Renewal of the authorisation for import and processing of genetically modified maize MIR162

COGEM advice CGM/210927-01

- The present application (EFSA/GMO/RX/025) concerns the authorisation for import and processing for use in feed and food of genetically modified (GM) maize MIR162;
- GM maize MIR162 was previously authorised for import and processing in 2012;

- Maize MIR162 expresses the genes *vip3Aa20* and *pmi*, conferring resistance to lepidopteran pests and enabling MIR162 to use mannose as a carbon source, respectively;

- In the Netherlands, feral maize populations have never been observed and the appearance of volunteers is rare;
- The wild relative of maize (teosinte) is not present in het natural environment of the Netherlands, therefore hybridisation of GM maize with other species is not possible;

- The molecular characterisation of maize MIR162 has been updated and meets the criteria of COGEM;
- The updated bioinformatics analysis, literature review, several unpublished studies and monitoring reports do not give any indication of a potential environmental risk

- COGEM is of the opinion that import and processing of maize MIR162 poses a negligible risk to the environment in the Netherlands;
- COGEM abstains from giving advice on the potential risks of incidental consumption since other organisations carry out a food/feed assessment.

1. Introduction

The present application (EFSA/GMO/RX/025), filed by Syngenta Crop Protection NV/SA, concerns the renewal of the authorisation for food, feed, import and processing of GM maize (*Zea mays*) MIR162. This authorisation was granted in 2012 (2012/651/EU).[1] Since market authorisations remain valid for a period of 10 years, the applicant filed an application for the renewal of the authorisation granted in 2012. The application contains, amongst others, monitoring reports, updated bioinformatics analyses, and a systematic literature search.

2. Previous COGEM advice

In 2010 COGEM advised positively on import and processing of maize line MIR162.[2] Additionally, COGEM has advised positively on import and processing of maize lines containing the event

MIR162, amongst which MON89034x1507xMIR162xNK603xDAS-40278-9[3] and Bt11xMIR162xMIR604xMON89034x5307xGA21.[4]

3. Environmental risk assessment

3.1 Characteristics of maize

Maize (*Zea mays*) is a member of the grass family *Poaceae*. It is a highly domesticated crop originating from Central America, but nowadays cultivated globally. Maize is wind pollinated[5,6] and has both male and female flowers that are spatially separated. The female flowers are not attractive to insect pollinators, because they do not produce nectar. Insect pollination of maize is highly limited but cannot be excluded.[7] Hybridisation of GM maize with other species than teosinte, the wild relative of maize, cannot occur.

Maize generally requires warm conditions in order to grow.[7,8] In cultivation areas with warm climatic conditions, the appearance of volunteers can occur the year following maize cultivation due to spilled cobs or kernels. Maize volunteers have also appeared in Austria (Central European continental climatic conditions).[9] However, these volunteers are usually killed by common mechanical pre-planting soil preparation practices.[7] Maize does not tolerate prolonged cold and frost.[10]

Maize is very sensitive to weed competition.[11] During the long process of domestication, maize has lost the ability to persist in the wild.[6] A soil seed bank, small seeds, and an extended period of flowering and seed production are characteristics often observed in persistent weeds.[12] Maize lacks all these characteristics. After ripening, the seeds (the kernels) adhere to the cob and do not scatter naturally.[7,13] Consequently, seed dispersal is severely hampered.

3.2 Receiving environment

In the Netherlands, the appearance of maize volunteers is rare, although maize plants occasionally have been observed outside agricultural fields.[14,15] Any volunteers emerging will be killed by frost at the onset of winter.[10] COGEM is not aware of any reports of feral maize populations in the Netherlands. Additionally, hybridisation of GM maize with teosinte is not possible, as teosinte is absent in maize fields and in nature in the Netherlands.[10]

Conclusion: In the Netherlands, feral maize populations do not occur and hybridisation of maize with other species is impossible.

3.3 Description of the introduced gene, trait and regulatory element

MIR162 was created by *Agrobacterium tumefaciens* mediated transformation. Descriptions of the inserted genetic elements in MIR162 are listed in the tables below. These lists are limited to information on the introduced genes, corresponding traits, and regulatory elements (promoters and terminators).

Introduced genes	Encoded products	Traits	Regulatory elements
Pmi, also known as *manA*	Phosphomannose isomerase (PMI) enzyme derived from *Escherichia coli* strain K-12.[16]	Enables transformed plant cells to use mannose as a sole carbon source	Polyubiquitin promoter and intron (Zm*Ubi*Int) sequences from *Z. mays* and nopaline synthase (*nos*) terminator sequence from *A. tumefaciens*
Vip3Aa20	Variant of a native vegetative insecticidal protein (Vip3Aa1) originating from *B. thuringiensis* strain AB88[17]	Resistance to certain lepidopteran pests	Polyubiquitin promoter and intron (Zm*Ubi*Int) sequences from *Z. mays* and *35S* terminator sequence from *Cauliflower mosaic virus*
For a detailed description of the introduced genes and traits, see references			

3.4 Updated bioinformatics analyses

Updated bioinformatics analyses were performed using updated databases and the original sequences that were submitted as part of two previous applications: EFSA/GMO/DE/2010/82 and EFSA/GMO/DE/2018/149, and the updated sequences of MIR162 obtained in 2019, named MIR162 hybrid Material ID 12MG000996. Comparing the insert sequence of MIR162 in Material ID 12MG000996 against the original MIR162 sequence, the applicant reports that no nucleotide changes were identified in the insert and flanking sequence of MIR162 present in Material ID 12MG000996 compared to the previously determined sequences, with the exception of a single nucleotide deletion. This concerns a cytosine in a cytosine homopolymer region in the second Zm*Ubi*Int promoter sequence, driving transcription of the *pmi* gene. According to the applicant, this deletion has no effect on human, animal and environmental safety.

of The entire MIR162 insert and junction DNA sequences were analysed for the presence of open reading frames in all six potential reading frames from stop to stop codon , including frames that overlap and are in frame with the coding sequences of the newly expressed Vip3Aa20 and PMI proteins. Bioinformatic alignment searches were performed using the COMPARE (Comprehensive Protein Database International Life Sciences Institute) 2020 database, and a customized toxin database (the Syngenta Toxin database 2020, created by retrieval of protein toxins, as curated and annotated at UniProt). The putative products of the identified ORFs do not reveal any relevant protein or amino acid similarities with known allergens or toxins. Additionally, no sequences potentially able to promote homologous recombination between the insert sequence and micro-organisms were identified by bioinformatic analyses. This was analysed using NCBI databases (complete genomes database, complete plasmid database and complete bacteriophages database).[18]

Considering the above, COGEM is of the opinion that the molecular characterisation of maize MIR162 has been performed correctly and meets the requirements of COGEM.[19] No new elements that would invalidate the conclusions of the initial risk assessment were identified.

Conclusion: The bioinformatics analyses of maize MIR162 have been updated and are adequate. No indications for potential environmental risks were identified.

3.5 Systematic literature search and unpublished studies

The applicant performed a literature search using several bibliographic databases and additional sources of information (e.g., web pages of regulatory authorities for food and feed safety, agriculture and biotechnology) covering a publication period from January 1st 2010 to April, May or June 2020, depending on the database and regulatory agency webpage. Additionally, an overview was provided of unpublished studies (produced, controlled or sponsored by the applicant, or provided to the applicant by a third party, not previously submitted to the EU) on maize line MIR162. No studies were identified with new data relevant to the risk assessment. Overall, no adverse effects on human and animal health, or the environment were identified in the literature searches and unpublished studies of the applicant.

Conclusion: The systematic literature search and unpublished studies of the applicant do not give any indication of potential environmental risk resulting from import and/or processing of maize line MIR162.

3.6 Annual monitoring reports

The applicant supplied annual reports on the post-market monitoring carried out between November 2013 and November 2020. Monitoring was performed by operators involved in import, handling and processing of viable GM maize MIR162, i.e. COCERAL, UNISTOCK and FEDIOL. The operators were to observe and report on any occurrence of unanticipated adverse effects, arising from MI162 maize; the results of which are summarised in the annual reports. As part of the monitoring reports, the applicant performed a yearly review of scientific publications to monitor the safety of maize MIR162. According to the applicant, the monitoring reports and scientific publications contained no indications of adverse effects or incidents.

Conclusion: The information in the annual monitoring reports gives no indication of adverse effects or incidents resulting from import and/or processing of maize line MIR162.

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 other organisations (EFSA, WFSR) was not known when this advice was completed.

5. Post-market environmental monitoring (PMEM)

The applicant did not propose any changes to the existing post-market environmental monitoring (PMEM) plan for maize line MIR162. COGEM has published several recommendations for further improvement of the general surveillance (GS) plan[20,21] but considers the current GS plan adequate for import and processing of maize MIR162.

6. Overall conclusion

COGEM is of the opinion that import and processing of maize MIR162 poses a negligible risk to the environment in the Netherlands. COGEM abstains from giving advice on the potential risks of incidental consumption since other organisations carry out a food/feed assessment.

References

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