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Testbiotech e. V.
Institute for Independent Impact Assessment in Biotechnology

EU about to approve genetically engineered maize with potential health risk

Christoph Then

The European Union Agriculture Council will on March 17 2011 deal with a market application of a so called 'stacked event' for MON 89034 × MON 88017 maize (Monsanto). Another new application for cotton GHB614 (Bayer) is on the agenda as well as renewal of application for maize 1507 (Pioneer). Testbiotech urges these applications be rejected, because necessary standards for assessing health risks are not met and recent publications show the need for further investigations.

1. On maize MON 89034 × MON 88017 (brand name: VT Triple Pro Corn)
This maize produces several insecticidal toxins derived from various strains of *Bacillus thuringiensis*. It is produced and sold by Monsanto company under its brand name VT Triple Pro Corn. The maize is made resistant against pest insects above ground (larvae from *Lepidotera* species) and in the soil (larvae from *Coleoptera* species).

Member states should take into account the fact that in maize 89034 (used for crossing in the stacked event) a highly synthetical Bt toxin is produced. This toxin is a combination of Cry1Ac, Cry1F and Cry1Ab (see digram). These proteins are produced by different strains of *Bacillus thuringiensis* (see table). There is no native form of this combined protein, so its risks can not be compared with the ones from native Bt toxins used before. In this case, synergistic effects, selectivity and toxicity have to assessed comprehensively to exclude risks for human health and farm animals.

Diagram: Combination of various Bt toxin and components from Bt toxins in VT Triple Pro Corn

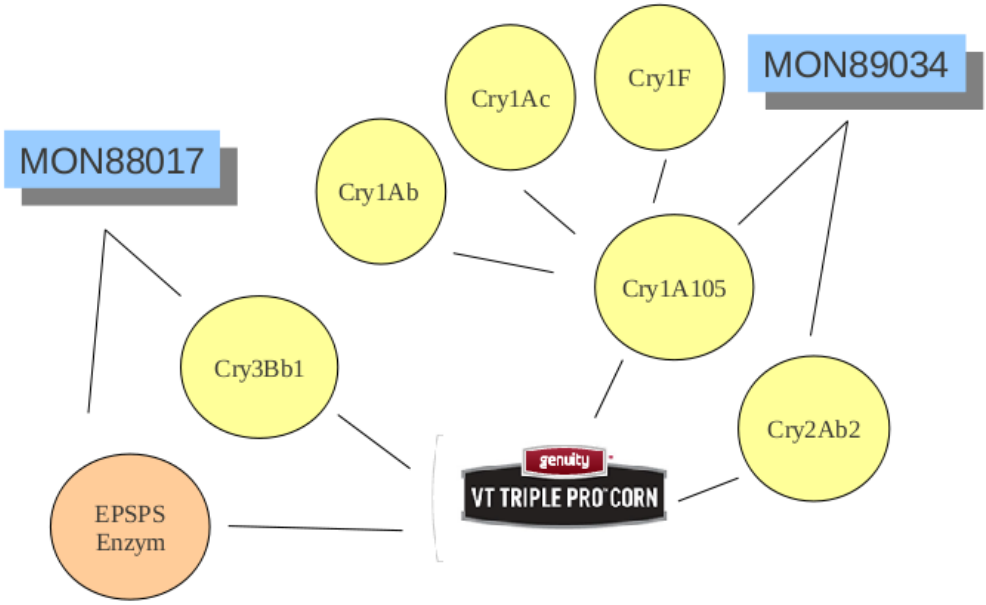

Table: origin of the proteins used in VT Triple Pro Corn

New protein produced in MON 89034 × MON 88017	Origin of the gene sequence
Cry1Ab (Cry1A.105)	*Bacillus thuringiensis*, subspecies *kurstaki*
Cry1Ac (Cry1A.105)	*Bacillus thuringiensis*, subspecies *kurstaki*
Cry1F (Cry1A.105)	*Bacillus thuringiensis*, subspecies *aizawai*
Cry2Ab2	*Bacillus thuringiensis*, subspecies *kurstaki*
Cry3Bb1	*Bacillus thuringiensis*, subspecies *kumamotoensis*
EPSPS enzyme	*Agrobacterium* sp. strain CP4

In the light of recent publications, the risk assessment of EFSA is not sufficient:

- As Pardo Lopez et al. (2009) and Pigott et al. (2008) show, synthetically derived and modified Bt toxins can show much higher toxicity than native proteins. Even small changes in the structure of the proteins can cause huge changes in its toxicity. EFSA did not evaluate this specific problem in the case of Cry1A.105. Moreover this is not the only protein that is changed in its structure, all the Bt toxins as produced in the plants are technically modified.
- EFSA discussed potential synergistic effects between the Bt toxins used in the plants and has come to the conclusion that these are not to be expected. EFSA herein refers to studies the Monsanto company performed on target organisms that only showed additive effects but no further interactivity between the proteins. However a recently published study of Sharma et

al. (2010) found synergistic effects of Cry1Ab and Cry1Ac in target pest insects. Further synergistic effects between Cry1Ac an other Bt toxins such as Cry2Ab2 and Cry1F are discussed in and Lee et al. (1996), Chakrabarti et al (1998), Stewart et al. (2001) and Kashdan et al (2007). Synergistic effects can become highly problematic for non target organisms: Interactivity between the toxins can cause unexpected higher toxicity and lower selectivity (Then, 2010). These effects also can impact human health.

- In general it is not sufficient to assess risks to human health such as potential synergies of the Bt proteins just by referring to experiments with insects (target organisms). At least in vivo studies on human cells should have been performed, to investigate effects of Bt toxins involved in this case. Especially the properties of the synthetic toxin Cry1A.105 are not known. But also the other Bt toxins have to be tested in appropriate biological systems to exclude risks for human health: The mode of action of Bt toxins is not fully understood. It is even a matter of controversial debate (Pigott & Ellar, 2007). Risks for human health can not be excluded by assumptions or considerations but only by empirical testing.
- Kidney problems were observed in animal feeding studies with MON89034 conducted by Monsanto (as presented in its market application for MON89034). These findings were considered as being not relevant by EFSA. Already at this point, EFSA should have requested further studies. But EFSA did not even request any feeding studies for health risks at the level of combining MON 89034 × MON88017 in a stacked event. In conclusion there is a high level of uncertainty regarding human health risks. The presence of these risks is supported by a report by Gallagher (2010) dealing with kidney problems that were observed in feeding studies with genetically engineered eggplant which also express a modified Cry1Ac protein.
- Also the potential synergies (and related risks) between Cry2Ab2 (as produced in MON88017) and the other Bt toxins in the stacked event were not investigated. It was overlooked that synergistic interactivity between Cry2Ab2 and Cry1Ab and between Cry2Ab2 and Cry1Ac has been discussed in Mattila et al. (2005) and Stewart et al. (2001).
- The necessary interplay between risk assessment in herbicides and the risk assessment of herbicide tolerant crops was omitted by EFSA. The maize is made tolerant against the use of Glyphosat preparations by introducing a gene construct for the EPSPS enzyme (see diagram). As a recent overview of the scientific literature shows (PAN AP, 2009) the toxicity of Glyphosat, its metabolites and its additive POEA (polyoxyethylene alkylamine) have to re-evaluated. EFSA should have at least requested detailed analyses of the residues from spraying various Glyphosate formulations on the genetically engineered plants.

In the light of these findings Testbiotech suggests the MON 89034 × MON 88017 stacked event not be approved and market authorisation for MON89034 be reassessed.

2. **Concerning the other applications** the following should be considered:

- In maize 1507 a Bt toxin being active against *Lepidoptera* species is combined with herbicide tolerance against Glufosinate. The Council should request a much more detailed risk assessment in this case. Some examples for the deficiencies of EFSA risk assessment: In maize 1507 the toxicity assessment by EFSA is largely derived by analogy with Cry1Ab. As Bauer-Panskus and Then (2010) show, this is an insufficient approach: The Cry1F protein (as produced in maize 1507) in comparison shows highly different toxicity in the model organism of the greater wax moth (Hanley et al., 2003), a finding that was overlooked by EFSA. Further, EFSA did not deal with the publication by Dona & Arvanitoyannis (2009). These experts come to the conclusion that the animal

feeding data as presented by Pioneer indicate severe health effects. No detailed analyses of the residues from spraying and its potential interactions with the Cry1F protein was conducted. A more detailed analyses of this case can be found at http://www.testbiotech.de/sites/default/files/table%20answer%20to%20EFSA_1507.pdf and http://www.testbiotech.de/sites/default/files/Stellungnahme%20Testbiotech%201507%20Mais_2.pdf.

- On Bt cotton GHB614 Testbiotech did not perform any detailed analysis. But what is evident from the opinions as presented by EFSA is that also in this case the interplay with the herbicide application is missing. The cotton is made tolerant against the use of Glyphosat preparations. As mentioned, a recent overview of the scientific literature shows (PAN AP, 2009) the toxicity of Glyphosat and its additive POEA (polyoxyethylene alkylamine) have to re-evaluated. EFSA should have at least requested detailed analyses of the residues from spraying various Glyphosate formulations on the genetically engineered cotton. Further it is a matter of concern that in the case of Bt cotton GHB614 no animal feeding studies for excluding health risks were conducted.

Testbiotech is therefore of the opinion that in these cases, too, the applications should be rejected because necessary standards of health risk assessment are not met by EFSA.

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