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KENMERK CGM/110520-01
ONDERWERP Advies m.b.t het concept van de herziene 'Guidance on the Post-Market Environmental Monitoring (PMEM) of GM plants' van de EFSA

Geachte heer Atsma,

De EFSA heeft haar richtsnoer voor 'post-market environmental monitoring' herzien. Het concept van dit richtsnoer is opengesteld voor commentaar. De COGEM heeft ervoor gekozen om haar commentaar gelijktijdig zowel aan u als direct aan de EFSA te doen toekomen.

Samenvatting
De EFSA heeft een conceptrichtsnoer opgesteld voor 'post-market environmental monitoring'. 'Post-market environmental monitoring' is een wettelijke verplichting bij het op de markt brengen van genetisch gemodificeerde gewassen en bestaat uit twee onderdelen. 'Case-specific monitoring' is ingesteld om te onderzoeken of aannames in de milieurisicobeoordeling over de eventuele aanwezigheid en het gevolg van schadelijke effecten correct zijn. 'General Surveillance' is ingesteld om onverwachte nadelige effecten van (het gebruik van) een gg-gewas zo goed mogelijk op te kunnen merken en is, in tegenstelling tot 'case-specific monitoring', in alle gevallen verplicht.
De COGEM kan instemmen met de inhoud van het conceptrichtsnoer. De EFSA beschrijft in haar conceptrichtsnoer de aanpak van 'case-specific monitoring' en 'general surveillance' en geeft voorbeelden van zaken die gemonitord zouden kunnen worden. De COGEM is van mening dat het richtsnoer 'post-market environmental monitoring' een stap verder brengt. Het richtsnoer is bovendien in lijn met eerdere COGEM adviezen over dit onderwerp.
De COGEM heeft enkele opmerkingen om het richtsnoer verder te verbeteren en wijst op enkele onduidelijkheden in de tekst van het richtsnoer. Ook vindt de COGEM dat in het richtsnoer minder nadruk moet worden gelegd op de statistische significantie van eventuele waargenomen effecten. De COGEM vindt het belangrijk dat ook bij effecten die niet statistisch significant zijn wordt overwogen of verder onderzoek noodzakelijk is.

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

Hoogachtend,

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Comments on the European Food Safety Authority draft version of the revised 'Guidance on the post-market environmental monitoring (PMEM)'

COGEM advice CGM/110520-01

Introduction

Upon a request from the European Commission, EFSA is revising the scientific opinion on Post-Market Environmental Monitoring (PMEM) of genetically modified (GM) plants. The draft version of the revised guidance on PMEM is open for public consultation.

COGEM welcomes the revised guidance on PMEM. COGEM is pleased with the document which brings PMEM to a more elaborate level. It clearly describes the monitoring approach and possible subjects for monitoring. The approach of PMEM that is described in the guidance document is in line with previous COGEM advices on this topic.[1,2] COGEM does have some remarks that could further improve the document and would remove remaining inconsistencies. The line numbers in COGEM's comments refer to the line numbers in the guidance document.

Background of PMEM
For each GM plant an environmental risk assessment is carried out to identify and evaluate potential adverse effects of a GM plant on human and animal health and the environment arising from its placing on the market. The outcome of this environmental risk assessment determines the requirements for Post-Market Environmental Monitoring (PMEM), i.e. the requirements for Case-Specific Monitoring.

The purpose of PMEM is to detect any direct or indirect, immediate, delayed or unforeseen effects on human health or the environment of GMOs after they have been placed on the market. Two types of monitoring are recognized: Case-Specific Monitoring (CSM) and General Surveillance (GS). The purpose of CSM is to confirm the correctness of any assumption in the ERA on the occurrence and impact of potential adverse effects of the GMO or its use. The outcome of the ERA determines whether CSM is required. The purpose of GS is to detect unanticipated adverse effects of the GM plant or its use. GS is required for all GM plants.

The presence of a PMEM plan is a legal requirement for each application for placing on the market a GMO or food/feed containing or consisting of that GMO (Directive 2001/18/EC and Regulation (EC) No 1829/2003).

General Remarks

Definitions of 'damage', 'harm' and 'adverse' should be clear and unambiguous
In a guidance on PMEM it is important to be unambiguous on the definitions of 'damage', 'harm' and 'adverse'. EFSA states that the subject of protection is considered to be damaged if it is *significantly* adversely affected. According to EFSA the identification of a *significant* adverse effect should consider both its intensity (e.g. extent of loss) and the value of the

impaired subject of protection (e.g. high value of the populations of a species protected by law) and the reversibility of, or recovery from, the damage (lines 492-496). However, EFSA's definition of damage is not introduced until the chapter on GS. Another definition (used in Directive 2004/35/EC) is mentioned earlier in the guidance (lines 134-147 and 466-468). This definition is different from EFSA's definition as it does not take reversibility into account. COGEM is of the opinion that EFSA's definition should be introduced early in the guidance document and that the differences with the definition in Directive 2004/35/EC should be explained. In addition, it should be made clear why EFSA prefers the definition which takes reversibility into account.

COGEM notes that EFSA does not clarify who decides if something is damaged. It should be clarified whether this is determined by the Member States or by the applicant.

Potential effects that do not reach statistical significance should not be neglected

In the EFSA guidance on PMEM apparently contrasting statements concerning difficulties in the design of PMEM are present. On one hand difficulties associated with the detection of effects are pointed out, but on the other hand EFSA seems to adhere to rather rigid criteria for statistical design and analysis.

In the section on CSM, EFSA elaborates on difficulties with regard to the statistical design, e.g. the selection of comparators, plot size, the need for considerable land resources to allow adequate replication and the control of between unit variability (lines 369-389); and in the section on GS, EFSA states that 'a thorough statistical analysis of the information collected by GS may not be possible for all cases' (lines 532-533).

However, in contrast to the attention for the difficulties of a proper statistical design and analysis in CSM and GS (lines 369-389 and 532-533), for CSM EFSA requires the applicant to state the minimum levels of data required to provide credible results and the minimum effect size to be detected. In addition, where appropriate a statistical power analysis should be done (lines 346-357). For GS EFSA states that, where appropriate, the requirements for statistical significance and the details of the statistical approaches should be given, i.e. effect size, sample sizes, sampling and recording methods (lines 530-531, 670-674 and 754-772). Although EFSA does not prescribe criteria for the statistical analysis of PMEM data, the requested information on statistical design suggest that EFSA is of the opinion that the statistical analysis of monitoring should adhere to high standards for data analysis.

COGEM agrees that care should be given to a proper set up of an experiment, but points out that it will be difficult, and might even be impossible, to obtain statistical significant data from monitoring because of the high variability present within the environment. This is true for both CSM and GS. In case of GS, the lack of a clear hypothesis on the type of adverse effects that might be caused by a GM plant further hampers the possibility to perform a proper statistical analysis and detect effects which are statistically significant. The 'general hypothesis' that was formulated by EFSA (lines 249-252 and 471-473) is not specific enough to be used as a starting point for statistically sound monitoring.

In view of the above described considerations, COGEM is of the opinion that not too much emphasis should be biven to the statistical significance of an observed effect when determining the need for further research. If too much emphasis is put on the statistical significance of an observed effect, a putative effect could be neglected because it does not reach statistical significance. COGEM is aware of the difficulties associated with the detection of an effect within the natural environmental variation. However, from situations in

the past it is known that too much emphasis on statistical significance could lead to unjust discarding of relevant effects. Therefore the guidance document should stress the possible importance of effects that do not fulfill the criteria of statistical significance. This aspect could be mentioned in paragraphs IV-B-1a and IV-B-1c of the guidance document.

COGEM agrees with EFSA on availability of raw data and analysis
COGEM notices that the guidance document is not consistent in its wording on the availability of raw data and analysis from CSM and GS data. In the section on CSM EFSA states that applicants should 'provide' the raw data and analysis of the CSM results to the Competent Authorities and the European Commission (lines 434-436). In the section on GS, EFSA 'recommends' that raw data and analysis of monitoring data are made available (lines 681-682) or states that applicants 'should make their raw data available' (lines 771 and 1075). COGEM is of the opinion that the requirements with regard to the availability of raw data should be consistent (i.e. 'to provide') throughout the guidance document.

Specific comments
III. Interplay between ERA, Risk management and PMEM

Presence of multiple GM plants important when investigating the cause of an observed effect
EFSA points out that future GS monitoring systems should not only consider individual events, but should also be concerned with the impacts on receiving environments of multiple GM plants, interactions between GM plants and their cultivation and management (lines 259-262). The purpose of GS is to detect unanticipated adverse effects of the GMO or its use. The set up of a system to detect unanticipated adverse effect is not significantly different when a single or when multiple GM events are present. Therefore, in COGEM's view it is questionable whether the presence of multiple GM events would impact the set up and realization of GS. The presence of multiple GM events is of importance in a later phase when investigating the cause of an observed effect.

IV. A. Case-specific monitoring

CSM should only be required in exceptional cases
According to EFSA, CSM should be carried out if significant levels of critical uncertainty are identified in the ERA (lines 271-273). COGEM points out that the box on page 11 could be interpreted in a way that CSM would seem to be a prerequisite for all GM plants and that all listed examples should be monitored. To avoid confusion, the text of the guidance document should emphasize that CSM is only required when effects are identified in the ERA that could lead to adverse effects on human health or the environment.

Development of resistant insects is not an environmental risk and should not be part of PMEM
Some of the examples listed in the box on page 11 refer to the development of insect-resistant pests (pest control, non-Bt refuge). If target pests become resistant this renders the GM plant useless and it could lead to crop losses and damage for farmers. COGEM is of the opinion that resistance of target pests is an agricultural economic risk, but does not result in an environmental risk and should therefore not be part of PMEM plans.

IV. B. General Surveillance

Responsibilities of different parties should be clear

GS focuses on the detection of unanticipated or unforeseen adverse effects. There is no underlying hypothesis on the nature of effects, which makes the detection of these effects difficult and results in problems with monitoring set up, problem formulation and statistical analysis. With regard to the set up of monitoring it is not completely clear which aspects of monitoring are the responsibility of the applicant. On one hand tables are included that list a variety of protection goals and tools (table 1 and 2) which suggests that the applicant should make sure that all the listed protection goals are monitored with the appropriate tools, but on the other hand the guidance document states that Member States have responsibilities with regard to the selection, adaptation and use of existing monitoring networks (lines 933-935), which is an important monitoring tool. To avoid confusion, the guidance should be very clear on the activities for which a party (e.g. applicant or Member State) is responsible.

GS for cultivation should also pay attention to monitoring of effects arising from import and processing

COGEM notes that the majority of the section on GS refers to cases where GM plants are cultivated. The set up of such a GS plan is focused on detecting unanticipated effects arising from growth of the GM plant. However, usually simultaneously with a license for cultivation, a license for import and processing of the GM plant is granted. As the effects that may arise from import and processing might differ from the effect that could arise from cultivation, COGEM is of the opinion that GS focused at the detection of unanticipated adverse effects in import and processing (described in lines 1020-1040) should also be part of a GS plan when a GM plant is cultivated.

COGEM is content with part in guidance on existing monitoring networks

EFSA states that GS plans should include the possibility of integrating GS with other plant production and appropriate terrestrial monitoring networks in Member States. EFSA mentions that the existing monitoring networks will differ from country to country (line 892). COGEM points out that differences in monitoring between countries are unavoidable. European initiatives that aim to reduce these differences should be welcomed and supported. One of these initiatives is Life Watch which aims to improve data availability and data usage within Europe. [3] This initiative could be mentioned in the guidance document.

Sustainability should be specified and should only be part of GS when possible environmental risks are concerned

COGEM notes that EFSA sees sustainable agriculture as one of the aspects that could be monitored in General Surveillance (line 283, 566, 710 tables 1 and 2). Sustainability is a dynamic concept and its interpretation depends on the context (e.g. society, culture and religion) and the spirit of the age. COGEM is of the opinion that only effects of the GM plant or of specific cultivation or management techniques directly linked to the GM plant should be considered in environmental risk analysis and post-market environmental monitoring. In the guidance an explicit delimitation of the sustainability aspects that should be considered in GS should be given.

Farmer questionnaires do not contain a proper comparator

EFSA states that a farmer questionnaire should be designed to ensure appropriate statistical validity (line 722 and 766). As mentioned before, COGEM questions whether monitoring data will allow the detection of statistical significant effects. In addition, in the questionnaires a proper comparator is missing. EFSA describes the inclusion of information on the location of a comparator site in the farmer questionnaire (line 780), but in practice farmer questionnaires use 'the usual situation' as the comparator. Solid data on the 'usual situation' are lacking. COGEM is of the opinion that specific attention is needed in order to obtain data on the 'usual situation'. Areas were conventional crops are grown could provide solid data on the 'usual situation', but COGEM is of the opinion that farmers can only be asked to provide data on the 'usual situation', when they grow conventional crops themselves.

EFSA states that the farmer questionnaire should provide information on other GM plants that are grown on the same sites or farms or on adjacent farms (lines 735-736 and lines 789-790). COGEM questions whether a farmer will be able to provide this information for adjacent farms. Therefore, COGEM is of the opinion that questions concerning the presence of GM plants on adjacent farms should not be part of the farmer questionnaire.

Sometimes sensitive data are required for PMEM

According to the guidance document the applicant is asked to describe the number of farmers/growers using a GM plant (line 765). In addition, in table 2 'economic data on crop production' is mentioned as an example of an assessment endpoint. COGEM notes that the data requirements for PMEM sometimes concern sensitive/confidential data.

COGEM assumes that 'economic data on crop production' refers to changes in crop yield. EFSA should change the wording of this example accordingly.

Guidance should be given on the duration of GS

In the paragraph on the duration of monitoring EFSA describes that GS plans should consider the possibility of unanticipated adverse effects occurring after cultivation of a GM plant (lines 840-848). However, in contrast to the title of the paragraph it is not mentioned how long GS has to be carried out. COGEM is of the opinion that EFSA should provide guidelines with regard to the duration of GS. COGEM is of the opinion that the duration of environmental exposure of the GM plant, which is a result of its life cycle and production cycle, should be considered when determining the duration of GS.

Conclusion

COGEM is pleased with the revised guidance document on PMEM which brings PMEM to a more elaborate level. It clearly describes the monitoring approach and possible subjects for monitoring. The approach of PMEM that is described in the guidance document is in line with previous COGEM advices on this topic.[1,2]

COGEM notes that the EFSA guidance contains apparent inconsistencies**.** On one hand difficulties associated with the detection of effects are pointed out, but on the other hand EFSA seems to adhere to rather rigid criteria for statistical design and analysis.

COGEM points out that due to the high variability present within the environment it is difficult, and might even be impossible, to obtain statistical significant data from monitoring (CSM and GS). Therefore**,** in first instance possible effects should not be neglected because

they do not reach statistical significance. If too much emphasis is put on the statistical significance of an observed effect, a possible relevant effect might be overlooked. In COGEM's view the guidance should also pay attention to observed effects when they do not reach statistical significance and should consider whether these effects require further research.

References

1. COGEM (2010). General Surveillance. CGM/100226-01
2. COGEM (2005). Post-market monitoring van genetisch gemodificeerde gewassen in Nederland. COGEM advice CGM/050414-03
3. LIFEWATCH (2011). LIFEWATCH. http://www.lifewatch.eu (May 20th, 2011)