GeneWatch UK comments on the opinion of the EFSA Scientific Panel on Genetically Modified Organisms on an application for the authorisation of GM soybean MON 87708 x MON 89788 for food and feed uses submitted under Regulation (EC) No. 1829/2003 by Monsanto

July 2015

The two-event stack GM soybean MON 87708 × MON 89788 was produced by conventional crossing of two GM crops to produce soybean tolerant to dicamba- and glyphosate-based herbicides. GeneWatch UK's comments are below.

3. Comments

a. Assessment:

Molecular characterisation
For the information on expression of the inserts, plants were grown at eight locations (four replicate blocks each) under field conditions in 2009 in the USA. Gene-environment interactions can affect food safety but the crops studied were grown only in the US, not in other potential export markets i.e. South America, so the analysis is incomplete. The potential production of novel dsRNA should also have been investigated.

Comparative analysis (for compositional analysis and agronomic traits and GM phenotype)
Based on the agronomic and phenotypic characteristics of soybean MON 87708 × MON 89788 under the tested conditions (treated and not treated with both intended herbicides), differences (non-equivalence) in some fatty acids and in trypsin inhibitor were observed in soybean MON 87708 × MON 89788 compared with its non-GM comparator. It is unclear why these differences were assumed to have no relevance to food safety or nutrition. These potential impacts of these differences should have been investigated further.

Again, field sites were limited to eight sites within the soybean cultivation areas in the USA, which is insufficient to examine gene-environment interactions, which were identified as of importance to many of the endpoints.

b. Food Safety Assessment:

Toxicology
Studies of the combined effects of the two herbicide residues have been omitted, as discussed further below.

Nutritional assessment
The risk assessment wrongly states that the nutritional characteristics of soybean MON 87708 × MON 89788-derived food and feed are not expected to differ from those of conventional soybean varieties, when in fact significant differences were detected in fatty acid composition during the compositional analysis. The impacts of these differences should have been assessed.

Others
The two-event stack GM soybean MON 87708 × MON 89788 was produced by conventional crossing of two GM crops to produce soybean tolerant to dicamba (3,6-dichloro-methoxy-benzoic acid) and glyphosate (N-(phosphonomethyl)glycine)-based herbicides. A major area of public interest will be the presence of residues of dicamba and glyphosate and their metabolites on the crop entering the

food chain, due to blanket spraying of the plants. Impacts on human and animal health due to these changes in management must be considered in the risk assessment according to Directive 2001/18/EC. The assessment completely omits this aspect of the analysis. From a food safety perspective, this means that the increased levels of dicamba- and glyphosate-based herbicides on the GM herbicide-tolerant soybean product being considered for approval have not been assessed.

Dicamba-tolerance is achieved by the expression of dicamba mono-oxygenase (DMO) proteins, which demethylates dicamba, producing 3,6-dichlorosalicylic acid and formaldehyde. However, information about the impacts of formaldehyde have been omitted, although it is a known carcinogen, implicated in some food safety alerts (e.g. http://www.foodsafetynews.com/2013/09/formaldehyde-detected-in-supermarket-fish-imported-from-asia/#.Unu3I-K7R0M).

For 3,6-dichlorosalicylic acid and dicamba residues, EFSA refers to the expertise of the EFSA Pesticides Unit in setting acceptable daily intakes (ADIs)and Maximum Residue Levels (MRLs). The Pesticides Unit has published a "Reasoned opinion on the modification of the MRL for dicamba in genetically modified soybean" (EFSA Journal 2013;11(10):3440) which states that "since the relevant component of the residues in dicamba-tolerant soybean was identified as the metabolite 3,6-dichlorosalicylic acid (DCSA) while dicamba was not detected at harvest, EFSA proposed to set a specific import tolerance of 0.4 mg/kg for the metabolite DCSA in soybean, and not to change the current MRL of 0.05* mg/kg set for dicamba". However, there are numerous gaps in information and thus little data to support the ADIs or how the relationship between the ADIs and MRLs has been set, especially as the metabolism pattern of the active substance in genetically modified plants was shown to be different and the available data did not allow EFSA to conclude whether dicamba and DCSA act through the same toxicological mode of action. Another metabolite, DCGA, was identified but there was insufficient toxicological data to set a specific ADI.

For glyphosate, a recent IARC publication identifies glyphosate as a probable human carcinogen (Guyton, K. Z., Loomis, D., Grosse, Y., El Ghissassi, F., Benbrahim-Tallaa, L., Guha, N., Scoccianti, C., Mattock, H., Straif, K. (2015). Carcinogenicity of tetrachlorvinphos, parathion, malathion, diazinon, and glyphosate. International Agency for Research on Cancer). This evidence was not taken into account when EFSA assessed MON 89788. EFSA cannot therefore rely on that earlier assessment. There is also evidence that glyphosate-based herbicides may be endocrine disruptors (e.g. Romano, R. M., Romano, M. A., Bernardi, M. M., Furtado, P. V., & Oliveira, C. A. (2010). Prepubertal exposure to commercial formulation of the herbicide glyphosate alters testosterone levels and testicular morphology. Archives of Toxicology, 84(4), 309–317. http://doi.org/10.1007/s00204-009-0494-z). Glyphosate residues are known to accumulate in glyphosate-tolerant soybeans (Bøhn, T., Cuhra, M., Traavik, T., Sanden, M., Fagan, J., & Primicerio, R. (2014). Compositional differences in soybeans on the market: Glyphosate accumulates in Roundup Ready GM soybeans. Food Chemistry, 153, 207–215. doi:10.1016/j.foodchem.2013.12.054). In addition the effects of adjuvants should have been considered. Many toxicological studies conducted with human, mouse and rat cells confirm findings from aquatic non-target organisms which suggest that looking at the effects of glyphosate alone is insufficient for a comprehensive assessment of the cultivation of glyphosate on human health (e.g. Young, F., Ho, D., Glynn, D., Edwards, V. (2015). Endocrine disruption and cytotoxicity of glyphosate and roundup in human Jar cells in vitro. Integrative Pharmacology, Toxicology and Genotoxicology. Vol. 1(1): 12-19. doi: 10.15761/IPTG.1000104.).

Furthermore, for the stacked trait MON 87708 × MON 89788 the combined residues of glyphosate-based and dicamba-based herbicide residues on human and animal health have not been considered, including potential synergistic effects. This is a very significant omission from the Opinion.

No information has been provided on how compliance with MRLs can be maintained over time as weeds will inevitably develop resistance to both glyphosate and dicamba (Mortensen, D. A., Egan, J. F., Maxwell, B. D., Ryan, M. R., & Smith, R. G. (2012). Navigating a Critical Juncture for Sustainable Weed Management. BioScience, 62(1), 75–84. doi:10.1525/bio.2012.62.1.12). In addition, no data has been provided regarding the potential use of other herbicides (especially as resistance develops) or the effects of consuming mixtures of the product with other products (such as RoundUp Ready soybeans).

No information was provided in the framework of this application on the effect of processing on the nature of dicamba or glyphosate residues.

Conclusions and recommendations
The risk assessment is incomplete and inadequate to support approval of the product.

5. Others
If the product were to be approved, extensive monitoring of herbicide residues (including metabolites) would be needed. However, it is unclear how this would be done in practice.