Insecticidal Bt toxins

Generally, the genetically engineered plants authorised for import into the EU already contain around a dozen different Bt toxins. These toxins originate from the soil bacteria Bacillus thuringiensis, which naturally produce around 200 insecticidal substances. The Bt toxins produced in the transgenic plants are, however, changed in their structure to enhance their toxicity. In addition, genetically engineered plants can be crossed to produce so-called stacked events. The stacked events that are then marketed not only contain a combination of toxins but have an overall higher concentration of the toxins (see below). The Bt toxins produced in the plants are considered to be mostly specific for targeted pest insects, and therefore safe for human and mammalian health in general. However, there is evidence that for several Bt toxins, the range of susceptible organisms is broader than assumed. Therefore, risks for human and animal health cannot be excluded a priori but need to be investigated empirically. In this context, there are some open questions that need to be considered:

• The detailed mode of action for most of the Bt toxins produced in genetically engineered plants is not known, and is different for each of the toxins. Further, there is a lack of relevant data and the existing data are partially contradictory (see Then, 2010; Hilbeck & Otto, 2016). As a result, the specificity of the toxins remains a matter of uncertainty. Also relevant in this context is – as mentioned – that the structure of the toxins produced in the plants is substantially changed. The Bt toxins produced in genetically engineered plants are not the same as natural Bt toxins and some do not even have a natural template. Consequently, there are substantial uncertainties regarding the safety assumed for health and the environment.

• There are some indications that Bt toxins can have negative effects in humans or, more generally, in mammals (Thomas and Ellar, 1983; Shimada et al., 2003; Huffmann et al. 2004; Ito et al. 2004; Mesnage et al., 2012; Bondzio et al., 2013). These effects might be substantially enhanced by interaction with other stressors such as residues from spraying with herbicides (Then, 2010). Combinatorial effects have already been described in some model organisms (Kramarz et al., 2007, Bohn et al., 2016). However, such interactions are not investigated in the context of EFSA risk assessment.

• The toxicity of Bt toxins can vary. Even small changes in their structure can render a higher toxicity (Pardo-López et al., 2009). However, even if the structure is deemed to be identical, toxicity can vary in dependency on the source as shown by Saeglitz et al. (2008). More detailed investigations are missing so far.

• There are further open questions about the true Bt content in the various parts of the plants, which can vary substantially in response to environmental conditions (Then & Lorch, 2008). But, as yet, evaluated methods to reliably determine the Bt content in the plants are largely missing (Szekacs et al., 2011). As investigations under defined stress conditions show, the Bt content in the plants can change unpredictably (Trtikova et al, 2015).

• It is known that at least some of the Bt toxins produced by transgenic plants can impact the immune system in mammals (see Rubio-Infante & Moreno-Fierros, 2015). In this context, it is a matter of special concern that Bt toxins are produced in some genetically engineered soybeans. Soybeans naturally produce a broad range of allergenic substances. Combinatorial effects may lead to an enhanced immune response to these allergens or cause new allergies (overview: Testbiotech 2012). To some extent these issues are also relevant to maize,
since some allergenic compounds have been described for maize plants. Furthermore, this adjuvant effect may also be relevant to other compounds that are mixed in food and feed along with the Bt producing plants. Contrary to claims made previously, after ingestion the Bt toxins are not rapidly degraded but can persist throughout the intestine in relatively large quantities (Chowdhury et al., 2003; Walsh et al. 2011). Consequently, there is sufficient time for the Bt toxins to interact with all kinds of compounds from the food plants to trigger or enhance immune responses.

**Figure 1: Overview of some problems in regard to the risk assessment of Bt toxins**

**Literature**

**Behn, T., Rover, C.M., Semenchuk, P.R. (2016)** Daphnia magna negatively affected by chronic exposure to purified Cry-toxins, Food and Chemical Toxicology, 91: 130-140.

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