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The AHTEG Guidance on Risk Assessment of LMOs

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Under the mandate of Decisions BS-IV/11 and BS-V/12, the Executive Secretary established the Ad Hoc Technical Expert Group on Risk Assessment and Risk Management (AHTEG) to develop further guidance on specific aspects of risk assessment and risk management.

The outcome is the AHTEG 'Guidance on Risk Assessment of Living Modified Organisms', which comprises three parts. Part I is the 'Roadmap' for risk assessment of living modified organisms (LMOs). Part II is a series of reports on conducting risk assessments on specific kinds of LMOs or traits. Part III is guidance on monitoring LMOs released into the environment.

Development of the Guidance

The Roadmap, and its graphic depiction as a flowchart (see Figure 1), as well as guidance on LM mosquitoes, abiotic stress tolerant LMOs, and LMOs with stacked genes, were first developed for and presented at the fifth Conference of the Parties serving as the Meeting of the Parties (COP-MOP5), in Nagoya, Japan in 2010. Since Nagoya, the AHTEG has worked to update the existing Guidance (after extensive testing and scientific review) and to introduce new specific guidance documents into the package.

Post-Nagoya revision of the exisiting Guidance

Part I – The Roadmap

The Roadmap was seen as the best way of presenting the phases and steps to be considered in a risk assessment. Importantly, the Roadmap shows how the conduct of the risk assessment relates to other stages in the entire risk appraisal process (including a pre-risk assessment scoping process and post-risk assessment evaluation of its outcomes), that leads to decision-making. Further, the Roadmap can be a navigational tool for training purposes.

The utility and legitimacy of any risk assessment is dependent on the degree to which the components are integrated and informed by the social, cultural, and policy context in which they apply. The risk assessment process, as any scientific process, is reliant on a number of implicit and explicit values and assumptions that set biases, criteria and standards within the risk assessement. The Roadmap formalizes the assessment framework as integrative, iterative and comparative, as well as sets realistic

and appropriate standards for scientific information.

The Roadmap provides guidance on conducting risk assessments that are for different potential receiving environments and societies, but based on consistent standards.

The Roadmap can provide the risk assessor with a sense of security as to what information they may legitimately ask for and, just as importantly, how to evaluate that information and integrate it into a package that is accessible to the decision-maker. This will lead to greater certitude in the expectations from both society and industry of what the regulator will require, leading to fewer conflicts and, ultimately, more efficient risk appraisal processes as well as will facilitate trade.

Part II – Specific guidance

Part II of the Guidance consists of advice on how to conduct risk assessments on particular kinds of LMOs because Parties requested additional direction on the risk issues special to their biology or in response to particular regulatory needs. The guidance on LM mosquitoes, stacked gene LMOs and abiotic stress-tolerant LMOs was updated after extensive testing since COP-MOP5.

New Developments to Part II

New in Part II is the addition of useful guidance on risk assessment of LM trees.

While there is debate on the biological definition of trees, what was considered relevant to the guidance were all organisms that shared the same spectrum of risk, containment or risk mitigation issues. The size and longevity of some trees may limit the power of glasshouse trials, contributing to greater uncertainty in the risk assessment. For this reason, additional controls and experiments may have to be conducted prior to field-testing.

The LM tree guidance considers risks based on:

- the way trees can be propagated (e.g., sexually, asexually, grafting);
- their potentially long lifetimes and sometimes great sizes (which can create many different kinds of exposure possibilities over time and bridge deep soil systems to many metres above the ground);
- how they disperse and how these mechanisms might be affected by climate changes (given their sometimes long lives);
- and management practices that could vary over the potentially long lives of trees, or between kinds of trees or by receiving environment and intent of the modification.

Introducing Part III of the Guidance - Monitoring

The AHTEG developed guidance on monitoring LMOs released into the environment because it was viewed as important for risk assessment and risk management because no specific guidance is available from the Protocol, or internationally.

LMO monitoring is the systematic approach for observing, collecting and analysing data on the potential adverse effects of an LMO, based on a risk assessment and after an LMO is released.[1]

Annex III recognizes monitoring of the LMO, among other things, as appropriate "where there is uncertainty regarding the level of risk". The source of this uncertainty could be, for example, unanticipated effects on human health, key ecological functions, interactions with future LMOs, changes in management of the LMO, or uncertainty as to whether the conclusions of safety that may have supported a decision for environmental release are indeed correct.

Step-by-step

Monitoring is applied to inform and complement step-by-step approaches to risk assessment. For example, applying monitoring at field testing stage or in a time-limited release approval can help to inform the risk assessment conducted for larger scale or longer term releases.

The new guidance on monitoring provides a sound conceptual basis that can help in the development of risk assessments that meet the objectives set out in Annex III of the Protocol. All monitoring plans are based on explicit or implicit hypotheses about rates of change in indicators or assessment endpoints. Likewise, they imbed assumptions about where in the environment monitoring will be most effective. Guidance developed under the AHTEG provides a robust, comprehensive approach to develop a monitoring plan focusing on "what to monitor", "how to monitor" "where to monitor", "how long to monitor", and "how to communicate" the results of monitoring, with the two types of monitoring

1 See Heinemann, J.A. and El-Kawy, O.A. Observational science in the environmental risk assessment and management of GMOs. Environment International 45 (2012) 68–71.

discussed below.

The monitoring guidance developed by the AHTEG breaks down the different applications of monitoring into two types of activities:

1. Case-specific monitoring (CSM), to address uncertainties identified in the risk assessment; and
2. General monitoring, to address uncertainties that were not identified in the risk assessment including long-term effects.

In the event that changes are observed during either type of monitoring activity, causality can be tested through the construction of more specific hypotheses.

Each of these types of monitoring has special roles and strengths.

- *Case-specific monitoring (CSM)*

CSM applies well at the field-testing stage, when much of the safety and performance testing is being conducted, and at larger scales with the intended use of the LMO. However, there is limited experience with the effectiveness or flaws of this approach, and no coordinated evaluation of existing plans are internationally available, largely because the countries that have undertaken the largest scale release of LMOs do not have validated or uniformly applied post-release monitoring programmes. Thus, there is little meaningful data to relate current experience with CSM to its efficacy to ensuring safety.

Causation-driven

CSM is often referred to as 'hypothesis-driven', but a better description might be that it is causation-driven. Proper case-specific hypotheses rigidly link an adverse effect to the LMO and determine if the LMO was the cause.

An example of a CSM hypothesis would be: Use of the herbicide tolerant (HT) rapeseed will cause an increase in HT volunteers in wheat fields. A monitoring plan might be imposed to determine if/when such resistant volunteers varieties could be detected in wheat fields.

CSM might also be part of a risk management strategy. Again using the HT rapeseed example, if a threshold detection limit were exceeded, farmers might be encouraged to use an alternative herbicide or switch away from no-till practices, or seed suppliers might be made contractually obligated to remove the volunteers. Further, monitoring for resistant volunteers could be enacted to test the efficacy of any weed resistance management strategies put in place along with the release of the LMO.

- *General monitoring*

General monitoring strategies apply well at larger scales but can also be applied at the field-testing stage. A form of general monitoring, called general surveillance, is already required in European Union (EU) member states. However, experience here is limited because there are few large-scale releases of LMOs in the EU. Nevertheless, evaluations of general surveillance plans is ongoing by the European Food Safety Authority, yet largely focus on farmer questionnaires, rather than actual field-collected data for its analysis. Independent scientists and their critical appraisals are however helping to build a knowledge base for effective implementation of general monitoring strategies.

Hypothesis-driven

General monitoring addresses broader questions on changes, and is also a hypothesis-driven and scientific approach. It is applied when regulators cannot be confident that all uncertainties were identified in a risk assessment. The strategies used to achieve a robust general monitoring plan are also useful to supplement CSM, especially when the adverse effect may be significant but of low probability or develops in the long-term.

Box 1: What are protection goals and assessment endpoints?

A protection goal is anything that you are concerned about. Preferably, these goals will have also been formally set in government policy or legislation. A protection goal could be, for example, human health in general or the conservation of a particular insect species endemic to the potential receiving environment.

An assessment endpoint is how effects on the protection goal will be measured or perceived. For example, if the protection goal is an endemic insect species, members of that species may be used as indicators and the assessment endpoint might be changes in indicator numbers, or qualitative changes in foraging behavior.

General monitoring is based on observation of indicators or assessment endpoints (Box 1). Changes in these indicators or parameters which indicate an adverse effect are used, when appropriate, to construct causation-driven hypotheses for testing of links to LMOs.

General hypotheses inform the choice of indicators and assessment endpoints and delineate the time period and geographical area under observation. Indicators and assessment endpoints may be defined by national protection goals and the conservation and sustainable use of biodiversity, taking into account human health.

As the underlying hypotheses are based on protection goals and are measured through assessment endpoints, it is essential that protection goals and endpoints be carefully and comprehensively identified. Failure at this stage may prevent achieving an effective detection limit. The Guidance advises on the choice of indicators and what parameters to use for measurement.

Oftentimes, existing monitoring or surveillance systems may be used to provide observations for a general monitoring plan. New diseases surveillance is an example of general monitoring that is relevant to Annex III of the Protocol but developed for broader purposes.1 The Guidance advises on what characteristics of existing or imposed monitoring plans are suited to addressing remaining uncertainties.

The success of a monitoring plan depends on its reference to an 'undisturbed' or baseline state. That is, some knowledge of the indicators and assessment endpoints must pre-exist release of the LMO. The Guidance advises that baseline data be collected, and how to appropriately collect these data.

Lastly, monitoring can only be effective if the results are properly communicated, for example to those that might benefit from the results during other risk assessment exercises, decision-makers or those who might be experiencing an adverse effect. In order to provide quality assurance and constructive feedback, the Guidance advises on how the monitoring plan and results can be communicated for independent evaluation and any potential follow up action, including changes to the monitoring plan, or to the decision on release.

Conclusions

The Guidance on Risk Assessment of Living Modified Organisms developed since 2009 includes the extensively 'road tested' and revised Roadmap along with the tested and revised guidance on LM abiotic stress-tolerant plants, stacked plants and LM mosquitoes. These documents were welcomed by Parties to the Protocol at COP-MOP5 and have benefited from numerous rounds of feedback and peer review. Incorporating the feedback from the first generation of documents, the AHTEG then developed new guidance on LM trees and monitoring, themselves subject to several rounds of review. Together, this package constitutes guidance in three parts that is very useful for the Parties to the Cartagena Protocol in implementing their risk assessment and risk management obligations under the Protocol and national legislation.

The package of guidance documents is both credible and consensus-building. Developed by a group of experts from industry, academia, government and civil society, it has achieved an effective compromise that adequately promotes safety without unduly burdening industry or inhibiting research, while bringing clarity and transparency to regulation.

The AHTEG has thus more than adeptly fulfilled the Parties' request for it to develop further guidance on risk assessment and risk management. It has also proved its utility in being able to respond to Parties' needs in addressing specific topics of risk assessment and risk management.

Therefore, at COP-MOP6, Parties should decide to:

- Endorse the Guidance on Risk Assessment of Living Modified Organisms, and ensure its wide accessibility, dissemination and usage.
- Integrate the Guidance into capacity-building activities on risk assessment, including into the training manual on risk assessment that has been developed by the Secretariat and used in training courses on risk assessment.
- Integrate the Guidance within the draft Results-Oriented Capacity-Building Action Plan (2012-2020), in its Focal Area 2 on Risk Assessment and Risk Management.
- Extend the mandate of the AHTEG, with the objective of developing guidance on new topics of risk assessment and risk management, including in relation to unintentional transboundary movement of LMOs.