Renewal of the authorisation for import and processing of genetically modified maize MIR604

COGEM advice CGM/190118-01

- The present application (EFSA/GMO/RX/013) concerns the renewal of the authorisation for import and processing of genetically modified (GM) maize MIR604;
- GM maize MIR604 was previously authorised for import and processing in 2009;
- COGEM advised positively on the import and processing of MIR604 in 2005;
- The GM maize expresses the genes *mcry3A* and *mir604pmi*;
- It is resistant to certain colepidopteran insects and able to use mannose as a carbon source;

- In the Netherlands, feral maize populations have never been observed and the appearance of volunteers is rare;
- In the Netherlands, the wild relative of maize, teosinte, is not present in maize fields or in nature and hybridisation of GM maize with other species is therefore not possible;

- The bioinformatic analyses of MIR604 has been updated and meets the criteria of COGEM;
- The updated bioinformatics analysis, literature review and monitoring reports do not give any indication of a potential environmental risk;

- COGEM is of the opinion that import and processing of maize MIR604 poses a negligible risk to the environment in the Netherlands;
- COGEM abstains from giving advice on the potential risks of incidental consumption since a food/feed assessment is carried out by other organisations.

1. Introduction

The present application (EFSA/GMO/RX/013), filed by Syngenta Crop Protection NV/SA, concerns the renewal of the authorisation for import and processing of GM maize MIR604. This authorisation was granted in 2009 (2009/866/EC).[1] Since import and processing authorisations remain valid for a period of 10 years, the applicant filed an application for the renewal of the authorisation granted in 2009. The application contains amongst others monitoring reports, an updated molecular characterisation and an updated literature search.

2. Previous COGEM advices

In 2005 COGEM advised positively on the import and processing of maize MIR604.[2] COGEM also advised positively on the import and processing of several stacked events including DP4114xMON810xMIR604xNK603 and Bt11xMIR162xMIR604xMON89034x5307xGA21.[3,4]

3. Environmental risk assessment

Potential environmental risks of GM maize MIR604 are assessed as part of the environmental risk assessment carried out by COGEM.

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 probably highly limited but cannot be excluded.[7]

Recently, the wild relative of maize, teosinte was detected in Spain[8,9,10] and France.[11,12] In these countries, it is present as a weed in some arable fields. In the Netherlands, teosinte is absent in maize fields and in nature.[13] Hybridisation of GM maize with other species than teosine, cannot occur.

Maize requires warm conditions in order to grow.[7,14] In cultivation areas with warm climatic conditions, the appearance of volunteers can occur the year following maize cultivation due to spilled cobs or kernels. However, these volunteers are usually killed by common mechanical pre-planting soil preparation practices.[7] Maize does not tolerate prolonged cold and frost. In the Netherlands, any volunteers emerging in or outside maize fields will be killed by frost at the onset of winter.[13]

Maize is very sensitive to weed competition.[15] 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.[16] Maize lacks all these characteristics. After ripening, the seeds (the kernels) adhere to the cob and do not shatter naturally.[7,17] Consequently, seed dispersal is severely hampered.

During field observations in Austria some volunteers and maize plants were observed in non-agricultural habitats.[18] In the Netherlands, the appearance of volunteers is very rare, although maize plants occasionally have been observed outside agricultural fields.[19] COGEM is not aware of any reports of feral maize populations in the Netherlands or elsewhere in Europe.

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

3.2 Description of the introduced genes, traits and regulatory elements

MIR604 was developed using *Agrobacterium tumefaciens* mediated transformation. A description of the inserted genetic elements is listed in the table below. The list is limited to information on the introduced genes, corresponding traits, and regulatory elements (promotors and terminators).

Introduced genes	Encoded proteins	Traits	Regulatory elements
mcry3A	Variant of the Cry3A protein derived from *Bacillus thuringiensis* subsp. *tenebrionis*[20,21,22]	Resistance against certain coleopteran insects	Metallothionein-like (*mtl*) promoter from *Zea mays* and nopaline synthase (*nos*) terminator from *Agrobacterium tumefaciens*
mir604pmi, also known as *manA*	Variant of phosphomannose isomerase (MIR604PMI) enzyme derived from *Escherichia coli* strain K12[23]	Enables transformed plant cells to use mannose as a sole carbon source	Polyubiquitin promoter and intron (Zm*Ubi*Int) from *Z. mays* and nopaline synthase (*nos*) terminator from *A. tumefaciens*
See references for a detailed description of the trait			

3.3 Updated bioinformatics analyses

The COGEM notes that the insert was not resequenced in the current application. However, the sequence of the event MIR604 has recently been confirmed in multiple stacked lines.

The bioinformatics analyses have been reconducted using updated databases. Using the original sequence and recent databases, the applicant updated the bioinformatics analyses of the inserted element and the sequences spanning the 5' and 3' junctions of the insert and its flanking regions. The sequences spanning the insertion site at the 5' and 3' flanking regions and the entire insert were screened to identify all open reading frames (ORFs) between stop codons. According to the applicant, no essential endogenous genes were disrupted at the insertion sites and the putative products of the ORFs did not generate any protein sequence similarities with known allergens or toxins. According to the applicant no new elements that would invalidate the conclusions of the initial risk assessment were identified.

Considering the above, COGEM is of the opinion that the molecular characterisation of maize MIR604 has been performed correctly and meets the requirements of COGEM.

Conclusion: The bioinformatics analyses of GM maize MIR604 has been updated and is adequate.

3.4 Annual monitoring reports and literature review

The applicant supplied annual reports on the monitoring carried out between 2009 and 2017. Monitoring was performed by operators involved in the import, handling and processing of viable maize MIR604 i.e., COCERAL, UNISTOCK and FEDIOL. As part of the monitoring reports, the applicant performed a yearly review of scientific publications to monitor the safety of maize MIR604. In addition, the applicant performed a review of the scientific literature published in the scientific literature and studies performed by the applicant within the period of 10 years prior to the

date of submission of this renewal application (since January 2007). The monitoring reports, the scientific publications and the safety studies performed by the applicant contained no indications of adverse effects or incidents.

Conclusion: The information in the annual monitoring reports, the literature review and safety studies performed by the applicant do not contain any indication of potential environmental risks or incidents resulting from import and/or processing of maize MIR604.

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, RIKILT carries out a food and/or feed assessment for Regulation (EC) 1829/2003 applications. The outcome of the assessment by other organisations (EFSA, RIKILT) was not known when this advice was completed.

5. Post-market environmental monitoring (PMEM)

The applicant supplied a new post-market environmental monitoring (PMEM) plan. COGEM has published several recommendations for further improvement of the general surveillance (GS) plan[24,25] but considers the current GS plan adequate for import and processing of maize MIR604.

6. Overall conclusion

COGEM is of the opinion that import and processing of maize MIR604 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

1. European Commission (2009). Commission Decision of 30 November 2009 authorising the placing on the market of products containing, consisting of, or produced from genetically modified maize MIR604 (SYN-IR6Ø4-5) pursuant to Regulation (EC) No 1829/2003 of the European Parliament and of the Council authorising the placing on the market of products containing, consisting of, or produced from genetically modified soybean A2704-12 (ACS-GMØØ5-3) pursuant to Regulation (EC) No 1829/2003 of the European Parliament and of the Council. Official Journal of the European Union 1.12.2009 L 314/102
2. COGEM (2005). Import and processing of maize variety MIR604 (EFSA/GMO/UK/2005/11) COGEM advice CGM/051122-02
3. COGEM (2018). Import and processing of genetically modified maize DP4114xMON810xMIR604xNK603 and sub-combinations. COGEM advice CGM/181019-01

4. COGEM (2018). Import and processing of genetically modified maize Bt11xMIR162xMIR604xMON89034x5307xGA21and sub-combinations. COGEM advice CGM/180924-01
5. Hin CJA (2001). Landbouwkundige risico's van uitkruising van GGO-gewassen. Centrum voor Landbouw en Milieu (CLM) [In Dutch]
6. Treu R & Emberlin J (2000). Pollen dispersal in the crops Maize (*Zea mays*), Oil Seed Rape (*Brassica napus* ssp. *oleifera*), Potatoes (*Solanum tuberosum*), Sugar Beet (*Beta vulgaris* ssp. *vulgaris*) and Wheat (*Triticum aestivum*). Evidence from Publications. Soil Association
7. Andersson M & Carmen de Vicente M (2010). Gene flow between crops and their wild relatives. The John Hopkins University Press, Baltimore, Maryland, The United States of America
8. Pardo G *et al.* (2014). El Teosinte (*Zea mays*, spp.). Cent. Sanid. y Certificación Veg. DGA [in Spanish]
9. Pardo G *et al.* (2015). Presencia de teosinte (*Zea* spp.) como mala hierba en los regadíos del valle del Ebro. XV Congr. la Soc. Española Malherbología La Malherbología y la Transf. tecnológica Sevilla, 417-424 [In Spanish]
10. Pardo G *et al.* (2016). El teosinte: descripción, situación actual en el valle del Ebro y resultados de los primeros ensayos. Vida Rural.408: 42-47 [In Spanish]
11. Agri79 (2013). Téosinte - La téosinte exige une vigilance toute particulière. http://agri79.reussir.fr/public/index.php?a=article&codeArticle=JFNK3KKU (visited: November 2nd2018) [In French]
12. Trtikova M *et al.* (2017). Teosinte in Europe - Searching for the origin of a novel weed. Sci. Rep. 7: 1560. doi: 10.1038/s41598-017-01478-w
13. Huiting HF *et al.* (2018). Are teosinte and feral maize present in the Netherlands? COGEM report CGM 2018-06
14. Miedema P (1982). The effect of low temperature on *Zea mays*. Advances in Agronomy 35: 93-128
15. CAB International (2007). Crop Protection Compendium. *Zea mays* (maize). CD-ROM edition, Wallingford
16. Kos SP *et al.* (2012). Can transgenic crops go wild? A literature study on using plant traits for weediness pre-screening. COGEM research report CGM 2012-01
17. Organisation for Economic Cooperation and Development (OECD) (2003). Consensus document on the biology of *Zea mays* ssp. *mays* (Maize)
18. Pascher K (2016). Spread of volunteer and feral maize plants in Central Europe: recent data from Austria. Environ. Sci. Eur. 28: 30
19. van de Wiel CCM *et al.* (2011). Crop volunteers and climate change. Effects of future climate change on the occurrence of Maize, Sugar Beet and Potato volunteers in the Netherlands. COGEM research report 2011-11
20. Murray EE *et al.* (1989). Codon usage in plant genes. Nucleic Acids Res. 17: 477-498
21. Sekar V *et al.* (1987). Molecular cloning and characterization of the insecticidal crystal protein gene of *Bacillus thuringiensis* var. *tenebrionis*. PNAS 84: 7036-7040
22. Chen E & Stacy C (2007). Modified Cry3A toxins. Syngenta Participations Ag, assignee. U.S. Patent No. 72, 76, 583. Washington, DC: U.S. Patent Office

23. Negrotto M *et al.* (2000). The use of phosphomannose-isomerase as a selectable marker to recover transgenic maize plants (*Zea mays* L.) via Agrobacterium transformation. Plant Cell Reports 19: 798-803
24. COGEM (2010). General Surveillance. COGEM report CGM/100226-01
25. COGEM (2015). Advice on improving the general surveillance of GM crops. COGEM advice CGM/150601-02