Comments on the European Food Safety Authority draft guidance on selection of comparators for the risk assessment of genetically modified plants

COGEM advice CGM/110114-01

Introduction

EFSA has launched an open consultation on a draft guidance document on the selection of comparators for the risk assessment of genetically modified (GM) plants. This document is an extension of subparagraph 2.3.1 'Cross cutting considerations for the choice of comparators' of the recently published EFSA guidance document 'the Environmental Risk Assessment of genetically modified plants', which is currently submitted for authorisation in The European Union.[1]

The risk assessment strategy for GM plants and derived food/feed comprises a molecular characterisation of the genetic modification, a comparative analysis of the compositional, agronomic and phenotypic characteristics of the GM plant and its appropriate comparator(s), and an assessment of their potential adverse environmental effects. To date, EFSA has required the use of non-GM lines with comparable genetic background, i.e. near-isogenic in the case of sexually propagated crops, or isogenic in the case of vegetatively propagated crops, as comparators in its evaluation of GMO applications.[2] Moreover, the non-GM lines should have a well-established history of safe use.

Comparator selection has to be considered from different points of view, each focusing on other aspects. Factors taken into account are for instance the number of introduced events, differences in genetical modification techniques used, and differences in the extent that the plant metabolism is affected. Due to the increasing complexity of GM plants, the ease in the identification of appropriate comparators is decreasing. In the draft guidance document, EFSA has extended her considerations on comparator selection.

COGEM welcomes the initiative of EFSA and acknowledges the difficulties in the selection of appropriate comparators due to the increasing complexity of GM plants. She supports the EFSA statement that the non-GM line which has a genetic background 'as close as possible' to the GM plant, is selected as comparator. However, COGEM has a few criticisms concerning the document. Starting with general comments, specific comments are listed according to the order in the text in the draft guidance. Numbered paragraph headings refer to the exact paragraph as found in the document.

In The Netherlands a food/feed risk assessment is carried out by other organizations and, therefore, the COGEM confines her comments on the selection of comparators concerning the environmental risk assessment (ERA).

General comments

COGEM notes that the document is difficult to read. This is partly due to the fact that the document discusses both the comparator selection for food/feed risk assessment and the ERA. To reduce the complexity of the text, it would be helpful if these items are better separated.

For specific cases, EFSA proposes to apply a segregant as an alternative for a comparator:
- the ERA of a GM plant containing three or more events combined by conventional crossing, shall cover all sub-combinations of these events as independent stacks (line 266-288). The way to obtain all possible sub-combinations is by segregation.
- in case that applicants convincingly demonstrate that a conventional counterpart cannot be made available, a negative segregant can alternatively be used (line 318 and 365)
- if a stacked event is obtained by re-transformation, EFSA requires that the new event is segregated from the original event and is risk assessed against a conventional counterpart (line 476-477)

To COGEMs point of view, differences in genetics of the parental lines are not taken into account when segregants are used as comparator. GM lines to be assessed can be homozygous, heterozygous or F1-hybrids. In case segregants are obtained from crosses between heterozygous or hybrid parental lines, all kind of combinations of alleles can occur resulting in different genetic backgrounds of segregant and event. COGEM points out that the current draft guidance focuses rather on homozygous than heterozygous GM lines. This should be emphasized in the guidance.

Specific comments per paragraph

2.3 Issues related to the sub-combinations of events present in stack

According to EFSA, in the case of applications for import and processing, the ERA of a GM plant containing three or more events shall *cover* all sub-combinations of these events as independent stacks (line 274). For applications for cultivation, the ERA of a GM plant containing three or more events shall *consider* all sub-combinations of these events as independent stacks (line 280 and 287).

COGEM supports the notion that there is a difference between the ERA of an application for import and processing and an application for cultivation. However, it is not clear how to interpret the differences in the terms ‘cover’ and ‘consider’. Furthermore, it is not clear whether the ERA has to consist of theoretical considerations or that comparative analysis has to be performed by experimental testing of all sub-combinations.

EFSA states that after cultivation of a stacked event, sub-combinations of events can arise by segregation. Therefore, for applications of stacked events, the risk of each sub-combination of events will have to be assessed too. (Line 273-288). COGEMs point of view is that the ERA of sub-combinations is not always relevant:
- in the case of crop cultivation, wild relatives are often lacking and volunteers are absent. This is for instance the case for Maize and Soybean. Consequently, sub-combinations will not occur in the field.
- Farmers do not propagate seeds for future use since F1 hybrids are involved and, due to patent restrictions, farmers are not allowed to. Consequently, sub-combinations will not occur in the field.

- It is not necessary to perform an ERA on each possible sub-combination of events present in the stack if there is no evidence that their gene products synergistically or antagonistically interact, e.g. when a Bt gene is combined with a herbicide tolerance gene.
- Sub-combinations obtained by segregation can differ markedly in their genetic background depending on the genetics of the parental lines. This hampers the comparison for the potential unintended effects of the inserted genes.

COGEM points out that assessing all sub-combinations of events is time consuming and cost demanding, raising the costs for notifications considerably without contributing significantly to the ERA. Therefore, the COGEM suggests requiring only evaluation of the different combinations of events, if these events will segregate in the field or in the environment, and if there is a scientific reason that there can be synergistic or antagonistic effects between the different events.

3.2 Comparators for event(s) stacked by conventional crossing

EFSA states that the risk assessment of the single events included in a stack is always a prerequisite for the risk assessment of stacked events (line 347, 358). However, an argumentation for this prerequisite is lacking. In the case of the ERA, COGEM fails to understand why the single events themselves have to be assessed if they never will be used for import, processing or cultivation. In case single events do not have a testable phenotype, a separate ERA of a single event is difficult or impossible, and in the best case only a theoretical consideration. Furthermore, the ERA of a single event is not relevant if it will not occur in the field (see above; first two comments on the ERA of sub-combinations discussed under 'specific comments on paragraph 2.3'). COGEMs point of view is that the ERA is only relevant for the stacked event applied for.

Conclusion

In the case of the risk assessment of a stacked event, several aspects concerning the ERA on sub-combinations of events present in stack are unclear. Moreover, the COGEM fails to understand why single events included in a stack have to be risk assessed separately if those single events will not be used for import, processing or cultivation. If segregants are choice of comparator, the document should more explicitly discuss plant genetics. In general, COGEM notes that the document is difficult to read.

References

1. EFSA panel on Genetically Modified Organisms (GM), 2010. Guidance document for the risk assessment of genetically modified plants and derived food and feed. EFSA journal 8(11):1879
2. EFSA panel on Genetically Modified Organisms (GM), 2006. Guidance document for the risk assessment of genetically modified plants and derived food and feed. EFSA journal 99, 1-100