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Impact Assessment in
Biotechnology

MON87701 x MON89788, Monsanto´s 'immune enhancing' stacked genetically engineered soy

Testbiotech comment on *EFSA (2011) Scientific Opinion on application (EFSA-GMO-NL-2009-73) for the placing on the market of insect resistant and herbicide tolerant genetically modified soybean MON 87701× MON 89788 for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto. The EFSA Journal 2012;10(2):2560. [34 pp.] doi:10.2903/j.efsa.2012.2560.*

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Comparative Analysis

In comparison to their conventional counterparts, both the stacked event and the parental plants show a number of significant differences. Using the ILSI database, which is known for its unreliability (http://www.testbiotech.org/en/node/619), these differences in phenotype and in plant composition were interpreted as having no biological relevance..

Instead of simply setting these differences aside, they should be explored further by subjecting the plants to stress tests under defined environmental conditions and conducting investigations into gene activity and metabolic profile.

Several investigations show that genetically engineered plants can exhibit unexpected reactions under stress conditions (see for example: Matthews et al., 2005). This can also impact the Bt content in the plants (Then& Lorch, 2008). Functional stability of the transgene under various defined environmental conditions was not shown. The number of field trials and geographical regions was too low to draw any final conclusions.

A number of relevant components were not investigated at all e.g. phosphatides, minerals and saponines. The observed environmental impacts on plant metabolism (such as C:N ratio) were not investigated further. No reason was given why the content of Cry 1 Ac toxin in the stacked event was much higher double that of the parental plant.

There is a specific need in this case for a more detailed investigation of changes in the plants´ composition since the expression of Cry1Ac was recently shown to disrupt regeneration, in vivo growth and development of transgenic tobacco and cotton (Rawat et el. 2011).

Toxicology:

The mode of action of Bt toxins is not fully understood. It is a matter of controversial debate (Pigott & Ellar, 2007). Strict selectivity of the Bt toxins is not shown by empirical evidence, but deduced from modes of action described previously. More recent research shows that there are mechanisms that might cause toxicity in other species and even in mammals (Soberon et al., 2009). Potential risks for human health are supported in a report by Gallagher (2010) dealing with kidney problems and immune reactions observed in feeding studies with genetically engineered eggplant, which also

express a modified Cry1Ac protein.

Several experts warn that a higher toxicity can be expected for glyphosate than previously thought (Antoniou, et al., 2010; Benachour, et al., 2007; Paganelli et al., 2010; PAN AP 2009). In this context, the additive POEA also has to be taken into account, as it is even more toxic than glyphosate in these plants. In 2010, German authorities prohibited the usage of certain glyphosate formulations with a high content of POEA for the production of animal feeds in order to avoid a risk of toxins being passed through the food chain.

The GMO panel decided to leave these questions concerning the risk assessment of residues from spraying to EFSA´s pesticide panel. In parallel, there is an ongoing EU process which is reviewing glyphosate under the pesticide regulation. This process has been postponed. Thus, the risk assessment of Roundup Ready soybeans will suffers on two levels – in the work of the GMO panel and the European pesticide regulation.

There are several reasons why risk assessment of genetically engineered plants with herbicide tolerance cannot leave aside the issue of residues from spraying:

1. Commercial large scale cultivation of these plants means there is a selective pressure on resistant weeds, thus increasing the amount of sprayed herbicides and the load of residues . The complementary herbicides are likely to be sprayed several times, thus the pattern of usage and the level of residues can be significantly higher compared to other plants.
2. Herbicide tolerant plants are meant to survive the application of the complementary herbicide while most other plants will be killed after short time. Thus, metabolites and the resulting residues can be rather specific.
3. In the case of stacked events, a combination of specific plant constituents is fixed in the genetically engineered plants. The combination of the residues from spraying and of insecticidal proteins (as it is the case in MON87701 x MON89788) causes a unique and unavoidable exposure of the feed and food chain with very specific residues. Possible interactions have to be investigated in detail.

So in conclusion, the residues and their combinatorial are inevitable constituents of the plants composition leading to specific pattern of exposure of the food chain. A basic prerequisite for risk assessment in this context are reliable data on residue loads from spraying with glyphosate formulations. The amount of these residues depends on the specific agronomic management used in the cultivation of the herbicide resistant plants. However, reliable data covering the actual range of residue load in the plants are not available (Kleter et al., 2011, EFSA 2011, Then 2011). Without such data, no sound risk assessment of this product can be made.

No feeding studies were performed with the stacked event, no acute, subchronic, long term and multigenerational study was requested. No tests were performed to determine potential combinatorial or accumulated effects of the toxins, nor of any other factors such as other toxic compounds, bacteria, plant enzymes (trypsin inhibitors) and especially the residues from the complementary herbicide.

No investigations were conducted to assess the impact of a permanent ingestion of these plants on the intestinal microbial composition in human and animals. No endocrinological studies were performed to investigate potential impacts on the reproductive system, despite the fact that soy produces hormonally active substances that might have been changed unintentionally.

The plants will go into feed and might be mixed with other genetically engineered plants. Tests need to be carried out to determine potential accumulative or combinatorial effects. But no assessment of

combinatorial effects with other genetically engineered plants used in food and feed was requested. Cry1Ac is also a Bt toxin known for its synergistic effects with other Bt toxins (Sharma et al., 2010). Synergistic effects can become highly problematic for non-target organisms. Interactivity of the toxins or the toxins in combination with environmental toxins, bacteria, plant enzymes or pesticides can cause higher than expected toxicity and lower selectivity (Then, 2010)

The effects of the different methods used for processing, and risks associated with particular usage of soybeans in human nutrition was not assessed.

All in all, this product has a substantial range of risks and there is a high level of uncertainty concerning its safety.

Allergy:
Insect-killing Soy MON87701 is engineered to produce insecticidal protein Cry1Ac. This is a Bt toxin which is known to enhance immune reactions and able to bind to epithelial cells in the intestine of mice (Vázquez-Padrón et al., 1999 and 2000). Soy is one of the most potent allergenic food plants, consequently, from a precautionary perspective, this protein should be avoided in these plants.

The findings in blood samples from individuals with a known allergy to soybeans, should have already triggered more investigations assessing the parental plants. EFSA should have at least requested further testing by now for stacked events.

Potential allergenicity in parental plants was assessed by applying in a pepsin digestion assay. In result, the Cry protein is thought to be degraded quickly in the gastrointestinal tract. However, Walsh et al. (2011) have found new evidence showing that the protein Cry1Ab can be found in the colon of pigs with a success rate of 80%. Thus, the Cry proteins can show much higher stability in monogastric species than predicted by current in vitro digestion experiments. These findings should require further assessment by EFSA.

Others:
No empirical investigation of the actual persistence of the Bt toxins and their potential accumulation in the environment was conducted. No investigation conducted for DNA traces in animal tissue after feeding was required. No plan for surveillance was made available that would allow identification of particular health impacts that might be related to the use of these genetically engineered plants in food and feed. The protocols used for conducting the measurements of the Bt toxins have not been fully published or evaluated by independent laboratories. As a result, independent institutions can hardly monitor the actual content of Bt concentration in the plants during cultivation or in food and feed products (Szekacs, 2011).

Monitoring health effects should be performed in regard to glyphosate formulations and their residues in the plants. This is also underlined by the fact that a significant proportion of consumers seem to have a substantial load of pesticide residues in their blood (Aris & LeBlanc, 2011).

Conclusion:
The opinion of EFSA should not be accepted. Genetically engineered soybeans producing additional proteins that are known to enhance immune reactions should not be authorised.

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