# Assessment of the safety of genetically modified MIR162 maize for renewal of authorisation under assimilated Regulation (EC) No. 1829/2003

## Reference number RP652


**Risk Assessment Unit**

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**Regulated Product Dossier Assessment**


**Assessment finalised: 05/04/2024**

# Contents

# Abbreviations

| Acronym | Definition |
|---|---|
| ACNFP | Advisory Committee on Novel Foods and Processes |
| ACRE | Advisory Committee on Releases to the Environment |
| DNA | Deoxyribonucleic acid |
| EC | European Commission |
| EFSA | European Food Safety Authority |
| EU | European Union |
| FSA | Food Standards Agency |
| FSS | Food Standard Scotland |
| GM | Genetically modified |
| GMO | Genetically modified organism |
| ORFs | Open reading frames |
| PMEM | Post-market environmental monitoring |

# Summary

Following the submission of application RP652 to the Food Standards Agency (FSA) under assimilated Regulation (EC) No. 1829/2003 from Syngenta Crop Protection NV/SA, represented by Syngenta Limited (Bracknell, UK), FSA/FSS (Food Standards Scotland) have undertaken a safety assessment on genetically modified MIR162 maize. To support the safety assessment by FSA/FSS, the Advisory Committee on Novel Foods and (ACNFP) provided advice to FSA/FSS on the data submitted for the renewal of authorisation for the genetically modified maize MIR162, as outlined in this document. The advice of the ACNFP has been taken into account in this safety assessment which represents the opinion of FSA/FSS on the safety of genetically modified MIR162 maize.

MIR162 maize is modified to express the Vip3a20 and PMI proteins; Vip3Aa20 – a variant of a protein from the soil bacterium *Bacillus thurigiensis* – is an insecticidal protein, active against certain lepidopteran pests of maize, including *Spodoptera frugiperda* (Fall armyworm) and *Helicoverpa zea* (Corn earworm). PMI (phosphomannose isomerase – from *E. coli* strain K-12) catalyses the reversible interconversion of mannose and fructose, and enables the plant to use mannose as a primary carbon source. It is used as a selectable marker in the development of MIR162 maize.

MIR162 maize has previously been authorised for food and feed uses and is most commonly used as animal feed. The scope of this application is for the renewal of the authorisation for placing on the market of food and feed products containing, consisting of, or produced from genetically modified MIR162 maize. This also includes products other than food or feed. The application does not cover cultivation and therefore no MIR162 maize will be grown in the UK.

In providing its advice on the safety of MIR162 maize for food and feed, the ACNFP considered data provided as part of application RP652 (post-market environmental monitoring reports, evaluation of systematic literature searches, additional studies performed by or on behalf of the applicant, and updated

bioinformatics analyses), additional information provided by the applicant, and analyses and reports from outside contractors. The ACNFP assessed these data for possible new hazards, modified exposures, or new scientific uncertainties identified during the authorisation period and not previously assessed in the context of the original application (EFSA GMO Panel 2012).

FSA/FSS concludes, based on ACNFP advice, that there is no evidence in the renewal application RP652 for new hazards, modified exposures, or new scientific uncertainties that would change the conclusions of the original risk assessment on genetically modified maize MIR162 (EFSA GMO Panel 2012).

# 1. Introduction

## 1.1 Background

On 11th March 2021, the Food Standards Agency (FSA) received application RP652 for the renewal of the authorisation of genetically modified maize MIR162 (unique identifier: SYN-IR162-4), submitted by Syngenta Crop Protection (hereafter referred to as "the applicant") according to Regulation (EC) No. 1829/2003, as assimilated into UK law.

FSA checked the application for compliance with the relevant requirements of Regulation (EC) No. 1829/2003, and assimilated Regulation (EU) No. 503/2013, and on 24th March 2021, declared the application valid.

Following the submission of application EFSA-GMO-DE-2010-82, and the publication of the EFSA (European Food Safety Authority) scientific opinion (EFSA GMO Panel 2012), the placing on the market of genetically modified maize MIR162 for products containing, consisting of, or produced from maize MIR162, excluding cultivation in the EU, was authorised by Commission Implementing Decision 2012/651/EU. A copy of Commission Implementing Decision 2012/651/EU was provided by the applicant.

FSA and FSS would like to thank the following members of the Advisory Committee on Novel Foods and Processes (ACNFP) who participated in the assessment: Dr Camilla Alexander White, Dr Andy Greenfield, Dr Anton Alldrick, Alison Austin, Dr Mark Berry, Prof Dimitris Charalampopoulos, Prof Susan Fairweather-Tait, Prof Paul Fraser, Dr Hamid Ghouddusi, Prof Wendy Harwood, Prof Huw Jones, Dr Ray Kemp, Dr Elizabeth Lund, Emeritus Prof Harry McArdle, Rebecca McKenzie, Prof Clare Mills, Dr Lesley Stanley, Prof Hans Verhagen, Dr Maureen Wakefield, Prof Bruce Whitelaw, and Emeritus Professor Pete Lund (co-opted member of ACNFP-PGT Subcommittee).

## 1.2 Terms of Reference

According to Articles 6 and 18 of assimilated Regulation (EC) No. 1829/2003, FSA/FSS were requested to carry out a scientific risk assessment of genetically modified maize MIR162 for the renewal of authorisation for placing on the market of products containing, consisting of, or produced from maize MIR162 in the context of its scope as defined in application RP652.

FSA/FSS sought safety advice from the ACNFP on genetically modified MIR162 maize, which will inform the FSA/FSS safety assessment. The FSA/FSS safety assessment is to be seen as the report requested under Articles 6(6) and 18(6) of that Regulation.

In addition to the present advice on the safety of genetically modified maize MIR162, the ACNFP were also asked to advise on the particulars listed under Articles 6(5) and 18(5) of assimilated Regulation (EC) No. 1829/2003. These articles concern details that must be included in positive opinions/outcomes of assessment of GMO foods and feeds, including labelling details, any relevant conditions or restrictions, and monitoring plans.

# 2. Applicant details

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(represented by)

Name: Syngenta Limited

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# 3. Data and methodologies

## 3.1 Data

The data for application RP652 submitted according to assimilated Regulation (EC) No. 1829/2003 and provided by the applicant at the time of submission are specified below. To inform the FSA/FSS safety assessment for the renewal of the authorisation of genetically modified maize MIR162 for food and feed uses in accordance with Articles 11 and 23 of Regulation (EC) No. 1829/2003, the ACNFP was asked to provide safety advice. It considered the requirements described in applicable guidance for the risk assessment of renewal applications of GM food and feed authorised under assimilated Regulation (EC) No. 1829/2003 and based its scientific safety assessment on the data within application RP652, additional

information provided by the applicant, and any relevant peer-reviewed scientific publications.

## 3.2 Methodologies

The ACNFP conducted its assessment in accordance with the principles described in assimilated Regulation (EU) No. 503/2013, applicable guidance, explanatory notes, and statements (EFSA GMO Panel, 2015; EFSA, 2019). Independent contractors performed preparatory work and delivered reports on the methods applied by the applicant in performing sequencing and bioinformatics analyses.

# 4. Assessment

## 4.1 Post-market environmental monitoring reports

The implementation of a PMEM (post-market environmental monitoring) plan was a condition of the authorisation, however since the previous environmental risk assessment of genetically modified maize MIR162 identified no potential adverse environmental effects, and the application did not cover cultivation, case-specific post-market environmental monitoring was not required.

The assessment of the PMEM reports provided in the renewal application are within the remit of the Advisory Committee on Releases to the Environment (ACRE), and their assessment of the PMEM reports forms part of the final scientific assessment published by FSA/FSS.

## 4.2 Systematic searches and evaluation of literature

A systematic literature search and review is required for renewal applications to identify new information relevant to the risk assessment of the GM food and feed that has become available since the previous authorisation. This includes

information relating to molecular characterisation, food and feed safety, and the environment.

In addition to the separate searches provided as part of the annual PMEM reports, the applicant also performed updated literature searches covering 2010 to 2020, in accordance with the recommendations on literature searches outlined in EFSA's explanatory note on literature searching (2010, 2019). Searches in electronic bibliographic databases and in websites of relevant organisations were also performed.

Altogether, 41 publications were identified as relevant (from 2852 publication identified after removal of duplicates), however none of these publications suggested that maize MIR162, or the expression of the newly expressed proteins (Vip3Aa20 and PMI), are likely to pose a risk to human and animal health, and the environment.

The ACNFP assessed the applicant's literature searches on genetically modified maize MIR162 and the newly expressed protein and found the overall quality of the performed literature searches to be acceptable.

The ACNFP acknowledged that no relevant publications raising a safety concern for human and animal health and the environment which would change the original risk assessment conclusions on maize MIR162 were identified by the applicant.

## 4.3 Updated bioinformatic data

The bioinformatics assessment of renewal applications for GM food and feed is focused on demonstrating that the conclusions of the original risk assessment remain applicable when considering the information from up-to-date methods of bioinformatics analysis. This includes analysis of the DNA sequence of the insertion site and flanking sequences to identify:

- disruption of endogenous genes

- open reading frames (ORFs) that potentially encode peptides with amino acid sequences similar to known toxins or allergenic proteins
- Similarity to microbial DNA sequences that may facilitate horizontal gene transfer

The amino acid sequence of the newly expressed protein(s) is also assessed, including for sequence similarity to known toxins and allergenic proteins, and their capacity to trigger coeliac disease.

An updated sequence analysis was performed to compare the DNA sequence of the MIR162 event (both insert and flanking sequences) to previously determined sequences for the MIR162 event. The DNA sequences of the insert and flanking DNA regions found a single nucleotide deletion in a promoter (which drives transcription of the *pmi* gene). Bioinformatics analysis of this deletion found no change in the safety assessment of MIR162 maize.

The updated bioinformatics analyses for the MIR162 event also found no DNA sequences able to promote homologous recombination between the MIR162 insert and micro-organisms.

The updated bioinformatics analyses found no interruption of endogenous maize genes at the insertion site. The updated bioinformatics analyses of the newly created ORFs within the insert, or spanning the junctions with the genomic DNA, did not indicate sequence similarities to toxins or allergens, nor did analysis of the coding frames of the MIR162 insert. In addition, the amino acid sequence of the newly expressed proteins did not have significant similarities with proteins known to cause coeliac disease.

The ACNFP reviewed the updated bioinformatics data and analyses provided by the applicant as part of the risk assessment process and concluded that the bioinformatics analyses performed using updated methodologies and tools identified no new information that would change the conclusions on the safety of MIR162 maize or change the parameters of the previous authorisation.

## 4.4 Additional documents or studies provided by the applicant

The applicant stated that no adverse effect reports from operators handling genetically modified maize MIR162 have been received, and no prohibitions or restrictions have been placed on MIR162 maize in any country.

Unpublished studies produced, controlled, or sponsored by, or on behalf of, the applicant, since genetically modified maize MIR162 was authorised were reviewed, and the relevance of the studies for molecular characterisation, human and animal safety, and the environment, was assessed by the applicant.

The ACNFP concluded that the new additional documents or studies provided by the applicant do not raise any concerns for human and animal health, and do not change the original risk assessment conclusions on genetically modified maize MIR162.

## 4.5 Overall assessment as provided by the applicant

The applicant provided an overall assessment concluding that the results of the monitoring reports and of the new information provided in the application for renewal of authorisation of genetically modified maize MIR162 for food and feed uses does not lead to the identification of new hazards, modified exposures, or uncertainties, and therefore does not change the outcome of the original risk assessment or the conditions set out in the original authorisation.

The ACNFP evaluated the overall assessment provided by the applicant and confirmed that there is no evidence in the renewal application that would indicate new hazards, relevant changes in exposure, or scientific uncertainties that would change the previous conclusions on genetically modified maize MIR162.

### 4.6 Environmental monitoring plan and proposal for improving the conditions of the original authorisation

The post-market environmental monitoring plan does not need revision as no adverse effects were reported during the authorisation period, nor was any literature identified that changes the conclusions of the previous assessment.

ACRE's advice is available on the GOV.UK website.

## 5. Analytical methods

The FSA and FSS have decided, where appropriate, to make use of the European Union Reference Laboratory (EURL) laboratory reports completed prior to the end of the transition period for a GMO for which an application has also now been made to GB.

The FSA and FSS accepted the European Union Reference Laboratory for Genetically Modified Food and Feed (EURL GMFF) report, showing that the detection methods for the single event SYN-IR162-4 were validated.

The methods and validation report are available on the European Commission website.

## 6. Overall conclusions and recommendations

FSA/FSS concluded, based on ACNFP advice, that there is no evidence in renewal application RP652 for new hazards, modified exposure, or scientific uncertainties

that would change the conclusion of the original risk assessment on genetically modified maize MIR162.

# 7. References


Regulation (EC) No. 1829/2003 of the European Parliament and of the Council of 22nd September 2003 on genetically modified food and feed.

Commission Implementing Regulation (EU) No. 503/2013 of 3rd April 2013 on application for authorisation of genetically modified food and feed in accordance with Regulation (EC) No. 1829/2003 of the European Parliament and of the Council and amending Commission Regulations (EUC) No. 641/2004 and (EC) No. 1981/2006.

Commission Implementing Decision (2012/651/EU) of 18 October 2012 authorising the placing on the market of the products containing, consisting of, or produced from genetically modified maize MIR162 (SYN-IR162-4 pursuant to Regulation (EC) No. 1829/2003 of the European Parliament and of the Council. Official Journal of the European Union L 290/14 20/10/2012.

EFSA GMO Panel (EFSA Panel on Genetically Modified Organisms), 2012. Scientific Opinion on application (EFSA-GMO-DE-2010-82) for the placing on the market of insect resistant genetically modified maize MIR162 for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Syngenta. EFSA Journal 2012;10(6): [27 pp.]. https://doi.org/10.2903/j.efsa.2012.2756. Available online: www.efsa.europa.eu/efsajournal.html

EFSA GMO Panel (EFSA Panel on Genetically Modified Organisms), 2015. Guidance for renewal applications of genetically modified food and feed authorised under Regulation (EC) No 1829/2003. EFSA Journal 2015;13(6):4129, 8 pp. https://doi.org/10.2903/j.efsa.2015.4129.

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EFSA (European Food Safety Authority), Devos Y, Guajardo IM, Alvarez F and Glanville J, 2019. Explanatory note on literature searching conducted in the context of GMO applications for (renewed) market authorisation and annual post-market environmental monitoring reports on GMOs authorised in the EU market. EFSA supporting publications 2019:EN-1614. 62 pp. https://doi.org/10.2903/sp.efsa.2019.EN-1614.