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KENMERK CGM/240819-01
ONDERWERP Advies hernieuwing import en verwerking van gg-Koolzaad MON88302

Geachte heer Jansen,

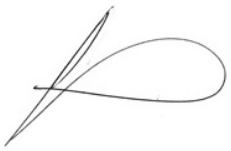
Naar aanleiding van een aanvraag voor een hernieuwing van de vergunning voor import en verwerking van genetisch gemodificeerde (gg-)Koolzaad MON88302 (GMFF-2023-21220), ingediend door Bayer Agriculture BV, namens Bayer CropScience LP, deelt de COGEM u het volgende mee.

Samenvatting:

De COGEM is gevraagd te adviseren over de hernieuwing van de vergunning voor import en verwerking van de genetisch gemodificeerde (gg-)Koolzaad MON88302. De COGEM heeft in 2012 positief geadviseerd over de import en verwerking van deze gg-Koolzaad. Vergunningen voor markttoelatingen moeten om de tien jaar hernieuwd worden. De gg-koolzaadlijn is door aanwezigheid van het *cp4 epsps* gen tolerant voor glyfosaat -bevattende herbiciden.
De aanvraag bevat onder andere geactualiseerde bioinformatische analyses, een recent literatuuronderzoek en de resultaten van de monitoring die tijdens de voorafgaande vergunningsperiode is uitgevoerd. Er zijn geen aanwijzingen dat MON88302 een risico kan vormen voor mens en milieu. Wel is de COGEM van oordeel dat het monitoringsplan uitgebreid moet worden. Door het morsen van zaden kunnen gg-koolzaadpopulaties zich namelijk vestigen in Nederland. Tussen verschillende gg-koolzaadplanten kan mogelijk ‘gene flow’ optreden, waardoor de ingebrachte eigenschappen stapelen en combinaties van transgenen ontstaan. Hierbij is een potentieel schadelijk milieueffect niet op voorhand uit te sluiten. Daarom is het noodzakelijk dat er gemonitord wordt op transportlocaties, zoals langs spoorwegen en op overslagplaatsen. De COGEM is van oordeel dat het monitoringsplan van MON88302 met bovenstaande punten moet worden uitgebreid alvorens de vergunning van voor import en verwerking kan worden hernieuwd.

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

Hoogachtend,



Prof. dr. ing. Sybe Schaap
Voorzitter COGEM

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- Ing. M.A.C. Möllers, Food-Feed loket

Advice on the renewal of the authorisation of import and processing of genetically modified oilseed rape MON88302

COGEM advice CGM/240819-01

- The present application (GMFF-2023-21220) concerns the renewal of the authorisation for import and processing for use in feed and food of genetically modified (GM) oilseed rape MON88302;
- MON88302 was previously authorized for import and processing in 2015;

- Oilseed rape MON88302 was produced by *Agrobacterium tumefaciens*-mediated transformation. It expresses the *cp4 epsps* gene, conferring tolerance to glyphosate containing herbicides;

- Feral oilseed rape populations occur across the Netherlands, with a small number of plants (25 or less) per location, along distribution routes and handling areas as a result of spillage of oilseed rape seeds during transport and transshipment;

- Oilseed rape can hybridise with *Brassica rapa* which is a common plant along Dutch roadsides. To a lesser extent it can also hybridise with *Brassica juncea* and *Brassica oleracea*;
- Stable incorporation (introgression) of genes from *B. napus* into wild populations of *B. rapa* and *B. napus* may be possible;

- The molecular characterisation of MON88302 has been updated and meets the criteria of COGEM
- Accidental spillage of GM oilseed rape seeds may lead to the establishment of feral GM *B. napus*, which could lead to plants with stacked events, or feral GM *B. rapa* harbouring GM traits like herbicide tolerance;

- COGEM is of the opinion that the monitoring plan for import and processing of GM oilseed rape should always include monitoring along transport routes (including roadsides and railway beddings), transshipment areas, and introduction through bird feed mixtures. As these aspects are not included in the current monitoring plan of MON88302, COGEM cannot advise positively on the application for import and processing for use in food and feed of MON88302 oilseed rape;
- COGEM abstains from giving advice on the potential risks of incidental consumption as a food/feed assessment is carried out by other organisations.

1. Introduction

The present application (GMFF-2023-21220), filed by Bayer Agriculture BV on behalf of Bayer CropScience LP, concerns the renewal of the authorisation for import and processing of genetically

modified (GM) oilseed rape (*Brassica napus*) MON88302 for use in food, feed and other products. Authorisation was previously granted in 2015.[1] In MON88302, the *cp4 epsps* gene is expressed, conferring tolerance to glyphosate containing herbicides. Because import and processing authorisations remain valid for a period of 10 years, the applicant has filed an application for the renewal of the authorisation granted in 2015. The application contains, amongst other things, monitoring reports, updated bioinformatics analyses, and a systematic literature search.

2. Previous COGEM advice

COGEM has issued a generic advice on aspects relevant to import and processing of GM oilseed rape in the Netherlands.[2] In addition, several advisory reports were issued on import and processing of GM oilseed rape lines with tolerance to various herbicides. COGEM was of the opinion that import and processing of these oilseed rape lines posed a negligible risk to the environment, but that the corresponding post-market environmental monitoring (PMEM) plan supplied by the applicant did not meet COGEM's requirements.[3,4,5,6,7,8] COGEM has previously advised similarly on the import and processing of GM oilseed rape MON88302, as well as the MON88302xMS8xRF3 line.[9,10]

3. Environmental risk assessment

The objective of an environmental risk assessment (ERA) is to identify and evaluate potential adverse effects of the genetically modified organism (GMO), direct or indirect, immediate or delayed, on human health and the environment. This ERA involves the import of GM oilseed rape, any concerns relating to cultivation, management or harvesting practices are beyond the scope of this advice. When assessing the environmental risk of incidental spillage of GM oilseed rape, COGEM assesses whether the event has an increased fitness under natural conditions. Other so-called 'areas of concern' (e.g. effects on non-target organisms) are only addressed if there is a reason to assume that the introduced traits might have a potential adverse effect on these areas.

3.1 Characteristics of the crop

Oilseed rape (*Brassica napus*) is a member of the *Brassicaceae* family, which also includes *Brassica rapa* (turnip, turnip-rape, and wild turnip), *Brassica juncea* (Chinese mustard), *Brassica oleracea* (cabbage), *Brassica nigra* (black mustard) and *Brassica carinata* (Ethiopian mustard). The allotetraploid *B. napus* is the result of natural hybridisation between *B. rapa* and *B. oleracea.*[2,11]

B. napus reproduces by self-pollination and cross-pollination. It produces large amounts of pollen, which are dispersed by both wind and insects. In fields, the average rate of cross-pollination is 30%. The seeds of *B. napus* are arranged in a single row in a fruit (a linear cylindrical silique), and are small, light and produced in large quantities.[2,12,13] Oilseed rape can cross-pollinate with its more common wild relative *B. rapa* and to a lesser extent with *B. juncea* and *B. oleracea*.[2,12]

3.2 Receiving environment

In the Netherlands, *B. napus* is grown as a crop and its seeds are imported for oil production. *B. napus* is able to form volunteers in disturbed environments near roadsides, railways and handling areas. The spillage of oilseed rape seeds during transport and transshipment has led to the establishment of feral

populations, with a small number of plants (25 or less) per location, along distribution routes and handling areas.[14]

Oilseed rape x *B. rapa* hybrid plants have been observed in the Netherlands.[15] Stable incorporation (introgression) of genes from *B. napus* into wild *B. rapa* has been reported in Canada, but has not been documented in the Netherlands.[16] In a survey performed in the Netherlands in 2019 to investigate the presence of GM oilseed rape along transport routes and locations where transhipment and processing of oilseed rape takes place, no GM oilseed rape was detected.[17,18] Recent investigation has shown that GM oilseed rape seeds can be present in bird feed mixtures.[19,20] This could pose a potential introduction route of GM oilseed rape into the Dutch environment.

Conclusion: Wild *B. napus* populations exist in the Netherlands. *B. napus* can hybridise with its wild relative *B. rapa*. Therefore, GM volunteers from spilled seeds can lead to dispersal of genes to wild populations of *B. napus* and *B. rapa*. To date, no GM oilseed rape has been detected in the Netherlands.

3.3 Description of the introduced genes and traits

MON88302 was produced by *Agrobacterium tumefaciens*-mediated transformation of conventional 'Ebony' oilseed rape hypocotyls using the PV-BNHT2672 plasmid. The genetic element introduced in MON88302, and a description thereof, is listed in the table below.

MON88302 is under the regulation of the *FMV/Tsf1* chimeric promoter, the *Tsf1* leader and intron sequences, and the *E9* 3' untranslated region. The *MV/Tsf1* chimeric promoter, which directs transcription in plant cells, contains enhancer sequences from the promoter of the figwort mosaic virus *35S* RNA combined with the promoter from the *Tsf1* gene of *Arabidopsis thaliana* that encodes elongation factor *EF-1α*. The *Tsf1* leader sequence is the 5' untranslated region from the *Tsf1* gene of *A. thaliana*. The *E9* 3' untranslated region is the 3' untranslated region of the pea (*Pisum sativum*) ribulose 1,5 bisphosphate carboxylase small subunit (*rbcS2*) *E9* gene and is present to direct polyadenylation of the *cp4 epsps* transcript. The chloroplast transit peptide CTP2 directs transport of the CP4 EPSPS protein to the chloroplast and is derived from *CTP2* target sequence of the *A. thaliana shkG* gene.

Introduced gene	Encoded proteins	Regulatory elements	Traits
cp4 epsps	CP4 5-enolpyruvylshiki-mate-3-phosphate synthase (EPSPS) originating from *Agrobacterium tumefaciens* strain CP4[21]	Chimeric promoter FMV/Tsf1, derived from enhancer sequences from the figwort mosaic virus 35S RNA together with the promoter from the *Tsf1* gene of *Arabidopsis thaliana*; the 5'UTR leader sequence of *Tsf1 A. thaliana*, the CTP2 target sequence of the *shkG* gene, from *A. thaliana*; the 3′ UTR of the rubisco subunit (rbcS2) E9 gene, from *Pisum sativum*	Confers tolerance to glyphosate herbicides

3.4 Updated bioinformatic analyses

In the current application, the applicant updated the bioinformatic analyses of the inserts, the sequences spanning the insertion sites from stop-to-stop codon and the 5' and 3' flanking regions, using databases assembled in January 2023 containing sequences from allergens, toxins, and proteins. According to the applicant there were no biologically relevant amino acid sequence similarities to known allergens, toxins, or other biologically active proteins with adverse effects for human or animal health.

As the reference genome was updated since the last application, the flanking regions were analysed to find the insertion site. Results indicate that the T-DNA was inserted without disrupting any endogenous genes.

The COGEM is of the opinion that the molecular characterisation of MON88302 meets the requirements of COGEM.[22]

Conclusion: The molecular characterisation was conducted according to the criteria previously laid down by COGEM. No indications were identified for potential environmental risks of the oilseed rape MON88302.

3.5 Systematic literature search

The systematic literature search – which was submitted as part of the renewal application – covered the period from 1 January 2014 to 16 November 2023 and addressed the question "Does MON88302 oilseed rape, derived food/feed products and the introduced glyphosate tolerance trait have adverse effects on human and animal health and the environment?" An overview of unpublished studies performed by the applicant that were not previously submitted to the EU was not provided. According to the applicant there were no unpublished studies that bring new information that might influence the risk assessment.

The literature search identified 344 publications in electronic databases and 550 records of internet pages of the relevant key organisations mentioned in the 2019 'Explanatory note on literature searching for GMO applications' EFSA publication.[23] Of the identified literature and records, only 2 records from internet pages of key organisations were considered relevant for the review question. According to the applicant, these records did not report any new hazards, modified exposure, or new scientific uncertainty of MON88302 and therefore did not have any implication for its risk assessment of MON88302.

Overall, no adverse effects on human and animal health, or the environment were identified in the literature searches of the applicant.

Conclusion: The literature searches do not give an indication of potential environmental risks resulting from import and processing of MON88302.

3.6 Annual monitoring reports

The annual Post Market Environmental Monitoring (PMEM) reports for GM oilseed rape MON88302 from October 2015 until May 2023 were provided. Based on the PMEM reports, the applicant states that no adverse health or environmental effects are associated with the import or use MON88302 oilseed rape.

These reports contain amongst others information on annual literature searches carried out by the applicant, and on the monitoring which is carried out by operators involved in import, handling and processing of viable GM oilseed rape. These operators are members of the European trade associations COCERAL, UNISTOCK or FEDIOL. They are expected to report any occurrence of potential adverse effects arising from MON88302 oilseed rape, including adventitious populations resisting routine eradication procedures. No adverse effects associated with the import or use of MON88302 were reported. According to the PMEM reports, no relevant publications that would invalidate the initial conclusions on the risk assessment of MON88302 were identified in the annual literature searches.

The PMEM of import and processing carried out between 2015 and 2023 did not provide any indications that import and processing of MON88302 poses a risk to the environment.

Conclusion: The information in the annual monitoring reports gives no indication of adverse effects or incidents resulting from import and/or processing of MON88302.

4. Food/feed assessment

This application is submitted under Regulation (EC) 1829/2003, therefore a food/feed assessment is carried out by EFSA and national organisations involved in the assessment of food safety. In the Netherlands, a food and/or feed assessment for Regulation (EC) 1829/2003 applications is carried out by Wageningen Food Safety Research (WFSR). The outcome of the assessment by these other organisations (EFSA, WFSR) was not known when this advice was completed.

5. Post-market environmental monitoring

The applicant did not propose any changes to the existing post-market environmental monitoring (PMEM) plan for the oilseed rape event MON88302 and argues that in the case of incidental release of oilseed rape seeds, these are unlikely to germinate, grow or reproduce in the environment around storage facilities and along transport routes.

COGEM has expressed concerns regarding the PMEM plan of GM oilseed rape events on several occasions. Feral oilseed rape populations can arise from GM oilseed rape seeds spilled during transshipment and transport.[24,25,26,27,28] Additionally, as GM oilseed rape seeds can potentially be introduced in the environment via bird feed mixtures, this introduction route should be considered in the PMEM plan.[19,20] Presence of feral GM oilseed rape could result in potential gene flow. As it cannot be excluded beforehand that such a newly generated stacked event may have an adverse effect, COGEM remains of the opinion that the monitoring plan for MON88302 should include periodical monitoring in transshipment areas and along transport routes such as railroads, etc. Additionally, the monitoring plan should include producers and distributors of seed mixtures in the PMEM plan, and should offer a place where adverse effects, and unexpected or notable events are reported.

Conclusion: The information in the annual monitoring reports gives no indication of adverse effects or incidents resulting from import and/or processing of MON88302. However, the current PMEM plan of MON88302 does not include monitoring along transport routes and transshipment areas, or its introduction via bird feed mixtures. COGEM is of the opinion that the PMEM plan should be adapted before market authorisation is granted.

6. Overall conclusion

Based on the above, COGEM is of the opinion that the molecular characterization and bioinformatic analysis are adequate and that there are no indications that MON88302 poses a risk to human health or the Dutch environment.

COGEM remains of the opinion that the PMEM plan for GM oilseed rape MON88302 needs to be adapted. Most importantly, the approval of the application should depend on the inclusion of monitoring along transport routes or transshipment areas in the general surveillance plan. Special attention should be paid to the areas where viable MON88302 oilseed rape seeds could be spilled unintentionally, enabling the identification of any direct or indirect, immediate, delayed or unanticipated environmental effects. COGEM abstains from giving advice on the potential risks of incidental consumption since other organisations carry out a food/feed assessment.

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