

ADOPTED: 1 September 2022

doi: 10.2903/j.efsa.2022.7562

Assessment of genetically modified maize MIR162 for renewal authorisation under Regulation (EC) No 1829/2003 (application EFSA-GMO-RX-025)

EFSA Panel on Genetically Modified Organisms (GMO),
Ewen Mullins, Jean-Louis Bresson, Tamas Dalmay, Ian Crawford Dewhurst,
Michelle M Epstein, Leslie George Firbank, Philippe Guerche, Jan Hejatko,
Francisco Javier Moreno, Hanspeter Naegeli, Fabien Nogué, Nils Rostoks,
Jose Juan Sánchez Serrano, Giovanni Savoini, Eve Veromann, Fabio Veronesi,
Ana Martín Camargo, Tilemachos Goumperis, Dafni Maria Kagkli, Paolo Lenzi,
Aleksandra Lewandowska, Tommaso Raffaello and Franz Streissl

Abstract

Following the submission of application EFSA-GMO-RX-025 under Regulation (EC) No 1829/2003 from Syngenta Crop Protection NV/SA, the Panel on Genetically Modified Organisms of the European Food Safety Authority was asked to deliver a scientific risk assessment on the data submitted in the context of the renewal of authorisation application for the insect-resistant genetically modified maize MIR162, for food and feed uses, excluding cultivation within the EU. The data received in the context of this renewal application contained post-market environmental monitoring reports, a systematic search and evaluation of literature, updated bioinformatic analyses, and additional documents or studies performed by or on behalf of the applicant. The GMO Panel assessed these data for possible new hazards, modified exposure or new scientific uncertainties identified during the authorisation period and not previously assessed in the context of the original application. The GMO Panel concludes that there is no evidence in renewal application EFSA-GMO-RX-025 for new hazards, modified exposure or scientific uncertainties that would change the conclusions of the original risk assessment on maize MIR162.

© 2022 Wiley-VCH Verlag GmbH & Co. KGaA on behalf of the European Food Safety Authority.

Keywords: maize, MIR162, renewal, Articles 11 and 23, Regulation (EC) No 1829/2003

Requestor: European Commission

Question number: EFSA-Q-2021-00122

Correspondence: nif@efsa.europa.eu

Panel members: Ewen Mullins, Jean-Louis Bresson, Tamas Dalmay, Ian Crawford Dewhurst, Michelle M Epstein, Leslie George Firbank, Philippe Guerche, Jan Hejatko, Francisco Javier Moreno, Hanspeter Naegeli, Fabien Nogué, Nils Rostoks, Jose Juan Sánchez Serrano, Giovanni Savoini, Eve Veromann and Fabio Veronesi.

Declarations of interest: If you wish to access the declaration of interests of any expert contributing to an EFSA scientific assessment, please contact interestmanagement@efsa.europa.eu.

Acknowledgements: The Panel wishes to thank the members of its standing Working Groups on Molecular Characterization, Food/Feed and Environmental Risk Assessment for the preparatory work on this scientific opinion, and the EFSA staff members Michele Ardizzone, Giuseppe Emanuele Condorelli, Antonio Fernandez Dumont and Pietro Piffanelli for the support provided to this scientific opinion.

Suggested citation: EFSA GMO Panel (EFSA Panel on Genetically Modified Organisms), Mullins E, Bresson J-L, Dalmay T, Dewhurst IC, Epstein MM, Firbank LG, Guerche P, Hejatko J, Moreno FJ, Naegeli H, Nogué F, Rostoks N, Sánchez Serrano JJ, Savoini G, Veromann E, Veronesi F, Camargo AM, Goumperis T, Kagkli DM, Lenzi P, Lewandowska A, Raffaello T and Streissl F, 2022. Scientific Opinion on the assessment of genetically modified maize MIR162 for renewal authorisation under Regulation (EC) No 1829/2003 (application EFSA-GMO-RX-025). EFSA Journal 2022;20(9):7562, 13 pp. <https://doi.org/10.2903/j.efsa.2022.7562>

ISSN: 1831-4732

© 2022 Wiley-VCH Verlag GmbH & Co. KGaA on behalf of the European Food Safety Authority.

This is an open access article under the terms of the [Creative Commons Attribution-NoDerivs](https://creativecommons.org/licenses/by/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited and no modifications or adaptations are made.



The EFSA Journal is a publication of the European Food Safety Authority, a European agency funded by the European Union.



Summary

Following the submission of application EFSA-GMO-RX-025 under Regulation (EC) No 1829/2003 from Syngenta Crop Protection NV/SA, the Panel on Genetically Modified Organisms of the European Food Safety Authority (GMO Panel) was asked to deliver a scientific risk assessment on the data submitted in the context of the renewal of authorisation application for the insect-resistant genetically modified maize MIR162. The scope of the renewal application EFSA-GMO-RX-025 is for the renewal of the placing on the market of products containing, consisting of, or produced from maize MIR162, excluding cultivation within the European Union (EU).

In delivering its scientific opinion, the GMO Panel took into account application EFSA-GMO-RX-025, additional information provided by the applicant, scientific comments submitted by the EU Member States and relevant scientific publications. The data received in the context of the renewal application EFSA-GMO-RX-025 contained: post-market environmental monitoring reports, an evaluation of the literature retrieved by a systematic search, additional studies performed by or on behalf of the applicant and updated bioinformatics analyses. The GMO Panel assessed these data for possible new hazards, modified exposure or new scientific uncertainties identified during the authorisation period and not previously assessed in the context of the original application.

The GMO Panel concludes that there is no evidence in the renewal application EFSA-GMO-RX-025 for new hazards, modified exposure or scientific uncertainties that would change the conclusions of the original risk assessment on maize MIR162 (EFSA, 2012).

Table of contents

Abstract.....	1
Summary.....	3
1. Introduction.....	5
1.1. Background	5
1.2. Terms of Reference as provided by the requestor	5
2. Data and methodologies	6
2.1. Data.....	6
2.1.1. Post-market monitoring reports	6
2.1.2. Systematic search and evaluation of literature	6
2.1.3. Updated bioinformatic data	6
2.1.4. Additional documents or studies provided by the applicant	7
2.1.5. Overall assessment as provided by the applicant	7
2.1.6. Monitoring plan and proposal for improving the conditions of the original authorisation	7
2.2. Methodologies.....	7
3. Assessment.....	7
3.1. Evaluation of the post-market monitoring reports	7
3.2. Evaluation of the systematic search and evaluation of literature.....	7
3.3. Evaluation of the updated bioinformatic data.....	7
3.4. Evaluation of the additional documents or studies provided by the applicant.....	8
3.5. Evaluation of the overall assessment as provided by the applicant	8
3.6. Evaluation of the monitoring plan and proposal for improving the conditions of the original authorisation.....	8
4. Conclusions.....	8
5. Documentation as provided to EFSA	8
References.....	9
Abbreviations.....	9
Appendix A – List of relevant publications identified by the applicant through systematic literature searches (January 2010–February 2022).....	10
Appendix B – List of additional studies performed by or on behalf of the applicant over the course of the authorisation period and not previously submitted to the EU with regard to the evaluation of the safety of the food and feed for humans, animal or the environment from maize MIR162	13

1. Introduction

1.1. Background

On 26 February 2021, the European Food Safety Authority (EFSA) received from the European Commission (EC) application EFSA-GMO-RX-025 for the renewal of the authorisation of maize MIR162 (Unique Identifier SYN-IR162-4), submitted by Syngenta Crop Protection NV/SA (hereafter referred to as 'the applicant') according to Regulation (EC) No 1829/2003¹.

Following receipt of application EFSA-GMO-RX-025, EFSA informed the Member States (MS) and made the summary of the application available to the public on the EFSA website.²

EFSA checked the application for compliance with the relevant requirements of Regulation (EC) No 1829/2003 and Regulation (EU) No 503/2013³ and, when needed, asked the applicant to supplement the initial application. On 16 July 2021, EFSA declared the application valid and made the valid application available to the MS and the EC.

Following the submission of application EFSA-GMO-DE-2010-82 and the publication of the EFSA scientific opinion (EFSA, 2012), the placing on the market of maize MIR162 for products containing, consisting of, or produced from this GM maize, excluding cultivation in the EU, was authorised by Commission Implementing Decision 2012/651/EU⁴ and Commission Implementing Decision (EU) 2019/60 amending Decision 2009/866/EC, Decision 2010/419/EU, Implementing Decision 2012/651/EU and Implementing Decision (EU) 2016/1685⁵. Copies of these authorisations were provided by the applicant.⁶

From the validity date, EFSA and its scientific Panel on Genetically Modified Organisms (hereafter referred to as 'the GMO Panel') endeavoured to respect a time limit of 6 months to issue a scientific opinion on application EFSA-GMO-RX-025. Such time limit was extended whenever EFSA and/or its GMO Panel requested supplementary information to the applicant. According to Regulation (EC) No 1829/2003, any supplementary information provided by the applicant during the risk assessment was made available to the MS and EC (for further details, see the section 'Documentation', below).

In accordance with Regulation (EC) No 1829/2003, EFSA consulted the nominated risk assessment bodies of the MS, including national Competent Authorities within the meaning of Directive 2001/18/EC⁷. The MS had 3 months to make their opinion known on application EFSA-GMO-RX-025 as of the date of validity.

1.2. Terms of Reference as provided by the requestor

According to Articles 6 and 18 of Regulation (EC) No 1829/2003, EFSA and its GMO Panel were requested to carry out a scientific risk assessment of maize MIR162 for the renewal of authorization for placing on the market of products containing, consisting of, or produced from GM maize MIR162 in the context of its scope as defined in application EFSA-GMO-RX-025.

According to Regulation (EC) No 1829/2003, this scientific opinion is to be seen as the report requested under Articles 6(6) and 18(6) of that Regulation including the opinions of the nominated risk assessment bodies of the MS.⁸

In addition to the present scientific opinion on maize MIR162, EFSA and its GMO Panel were also asked to report on the particulars listed under Articles 6(5) and 18(5) of Regulation (EC) No 1829/2003.

¹ Regulation (EC) No 1829/2003 of the European Parliament and of the Council of 22 September 2003 on genetically modified food and feed. OJ L 268, 18.10.2003, pp. 1–23.

² Available online: <https://open.efsa.europa.eu/questions/EFSA-Q-2021-00122>

³ Commission Implementing Regulation (EU) No 503/2013 of 3 April 2013 on applications 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 (EC) No 641/2004 and (EC) No 1981/2006. OJ L 157, 8.6.2013, pp. 1–48.

⁴ Commission Implementing Decision of 18 October 2012 authorising the placing on the market of 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.

⁵ Commission Implementing Decision (EU) 2019/60 of 11 January 2019 amending Decision 2009/866/EC, Decision 2010/419/EU, Implementing Decision 2012/651/EU and Implementing Decision (EU) 2016/1685 as regards the representative of the authorisation holder. Official Journal of the European Union L 12/31, 15.1.2019.

⁶ Dossier: Maize MIR162 – Annex I.

⁷ Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC. OJ L 106, 12.3.2001, pp. 1–38.

⁸ Opinions of the nominated risk assessment bodies of EU Member States can be found at the Open EFSA Portal <https://open.efsa.europa.eu/questions>, querying the assigned Question Number.

The relevant information is made available in the Open EFSA portal,⁹ including the information required under Annex II to the Cartagena Protocol, a labelling proposal, a post-market environmental monitoring (PMEM) plan as provided by the applicant; the method(s), validated by the Community reference laboratory, for detection, including sampling, identification of the transformation event in the food-feed and/or foods-feeds produced from it and the appropriate reference materials.

2. Data and methodologies

2.1. Data

The data for application EFSA-GMO-RX-025 submitted according to EFSA requirements (EFSA GMO Panel, 2015; EFSA, 2019a) and provided by the applicant at the time of submission, or in reply to requests for additional information, are specified below.

In the frame of the contracts OC/EFSA/GMO/2020/01 and OC/EFSA/GMO/2018/04, contractors performed preparatory work and delivered reports on the methods applied by the applicant in performing sequencing and literature search, respectively.

2.1.1. Post-market monitoring reports¹⁰

Based on the outcome of the initial food and feed risk assessment, a post-market monitoring plan for monitoring of GM food and feed was not required by the authorisation decision. The implementation of a PMEM plan, consisting of a general surveillance plan to check for any adverse effects on the environment arising from maize MIR162, was a condition for the authorisation. As no potential adverse environmental effects were identified in the environmental risk assessment of maize MIR162 (EFSA, 2012), case-specific monitoring was not considered necessary by the GMO Panel.

The applicant provided nine annual PMEM reports covering a reporting period from October 2012 to June 2021. The annual PMEM plans submitted by the applicant included (1) commodity crop (GM and non GM) imports into the EU by country of origin and destination; (2) the description of a centralised system managed by EuropaBio¹¹ for the collection of information recorded by various operators (federations involved in maize grains import, storage and processing) on any observed adverse effect(s) on human health and the environment arising from handling of maize possibly containing maize MIR162; (3) the reports of the surveillance activities conducted by such operators; and (4) the review of relevant scientific peer-reviewed studies retrieved from literature searches.

2.1.2. Systematic search and evaluation of literature¹²

In addition to the separate searches provided as part of the annual PMEM reports, the applicant performed two systematic literature searches covering the period from January 2010 until February 2022, in accordance with the recommendations on literature search outlined in EFSA (2010, 2019b).

Searches in electronic bibliographic databases and in websites of relevant organisations were performed to identify relevant publications. Altogether 3,411 publications were identified (after removal of duplicates). After applying the eligibility/inclusion criteria defined a priori by the applicant, 50 peer-reviewed and non-peer-reviewed publications were identified as relevant for food and feed safety assessment or molecular characterisation. The relevant publications are listed in Appendix A.

2.1.3. Updated bioinformatic data¹³

At the time of submission of the renewal dossier, the applicant provided a complete bioinformatic data set for maize MIR162 event including an analysis of the insert and flanking sequences, an analysis of the potential similarity to allergens and toxins of the newly expressed protein and of all possible open reading frames (ORFs) within the insert and spanning the junction sites, an analysis of possible horizontal gene transfer (EFSA, 2017), and a safety assessment of the newly expressed proteins VIP3Aa20 and PMI regarding their capacity to trigger celiac disease (EFSA GMO Panel, 2017). The outcome of the updated bioinformatic analyses is presented in Section 3.3.

⁹ Available online: <https://open.efsa.europa.eu/questions/EFSA-Q-2021-00122>

¹⁰ Dossier: Maize MIR162 – Annex II; additional information: 28/4/2022.

¹¹ The responsibilities of EuropaBio in coordinating activities of technology providers on the post-market environmental monitoring of GM crops were taken over by CropLife Europe as of 1 January 2021.

¹² Dossier: Maize MIR162 – Annex III; additional information: 28/4/2022.

¹³ Dossier: Maize MIR162 – Annex III; additional information: 11/10/2021, 28/4/2022, 19/7/2022.

2.1.4. Additional documents or studies provided by the applicant¹⁴

In line with the renewal guidance requirements (EFSA GMO Panel, 2015; EFSA, 2019a), the applicant provided an overview on the worldwide approvals of maize MIR162 and searched for any available full reports of studies performed by or on behalf of the applicant over the course of the authorisation period and not previously submitted to the EU (Appendix B).

The relevance of the listed studies for molecular characterisation, human and animal safety and the environment was assessed by the applicant.

2.1.5. Overall assessment as provided by the applicant¹⁵

The applicant provided an overall assessment concluding that information provided in the application for renewal of authorisation of maize MIR162 for food and feed uses in the EU does not change the outcome of the original risk assessment (EFSA, 2012).

2.1.6. Monitoring plan and proposal for improving the conditions of the original authorisation¹⁶

The applicant indicated in the dossier that the environmental post-market monitoring plan is appropriate and does not need any changes.

2.2. Methodologies

The GMO Panel assessed the application for renewal of the authorisation of maize MIR162 for food and feed uses in accordance with Articles 11 and 23 of Regulation (EC) No 1829/2003. The GMO Panel took into account the requirements described in its guideline for the risk assessment of renewal applications of GM food and feed authorised under Regulation (EC) No 1829/2003 (EFSA GMO Panel, 2015). The comments raised by the nominated risk assessment bodies of EU Member States were taken into consideration during the scientific risk assessment.

3. Assessment

3.1. Evaluation of the post-market monitoring reports

During the general surveillance activities covering the authorisation period of maize MIR162, no adverse effects were reported by the applicant.

3.2. Evaluation of the systematic search and evaluation of literature

The GMO Panel assessed the applicant's literature searches on maize MIR162 and the newly expressed proteins VIP3Aa20 and PMI. The overall quality of the performed literature searches is acceptable.

The GMO Panel acknowledges that no publications raising a safety concern for human and animal health and the environment which would change the original risk assessment conclusions on maize MIR162 (EFSA, 2012) have been identified by the applicant.

3.3. Evaluation of the updated bioinformatic data

The results of the updated bioinformatic analyses to assess the interruption of maize endogenous genes confirm previous results indicating that no endogenous genes have been interrupted by event MIR162 (EFSA, 2012; EFSA GMO Panel, 2019, 2021).

Analyses of the amino acid sequence of the newly expressed proteins VIP3Aa20 and PMI reveal no significant similarities to toxins, allergens or immunogenic gluten-related epitopes. The updated bioinformatic analyses of the newly created ORFs within the insert do not indicate sequence similarities to toxins or allergens in maize MIR162. In addition, the updated bioinformatic analysis of the newly created ORFs spanning the junctions with genomic DNA confirms previous results which did not indicate sequence similarities to toxins or allergens in maize MIR162 (EFSA, 2012; EFSA GMO Panel, 2019, 2021).

¹⁴ Dossier: Maize MIR162 – Annex III; additional information: 11/10/2021, 28/4/2022.

¹⁵ Dossier: Maize MIR162 – Annex III.

¹⁶ Dossier: Maize MIR162 – Part III – Summary.

The updated bioinformatic analyses for event MIR162 did not reveal any DNA sequence that could provide sufficient length and identity which could facilitate horizontal gene transfer (HGT) by double homologous recombination, confirming previous conclusions (EFSA, 2012; EFSA GMO Panel, 2019, 2021). Given the results of this analysis and that the recombinant DNA in maize MIR162 does not confer selective advantages to microorganisms, the GMO Panel identified no safety concern linked to an unlikely but theoretically possible HGT.

3.4. Evaluation of the additional documents or studies provided by the applicant

The GMO Panel evaluated the full study reports of the additional studies provided, including a new sequencing study (Appendix B). The sequencing data are compliant with the requirements laid down in the EFSA Technical Note on the quality of DNA sequencing for the molecular characterisation of genetically modified plants (EFSA GMO Panel, 2018). The study reports a nucleotide difference in the sequence of the event in recent plant material (year of collection 2018), compared to the sequence of the event in the originally assessed application (EFSA, 2012). The difference is located in a cytosine homopolymer region in the second of the two ZmUbiInt promoters contained in the MIR162 insert (bp 6,770–6,782). The location of the difference suggests that it is due to the technical difficulties with sequencing the homopolymer regions. Bioinformatic analyses identified no risks for human and animal safety related to the nucleotide difference.

Overall, the new additional documents or studies provided by the applicant do not raise any concern for human and animal health and the environment, which would change the original risk assessment conclusions on maize MIR162.

3.5. Evaluation of the overall assessment as provided by the applicant

The GMO Panel evaluated the overall assessment provided by the applicant and confirms that there is no evidence in renewal application EFSA-GMO-RX-025 indicating new hazards, relevant changes in exposure or scientific uncertainties that would change previous conclusions on maize MIR162.

3.6. Evaluation of the monitoring plan and proposal for improving the conditions of the original authorisation

The PMEM plan covers general surveillance of imported GM plant material, including maize MIR162. This general surveillance is coordinated by CropLife Europe and implemented by selected operators (federations involved in maize grains import and processing). In addition, the applicant reviews relevant scientific publications retrieved from literature searches on an annual basis. The GMO Panel is of the opinion that the scope of the plan provided by the applicant is consistent with the scope of application EFSA-GMO-RX-025, but reminds that monitoring is related to risk management, and thus the final adoption and implementation of the PMEM plan falls outside the mandate of EFSA.

4. Conclusions

The GMO Panel concludes that there is no evidence in renewal application EFSA-GMO-RX-025 for new hazards, modified exposure or scientific uncertainties that would change the conclusions of the original risk assessment on maize MIR162 (EFSA, 2012).

5. Documentation as provided to EFSA

- 1) Letter from the European Commission to EFSA received on 26 February 2021 for the continued marketing of genetically modified maize MIR162 submitted in accordance with articles 11 and 23 of Regulation (EC) No 1829/2003 by Syngenta Crop Protection NV/SA (EFSA-GMO-RX-025).
- 2) Application EFSA-GMO-RX-025 validated by EFSA, 16 July 2021.
- 3) Request for supplementary information to the applicant, 11 August 2021.
- 4) Receipt of supplementary information from the applicant, 10 November 2021.
- 5) Request for supplementary information to the applicant, 2 February 2022.
- 6) Receipt of supplementary information from the applicant, 28 April 2022.
- 7) Request for supplementary information to the applicant, 20 May 2022.
- 8) Receipt of supplementary information from the applicant, 19 July 2022.

References

- EFSA (European Food Safety Authority), 2010. Application of systematic review methodology to food and feed safety assessments to support decision making. *EFSA Journal* 2010;8(6):1637, 90 pp. <https://doi.org/10.2903/j.efsa.2010.1637>
- EFSA (European Food Safety Authority), 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. <https://doi.org/10.2903/j.efsa.2012.2756>
- EFSA (European Food Safety Authority), Gennaro A, Gomes A, Herman L, Nogué F, Papadopoulou N and Tebbe C, 2017. Technical report on the explanatory note on DNA sequence similarity searches in the context of the assessment of horizontal gene transfer from plants to microorganisms. EFSA supporting publication 2017:EN-1273, 11 pp. <https://doi.org/10.2903/sp.efsa.2017.EN-1273>
- EFSA (European Food Safety Authority), 2019a. Administrative guidance on the submission of applications for renewal of authorisation of genetically modified food and feed under Articles 11 and 23 of Regulation (EC) No 1829/2003. EFSA supporting publication 2019:EN-1668, 19 pp. <https://doi.org/10.2903/sp.efsa.2019.EN-1668>
- EFSA (European Food Safety Authority), Devos, Y, Guajardo, IM, Álvarez, F and Glanville, J, 2019b. 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;16(4):EN-1614, 62 pp. <https://doi.org/10.2903/sp.efsa.2019.en-1614>
- 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>
- EFSA GMO Panel (EFSA Panel on Genetically Modified Organisms), Naegeli H, Birch AN, Casacuberta J, De Schrijver A, Gralak MA, Guerche P, Jones H, Manachini B, Messean A, Nielsen EE, Nogue F, Robaglia C, Rostoks N, Sweet J, Tebbe C, Visioli F, Wal J-M, Eigenmann P, Epstein M, Hoffmann- Sommergruber K, Koning F, Lovik M, Mills C, Moreno FJ, van Loveren H, Selb R and Fernandez Dumont A, 2017. Guidance on allergenicity assessment of genetically modified plants. *EFSA Journal* 2017;15(5):4862, 49 pp. <https://doi.org/10.2903/j.efsa.2017.4862>
- EFSA GMO Panel (EFSA Panel on Genetically Modified Organisms), Casacuberta J, Nogué F, Naegeli H, Birch AN, De Schrijver A, Gralak MA, Guerche P, Manachini B, Messéan A, Nielsen EE, Robaglia C, Rostoks N, Sweet J, Tebbe C, Visioli F, Wal J-M, Moxon S, Schneeberger K, Federici S, Ramon M, Papadopoulou N and Jones H, 2018. Scientific Opinion on the technical Note on the quality of DNA sequencing for the molecular characterisation of genetically modified plants. *EFSA Journal* 2018;16(7):5345, 11 pp. <https://doi.org/10.2903/j.efsa.2018.5345>
- EFSA GMO Panel (EFSA Panel on Genetically Modified Organisms), Naegeli, H, Bresson, J-L, Dalmay, T, Dewhurst, IC, Epstein, MM, Firbank, LG, Guerche, P, Hejatko, J, Moreno, FJ, Mullins, E, Nogué, F, Rostoks, N, Serrano Sánchez, JJ, Savoini, G, Veromann, E, Veronesi, F, Álvarez, F, Ardizzone, M, De Sanctis, G, Dumont, AF, Gennaro, A, Gómez Ruiz, JÁ, Lanzoni, A, Neri, FM, Papadopoulou, N and Paraskevopoulos, K, 2019. Scientific Opinion on the assessment of genetically modified maize MON 87427 × MON 89034 × MIR162 × MON 87411 and subcombinations, for food and feed uses, under Regulation (EC) No 1829/2003 (application EFSA-GMO-NL-2017-144). *EFSA Journal* 2019;17(11):5848, 33 pp. <https://doi.org/10.2903/j.efsa.2019.5848>
- EFSA GMO Panel (EFSA Panel on Genetically Modified Organisms), Naegeli, H, Bresson, J-L, Dalmay, T, Dewhurst, IC, Epstein, MM, Firbank, LG, Guerche, P, Hejatko, J, Moreno, FJ, Mullins, E, Nogué, F, Rostoks, N, Sánchez Serrano, JJ, Savoini, G, Veromann, E, Veronesi, F, Álvarez, F, Ardizzone, M, De Sanctis, G, Devos, Y, Fernandez, A, Gennaro, A, Gómez Ruiz, JÁ, Lanzoni, A, Neri, FM, Papadopoulou, N, Paraskevopoulos, K and Raffaello, T, 2021. Scientific Opinion on the assessment of genetically modified maize 1507 × MIR162 × MON810 × NK603 and subcombinations, for food and feed uses, under Regulation (EC) No 1829/2003 (application EFSA-GMO-NL-2015-127). *EFSA Journal* 2021;19(1):6348, 40 pp. <https://doi.org/10.2903/j.efsa.2021.6348>

Abbreviations

GM	genetically modified
GMO	genetically modified organism
GMO Panel	EFSA Panel on Genetically Modified Organisms
HGT	horizontal gene transfer
ORFs	open reading frames
PMEM	post-market environmental monitoring
PMI	phosphomannose isomerase
VIP3Aa20	vegetative insecticidal protein (vip3Aa variant)

Appendix A – List of relevant publications identified by the applicant through systematic literature searches (January 2010–February 2022)

References

- Dively GP, Huang F, Oyediran I, Burd T, Morsello S. 2020. Evaluation of gene flow in structured and seed blend refuge systems of non-Bt and Bt corn. *J Pest Sci* 93:439–447.
- Food Standards Australia New Zealand. 2011a. A1060 GM Corn Line 5,307 AR FINAL. <https://www.foodstandards.gov.au/code/applications/Documents/A1060%20GM%20Corn%20Line%205307%20AR%20FINAL.pdf>
- Food Standards Australia New Zealand. 2011b. A1060. <https://www.foodstandards.gov.au/code/applications/Documents/A1060.zip>
- Food Standards Australia New Zealand. 2012. A1060 GM Corn Line 5,307 AppR FINAL. <https://www.foodstandards.gov.au/code/applications/Documents/A1060%20GM%20Corn%20Line%205307%20AppR%20FINAL.pdf>
- Food Standards Australia New Zealand. 2016. A1138 Application_Redacted. https://www.foodstandards.gov.au/code/applications/Documents/A1138%20Application_Redacted.pdf
- Food Standards Australia New Zealand. 2017a. A1138_SD1_at approval. https://www.foodstandards.gov.au/code/applications/Documents/A1138_SD1_at%20approval.pdf
- Food Standards Australia New Zealand. 2017b. A1138 SD1. <https://www.foodstandards.gov.au/code/applications/Documents/A1138%20SD1.pdf>
- Food Standards Australia New Zealand. 2020a. A1060 GM Corn Line 5,307 AppR SD1 Safety Assess. <https://www.foodstandards.gov.au/code/applications/Documents/A1060%20GM%20Corn%20Line%205307%20AppR%20SD1%20Safety%20Assess.pdf>
- Food Standards Australia New Zealand. 2020b. A1060 GM Corn Line 5,307 AR SD1 Safety Assess. <https://www.foodstandards.gov.au/code/applications/Documents/A1060%20GM%20Corn%20Line%205307%20AR%20SD1%20Safety%20Assess.pdf>
- Food Standards Australia New Zealand. 2020c. A1202 Executive Summary_Redacted. https://www.foodstandards.gov.au/code/applications/Documents/A1202%20Executive%20Summary_Redacted.pdf
- Food Standards Australia New Zealand. 2020d. A1202 SD1. <https://www.foodstandards.gov.au/code/applications/Documents/A1202%20SD1.pdf>
- Health Canada. 2010a. Decision Document DD2010-79 Determination of the Safety of Syngenta Seeds Canada Inc.'s Corn (*Zea mays* L.) Event MIR162. <https://www.canada.ca/en/news/archive/2010/07/decision-document-dd2010-79-determination-safetysyngenta-seeds-canada-inc-corn-zea-mays-eventmir162.html>
- Health Canada. 2010b. DD2010-79: Determination of the Safety of Syngenta Seeds Canada Inc.'s Corn (*Zea mays* L.) Event MIR162 - Canadian Food Inspection Agency. <https://www.inspection.gc.ca/plant-health/plants-with-novel-traits/approved-under-review/decisiondocuments/dd2010-79/eng/1310494079263/1310494159104>
- Health Canada. 2011. DD2007-68: Determination of the Safety of Syngenta Seeds Inc.'s Corn (*Zea mays* L.) Event MIR604 - Canadian Food Inspection Agency. <https://inspection.canada.ca/plant-varieties/plants-with-novel-traits/approved-under-review/decisiondocuments/dd2007-68/eng/1310746461506/1310746547873>
- Health Canada. 2013. Decision Document DD 2013–96: Determination of the Safety of Syngenta Canada Inc.'s Corn (*Zea mays* L.) Event 5,307 - Canadian Food Inspection Agency. <https://www.inspection.gc.ca/plants/plants-with-noveltraits/approved-under-review/decision-documents/dd-2013-96/eng/1378914978025/1378915059235>
- Health Canada. 2015a. Novel Food Information – Insect Resistant Corn 5,307. <https://www.canada.ca/en/health-canada/services/foodnutrition/genetically-modified-foods-other-novelfoods/approved-products/novel-food-informationinsect-resistant-corn-5307.html>
- Health Canada. 2015b. Novel Food Information – Insect Resistant Corn Event MIR 162. <https://www.canada.ca/en/health-canada/services/foodnutrition/genetically-modified-foods-other-novelfoods/approved-products/novel-food-informationinsect-resistant-corn-event-162.html>
- Health Canada. 2018. Novel Food Information – Provitamin A Biofortified Rice Event GR2E (Golden Rice). <https://www.canada.ca/en/health-canada/services/foodnutrition/genetically-modified-foods-other-novelfoods/approved-products/novel-food-informationgolden-rice-gr2e.html>
- Herman, R. A., Hou, Z., Mirsky, H., Nelson, M. E., Mathesius, C. A., Roper, J. M. 2021. History of safe exposure and bioinformatic assessment of phosphomannose-isomerase (PMI) for allergenic risk. *Transgenic Res* 30:201–206.

References

- Liu W, Liu X, Liu C, Zhang Z, Jin W. 2020. Development of a sensitive monoclonal antibody-based sandwich ELISA to detect Vip3Aa in genetically modified crops. *Biotechnol Lett* 42:1467–1,478.
- Long, N, Bottoms, J, Meghji, M, Hart, H, Que, Q, Pulliam, D. 2012. Corn event MIR162. Syngenta Participations AG, assignee. U.S. Patent No. 8,232,456. Washington, DC: U.S. Patent Office.
- Long, N, Bottoms, J, Meghji, M, Hart, H, Que, Q, Pulliam, D. 2013a. Corn event MIR162. Syngenta Participations AG, assignee. U.S. Patent No. 8,455,720. Washington, DC: U.S. Patent Office.
- Long, N, Bottoms, J, Meghji, M, Hart, H, Que, Q, Pulliam, D. 2013b. Corn event MIR162. Syngenta Participations AG, assignee. U.S. Patent No. 8,618,272. Washington, DC: U.S. Patent Office.
- Long, N, Bottoms, J, Meghji, M, Hart, H, Que, Q, Pulliam, D. 2017. Corn event MIR162. Syngenta Participations AG, assignee. U.S. Patent No. 9,752,198. Washington, DC: U.S. Patent Office.
- Ministry of Agriculture, Forestry and Fisheries. 2010a. Safety confirmation related to "heat-resistant? -amylase-producing corn 3,272 line". http://www.maff.go.jp/j/press/syouan/tikusui/pdf/100326_1-01.pdf
- Ministry of Agriculture, Forestry and Fisheries. 2010b. Coleoptera pest-resistant corn (ecry3.1Ab, Zea mays subsp . . .) https://www.affrc.maff.go.jp/docs/committee/diversity/100201/pdf/siryu_2-2.pdf
- Ministry of Agriculture, Forestry and Fisheries. 2018. Document 5–2. <https://www.affrc.maff.go.jp/attach/pdf/20190201-13.pdf>
- Ministry of Agriculture, Forestry and Fisheries. N.d. Document 5–2. http://www.maff.go.jp/j/council/sizai/siryu/22_21/pdf/data5-2.pdf
- Ministry of Agriculture, Forestry and Fisheries. N.d. Document 5–3. http://www.maff.go.jp/j/council/sizai/siryu/25_24/pdf/data5-3.pdf
- Ministry of Agriculture, Forestry and Fisheries. N.d. Document 7. <http://www.maff.go.jp/j/council/sizai/siryu/33/pdf/data7.pdf>
- Ministry of Agriculture, Forestry and Fisheries. N.d. Safety confirmation for "Lepidoptera pest resistant corn MIR162 line". http://www.maff.go.jp/j/press/syouan/tikusui/pdf/100326_1-02.pdf
- Ministry of Agriculture, Forestry and Fisheries. N.d. vip3A, pat, mEPSPS, Zea mays subsp. Mays. http://www.affrc.maff.go.jp/docs/committee/diversity/091217/pdf/siryu_3-1.pdf
- National Technical Commission on Biosafety. 2016. Opinion Views Rapporteur Karen. <http://ctnbio.mctic.gov.br/documents/566529/2076451/Parecer+Vistas+Relator+Karen/403c4035-8db2-4422-8d61-055e1b44c414>
- Raybould A, Higgins, LS, Horak, MJ, Layton, RJ, Storer, NP, De La Fuente, J M, Herman, RA. 2012. Assessing the ecological risks from the persistence and spread of feral populations of insect-resistant transgenic maize. *Transgenic Res*, 21:655–664.
- Raybould A, Vlachos D. 2011. Non-target organism effects tests on Vip3A and their application to the ecological risk assessment for cultivation of MIR162 maize. *Transgenic Res* 20:599–611.
- United States Department of Agriculture. 2010. 20,560 Federal Register /Vol. 75, No. 75/Tuesday, April 20, 2010 - Syngenta Biotechnology, Inc.; Determination of Nonregulated Status for Corn Genetically Engineered for Insect Resistance. https://www.aphis.usda.gov/brs/fedregister/BRS_20100420.pdf
- United States Department of Agriculture. 2011a. NATIONAL ENVIRONMENTAL POLICY ACT DECISION AND FINDING OF NO SIGNIFICANT IMPACT: MIR162 Maize SYN-IR162-4. https://www.aphis.usda.gov/brs/aphisdocs2/07_25301p_com.pdf
- United States Department of Agriculture. 2011b. NATIONAL ENVIRONMENTAL POLICY ACT DECISION AND FINDING OF NO SIGNIFICANT IMPACT: ALPHA-AMYLASE MAIZE EVENT 3272. https://www.aphis.usda.gov/brs/aphisdocs/05_28001p_fonsi_rtc.pdf
- United States Department of Agriculture. 2011c. Event 5,307 USDA Petition – USDA-APHIS. https://www.aphis.usda.gov/brs/aphisdocs/10_33601p.pdf
- United States Department of Agriculture. 2011d. ENVIRONMENTAL REPORT Petition for Determination of Nonregulated Status of Event 5,307 Corn. https://www.aphis.usda.gov/brs/aphisdocs/10_33601p_syngenta_er.pdf
- United States Department of Agriculture. 2013. Final Environmental Assessment - USDA-APHIS. https://www.aphis.usda.gov/brs/aphisdocs/10_33601p_fea.pdf
- United States Department of Agriculture. 2019. Petition for the Determination of Nonregulated Status of Maize Event PY203. https://www.aphis.usda.gov/brs/aphisdocs/19_17601p.pdf
-

References

- United States Department of Agriculture. N.d. I. Summary – USDA-APHIS.
https://www.aphis.usda.gov/brs/aphisdocs/04_36201p_pea.pdf
- United States Department of Agriculture. N.d. Plant Pest Risk Assessment for MIR162 Corn - USDA-APHIS.
https://www.aphis.usda.gov/brs/aphisdocs/07_25301_pra.pdf
- United States Department of Agriculture. N.d. Plant Pest Risk Assessment for Event 3,272 Corn – USDA.
https://www.aphis.usda.gov/brs/aphisdocs/05_28001p_pra.pdf
- United States Department of Agriculture. N.d. Plant Pest Risk Assessment for Event 3,272 Corn.
https://www.aphis.usda.gov/brs/aphisdocs/05_28001p_ppra.pdf
- United States Environmental Protection Agency. N.d. Bacillus thuringiensis Cry1Ab Delta-Endotoxin Protein and the Genetic Material Necessary for Its Production (via Elements of Vector pZO1502) in Event Bt11 Corn (OECD Unique Identifier: SYN-BTØ11-1)(006444) & Bacillus thuringiensis Vip3Aa20 Insecticidal Protein and the Genetic Material Necessary for Its Production (via Elements of Vector pNOV1300) in Event.
https://www3.epa.gov/pesticides/chem_search/reg_actions/registration/fs_PC-006444_01-Mar-09.pdf
- United States Food and Drug Administration. 2018. Biotechnology Notification File No. 000158 Note to the File.
<https://www.fda.gov/media/113374/download>
- Wang, X, Zhang, S, Hu, D, Zhao, X, Li, Y, Liu, T, Li, Y. 2014. BcPMI2, isolated from nonheading Chinese cabbage encoding phosphomannose isomerase, improves stress tolerance in transgenic tobacco. *Mol Biol Rep* 41:2207–2,216.
- Zhang, M, Zhuo, X, Wang, J, Yang, C, Powell, CA, Chen, R. 2015. Phosphomannose isomerase affects the key enzymes of glycolysis and sucrose metabolism in transgenic sugarcane overexpressing the manA gene. *Mol Breeding* 35:100.
-

Appendix B – List of additional studies performed by or on behalf of the applicant over the course of the authorisation period and not previously submitted to the EU with regard to the evaluation of the safety of the food and feed for humans, animal or the environment from maize MIR162

Study identification	Title
TK0060148	Metabolic Profiling of Sugars and Sugar Phosphates in Grain Derived from MIR162 Maize
JY150240-1	Report of oral acute toxicity study of PMI protein
TK0107154	Characterisation of Vegetative Insecticidal Protein (Vip3Aa20) Test Substance and Certificate of Analysis
TK0235588	Characterisation of Microbially Produced Test Substance PMI-0114 Containing Phosphomannose Isomerase (PMI) Protein and Certificate of Analysis
TK0285529	In vitro Digestibility of Phosphomannose Isomerase (PMI) Protein Under Simulated Mammalian Gastric Conditions for China
TK0329350	Effect of Temperature on the Stability of Phosphomannose Isomerase (PMI) Protein
WIL-639227; TK0256516	A Single-Dose Oral Gavage Toxicity Study of PMI-0114 in CD-1 Mice with a 14-Day Recovery Period
TK0428575	Event MIR162: Insert and Flanking Sequence Analysis of Event MIR162 in Material ID 12MG000996
TK0537123	Storage Stability Assessment of Microbially Produced Test Substance VIP3A20-0111 Containing Vip3Aa20 Protein