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General Surveillance of Genetically Modified Organisms – the Importance of Expected and Unexpected Environmental Effects

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Abstract: GMO Monitoring was made mandatory in the European Union. The according regulatory practice, however, is still under development. Recently, the European Food Safety Authority completed a guidance document which attempts to specify the requirements for general surveillance, i. e. the monitoring aspects that go beyond case-specific issues. While case-specific monitoring (CSM) follows relevant or unclear effects of a particular trait, as identified during risk assessment, general surveillance (GS) covers entirely unforeseen effects or those that are cross-functional and difficult to predict (indirect, delayed, or combinatory).

Here, we outline an approach how to systemise monitoring issues, give examples for typical General Surveillance topics of oilseed rape and maize and then discuss the guidance how to set-up GS monitoring plans.

1. Introduction

Before a genetically modified organism (GMO) is admitted in the European Union for commercial use (notification), a thorough risk assessment is required. Due to the complexity and variability of environmental relations, it is not possible to predict all potential effects for all regions where a GMO might be exposed. Thus it remains uncertain whether the results of risk analysis obtained on a temporally and spatially limited basis, actually hold under conditions of commercial use on larger spatio-temporal scales.

GMO Monitoring therefore was made mandatory in the European Union (Directive 2001/18/EC). The according regulatory practice, however, is still under development. Recently, the European Food Safety Authority (EFSA) completed a guidance document which attempts to specify the requirements for general surveillance, i. e. the monitoring aspects that go beyond case-specific issues (EFSA 2005). While case-specific monitoring (CSM) follows relevant or unclear effects of a particular trait, as identified during risk assessment, general surveillance (GS) covers entirely unforeseen effects or those that are cross-functional and difficult to predict (indirect, delayed, or combinatory).

Here, we outline an approach how to systemise monitoring issues, give examples for typical General Surveillance topics of oilseed rape and maize and then discuss the guidance how to set-up GS monitoring plans.

2. What to monitor: A Hierarchical Systematisation of Potential Environmental Effects with a Focus on GM Maize and Oilseed Rape

Because of experimental limitations in spatial scale and temporal extent, not all relevant environmental effects can be tested during risk analysis. Though it is possible to identify potentially relevant starting points of cause-effect chains during risk analysis, it may not be possible to predict how these effects combine in different regional contexts or crop rotation pattern. Scaling, aggregation or combinatory effects make an important part of the GS context. Therefore it is useful to go through the levels of ecological organisation and identify aspects that require further observation (Züghart and Breckling, 2003):

- The molecular and organismic level
  e. g. stability and integrity of the transformant, identity of the commercialised product with the notified.
- The level of field cultivation and the farm-scale level
  e. g. implications of the intended use, changes in crop management, implications from other than the intended use – including abuse, combinatory effects.
- The population level
  e. g. population dynamics of the transgenic focal species in terms of farm-to-farm interactions by cross-pollination, joint use of machinery, etc.

- The ecosystem level
  e. g. local organisms-environment interactions, food chains, soil interactions, remineralisation (bio-element cycling), and farmland biodiversity including field margins and bordering ecosystems.
- The landscape- and regional level
  i. e. relations beyond the extent of a certain ecosystem type – e. g., biodiversity implications of organisms which use different habitats; changes in land cover and land use. Also general background information on climate and regional infrastructure, farm types and spatio-temporal variability in management pattern belong to this level, and where, in which (non-target) ecosystems any transgenic material occurs.

Any of the potential effects of a GMO can be assigned to one of these levels. Effects are frequently relevant to more than one level (cross-level causation).

A GS topic for herbicide tolerant **oilseed rape** (OSR, *Brassica napus*) results from the fact that transgenes may escape cultivation and survive for decades in other environments. Seeds can persist for long in the seed bank and OSR plants frequently occur as volunteers in other crops. Abundant feral populations are found in the countryside as well as in industrial terrains, along roadsides or in urban housing areas (Menzel, 2006), where also a variety of potential hybridisation partners grow. Some of them (OECD, 1997) are relevant weeds. It is not sufficiently predictable:

- whether and to where transgenes disperse,
- whether weedy transgenic populations occur and interfere with herbicide use, colonise new habitats where transgenes convey a selective advantage (e. g., along herbicide treated rail tracks),
- whether and where stacking of transgenes may convey multiple resistance.

The causal interactions to enable such a potential are known from isolated processes, however, the self-amplification probabilities of certain genotypes in different environments are not predictable. The involved combinatory effects are topics for GS. Tracing each event in separation (as in CSM) would unnecessarily multiply the effort.

Central issues for the monitoring of **insect resistant maize** (*Zea mays*) are biodiversity effects (Züghart and Breckling, 2003). Target- as well as non-target-organisms are exposed to the toxin. Development of resistance is possible. Only selected species can be tested for sensitivity. Largely, this is done under controlled laboratory conditions (Hilbeck et al., 1999). It is not possible to analyse all food chains. Changes in crop management may have beneficial as well as harmful effects. How food chains and neighbouring ecosystems are affected is difficult to predict. In southern Europe, feral and volunteer growth of maize occurs. There are biodiversity impacts expected due to the altered use of insecticides which in case of a combination with herbicide tolerance may have further effects on the landscape and regional level. Biodiversity monitoring is a typical aspect of GS.

In both cases, for oilseed rape as for maize, there are environmental effects identified in experimental research. The impact on environmental dynamics at regional scale is not fully predictable. *Anticipated and unanticipated effects are not completely and consistently separable.*

3. The General Surveillance approach of EFSA

The European Food Safety Authority has a prominent role in providing guidance in the GMO notification process. In a new chapter of the Guidance Document for General Surveillance, EFSA (2005) provides a specific interpretation.

- EFSA (2005) focuses GS on unanticipated adverse effects: "The objective of General Surveillance is to identify the occurrence of unanticipated adverse effects ... Monitoring of potential adverse cumulative long-term effects and areas of uncertainty identified in the environmental risk assessment ... should be considered initially within Case-Specific Monitoring." (p. 2)
- EFSA (2005) suggests to execute GS without underlying hypotheses: "... General Surveillance is a general overseeing of the geographical regions where GM plants are grown without having any specific hypothesis on adverse effects on human health or the environment. As General Surveillance is not hypothesis-driven, it is not conducted using directed experimental approaches ... However, robust scientific methodology should be applied wherever possible in order to ... produce statistically valid data for determining causes and effects." (p. 3, 4)[1]. ... "Additionally, when several GM plants have been commercialised, the interactions between these GM plants and their management may need to be considered where appropriate." (p. 4)[2].
- EFSA emphasises that "The establishment, persistence and spread of a GM plant is not an environmental hazard in itself. Similarly, dispersal of pollen and seeds and gene flow *per se* are not environmental hazards and thus the focus of General Surveillance should be on recording any unanticipated consequences of the cultivation of the GM plant, such as unforeseen weediness, invasiveness or changes in plant population dynamics or populations of biota associated with the GM plants." (p. 4)[3]

4. ACRE about General Surveillance

ACRE is an advisory body under the UK Department for Environment, Food and Rural Affairs (DEFRA). In its Guidance Note 16, ACRE describes "Best Practice in the Design of Post-market monitoring Plans".

The document distinguishes 3 categories of effects to be monitored: **I: anticipated effects** which fall mainly but not exclusively under CSM, **II: Interactive or cumulative effects**

[1] It is problematic how to apply robust science in this context, as the specification of hypotheses is inherent to the scientific method.
[2] This would not be possible without the implicit hypothesis of interaction to exist.
[3] The question arises how this should be possible without investigating the hypothesis that weediness etc. might occur. In addition, it is useful to state that transgenes outside the intended area of use provide a potential indicator for unintended self-organising environmental effects.

that are difficult or impossible to predict. [These are "e. g. effects that might arise as a result of an increase in the scale of cultivation and potential effects arising as a result of interactions between the GM crop and future varieties." (ACRE p. 7)] and **III: Unanticipated effects** ["i. e. potential effects not identified in the ERA (environmental risk assessment), which can only be addressed by general surveillance." (p. 7)].

For category II effects, ACRE states, that "Even though the potential outcome of interactions between releases of GM crops may not be assessed fully within one individual dossier, it remains possible to predict that interactions between GM crops may occur and also what characteristics might reasonably be expected to be affected if they do." (p. 7)

This qualifies category II effects for GS: GS "is pertinent for longer-term observation and detection of unexpected developments. Some of these developments will be in *category II*, i. e. associated with cumulative effects and interactions between crop varieties." (p. 9)

ACRE explicitly states one form of hypotheses relevant for GS: "General surveillance may be null hypothesis driven, i. e. testing the prediction that there is no change compared with conventional agriculture." (p. 9)

While EFSA and ACRE agree in the relevance of statistical data analysis, ACRE adds time management and quality implications: "Accurate, well written and timely reporting is central to the principles of PMM (post market monitoring). This is particularly important in view of the need to ensure that any further investigation that is needed can be planned, agreed and implemented in a timely fashion. ... Results should be given in a way that is clearly explained including the power and appropriateness of the data to answer the hypotheses." (p. 10)

5. Discussion: Monitoring Unexpected Effects without Underlying Hypotheses is Epistemologically Impossible

Hypotheses are central in scientific investigation. They define what is looked for. Hypotheses predict alternative results of experiments. Hypotheses have the same role in environmental observation. They specify the (range of) targets. Entirely untargeted observation is impossible, i. e. an antinomy in an epistemological sense. In this respect, the questionnaire approach EFSA (2005) suggests as a hypotheses-free investigation instrument tests a set of dedicated hypotheses: e. g. the one that there are no relevant changes that a scientifically untrained and unequipped person being involved in agriculture would attribute to the cultivation of GMO.

A similar situation exists concerning expected and unexpected effects. Both may be linked, as expected effects may have implications that escaped attention. Once identified, an unexpected effect will be known and thus anticipated in the next season. If anything expected is ruled out, nothing is left and monitoring becomes an empty set. The Directive 2001/28 EC clearly specifies that: "The objective of a monitoring plan is to: (i) confirm that any assumption regarding the occurrence and impact of potential adverse effects of the GMO or its use in the e. r. a. are correct, and (ii) identify the occurrence of adverse effects of the GMO or its use on human health or the environment which were not anticipated in the e. r. a. (= environmental risk assessment) (Annex VII of Directive 2001/28 EC)."

Handling hypotheses and unexpected effects, the EFSA Guidance remains less operational than previous approaches like ACRE or Züghart and Breckling (2003). We are convinced that a hypothesis-guided framework is necessary to achieve the legal requirements of the Directive 2001/18 EC.

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