COMMISSIE
COGEM
GENETISCHE
MODIFICATIE

BEZOEKADRES:
A. VAN LEEUWENHOEKLAAN 9
3721 MA BILTHOVEN

POSTADRES:
POSTBUS 578
3720 AN BILTHOVEN

TEL.: 030 274 2777
FAX: 030 274 4476
INFO@COGEM.NET
WWW.COGEM.NET

Aan de staatssecretaris van
Infrastructuur en Milieu
Dhr. J.J. Atsma
Postbus 30945
2500 GX Den Haag

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KENMERK CGM/110311-03
ONDERWERP Advies m.b.t de ‘guidance on risk assessment of living modified organisms’ van de ‘Convention on Biodiversity’

Geachte heer Atsma,

Naar aanleiding van uw verzoek om een wetenschappelijke beoordeling van het conceptrichtsnoer die in het kader van het ‘Cartagena Protocol’ is opgesteld, stuurt de COGEM u de volgende reactie.

Samenvatting
In het kader van het ‘Cartagena Protocol’ heeft een zogenaamde technische werkgroep een conceptrichtsnoer opgesteld dat bestaat uit twee delen: de zogenaamde ‘roadmap’ en drie specifiekere richtsnoeren over gestapelde genen, abiotische stresstolerantie en genetisch gemodificeerde muggen. In het richtsnoer is het risicobeoordelingsproces van zogenaamde ‘living modified organisms’ beschreven en zijn de stappen die hierbij worden doorlopen uitgewerkt. Het richtsnoer is geschreven als naslagwerk voor risicobeoordelaars en daarnaast bedoeld om te gebruiken bij scholing in risicobeoordeling en risicomanagement (capacity building).
Het richtsnoer beschrijft in algemene termen hoe het proces van risicobeoordeling van zogenaamde ‘living modified organisms’ verloopt en volgt hierbij de algemeen geaccepteerde methodologie. De ‘roadmap’ zou geschikt moeten zijn voor de risicobeoordeling van alle ‘living modified organisms’. De COGEM is van mening dat dit niet het geval is. De gekozen bewoordingen zijn vaak specifiek voor gewassen en bepaalde aspecten die bij de risicobeoordeling van andere organismen van belang zijn, komen in de ‘roadmap’ onvoldoende aan bod. De COGEM stelt voor om specifiekere richtsnoeren te ontwikkelen voor groepen van organismen (vissen, insecten, virussen en bacteriën).
De COGEM is verder van mening dat het proces van de risicobeoordeling inzichtelijker zou worden wanneer het richtsnoer aangevuld zou worden met verhelderende voorbeelden. De toepasbaarheid van het richtsnoer zou verder vergroot worden wanneer in het richtsnoer ook verhelderd zou worden wanneer informatie noodzakelijk is bij de risicobeoordeling van een bepaalde ‘living modified organism’ en wanneer informatie voor de risicobeoordeling van dit organisme niet aanwezig hoeft te zijn.

De door de COGEM gehanteerde overwegingen en het hieruit voortvloeiende advies treft u hierbij aan als bijlage.

Hoogachtend,

Prof. dr. ir. Bastiaan C.J. Zoeteman
Voorzitter COGEM

c.c. Dr. I. van der Leij
Drs. H.P. de Wijs

Comments on the draft 'guidance on risk assessment of living modified organisms' from the Convention on Biodiversity

COGEM advice CGM/110311-03

1. Introduction

An Ad Hoc Technical Expert Group (AHTEG) on risk assessment and risk management under the 'Cartagena Protocol', recently published a draft guidance document entitled "guidance on the risk assessment of living modified organisms (LMOs). The purpose of this document is to facilitate and enhance the use of the part of the 'Cartagena Protocol' that describes the LMO risk assessment methodology (Annex III) by elaborating the technical and scientific process of how to apply the steps and points to consider in the process of risk assessment. The guidance document is being developed to be used as a reference for risk assessors when conducting or reviewing risk assessments and for use in risk assessment and risk management training programs (capacity-building activities).

According to the Cartagena Protocol on Biosafety the risk assessment of an LMO is required in all cases of deliberate release (field trials as well as commercial applications). In the 'Cartagena Protocol' an LMO is defined as 'any living organism that possesses a novel combination of genetic material obtained through the use of modern biotechnology'. The term 'living organism' refers to any biological entity capable of transferring or replicating genetic material, including sterile organisms, viruses and viroids.

The published guidance consists of two parts. Part I of the guidance is the 'roadmap for risk assessment of LMOs. The roadmap provides an overview of the process of environmental risk assessment of an LMO. It applies to all types of LMOs (and products thereof) and their intended uses. The roadmap has, however, been developed on the basis of experiences with the risk assessment of living modified crop plants. Part II of the guidance focuses on 'specific types of LMOs and traits' and contains three more specific guidance documents. The topics of the specific guidance documents are 'LMOs with stacked genes or traits', 'living modified crops with tolerance to abiotic stress' and on 'living modified mosquitoes'.

The Parties of the Convention on Biodiversity noted that the guidance requires further scientific review and testing to establish its overall utility and applicability to living modified organisms of different taxa introduced into various environments. Therefore, a review process of the first version of the AHTEG guidance document was started. COGEM was asked by the Dutch ministry of Infrastructure and Environment for a scientific review of the guidance and the concepts mentioned therein. Due to the limited time available for this review COGEM focussed on major criticisms.

Comments on the roadmap

More guidance needed with regard to the aspects that are crucial when determining the scope of the risk assessment

COGEM is of the opinion that the roadmap is a well-considered document. The roadmap starts with an introduction on the risk assessment process and describes the overarching issues that should be considered in the design/planning phase of the risk assessment process to ensure the quality and relevancy of the information used. According to the roadmap one of the questions that should be answered in the planning phase is which data are considered relevant for the risk assessment (page 3). The roadmap also states that the data should be of an acceptable scientific quality (page 4). There is, however, no further guidance present on these issues and examples of relevant or irrelevant data or of scientifically acceptable or unacceptable data are not given. In addition, a number of aspects are listed that should be taken into consideration when setting the context and scope for a risk assessment. These aspects are, amongst others, protection goals, assessment end-points, risk thresholds, management strategies and methodological and analytical requirements (page 5). According to the guidance document the protection goals are chosen by the Party (page 1). COGEM points out that the competent authority should also determine the assessment endpoints and risk thresholds. COGEM notes that there is no guidance available on the process of identification of protection goals, assessment endpoints and risk thresholds or on the identification of methodological and analytical requirements. The above-mentioned aspects play a crucial role in the risk assessment process and therefore guidance on the determination of these aspects should be incorporated in the document.

Road map gives general description but lacks examples

The described risk assessment process follows the generally accepted risk assessment methodology consisting of five steps. For each step a rationale and points are listed that should be considered. The description of the risk assessment process is general and does not give indications on the aspects that are considered important for specific LMOs. The risk assessment process is only limitedly explained. The risk assessment approach would be clarified by the inclusion of more detailed explanation and examples that demonstrate the use of the guidance in practice. More detailed explanation and examples could be given in an annex to the guidance document or in an accompanying document that is clearly identifiable as an example of the risk assessment approach.

Roadmap not applicable to all types of LMOs

The roadmap is meant to provide guidance on the risk assessment process for all types of LMOs (page 1). In the roadmap the generally accepted risk assessment methodology is followed, but the roadmap focuses on living modified (LM) crops. This is reflected in the terminology used and in the aspects that are included in the roadmap. As the terminology in the roadmap is not appropriate for all types of LMOs and because not all aspects are included that are relevant for the risk assessment of other types of LMOs, the use of this roadmap for other types of LMOs, such as viruses and bacteria, is limited.

For instance, the aspects that are relevant for determining the risk of living modified micro-organisms such as the host organism of the wild type micro-organism or the occurrence of shedding (excretion of living modified micro-organisms) are not mentioned at all. COGEM

suggests to develop more guidance documents for different types of living modified organisms (fish, insects, viruses, bacteria).

In addition, it is stated that the roadmap applies to all types of LMOs and products thereof (footnote 4 page 1). This suggests that the roadmap also applies to products that no longer contain living modified organisms. COGEM is aware that in the roadmap the terminology of the 'Cartagena Protocol' is used and that the roadmap only applies to products with living modified organisms. However, as the roadmap is developed to be used in capacity building activities COGEM is of the opinion that it should be clarified that the roadmap only applies to those products that still contain living modified organisms.

Inclusion of non-scientific scenarios in the risk assessment process is possible

The concepts in the roadmap are recognisable and are often used in the process of risk assessment. The wording in the roadmap is however not unequivocal and leaves room for interpretation. For instance, the heading of step 1 is "an identification of any novel genotypic and phenotypic characteristics associated with the LMO, that may have adverse effects on biological diversity in the likely potential receiving environment, taking also into account risks to human health" (page 6). 'May have adverse effects' can be interpreted broadly. In addition, although it is mentioned that scientifically plausible scenarios should be identified in step 1 (page 6), it is not clear who determines whether scenarios are scientifically plausible or when they should be considered scientifically plausible. Therefore, the inclusion of scenarios that are not scientifically plausible in the risk assessment process remains possible. The inclusion of criteria that could be used to assess the scientific plausibility of a scenario would reduce the likelihood that other scenarios are accidentally included in the risk assessment process.

More guidance on the necessity of information

When identifying the characteristics of the LMO that may have an adverse effect (step 1 of the risk assessment) one of the points that should be considered is the molecular characteristics that are related to the modification. Several molecular aspects are listed that may be important for the molecular characterization of the LMO e.g. stability within the genome and the expression level (page 7). Although it is mentioned that the relevance of the aspects may vary according to the type of application, it is not mentioned when this information is considered relevant. Throughout the document more attention should be paid to the intended use of an LMO (for instance cultivation vs. import and processing). In general, more guidance should be given in the text on those cases where information is necessary for the risk assessment and on the cases where this information is not needed. The assessment of potential adverse effects on non-target organisms is for instance less relevant when an LM crop is not cultivated.

Different definitions of transgene in the document

COGEM points out that the definition of a transgene is not consistent throughout the document. On page 3 a transgene is defined as "a nucleic acid sequence *in an LMO* that results from the application of modern biotechnology" (footnote 11). According to page 15 a transgene is "a nucleic acid sequence that results from the application of modern biotechnology" (footnote 23). COGEM is of the opinion that the same definition should be used throughout the document.

Determination of sub-lethal effects important when assessing adverse effects on non-target organisms

According to the roadmap one of the points that should be considered when evaluating the magnitude of potential consequences of an adverse effect (step 3) is the result from laboratory experiments. One of the examples that is mentioned is the dose-response relationship (EC50, LD50) (page 10). EC50 or LD50 values are used to establish the toxicity of a substance and reflect the concentration that produces a response in 50% of the test population (EC50) or the dose that is lethal to 50% of the test population (LD50). Studies that determine LD50 are often present to assess the effect of an insect resistant LM crop on non-target organisms. COGEM is of the opinion that the effect of an LM crop on non-target organisms should only be assessed if there is an indication that expression of the transgene could adversely affect non-target organisms. COGEM points out that sub-lethal effects can have a large influence on populations of non-target organisms. Therefore, COGEM is of the opinion that the assessment of sub-lethal effects on non-target organisms should be part of the assessment of the effect of an LM crop on non-target organisms. Both lethal and sub-lethal effects are reflected in measurements of population growth. Therefore, COGEM considers data on the population growth of non-target organisms of fundamental importance for the assessment of the effect of an LM crop on non-target organism. COGEM is of the opinion that the assessment of sub-lethal effects should be included in the guidance document.

Monitoring important when dealing with uncertainty

In step 4 the level of overall risk of an LMO is determined and characterized. In the guidance it is mentioned that when there is uncertainty regarding the level of risk, this uncertainty may be addressed by requesting further information, by implementing appropriate risk management strategies and/or monitoring the LMO in the receiving environment (page 10). COGEM is of the opinion that monitoring is a helpful tool to detect unexpected adverse effects of an LMO and stresses the importance of monitoring in dealing with uncertainty. In COGEMs view monitoring should receive more attention in the guidance document.

More guidance on the assessment of cumulative effects caused by multiple single events

According to the guidance document one of the points to consider when determining the overall risk posed by the LMO is any cumulative effect due to the presence of multiple LMOs in the receiving environment (page 11). The assessment of cumulative effects is mentioned in the guidance of stacked events, but there is no guidance available on the assessment of cumulative effects for unintended stacked events. In addition, in the roadmap no guidance is given on the assessment of cumulative effects caused by multiple single events. COGEM is of the opinion that the guidance should elaborate on this topic. In practice, cumulative effects caused by multiple single events can probably only be detected through monitoring.

(Ir)reversibility of effect should be part of the consideration

The individual risks are determined on the basis of the identified potential adverse effects and their likelihood and consequences (page 10). Subsequently, the risk of an LMO is greater if the possible adverse effect of an LMO is irreversible. An effect that could be irreversible is for instance the transfer of a transgene to wild relatives by outcrossing. COGEM is of the

opinion that it is important to consider whether an effect is reversible. Therefore this aspect should be mentioned in the guidance.

Conclusion on acceptability of a risk should not be made by applicants
According to step 5 of the roadmap the risk assessor should recommend whether or not the risks are acceptable or manageable (page 11). COGEM points out that in step 5 some aspects are mentioned that are not related to risk assessment but which are part of the decision-making process. It is important to note that the acceptability of a risk is a decision of the competent authorities and should not be determined by other risk assessors, e.g. by an applicant. Information on the possible benefits of an LMO could be important when evaluating the acceptability of a risk. This aspect could be mentioned in the roadmap.

Risk management measures part of step 5 of the risk assessment process, but outside scope of roadmap
The roadmap lists some issues that are related to risk assessment and the decision making process but which are considered to be outside the scope of the roadmap (e.g. co-existence, risk management, public awareness) (page 12). One of the listed issues is 'risk management' which is confusing since a major part of the considerations in step 5 of the risk assessment process refers to risk management measures.

Figure 1 should mention that objectives and criteria should be set at the beginning of the risk assessment
In figure 1 the roadmap is depicted (page 13). In this figure it is mentioned that after step 5 one should evaluate whether the objectives and criteria that were set at the beginning of the risk assessment are met. The determination of objectives and criteria are not included in the figure. These aspects should be added to the figure.

Comments on the risk assessment of LMOs with stacked genes or traits

Overall effect of an LMO is important, whether the effect is the result from interactions between proteins is of less importance
The guidance in this part focuses on those aspects that should receive special attention when assessing the risk of LM plants with stacked genes or traits. The potential interactions between the combined events and the combinatorial and cumulative effects of the stacked event should be assessed. The process of risk assessment that is described seems to be straightforward. It is however important to realize that the assessment of potential interactions and effects from stacked events could be very complex. COGEM points out that for the final conclusion on the eventual risks of an LMO the overall effect of an LMO is important. The underlying mechanism of an adverse effect or whether an adverse effect is the result from interactions between proteins is of less importance.

Adverse effects of management procedures that are not a direct effect of the LM crop should not be included in the risk assessment
In the document it is stated that indirect effects due to changed agricultural management procedures should be taken into consideration (page 16). It is not clear to what extent this should be done. 'Agricultural management procedures' could refer to many different aspects.

COGEM is of the opinion that adverse effects originating from agricultural management procedures that are not a direct effect of the LM crop should not be part of the risk assessment.

Comments on the risk assessment of LM crops with tolerance to abiotic stress

More explanation necessary with regard to the possible adjustments of the characterization of the LM crop

The guidance on the risk assessment of living modified crops with abiotic stress tolerance mentions that the characterization of the LM crop (step 1) could be a challenge (page 19). It is mentioned that when the non-modified crop has never been grown in the receiving environment because its growth is prevented by the abiotic stress conditions the comparative approach will need to be adjusted. How the approach should be adjusted is not mentioned. In COGEMs view this aspect should receive more attention. In the guidance document it should be explained how the comparative approach should be adjusted. The characterization of the LM crop will be based on a theoretical consideration rather than on a real-life comparative approach.

Comments on the risk assessment of LM mosquitoes

Effect of the introduced trait on the biology of the LM mosquito should be considered

The guidance on the risk assessment of living modified (LM) mosquitoes mentions several aspects that should be taken into account in the risk assessment, e.g. the species of mosquito, the introduced trait, the intended receiving environment and the objective and scale of the intended release (page 23). However, the effect of the introduced trait on the LM mosquito itself e.g. on fitness, life span and/or developmental rate is not mentioned as one of the aspects that should be considered. The biology of a mosquito could be altered by the introduced trait. As an altered biology could influence the possible risk of an LM mosquito the possible effect of the introduced trait on the biology of an LM mosquito should be considered in the risk assessment.

Potential effect of altered host range and impact of diseases on the ecosystem should be mentioned in the guidance

In the part of the guidance that assesses the possible effects on biological diversity several aspects are mentioned through which an LM mosquito could have an effect on the ecosystem (page 23 and 24). It is not mentioned that the LM mosquito could influence the ecosystem if the host range of an LM mosquito is altered compared to the non-modified mosquito. This aspect should be included in the guidance as one of the aspects that could affect the ecosystem and also as one of the points that should be considered in the assessment of possible effects of an LM mosquito on biodiversity.

In addition, this part of the guidance does not recognize the impact of diseases on the ecosystem. Diseases have a direct impact on the occurrence of their host organisms and could also indirectly affect the occurrence of other organisms. Diminishing the occurrence of a disease through the release of LM mosquitoes will therefore almost by definition have an effect on the ecosystem.

Spread of transgenes is affected by the fitness effect of the trait on the LM mosquito
Gene flow is one of the issues that should be considered in the risk assessment. In the paragraph on 'gene flow through cross-fertilization' it is mentioned that the likelihood and rate of spread of the transgenes or genetic elements is (amongst others) determined by the fitness conferred by the introduced trait (page 25). In this sentence it is not clarified that the fitness effect on the insect in the relevant receiving environment is meant. Therefore, this sentence should be changed in order to reflect that the fitness advantage/disadvantage of the trait on the LM mosquito in the receiving environment affects the rate of spread of the transgenes.

Unclear which mechanisms could be used to recall LM mosquitoes
In the paragraph on risk management strategies (step 5) one of the points to consider is the availability of mechanisms to recall the LM mosquitoes and transgenes if they spread unexpectedly (page 27). COGEM seriously doubts whether mechanisms that could be used to recall LM mosquitoes are available. COGEM is of the opinion that the guidance document should elaborate on the availability of recall mechanisms. If recall mechanisms are not present, this is an important point to consider in the earlier steps of the risk assessment of LM mosquitoes.

Conclusion
In general, the roadmap and the more specific guidance documents follow the generally accepted risk assessment methodology. The risk assessment process is described in general terms. The roadmap is meant to give guidance on the risk assessment process for all types of LMOs. In COGEMs view this aim is not met. The terminology that is used focuses too much on LM crops and not all aspects that are relevant in the risk assessment of other types of LMOs are included. Therefore the use of the roadmap for other LMOs, such as viruses and bacteria, is limited. COGEM suggests to develop more guidance documents for different types of living modified organisms (fish, insects, viruses, bacteria).

The documents do not indicate which aspects are considered important for certain types of LMOs. COGEM is of the opinion that the inclusion of clarifying examples would enhance the usefulness of the guidance. These examples could be included in an annex to the guidance document or in an accompanying document that is clearly identifiable as an example of the risk assessment approach. In addition, the guidance should indicate when information is necessary for the risk assessment and when this information is not needed

According to the document a recommendation as to whether or not the risks are acceptable or manageable is asked from the risk assessor in step 5 of the risk assessment process. Risk assessors can describe the magnitude of the overall risk and evaluate the effect of risk management measures on the overall risk. It is important to note that the acceptability of a risk is a decision of the competent authorities and should not be determined by other risk assessors, e.g. by an applicant.