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Lecture

Bt Crops - Controversies Around the Science Necessary for Risk Assessment

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Session

Risk Assessment

An Appraisal of Current Approaches

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Despite 15 years of industrial scale production of genetically modified (GM) crops at least in five countries, no consensus on the applied environmental risk assessment (ERA) methodologies, let alone agreed standardized testing procedures exist. But all regulations of GM organisms call for some risk assessment to be carried out. Hence, I will provide a review of the current implementation of risk assessment in relation to GM crops and identify the most severe shortcomings that we propose to alleviate with an alternative concept for ERA for GM plants.

The ERA currently focuses only on the novel trait expressed by the introduced transgenes and novel substances (e.g. Bt-toxins) produced in the GM plant. This current interpretation of the regulations of GM plants, including those laid down in the Cartagena Protocol, was made precedent by the US regulations (Mendelsohn et al. 2003) and is grounded in the concept of 'substantial equivalence' of GM plants and its non-transformed counterparts (FAO/WHO 1996; OECD 2000). Despite the fact that OECD consensus documents on compositional considerations have been published for various crops, no obligatory guidelines exist regarding what to test and how similar the values should be in order to still comply with being 'equivalent'. For example, the degree of acceptable difference between a non-transformed parent cultivar or any other cultivar of the same plant species and the GM event is not defined (Millstone et al. 1999). Often, substantial equivalence data do yield significant differences even outside of reported ranges for other (at times 'historic') cultivars but are then dismissed as 'biologically irrelevant'. The substantial equivalence (or familiarity) concept is therefore highly contested in particular with regard to its relevance for biosafety evaluations as it serves as the prime screen for unintended effects (Royal Society of Canada 2001; Freese and Schubert 2004). According to the developers of GM plants and some government regulators, the declaration of substantial equivalence legitimizes the omission of testing for anything but initial acute short-term effects of the isolated microbial toxin (Garcia-Alonso et al. 2006; Romeis et al. 2008).

An improved ERA concept for the assessment of potential adverse effects of GM plants has been proposed that is tailored to the GM case and the receiving environment and system-oriented with the GM plant at the center. The proposed testing strategy builds on the outcome of the 'GMO ERA Project' produced by an international group of scientists from the global working group 'Transgenic Organisms in IPM and Biocontrol' run under the auspices of the IOBC (International Organisation for Biological Control) (Hilbeck and Andow 2004, Hilbeck et al. 2006, Andow et al. 2008). It has been further developed and embedded into the EU provisions for ERA of GM plants (EC 2001 and 2002) in a project commissioned by the German Federal Agency for Nature Conservation (Hilbeck et al. 2008a). The concept focuses on sequential testing from laboratory to the field and is prescriptive with regard to a procedure developed for selection of testing organisms that do occur in the receiving environment and the proper protocols for testing them. It further includes potential adverse effects arising from direct and indirect exposure to the whole GM plant and from secondary stressors that are required to realize the benefit and intended effect(s) of the GM plant, such as the application of broad spectrum herbicides.

Hazard Identification

Information on the GM plant's biology, ecology and current spatio-temporal agronomic use and limitations of use is compiled. This includes comprehensive information on the molecular characterization of the GM plant, its introduced genetic material and tissue-specific expression of the

novel proteins. Information on the intended effect(s) include(s) data on the problem to be solved with the proposed GM plant, efficacy data of it demonstrating the ability to solve that problem, the severity of the problem, how widespread the problem is and who is mostly affected by it. To do that in an inclusive and transparent manner, scientists have developed a stakeholder process and tested it for the use in ERA of GM organisms (Hilbeck et al. 2004; Nelson & Banker 2007). Such a systematic process allows one to identify the main users of the GM plant, and to estimate the likely adoption rate and spread of the GMO after release. This in turn allows one to delineate the potential receiving environments and focus the analysis on those where the adoption is expected to be greatest with the assumption that potential adverse environmental effects will likely manifest where the GM crop is grown most frequently and is most widespread.

Selection of testing species

In current risk assessments, ecotoxicological testing that is carried out for Bt plants follows closely the methodologies developed for environmental chemicals like pesticides. Testing organisms are chosen from a list of universal standard species that are representative of trophic levels in general, rather than present in a given receiving environment (Andow and Hilbeck 2004). Our proposed methodology for testing of non-target organisms is prescriptive with regard to the use of a procedure for selection of testing species and the development of proper testing protocols and risk hypotheses tailored to each case and receiving environment.

Exposure Assessment – from pathways to scenarios and protocols

For the species ranked highest in the previous component, an exposure analysis is conducted to determine whether or not and to what degree the species come into contact with the primary stressor, i.e. the GM plant including the transgene product or the altered composition of primary metabolic compounds, or any secondary stressor required for realizing the transgenic function of the GM plant, e.g. the broad spectrum herbicide for herbicide tolerant GM plants. Because GM plants can multiply and spread via pollen and seed flow, this exercise will differ significantly from an exposure analysis of chemicals and will include also an analysis of the spread of GM plants into other ecosystems, including aquatic systems. Currently, there exists very little if any data on biogeochemical cycling, spread and fate of transgene products in the above- and below-ground ecosystems of the receiving environments and their potentially changing bioactivity and metabolites in the varying environmental media. Some studies published to date have confirmed the suspected spread of Bt toxins through food chains (Harwood et al. 2005; Zwahlen and Andow 2005; Obrist et al. 2006; Harwood et al. 2007). However, the bioactivity of such metabolites remains unknown to date. Several experiments studied the impact of Bt crop plant material on soil organisms with variable results ranging from some effects to transient effects to no effects (e.g. Zwahlen et al. 2003; Blackwood and Buyer 2004).

Effect Determination – doing the testing and generating the data

The main step here is the implementation of the testing plan developed before. However, again, controversy exists over whether the evidence for ‘reason for concern’ should be experimental or could be extrapolated from theory and experience in related fields of science (Zwahlen and Andow 2005; Andow et al. 2006; Garcia-Alonso et al. 2006; Lang et al. 2007; Romeis et al. 2008). Secondly, whether or not an absence of a ‘reason for concern’ (i.e. evidence) constitutes evidence for safety to the effect that no more testing at higher levels is re-

quired is subject to debate. As GM plants and their biochemical products can take on different properties in different environments and at different ecological organisational levels, data documenting/confirming the lack of evidence of adverse effects must be produced at every testing level.

Risk Characterization – synthesizing all information

In this component of the ERA framework, the risk is characterized by combining and comparing the obtained data and information. While the emphasis is placed on quantitative data, all gathered qualitative information is also integrated here. The outcome of activities in this component is a list of potential risks with an estimation of their strength (high, moderate or low) that were experimentally confirmed. Rejected potential adverse effect hypotheses that could experimentally be proven as unlikely or minor or non-existent are excluded. Equally important, the delimitation of the ERA and transparent documentation of remaining uncertainties is identified here. From this, guidance for possible risk management strategies and monitoring plans can be derived. With this proposal, we distinctly disagree with the proposal that ERA of GMOs could be entirely a desk exercise based on 'data collected for other purposes' and may not require the 'acquisition of new data' as put forward by developers (Raybould 2006; Raybould 2007). This leads to the current situation that new GM maize cultivars combining and stacking different Bt toxins by conventional crossing of various GM maize varieties enter the market largely untested. Bt maize event called 'Smartstax' (AGBIOS GM Database 2009) that combines 6 insecticidal Bt toxins and resistance genes for 2 broad-spectrum herbicides could enter the market with close to no testing for toxic or environmental impacts relying entirely on 'the environmental risk assessment of the individual events' – except for one additional study with an unspecified non-target organism, the results of which are not even summarized (EPA OPPTS 7501P). This in our view is not science-based, lacks the required precaution and entirely puts the discovery of any potential interaction, cumulative, indirect and long-term effect of the combined potpourri of 6 toxins and 2 herbicide residues on human and animal health and the environment in the marketing phase, i.e. the farmer and consumer.

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