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Impact Assessment in
Biotechnology

Testbiotech comment on EFSA Scientific Opinion on the application (EFSAGMO-NL-2010-78) for the placing on the market of herbicide tolerant genetically modified soybean MON 87705 for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto.

This is a comment concerning a genetically engineered, herbicide-tolerant (glyphosate) soybean with an increased oleic acid for food and feed uses, import and processing.

Molecular data

The expression of the gene construct and the functional stability of the gene construct were, for example, not tested under extreme climate conditions such as drought and flooding which are likely to occur under present ongoing climate change. Investigations under controlled environmental conditions including various biotic and abiotic stressors should have been performed to determine the actual range of variation and to identify relevant impact factors. Further, the effects of the additional genes on the activity of the plants´ genome and the plants´ metabolism were not investigated by using methods such as metabolic profiling.

The genetic modification to change the oil composition in the soybeans is based on an inhibition of the expression of endogenous plants genes by RNAi interference (RNAi), resulting in reduced levels of the corresponding plant enzymes. The underlying molecular process is complex and encompasses the degradation of endogenous mRNAs. In this process, small interference RNA molecules might be produced such as secondary (double stranded) dsRNAs, which can be biologically relevant to human health and the environment. (Short inhibitory) siRNA molecules may both cause intended gene silencing and have off-target effects, i.e. may silence genes other than those intended (Senthil-Kumar et al., 2011). These effects can be passed from the plant to human or animal at the consumption stage. Potential biological effects will depend on similarities between the cell regulation in mammals and plants. These biological effects based on these similarities are shown by Zhang, et al., 2011. Thus, for the risk assessment of plants that produce new dsRNA , it is necessary to conduct bioinformatics studies to identify any likely unintended targets of the intended siRNAs in humans or animals. But no such studies were conducted.

References:

Senthil-Kumar, M., Kirankumar, S., Mysore, K.S. (2011) Caveat of RNAi in Plants: The Off-Target Effect. In: H. Kodama, A. Komamine (eds.), RNAi and Plant Gene Function Analysis, Methods in Molecular Biology 744, DOI 10.1007/978-1-61779-123-9_2, © Springer Science+Business Media, LLC 2011

Zhang, L., Hou, D., Chen, X., Li, D., Zhu, L., Zhang, Y., Li, J., Bian, Z., Liang, X., Cai, X., Yin, Y., Wang, C., Zhang, T., Zhu, D., Zhang, D., Xu, J., Chen, Qu., Ba, Y., Liu, J., Wang, Q., Chen, J., Wang, J., Wang, M., Zhang, Q., Zhang, J., Zen, K., Zhang, C.Y. (2011) Exogenous plant MIR168a specifically targets mammalian LDLRAP1: evidence of cross-kingdom regulation by microRNA, Cell Research: 1-10.

Comparative assessment (for compositional analysis and agronomic traits and GM phenotype)

Several significant differences were observed in composition data on unintended changes in fatty acids, differences in amino acids and protein content. Further, the data also show significant differences in agronomic performance. These differences have been declared irrelevant by EFSA through reference to historical data from the ILSI Database, which is known to be unreliable. EFSA declared further data showing significant differences to be of either no significance to safety concerns or not relevant for intended uses. For example, in response to the comments from the experts of Member States, EFSA states: “Even in the case of instability of the trait, it would not raise a safety issue.” This statement shows a surprising level of ignorance in assessing biological effects that can impact the safety of genetically engineered plants.

In conclusion, EFSA´s risk assessment is flawed because it is based on cherry picking, wrong comparisons and questionable assumptions. If the significant differences are taken into account as necessary, the plants cannot be regarded as substantially equivalent. Thus, according to EFSA Guidance, a much more comprehensive risk assessment would have been necessary.

Further, EFSA overlooked that spraying the plants with complementary herbicide (glyphosate) can significantly change their composition (see a full list of references in Testbiotech, 2012). EFSA should have requested data from all field trials with and without application of the herbicide and a comprehensive comparison of the relevant data.

Reference:

Testbiotech, 2012, Technical background for a complaint under Article 10 of Regulation (EC) No. 1367/2006 against decision of EU Commission to give market authorisation to stacked soy MON87701 x MON89788, http://www.testbiotech.de/node/691

Toxicology

The 90 days study was performed with defatted meal from soybean. Those characteristics of the beans that are changed by genetic engineering (composition of oil) were not tested by the 90 days study. Thus, no conclusion can be drawn on potential health effects of consuming the whole beans or oil derived from the beans. EFSA should have requested long-term (chronic) studies with whole soybeans to judge their safety and to investigate further the significant findings from the study as presented by Monsanto.

Further, OECD guidelines were contravened because only one dosage of the soybeans was tested. There was also no comparison between the soybeans that were sprayed and those that were not sprayed with the complementary herbicide (glyphosate).

Further, only particular usages in food and feed were considered, while the application is not restricted to such uses. All potential uses in food and feed have to be assessed before any product derived from genetically engineered organisms is approved. Otherwise consumer could be exposed to risks that had not been assessed.

Allergenicity

EFSA (2010) speaks about the need for detailed investigations into allergenic risks for infants and individuals with impaired digestive functions. “The specific risk of potential allergenicity of GM products in infants as well as individuals with impaired digestive functions (e.g. elderly people, or individuals on antacid medications) should be considered, taking into account the different digestive physiology and sensitivity towards allergens in this subpopulation.” However, these specific risks were left aside during EFSA risk assessment.

Further, the soybeans were tested with sera from small groups of individuals known to react to allergens from soybeans. Several differences were observed but not deemed relevant. Instead, EFSA should have requested much more detailed investigations. As the minutes of a meeting of the working group (WG) “Self Task on Allergenicity” of 24 September 2007 shows, EFSA has serious doubts about the reliability of investigations with such a small number of patients as conducted in this case. “More sera from patients are needed but they also need to be well characterised. Statistical calculations have been done showing that 60-70 well characterised sera are needed based on variability. Since this might not be feasible, the WG has to consider the reliability of studies with a lower number of sera.” In result, the assessment as conducted by EFSA cannot be seen as sufficient.

References:

EFSA (2010) EFSA Panel on Genetically Modified Organisms (GMO); Scientific Opinion on the assessment of allergenicity of GM plants and microorganisms and derived food and feed. EFSA Journal 2010; 8(7):1700. [168 pp.] doi:10.2903/j.efsa.2010.1700. Available online: www.efsa.europa.eu

EFSA (2007), Minutes of the meeting of the EFSA working group (WG) “Self Task on Allergenicity” of 24 September 2007,

Nutritional Assessment

There are no data on the equivalence and quality of the products that are processed such as soybean sprouts, milk and baby food, or for products undergoing fermentation and heat treatment. Without such data, no conclusion can be drawn upon equivalence and food safety:

Data are necessary to assess effects of processing on the naturally occurring antinutrients such as the trypsin inhibitor. Its degradation can be impacted due to unintended effects in the plants. Other antinutrients should also be considered.

Others
In its answers to experts of member states, EFSA states several times that the application fulfils the requirements of older guidelines (such as EFSA, 2006) that were valid at the time of application. However, it has to be made clear that EU regulation 1829/2003 requests that risk assessment is carried out according to highest possible standards. Thus, guidelines that were valid years ago cannot now be considered as a sufficient standard for risk assessment.

As a recent legal dossier compiled by Professor Ludwig Kraemer shows, the decision not to monitor any health effects at the stage of consumption of genetically engineered food, violates the requirements of EU regulations. Directive 2001/18 and Regulation 1829/2003 both require that potential adverse effects on human health of genetically modified plants are controlled during the use and consumption stage, including in those cases where such effects are unlikely to occur. Monitoring also has to include residues from spraying with the complementary herbicide.
Thus, the EFSA opinion that monitoring of health effects is unnecessary, is wrong and contradicts current EU regulations.

References:
Kraemer, L. (2012) The consumption of genetically modified plants and the potential presence of herbicide residues, legal dossier compiled on behalf of Testbiotech, http://www.testbiotech.de/sites/default/files/Legal_Dossier_Kraemer_Pesticide_RA_PMP.pdf

Conclusion and recommendations: The opinion of EFSA should be rejected.