

## Comments from the public: 40-3-2 soybean

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**Organisation: Testbiotech**

**Country: Germany**

**Type: Non Profit Organisation**

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### **a. Assessment:**

#### **Comparative analysis (for compositional analysis and agronomic traits and GM phenotype)**

Using comparative assessment (also known as the concept of substantial equivalence) as a starting point means that the risks associated with the genetic engineering method are not sufficiently scrutinized. Gene constructs inserted through genetic engineering are not subject to normal gene regulation. As we know from several publications (see for example Zeller et al., 2010), this can give rise to unexpected effects in genetically engineered plants under certain environmental conditions.

There are some indications that these issues are especially relevant for soy 40-3-2. With regard to soybean 40-3-2, it is known that the insert with flanking soybean genomic sequences might produce a fusion protein (Rang et al., 2005). Further, it is known that soybean 40-3-2 can react unexpectedly to dry hot weather conditions (Gertz et al., 1999). Windels et al. (2001) show unintended insertion of DNA. Lappe et al. (1999) show alterations in phytoestrogen content. Zobiolo et al. (2010) show that the composition of lignin and other parameters are impacted by the newly introduced metabolism of glyphosate. These observations show the necessity of carrying out experiments systematically under changing environmental conditions to find out how the newly introduced metabolism interacts with the plant's own genome regulation and to investigate if, and how, the amounts of pesticide residues are related to these effects. Immunologically relevant proteins and hormonally active ingredients should also be taken into account.

Gertz J.M., Vencill W.K., Hill N.S. (1999) Tolerance of Transgenic Soybean (*Glycine max*) to Heat Stress. British Crop Protection Conference – Weeds, 15-19 Nov 1999, Brighton: 835-840.

Lappe, M.A., Bailey, E.B., Childress, C. & Setchell, K.D.R. 1999. Alterations in clinically important phytoestrogens in genetically modified, herbicide-tolerant soybeans. *J. Med. Food* 1, 241-245.

Rang, A., Linke, B., Jansen, B. (2005) Detection of RNA variants transcribed from the transgene in Roundup Ready soybean. *European Food Research and Technology* 220(3-4): 1438-2377.

Ran, T., Mei, L., Lei, W., Aihua, L., Ru, H., Jie, S (2009) Detection of transgenic DNA in tilapias (*Oreochromis niloticus*, GIFT strain) fed genetically modified soybeans (Roundup Ready). *Aquaculture Research*, Volume 40 (12): 1350-1357

Windels, P., Taverniers, I., Depicker, A., Van Bockstaele, E. & De Loose, M. 2001. Characterisation of the Roundup Ready soybean insert. *Eur Food Res Technol* 213, 107-112.

Zeller S.L., Kalininal, O., Brunner, S., Keller B., Schmid B., 2010, Transgene × Environment Interactions in Genetically Modified Wheat:  
<http://www.plosone.org/article/info:doi/10.1371/journal.pone.0011405>

Zobiolo, L.H.S., Bonini, E.A., de Oliveira R.S., Kremer, R.J., Ferrarese-Filho, O., 2010, Glyphosate affects lignin content and amino acid production in glyphosate-resistant soybean, *Acta Physiol Plant* (2010) 32:831–837, DOI 10.1007/s11738-010-0467-0

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## **b. Food Safety Assessment: Toxicology**

EFSA cites several toxicity studies to underpin its findings that there are no toxicological risks associated with RR soybean. All the studies in line with the EFSA view are quoted without any criticism, whereas studies that are critical in their findings (most of them published by the Italian Malatesta team e.g. Malatesta et al. 2008, Cisterna et al. 2008) are dismissed for assumed faults in experimental design, statistical evaluation etc. The same is true for a study by Magaña-Gómez et al. (2008) who reported that pancreatic microscopic features were disturbed by a diet containing RR soybean. A review article by Magaña-Gómez et al. (2009) is not included in the EFSA opinion. In the publication, the authors declare that in quite a few of studies concerning soybean 40-3-2 “a tendency towards microscopic and molecular changes was observed, suggesting some kind of cell damage. These studies should be used to support further experiments using profiling techniques to screen for potential changes at different cellular levels: gene expression, protein translation, or metabolic pathways.”

The EFSA is obviously applying double standards in assessment because the studies that EFSA is relying on as proof for the safety of RR soybean are themselves not incontestable. For example, EFSA quotes a multi-generational study, which analysed the effect of a diet containing RR soybean on the testicle development of male mice (Brake & Evenson 2004). This study can be criticised for having no feeding protocols, no data on weight, on feed intake or on growth pattern related to feed intake. The results of a publication by Teshima et al. (2000), another study quoted by EFSA, are questionable because only five animals were tested per group.

Brake D.G. and Evenson D.P. (2004) A generational study of glyphosate-tolerant soybeans on mouse fetal, postnatal, pubertal and adult testicular development. *Food Chemistry and Toxicology* 42, 29-36.

Cisterna, B., Flach, F., Vecchio, L., Barabino, S.M.I., Battistelli, S., Martin, T.E., Malatesta, M. and Biggiogera, M. (2008) Can a genetically-modified organism-containing diet influence embryo development? A preliminary study on pre-implantation mouse embryos. *European Journal of Histochemistry* 52, 263-267.

Magaña-Gómez, J.A., Cervantes, G.L., Yepiz-Plascencia, G. and Barca, A.M.C.d.l. (2008) Pancreatic response of rats fed genetically modified soybean. *Journal of Applied Toxicology* 28, 217–226.

Magaña-Gómez, J. A. and Calderón, A.M.C.d.l. (2009), Risk assessment of genetically modified crops for nutrition and health. *Nutrition Reviews* 67, 1–16.

Malatesta, M., Boraldi, F., Annovi, G., Baldelli, B., Battistelli, S., Biggiogera, M., Quaglino, D. (2008) A long-term study on female mice fed on a genetically modified soybean: effects on liver ageing. *Histochem Cell Biol* 130, 967-977

Teshima, R. Akiyama, H., Okunuki, H., Sakushima, J., Goda, Y. Onodera, H., Sawada, J. and Toyoda, M. (2000) Effect of gm and non-gm soybeans on the immune system of BN rats and B10A mice. *J. Food Hyg. Soc. Japan* 41, 188-193.

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## Allergenicity

EFSA forgot to take into account a study that appears important for the assessment of the allergenic properties of RR soybean. Yum et al. (2005) reported the details of skin tests with the RR- and non-transgenic soybean. They found that the RR soybean shows a different binding band compared with wild soy. Furthermore, one patient had a positive skin test result to GMO soybeans only.

Yum, H.Y., Lee, S.Y., Lee, K.E., Sohn, M.H., Kim, K.E. (2005) Genetically modified and wild soybeans: an immunologic comparison. *Allergy and Asthma Proc* 26, 210–6.

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## Nutritional assessment

One of the most controversially debated subjects in GMO research is the question of whether transgenic DNA can be found in animal tissue such as meat, milk or eggs. DNA from transgenic plants has been found in the tissue of some animals such as fish and pigs (Chainark, 2008; Ran et al., 2009; Mazza et al., 2005, Sharma et al 2006). In 2010, Italian researchers detected fragments of the cp4 epsps gene (the gene incorporated in RR soybean) in the liver, kidney, heart and muscle of goats (Tudisco et al. 2010). Changes were even found in the production of a specific enzyme in kid goats. EFSA does not even mention these studies.

Chainark, P. (2008) Availability of genetically modified feed ingredient II: investigations of ingested foreign DNA in rainbow trout *Oncorhynchus mykiss*. *Fisheries Science*, 74(2): 380-390(11)

Mazza, R., Soave, M., Morlacchini M., Piva, G., Marocco, A. (2005) Assessing the transfer of genetically modified DNA from feed to animal tissues, *Transgenic Res.* 14: 775-784

Ran, T, Mei, L., Lei, W., Aihua, L., Ru, H., Jie, S (2009) Detection of transgenic DNA in tilapias (*Oreochromis niloticus*, GIFT strain) fed genetically modified soybeans (Roundup Ready). *Aquaculture Research*, Volume 40 (12): 1350-1357

Sharma R., Damgaard D., Alexander T.W., Dugan M.E.R., Aalhus J.L., Stanford K., McAllister T.A. (2006) Detection of transgenic and endogenous plant DNA in tissues of sheep and pigs fed Roundup Ready canola meal. *Journal of Agricultural Food Chemistry* 54: 1699–1709.

Tudisco, R., Mastellone, V., Cutrignelli, M.I, Lombardi, P, Bovera, F., Mirabella, N., Piccolo, G., Calabro, S., Avallone, L., Infascelli, F. 2010. Fate of transgenic DNA and evaluation of

metabolic effects in goats fed genetically modified soybean and in their offsprings. *Animal* 4, 1662-1671.

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## Others

There are many new studies and reviews being published showing that low concentrations of glyphosate and, in particular, the additive POEA (polyoxyethylene alkylamine) are much more toxic than previously thought (see for example publications reviewed by PAN AP, 2009, see also Paganelli et al, 2010). Further, Zobiolo et al (2010) show there is a highly specific relationship between glyphosate application and the plant's components. The EFSA opinion does not address these issues. It only refers to pesticide regulation and the work of the EFSA pesticide panel. The GMO panel thereby overlooks the fact that these new publications were never assessed by any other EFSA panels, and that many of these risk issues are closely related to both the genetically engineered trait and the assessment of the herbicide. That is why a systematic interplay is required to assess the actual risks for human health. This is also required for example by Directive 2001/18, Recital 16. The necessary interplay between these sectors of risk assessment is completely missing in EFSA's opinion.

PAN AP, Pesticide Action Network Asian Pacific, 2009, Monograph on Glyphosate, <http://www.panap.net/en/p/post/pesticides-info-database/115>

Paganelli, A., Gnazzo, V., Acosta, H., López, S.L., Carrasco, A.E. 2010. Glyphosate-based herbicides produce teratogenic effects on vertebrates by impairing retinoic acid signalling. *Chem. Res. Toxicol.*, August 9. <http://pubs.acs.org/doi/abs/10.1021/tx1001749>

Zobiolo, L.H.S., Bonini, E.A., de Oliveira R.S., Kremer, R.J., Ferrarese-Filho, O., 2010, Glyphosate affects lignin content and amino acid production in glyphosate-resistant soybean, *Acta Physiol Plant* (2010) 32:831–837, DOI 10.1007/s11738-010-0467-0

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## 4. Conclusions and recommendations

The EFSA opinion on the renewal application for the Monsanto Roundup Ready variety of soybean (soybean 40-3-2) is basically incomplete and flawed and should not be accepted by the risk manager.

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## 5. Others

Legally required post market monitoring of health effects is still not in place. In Testbiotech's opinion a monitoring system is essential because otherwise the legal requirements for market authorisation of food and feed from genetically engineered plants cannot be met.

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