TESTBIOTECH Background 09 - 11 - 2013

Testbiotech comment on the Scientific Opinion of EFSA on application EFSA-GMO-RX-T25 and EFSA-GMO-NL-2007-4 for the placing on the market of herbicide-tolerant genetically modified maize T25 for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Bayer

Christoph Then & Andreas Bauer-Panskus

Introduction
Maize T25 was one of the first genetically engineered crops to enter the market. It was first evaluated in the EU in 1998. T25 contains a gene that makes maize plants tolerant to glufosinate (brand names such as Liberty or Basta). Glufosinate is a broad-spectrum herbicide and is highly controversial because of its toxicity to mammals.

Molecular data
The genetic modification led to the formation of several open reading frames (ORFs). The molecular characterisation should take into account not only the possible emergence of new proteins and tRNA but also the new double stranded RNA products that might be transmitted at the consumption stage as a biological active substance.

Data should be requested on the impact of the newly introduced DNA, its gene products and the new metabolic pathway in the plants own gene regulation.

Comparative assessment (for compositional analysis and agronomic traits and phenotype)
Several field trials were conducted to prove that maize T25 is compositionally equivalent to its isogenic line. There were several findings indicating that site-specific effects led to significant differences between T25 and its comparator. Further, the expression of the PAT protein in the kernels shows considerable variation, which seem to be impacted by specific environmental conditions. But instead of systematic investigation of environmental x genome interaction, EFSA just gives a very general statement that cannot be considered as a scientific conclusion based on verifiable facts:

> *"The EFSA GMO Panel considered the observed compositional differences between maize grain produced from maize T25 and its conventional counterparts in the light of the field trial design, measured biological variation and the level of the studied compounds in non-GM commercial varieties, and concluded that no biologically relevant differences were identified in the compositional characteristics of grain produced from maize T25 compared with its conventional counterpart, and that its composition falls within the range of non-GM commercial varieties, except for the expression of the PAT protein."*

Furthermore, data from sweet maize T25 (the most relevant product for human consumption) showed several significant findings which were not assessed by EFSA because

> "*compositional changes during post-harvest storage of the sweet maize could not be*

excluded"

This statement raises questions about why EFSA did not request any new data to find out if, and which, compositional changes occur during storage. Such changes are relevant for risk assessment if meaningful differences between T25 and its comparator are identified.

Toxicology
A 90-day rodent study carried out by the applicant was rejected because of fundamental flaws in study design. A 42-day nutritional study was also rejected by the panel. Instead of asking the applicant to produce valid toxicological data, EFSA refers to the outcomes of a second 42-day nutritional study, which showed no differences between a diet containing maize T25 and a diet containing the isogenic line. However, the results from nutritional studies are only of minor relevance for toxicity assessment.

It is a matter of concern that more than 15 years after T25 was developed, there is still no reliable long-term feeding study or targeted monitoring of the effects on health. No final conclusion regarding the toxicity of maize T25 can be drawn based on the data available.

Allergenicity
Although EFSA guidance requires an investigation into the changes in the overall allergenicity of the maize, this was not carried out, and the only publication mentioned in the EFSA opinion was identified as unreliable. Instead of requesting reliable data EFSA concludes:

> *"In the context of this application, and based on the available information, there is no evidence that the genetic modification might significantly change the overall allergenicity of maize T25."*

This statement shows that EFSA´s opinion follows a do not seek and you will not find approach.

Others
Several other genetically engineered plants with tolerance to various herbicides have pending applications for market authorisation in the EU, making a systematic approach necessary to deal with new patterns of exposure, with interactions between the substances and the accumulated impact on human and animal health. Risk assessment should take potential interactions and accumulated effects between the residues from spraying with glufosinate and residues from spraying with other herbicides into account. Furthermore, the residues left in other genetically engineered plants from spraying with herbicides, potential interactions and accumulated effects should all be taken into account as these plants can be mixed with T25 in food and feed.

Glufosinate is regarded as potentially damaging to health (EFSA, 2005). According to the German Agricultural Ministry, glufosinate will be phased out in the EU in 2017 for reasons of reproductive toxicity (BMELV, 2009). Furthermore, it has been shown that the metabolite of glufosinate (called NAG) produced by the transgenic plants can be partially reconverted into the pesticide itself by gut bacteria, leading to increased health risks for animals and consumers (Bremmer & Leist, 1997).

Conclusion and recommendations
There was no investigation of indications for site-specific impacts on the plant's genome. Toxicology and allergenicity was not investigated properly. Instead, EFSA made several assumptions not based on verifiable data. Residues from spraying with glufosinate were not considered.
Therefore, no final conclusion on the safety maize T25 can be reached. EFSA's opinion should be

rejected.

Monitoring
Monitoring taking the residues from spraying into account must be carried out at the consumption stage. If T25 is authorised, main use of T25 is likely to be in feed products. Thus national veterinary networks and services should be involved in the monitoring of effects on animal health.

References:
BMELV, Bundesministerium für Ernährung, Landwirtschaft und Verbraucherschutz (2009) Neue Bewertungskriterien für Wirkstoffe in Pflanzenschutzmitteln [German language only]. http://www.fao.org/ag/agp/agpp/pesticid/jmpr/Download/98/glufosi3.pdf

Bremmer, J.N. and Leist, K.-H. (1997) Disodium-N-acetyl-L-glufosinate; AE F099730 - Hazard evaluation of Lglufosinate produced intestinally from N-acetyl-L-glufosinate. Hoechst Schering AgrEvo GmbH, Safety Evaluation Frankfurt. TOX97/014. A58659. Unpublished. (see FAO publication on www.fao.org/ag/agp/agpp/pesticid/jmpr/Download/98/glufosi3.pdf)

EFSA (2005) Conclusion regarding the peer review of the pesticide risk assessment of the active substance glufosinate. EFSA Scientific Report 27: 1-81.