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Testbiotech analysis of EFSA *Guidance* on the environmental risk assessment of genetically modified plants

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EFSA´s standards for environmental risk assessment not sufficient

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Table of Contents

Summary

EFSA *Guidance* on environmental risk assessment (ERA) is inadequate to assess the risks of genetically engineered plants. It is based upon *comparative assessment* – a concept that is far too narrow and biased. It does not define any cut off criteria even for plants that are persistent and might become invasive. It is not sufficiently clear on the risk assessment of stacked events and does not integrate all relevant levels of the food web. For example, wildlife vertebrates are completely omitted. Further deficiencies are listed in previous documents prepared by Testbiotech.

Introduction:

In its recent comment on the *Draft Guidance* document, Testbiotech (2010) proposed a list of ten points essential for the risk assessment of genetically engineered plants (link). These recommendations are based on a more detailed analysis (Then, 2010a) – and are as follows:

- generate a broad range of non biased data and drop the concept of substantial equivalence
- develop a coherent step by step procedure that includes a set of mandatory investigations before and during experimental field trials
- make it compulsory for applicants to reveal all existing studies and data
- include all levels of the food web, not rely on a tiered approach, make it compulsory for applicants to present data from different receiving environments
- take into account accumulated, combinatorial and delayed effects
- treat stacked events as new products that need independent assessment
- request feeding studies over the lifetime of certain animal species including the following generations
- develop an integrated approach for risk analysis including criteria for ethical, socio economic issues
- define some cut off criteria for the rejection of market applications such as invasiveness and persistence
- establish comprehensive monitoring

In the opinion of Testbiotech, EFSA *Guidance* on environmental risk assessment (EFSA 2010a) still mostly lacks these crucial elements and the ten points remain valid. Some changes were introduced into the final EFSA *Guidance* and therefore the following points are addressed in this background paper:

1. Substantial equivalence, familiarity and comparative assessment
2. Persistence and invasiveness
3. Stacked events
4. Food web and animal feeding studies

1. Substantial equivalence, familiarity and comparative assessment

In its previous draft, EFSA reverted to the concept of *substantial equivalence* as the underlying paradigm of risk assessment. In the final *Guidance* (EFSA 2010a), the term *substantial equivalence* is deleted from the text. *Comparative safety assessment* and the concept of *familiarity* are, nevertheless, still used to describe the very basic ERA concept (see Figure 1). The substance of the *Guidance* has not been changed. EFSA *Guidance* still relies on the concept of *substantial equivalence* as proposed by the OECD (1993). The terms *comparative assessment*, *familiarity* and *substantial equivalence* are simply used as synonyms for the same concept:

> *"The ERA of GM plants involves generating, collecting and assessing information on a GM plant in order to determine its potential adverse impact relative to its non-GM plant comparator, and thus assessing its comparative safety. The underlying assumption of the comparative assessment for GM plants is that the biology of traditionally cultivated plants from which the GM plants have been derived, and the appropriate comparators is well known. To this end the concept of familiarity was developed by the OECD (OECD, 1993)." (page 11).*

As a recent Testbiotech background paper shows (Then & Bauer-Panskus, 2010), the concept of *comparative assessment* as used by EFSA was substantially developed by industry and the International Life Sciences Institute (ILSI) between 2001 and 2003. During this period, Harry Kuiper and Gijes Kleter (both members of the EFSA *GMO Panel*) were active within the ILSI *Task Force* as experts and as authors of the relevant scientific publications. In 2004, the concept was adopted in the first GMO Panel (EFSA 2004) food and feed *Guidance document.*

The main problem with *comparative assessment* as proposed by EFSA is that genetically engineered plants are not seen as basically different from conventionally bred plants. Therefore, genetically engineered plants are not assessed as technical products inheriting specific risks and technical qualities – to the opposite they are assessed by comparing them with plants derived from conventional breeding. This has huge impact on the overall process of risk assessment. According to EFSA *Guidance*, *comparative assessment* will largely influence and substantially narrow the outcome of *hazard identification* and *hazard characterization comparative assessment* (see for example Figure 1 of EFSA´s *Guidance*).

As Testbiotech explained (Then & Bauer-Panskus, 2010; Then&Potthof, 2009), the comparison of genetically engineered plants and their conventional counterparts can be seen as an important tool, but should not be used as starting point or general concept of risk assessment. Instead of using *comparative assessment*, a broad range of non-biased and specific technical data should be generated by subjecting the genetically engineered plants to a range of standardized conditions. These data should, for example, cover genetic stability, interactivity between the genome and the environment, potential impact of climate change and also include reactions to specific abiotic and biotic stressors.

Metabolic profiling, measurement of gene activity and determining the content of decisive components (such as Bt toxins or metabolities from application of herbicides) are crucial elements when investigating the impact that defined environmental conditions have on genetically engineered plants, and for performing proper *hazard identification* at the beginning of risk assessment. In 2009, Testbiotech presented this overall concept as a "stress test" or "crash test" (Then & Potthof, 2009).

These more specific investigations are decisive for risk assessment because genetic engineering in plants is the only technology in the sector of plant breeding that does not rely on the plants´ own genome regulation, but on technically enforced gene activity, and in many cases also involves the insertion of additional genetic information from other species. EFSA *Guidance* fails to provide an adequate scientific concept on how to generate and how to assess the relevant data prerequisite for *hazard identification* and *hazard characterization*.

2. Persistence and invasiveness

EFSA *Guidance* (EFSA, 2010a) does not consider gene flow as such to be a problem. Even if plants are likely to persist in the environment and are able to exchange their genetic information with wild species, EFSA will not regard this as a risk per se (e.g. see decision-making tree, Figure 4 of EFSA *Guidance*).

This position of EFSA is not acceptable from the perspective of the precautionary principle. The long-term impact of gene flow in the fields and in the surrounding environment (as is the case with rape seed or poplar trees) can scarcely be assessed by existing scientific methods. For example, under current climate change, genetically engineered plants might show unintended effects that cannot be taken into account during risk assessment because they are triggered only by certain environmental conditions. There are several publications that show unintended effects in genetically engineered plants that cannot be predicted (see list of publications in Then, 2010). For example, higher fitness can emerge via hybridization with wild relatives as observed in rice (Lu&Yang, 2009). In this context, non-knowledge is a significant factor that must be taken into account in risk assessment.

Thus, unequivocal cut off criteria should not be designed to favour the authorization of genetically engineered plants that cannot be recalled from the fields and / or the environment. This approach also is necessary in regard to the general requirements of the EU regulation (Dir 2001/18), that foresees reevaluation of genetically engineered plants every ten years, and allows the withdrawal of products from the market if new risks or technical failures become apparent. Current EU regulations would be contradicted if genetically engineered plants could not be controlled in their distribution and persistence.

3. Stacked events

The wording of EFSA *Guidance* (EFSA 2010a) on the risk assessment of stacked events is not clear and in some ways ambiguous. For example, in the summary it says:

> *"Further, GM plants containing stacked events are considered with respect to specific areas of risk."*

The relevant chapters of EFSA *Guidance* contain a confusing mixture of criteria and measures that can be applied to stacked events. It leaves out any clarification that the risk assessment of stacked events cannot rely on the assessment of single traits. Undoubtedly, stacked events should undergo full risk assessment and be treated as new applications.

The general need for empirical investigation into the combinatorial effects of stacked events cannot be denied. Currently, six different and technically modified Bt-toxins are being combined in a single

plant (see http://www.testbiotech.org/en/node/423). In addition, these plants even incorporate gene constructs for conferring herbicide tolerance. It is not possible to deduce possible interactions within these plants from the properties of single traits.

4. Non target organisms and animal feeding studies

Testbiotech is concerned that the tiered approach described by EFSA, will be influenced by linked working groups whose members are from the EFSA GMO panel (e.g. Detlev Bartsch and Jeremy Sweet) and industry (see Romeis et al, 2008). In the EFSA document on non-target organisms (EFSA 2010b), there are even some passages plagiarized from Romeis et al (2008) (see table):

Romeis et al (2008) (including follwing authors: Jörg Romeis, Detlef Bartsch (EFSA), Franz Bigler, Marco P Candolfi (BASF), Marco M C Gielkens, Susan E Hartley, Richard L Hellmich, Joseph E Huesing (Monsanto), Paul C Jepson, Raymond Layton (DuPont), Hector Quemada, Alan Raybould (Syngenta), Robyn I Rose, Joachim Schiemann, Mark K Sears, Anthony M Shelton, Jeremy Sweet (EFSA), Zigfridas Vaituzis & Jeffrey D Wolt	EFSA (2010b) Scientific Opinion on the assessment of potential impacts of genetically modified plants on non-target organisms
More specific, crop-associated species may be selected that represent an important genus (e.g., Orius spp.), and other taxa may be selected that are broadly representative of whole families (e.g.,parasitic wasps of the Ichneumonidae) or orders (e.g., Coleoptera) that are known to be important.	More specific, crop-associated species may be selected that represent an important genus (e.g. Orius spp.), and other taxa may be selected that are broadly representative of whole families (e.g. Aphidius spp.) that are known to be important for ecosystem services.
Even the nontarget pest species that are screened for their sensitivity to the insecticidal protein during product development can serve as surrogates for NTAs.	The pest species that are screened for their sensitivity to the insecticidal protein during product development can also serve as surrogates for NTO's.
In addition, the risk assessment may consider species with special aesthetic or cultural value or species classified as threatened or endangered.	In addition, the problem formulation may consider species of anthropocentric significance, including those with special aesthetic or cultural value (e.g. the peacock butterfly, Inachis io) or species classified as threatened or endangered.

In general, combinatorial effects and additional stressors from the receiving environment will require empirical tests on all levels of the food web, regardless of whether effects are found on lower levels or not. This basic requirement is not incorporated in EFSA *Guidance*. By focussing on the tiered approach, the higher levels of the food web i.e. the vertebrate levels, are completely omitted. Two aspects are relevant for this food web level. Firstly, there are certain risks for wildlife such as birds that are not assessed under food and feed, and secondly, wild animals can contribute to the dissemination of viable seeds and plant material.

The conclusions from these observations are that risk assessment of non-target organisms should not be reduced to specific tiers. Investigations should be continued even if no risks are identified on the first tier. Furthermore, feeding studies to investigate health risks for wildlife vertebrates should be included.

At present, if *comparative assessment* does not reveal any significant findings, EFSA does not even require feeding studies with genetically engineered plants to investigate any health risks for humans or livestock. This kind of risk assessment concept is not acceptable and inadequate to provide necessary consumer and environmental protection.

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