinositol (PI), phosphatidylserine (PS) and phosphatidic acid (PA). The most frequent fatty acid component of soybean phospholipids is 18:2n-6 linoleic acid (Liu and Ma 2011). The genetic modification conducted on soybean MON 87705 × MON 87708 × MON 89788, with the significantly reduced fraction of 18:2n-6 linoleic acid is thus likely to also influence the nature and possibly also amount of soybean phospholipids. This should have been characterised by phospholipid analysis and also argues for the need for in vivo nutritional studies. The modern rapeseed (also called canola with low levels of erucic acid and glucosinolates) is the third largest source of oil for human consumption and is the main vegetable oil used in Norwegian salmon feed (Ytrestøyl et al 2014). Rapeseed oil is characterized as a high phytosterol-oil, while soybean oil and olive oil are in the group low/intermediate-phytosterols. Phytosterols have the ability to inhibit the uptake of cholesterol from the intestine and lower plasma cholesterol and triacylglycerol (TAG) in humans (Bernacer et al. 2015). The effects of phytosterols on Atlantic salmon metabolism and health, however, are not completely known, but it has been suggested that high concentrations of dietary phytosterols (>1.1 g kg^{-1} diet) can lead to some unwanted metabolic changes, like increased liver and plasma TAGs (Liland 2014). We do not know if the levels of phytosterols or other lipid-soluble components in the soybean MON 87705 × MON 87708 × MON 89788 have been affected by the genetic modification. If there are changes in phytosterol levels in soybean MON 87705 × MON 87708 × MON 89788, this may affect bioavailability of other sterols. Thus, analysis of phytosterol levels would be of importance to help mitigate possible negative effects that any changes in their concentration may have on consumer health.

Furthermore, other unintended effects in soybean MON 87705 × MON 87708 × MON 89788 regarding saponin and lectin levels are not provided by the applicant. These are not among the list of suggested components in the OECD guideline for new varieties of soybeans, but with major nutrient changes as observed in soybean MON 87705 × MON 87708 × MON 89788, a more thorough compositional screening should be performed and this should also be requested in an updated OECD guideline. Lectins and heat-stable, amphipathic saponins present in soybean have been implicated as contributing factors in the development of soybean meal-induced enteropathy in Atlantic salmon and rainbow trout (Krogdahl et al. 2015; Iwashita et al. 2008). Their involvement in the development of a similar condition observed in calves and piglets cannot be excluded. Thus any changes in the levels of these antinutritional factors in MON 87705 × MON 87708 × MON 89788 soybean would be of practical importance for the aquafeed industry.

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A, 6.2. Nutritional assessment of the GM food and feed

We agree with the applicant that soybean MON 87705 × MON 87708 × MON 89788 with its changes in fatty acid profile can represent a nutritional improvement in both food and feed. Soybean MON 87705 × MON 87708 × MON 89788 could improve the disequilibrium in the intakes of n-6 to n-3 fatty acids, as we know today that the ratios between n-6 and n-3 FAs in traditional soybean oil are above the recommended levels for humans.

In the case of GM plants modified for altered content of nutrients, livestock studies with model or target species should be performed in order to determine the bioavailability of individual nutrients in the feed derived from a GM plant compared to its comparator (ILSI, 2003, 2007). The Norwegian GMO panel is of the opinion that a nutritional assessment study should have been performed with the stacked soybean MON 87705 × MON 87708 × MON 89788.

References

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