

Testbiotech comment on EFSA Panel on Genetically Modified Organisms (GMO); Scientific Opinion on an application (EFSAGMO-NL-2012-107) for the placing on the market of maize MON 810 pollen under Regulation (EC) No 1829/2003 from Monsanto. EFSA Journal 2012;10(12):3022

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Maize MON810 produces an insecticidal Bt protein, Cry1Ab, which is under control of the promoter of the cauliflower mosaic virus. It was produced using the particle gun method (for more details see <http://www.testbiotech.org/en/node/535>).

Molecular data

The EFSA risk assessment suffers from a lack of data on the actual Bt content in pollen. The original data from Monsanto are around 20 years old. Since then only very few data were made available.

Further, the methods for measuring the Bt content were never evaluated for reliability and comparability (Szcak, et al., 2011). It is known that environmental conditions can influence the content of the Bt in the plants – but no data are available for Bt content in pollen under defined environmental conditions (Then & Lorch, 2008).

Thus, the whole risk assessment is based on insufficient data.

Comparative assessment

The EFSA risk assessment suffers from a complete lack of data on compositional analysis of the pollen. Without data for compositional analysis, no comparative risk assessment can be applied (as performed by EFSA).

The complete lack of any data on compositional analysis should have led EFSA to reject the assessment of this application as long as no data are available.

Toxicology

The mode of action of the Bt toxin still is not known in all its details (Vachon et al 2012). The impact on human cells was described recently (Mesnage et al., 2012). Since no reliable data are available for the Bt content in the pollen and no final conclusion can be drawn upon the safety of the pollen.

Allergenicity

The opinion of EFSA ignores the findings on immune reactions triggered by Bt plants. There are already several studies showing that genetically engineered plants producing Cry proteins interact with the immune system in vertebrates. Such examples include fish (Sagstad et al., 2007), pigs (Walsh et al., 2011), mice (Finamore et al., 2008), and rats (Kroghsbo et al., 2008). Further, Gu et al (2012) suggest that Bt-maize can potentiate oxidative cellular stress in immune-sensitised animals (fish), thus specific attention should be paid to interactions of the Bt proteins with other food components and the immune status of the individual.

Further, the weight of evidence brought forward by EFSA is based on investigations that do not allow the assessment of digestion of the protein under realistic conditions. For example, feeding studies with pigs conducted by Chowdhury et al. (2003) as well as Walsh et al. (2011) found that Cry1A proteins can frequently be found in the colon of pigs. This shows Cry1A proteins can show much higher stability in monogastric species than predicted by current in vitro digestion experiments. It should be taken into consideration that pollen is likely to resist digestion more than other foodstuff and as result the Bt proteins are likely to survive to an ever higher percentage than in other food.

In this context, risk assessment should also include the exposure via the respiratory system, because this question was not fully investigated in the risk assessment of MON810 for cultivation.

Thus, no conclusion can be made upon the safety of the pollen in regard to the immune system.

Nutritional Assessment

The EFSA risk assessment suffers from a complete lack of nutritional data.

Pollen is seen as a health food and dietary supplement, so it is astonishing that EFSA has not even tried to assess the nutritional quality of pollen that contains Bt-toxins. EFSA should have undoubtedly requested data from the applicant.

Environmental risk assessment

Risk assessment should also include the exposure via the respiratory system since so far no detailed investigations are available, while some data indicate risks for human health (Bernstein et al., 1999; Doekes et al., 2004).

Conclusion and recommendations:

The risk assessment of EFSA is not based on any reliable data. Further, the opinion of EFSA does not identify the true range of uncertainties (as requested by Regulation 178/2002) and the current limits of knowledge. The risk manager should therefore reject this opinion.

References:

Bernstein, I. L.; Bernstein, J. A.; Miller, M.; Tierzieva, S.; Bernstein, D I.; Lummus, Z.; Selgrade, M. K.; Doerfler, D. L; Seligy, V. L. (1999) Immune responses in farm workers after exposure to *Bacillus thuringiensis* pesticides. *Environ. Health Perspect*, 107, 575–582.

Chowdhury, E. H., Kuribara, H., Hino, A., Sultana, P., Mikami, O., Shimada, N., Guruge, K. S., Saito, M., Nakajima, Y. (2003). Detection of corn intrinsic and recombinant DNA fragments and Cry1Ab protein in the gastrointestinal contents of pigs fed genetically modified corn Bt11. *J. Anim. Sci.* 81: 2546-2551.

Doekes, G.; Larsen, P.; Sigsgaard, T.; Baelum, J. (2004) IgE sensitization to bacterial and fungal biopesticides in a cohort of Danish greenhouse workers: the BIOGART study. *Am. J. Ind. Med.*, 46, 404–407.

Finamore, A., Roselli, M., Britti, S., Monastra, G., Ambra, R., Turrini, A. & Mengheri, E., 2008, Intestinal and peripheral immune response to MON810 maize ingestion in weaning and old mice. *Journal of Agricultural and Food Chemistry* 56: 11533–11539

Gu, J., Krogdahl A., Sissener, N.H., Kortner, T.M., Gelencser E., Hemre G.I., Bakke A.M. (2012) Effects of oral Bt-maize (MON810) exposure on growth and health parameters in normal and sensitised Atlantic salmon, *Salmo salar* L., *British Journal of Nutrition*, doi:10.1017/S000711451200325X

Kroghsbo, S., Madsen, C., Poulsen, M., Schrøder, M., Kvist, P.H., Taylor, M., Gatehouse, A., Shu, Q., Knudsen, I., 2008, Immunotoxicological studies of genetically modified rice expressing PHA-E lectin or Bt toxin in Wistar rats. *Toxicology*. 245, 24-34.

Mesnage R., Clair E., Gress S., Then C., Székács A., Séralini G.-E., 2012, Cytotoxicity on human cells of Cry1Ab and Cry1Ac Bt insecticidal toxins alone or with a glyphosate-based herbicide, *Journal of Applied Toxicology*, <http://onlinelibrary.wiley.com/doi/10.1002/jat.2712/abstract>

Sagstad, A., Sanden, M., Haugland, O, Hansen A.C., Olsvik P.A., Hemre G.I., 2007, Evaluation of stress- and immune-response biomarkers in Atlantic salmon, *Salmo salar* L., fed different levels of genetically modified maize (Bt maize), compared with its near-isogenic parental line and a commercial suprex maize, *Journal of Fish Diseases*, 30: 201–212

Székács, A., Weiss G., Quist, D., Takács, E., Darvas, B., Meier, M., Swain T., Hilbeck A., (2011): Inter-laboratory comparison of Cry1Ab toxin quantification in MON 810 maize by enzyme-immunoassay, *Food and Agricultural Immunology*, DOI:10.1080/09540105.2011.604773.

Then, C. & Lorch, A., 2008, A simple question in a complex environment: How much Bt toxin do genetically engineered MON810 maize plants actually produce?, in: Breckling, B., Reuter, H. & Verhoeven, R. (eds), 2008, *Implications of GM-Crop Cultivation at Large Spatial Scales*, *Theorie in der Ökologie* 14. Frankfurt, Peter Lang, <http://www.mapserver.uni-vechta.de/generisk/gmls2008/index.php?proceedings=ja&call=ja>

Vachon, V., Laprade, R., Schwartz, J.L., 2012, Current models of the mode of action of *Bacillus thuringiensis* insecticidal crystal proteins: A critical review, *J. Invertebr. Pathol.* <http://dx.doi.org/10.1016/j.jip.2012.05.001>

Walsh, M.C., Buzoianu, S.G., Gardiner, G.E., Rea M.C., Gelencsér, E., Jánosi A., Epstein M.M., Ross, R.P., Lawlor, P.G. (2011) Fate of Transgenic DNA from orally administered Bt MON810 maize and effects on immune response and growth in pigs. *PLoS ONE* 6(11): e27177, doi:10.1371/journal.pone.0027177.