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# Assessment of genetically modified oilseed rape T45 for renewal of authorisation under Regulation (EC) No 1829/2003 (application EFSA-GMO-RX-012)

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## Abstract

Following the submission of application EFSA-GMO-RX-012 under Regulation (EC) No 1829/2003 from Bayer CropScience N.V., 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 herbicide-tolerant genetically modified oilseed rape T45, for food and feed uses, excluding cultivation within the European Union. 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. Under the assumption that the DNA sequence of the event in oilseed rape T45 considered for renewal is identical to the sequence of the originally assessed event, the GMO Panel concludes that there is no evidence in the renewal application EFSA-GMO-RX-012 for new hazards, modified exposure or scientific uncertainties that would change the conclusions of the original risk assessment on oilseed rape T45.



**Keywords:** oilseed rape, T45, renewal, articles 11 and 23, Regulation (EC) No 1829/2003

**Requestor:** European Commission (DG SANTE)

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## Summary

Following the submission of application EFSA-GMO-RX-012 under Regulation (EC) No 1829/2003 from Bayer CropScience N.V., 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 herbicide-tolerant genetically modified oilseed rape T45. The scope of renewal application EFSA-GMO-RX-012 is for placing on the market of products containing or produced from oilseed rape T45, resulting from the commercialisation of this oilseed rape in third countries until 2005, excluding cultivation in the European Union.[1]

In delivering its scientific opinion, the GMO Panel took into account application EFSA-GMO-RX-012, additional information provided by the applicant, scientific comments submitted by the Member States and relevant scientific publications. The data received in the context of the renewal application EFSA-GMO-RX-012 contained: post-market environmental monitoring reports, an evaluation of the literature retrieved by two systematic searches, updated bioinformatic analyses, and additional 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.

Under the assumption that the DNA sequence of the event in oilseed rape T45 considered for renewal is identical to the sequence of the originally assessed event, the GMO Panel concludes that there is no evidence in renewal application EFSA-GMO-RX-012 for new hazards, modified exposure or scientific uncertainties that would change the conclusions of the original risk assessment on oilseed rape T45 (EFSA, 2008).


[1] According to the information provided by the applicant, the de-registration of the oilseed rape T45 derived varieties was completed in 2004 with the exception of a single line that was still sold in limited quantities until 2005. Oilseed rape T45 grown historically in Canada and USA on a very limited surface may only enter the EU by import at low level in commodity rapeseed.

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# 1. Introduction

## 1.1. Background

On 1 March 2018, the European Food Safety Authority (EFSA) received from the European Commission (DG SANTE) application EFSA-GMO-RX-012 by Bayer CropScience N.V. for the renewal of authorisation of genetically modified (GM) oilseed rape T45 (Unique Identifier ACS-GMØØ8-2) for the placing on the market of products containing or produced from this GM oilseed rape for submitted within the framework of Regulation (EC) No 1829/2003[2]. Before sending the application to EFSA, the European Commission confirmed that the data submitted in the context of this renewal application were in line with the legal requirements laid down in Articles 11 and 23 of Regulation (EC) No 1829/2003.

After receiving application EFSA-GMO-RX-012, and in accordance with Articles 5(2)(b) and 17(2)(b) of Regulation (EC) No 1829/2003, EFSA informed Member States and made the summary of the application available to the public on the EFSA website.[3]

On 5 June 2018, EFSA declared the application valid in accordance with Articles 6(1) and 18(1) of Regulation (EC) No 1829/2003. EFSA made the valid application available to Member States and the European Commission, and consulted nominated risk assessment bodies of Member States, including national Competent Authorities within the meaning of Directive 2001/18/EC following the requirements of Articles 6(4) and 18(4) of Regulation (EC) No 1829/2003, to request their scientific opinion. Member States had three months after the opening of the Member State commenting period (until 10 September 2018) to make their opinion known.

Following the submission of applications EFSA-GMO-UK-2005-25 and EFSA-GMO-RX-T45, for which one EFSA scientific opinion was published (EFSA, 2008), the placing on the market of oilseed rape T45 for products containing or produced from this GM oilseed rape resulting from the commercialisation of this oilseed rape in third countries until 2005, excluding cultivation in the European Union (EU), was authorised by Commission Decision 2009/184/EC[4]. A copy of this authorisation was provided by the applicant.[5]

EFSA requested additional information on 19 June 2018, 10 October 2018, 22 October 2018 and 3 December 2018. The applicant submitted their replies on 17 August 2018, 6 November 2018, 6 December 2018 and 10 January 2019, respectively.

In giving its scientific opinion to the European Commission, the Member States and the applicant, and in accordance with Articles 6(1) and 18(1) of Regulation (EC) No 1829/2003, EFSA has endeavoured to respect a time limit of six months from the acknowledgement of the valid application. As additional information was requested by the Panel on Genetically Modified Organisms of the European Food Safety Authority (GMO Panel), the time limit of 6 months was extended accordingly, in line with Articles 6(1), 6(2), 18(1), and 18(2) of Regulation (EC) No 1829/2003.

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 and thus will be part of the EFSA overall opinion in accordance with Articles 6(5) and 18(5).

## 1.2. Terms of Reference as provided by the requestor

The GMO Panel was requested to carry out a scientific risk assessment on the data submitted in the context of the renewal of authorisation application for the placing on the market of products containing or produced from GM oilseed rape T45, in accordance with Articles 11 and 23 of Regulation (EC) No 1829/2003.

Where applicable, any conditions or restrictions which should be imposed on the placing on the market and/or specific conditions or restrictions for use and handling, including post-market monitoring requirements based on the outcome of the risk assessment and, in the case of GMOs or food and feed containing or consisting of GMOs, conditions for the protection of particular ecosystems/environment

[2] 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, p. 1–23.
[3] Available online: http://registerofquestions.efsa.europa.eu/roqFrontend/questionDocumentsLoader?question=EFSA-Q-2018-00229
[4] COMMISSION DECISION of 10 March 2009 authorising the placing on the market of products containing or produced from genetically modified oilseed rape T45 (ACS-GMØØ8-2) resulting from the commercialisation of this oilseed rape in third countries until 2005, pursuant to Regulation (EC) No 1829/2003 of the European Parliament and of the Council. Official Journal of the European Union L 68/28, 13.3.2009.
[5] Dossier: Oilseed rape T45 renewal – Annex 1.

and/or geographical areas should be indicated in accordance with Articles 6(5)(e) and 18(5)(e) of Regulation (EC) No 1829/2003.

The GMO Panel was not requested to give an opinion on information required under Annex II to the Cartagena Protocol. Furthermore, the GMO Panel did not consider proposals for labelling and methods of detection (including sampling and the identification of the specific transformation event in the food and feed and/or food and feed produced from it), which are matters related to risk management.

# 2. Data and methodologies

## 2.1. Data

The data for application EFSA-GMO-RX-012 provided by the applicant at the time of submission, or in reply to requests for additional information are specified below.

In the context of this renewal application, no new sequence study was submitted among the additional documents or studies performed by or on behalf of the applicant.[6] In accordance with the GMO Panel guidelines for renewal of applications of GM food and feed authorised under Regulation (EC) No 1829/2003 (EFSA GMO Panel, 2015), the GMO Panel evaluated the data provided in the context of this oilseed rape T45 renewal application under the assumption that the T45 event sequence is identical to the sequence of the originally assessed event (EFSA, 2008).

### 2.1.1. Post-market monitoring reports[7]

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 post-market environmental monitoring (PMEM) plan, consisting of a general surveillance plan to check for any adverse effects on the environment arising from oilseed rape T45, was a condition for the authorisation. As no potential adverse environmental effects were identified in the environmental risk assessment of oilseed rape T45 (EFSA, 2008), case-specific monitoring was not considered necessary by the GMO Panel.

The applicant provided ten annual PMEM reports covering a reporting period from March 2009 to June 2018. 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 established by EuropaBio for the collection of information recorded by various operators [federations involved in oilseed rape seeds import and processing] on any observed adverse effect(s) on human health and the environment arising from handling of oilseed rape possibly containing oilseed rape T45; (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 literature[8]

In addition to the ten separate literature searches provided as part of the annual PMEM reports, the applicant performed two systematic literature searches for oilseed rape T45 and the newly expressed phosphinothricin *N*-acetyltransferase (PAT) protein covering the period from 1 March 2009 till 30 September 2018, in accordance with the recommendations on literature searching outlined in EFSA (2010, 2017a).

Searches in electronic bibliographic databases and in websites of relevant organisations were performed to identify relevant publications. Altogether, 667 publications were retrieved. After applying the eligibility/inclusion criteria defined *a priori* by the applicant, five publications were identified as relevant for food and feed safety assessment, molecular characterisation and environmental safety assessment. The list of relevant publications is provided in Appendix A.

### 2.1.3. Updated bioinformatic data[9]

At the time of submission of the renewal dossier, the applicant provided a complete bioinformatic dataset for the oilseed rape T45 event including an analysis of the insert and flanking sequences, an

[6] ossier: Oilseed rape T45 renewal – Section 2.3; additional information: 6/11/2018.
[7] Dossier: Oilseed rape T45 renewal – Section 2.2; Annex 2; additional information: 10/1/2019.
[8] Dossier Oilseed rape T45 renewal – Section 2.3.1; additional information: 17/8/2018 and 6/12/2018.
[9] Dossier: Oilseed rape T45 renewal – Section 2.3.2.

analysis of the potential similarity to allergens and toxins of the newly expressed protein and of all possible ORFs within the insert and spanning the junction sites, and an analysis of possible horizontal gene transfer (EFSA, 2017b). The outcome of the updated bioinformatic analyses is presented in Section 3.3.

#### 2.1.4. Additional documents or studies provided by the applicant[10]

The applicant provided an overview on the worldwide approvals of oilseed rape T45 and the full study reports of all 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 these 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 applicant[11]

The applicant provided an overall assessment concluding that information provided in the application for renewal of authorisation of oilseed rape T45 for food and feed uses in the EU does not change the outcome of the original risk assessment (EFSA, 2008).

#### 2.1.6. Monitoring plan and proposal for improving the conditions of the original authorisation[12]

The applicant indicated in the dossier that the environmental 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 oilseed rape T45 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 Member States are addressed in Annex G of EFSA's overall opinion[13] and 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 oilseed rape T45, 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 oilseed rape T45. Although the overall quality of the performed literature searches is acceptable, the GMO Panel considers that future searches could be improved. The GMO Panel therefore recommends the applicant for future searches to:

- ensure that enough search term variation is used (covering possible synonyms, related terms, acronyms, spelling variants, old and new terminology, brand and generic names, lay and scientific terminology, common typos, translation issues);
- include intended trait-specific search terms;
- ensure that enough truncation is used and use truncation consistently;
- include controlled vocabulary (subject indexing) in the searches when available, and, where subject headings are available, use both free-text terms and controlled vocabulary in the searches.

[10] Dossier: Oilseed rape T45 renewal – Section 2.3.3.
[11] Dossier: Oilseed rape T45 renewal – Section 2.3.4.
[12] Dossier: Oilseed rape T45 renewal – Section 2.4.
[13] Available online: http://registerofquestions.efsa.europa.eu/roqFrontend/questionDocumentsLoader?question=EFSA-Q-2019-00031

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 oilseed rape T45 (EFSA, 2008) have been identified by the applicant.

### 3.3. Evaluation of the updated bioinformatic data

The results of the updated bioinformatic analysis of oilseed rape T45 confirms that no known endogenous genes were disrupted by the insert. Analyses of the amino acid sequence of the newly expressed PAT protein reveal no significant similarities to toxins or allergens. In addition, bioinformatic analyses of the newly created ORFs within the insert or spanning the junctions with genomic DNA reveal no significant similarities to toxins and allergens.

The updated bioinformatic analysis for oilseed rape event T45 does not reveal any DNA sequence that could provide sufficient length and identity which could facilitate horizontal gene transfer by double homologous recombination (HR), confirming the previous conclusions (EFSA, 2008). Given the results of this analysis and the potential of the recombinant DNA in oilseed rape T45 to confer selective advantages or increased fitness 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 (Appendix B). This new information does not raise any concern for human and animal health and the environment, which would change the original risk assessment conclusions on oilseed rape T45.

### 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-012 indicating new hazards, relevant changes in exposure or scientific uncertainties that would change previous conclusions on oilseed rape T45.

### 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 oilseed rape T45. This general surveillance is coordinated by EuropaBio and implemented by selected operators (federations involved in oilseed rape seeds 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 oilseed rape T45, 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

Under the assumption that the DNA sequence of the event in oilseed rape T45 considered for renewal is identical to the sequence of the originally assessed event, the GMO Panel concludes that there is no evidence in the renewal application EFSA-GMO-RX-012 for new hazards, modified exposure or scientific uncertainties that would change the conclusions of the original risk assessment on oilseed rape T45 (EFSA, 2008).

## Documentation provided to EFSA

1) Letter from the European Commission to EFSA received on 1 March 2018 for the continued marketing of genetically modified oilseed rape T45 in accordance with articles 11 and 23 of Regulation (EC) No 1829/2003 by Bayer (EFSA-GMO-RX-012).
2) Acknowledgement letter, dated 9 March 2018, from EFSA to the European Commission.
3) Letter from EFSA to applicant dated 17 April 2018 requesting additional information under completeness check.
4) Letter from applicant to EFSA received on 14 May 2018 providing additional information under completeness check.

5) Letter from EFSA to applicant dated 5 June 2018 delivering the 'Statement of Validity' for application EFSA-GMO-RX-012.
6) Letter from EFSA to applicant dated 19 June 2018 requesting additional information and stopping the clock.
7) Letter from applicant to EFSA received on 17 August 2018 providing additional information.
8) Letter from EFSA to applicant dated 20 August 2018 re-starting the clock from 17 August 2018.
9) Letter from EFSA to applicant dated 10 October 2018 requesting additional information and stopping the clock.
10) Letter from EFSA to applicant dated 22 October 2018 requesting additional information and remaining the clock stop.
11) Letter from applicant to EFSA received on 6 November 2018 providing additional information.
12) Letter from EFSA to applicant dated 3 December 2018 requesting additional information and remaining the clock stop.
13) Letter from applicant to EFSA received on 6 December 2018 providing additional information.
14) Letter from applicant to EFSA received on 10 January 2019 providing additional information.
15) Letter from EFSA to applicant dated 11 January 2019 re-starting the clock from 10 January 2019.

## References

EFSA (European Food Safety Authority), 2008. Opinion of the Scientific Panel on Genetically Modified Organisms on an application (Reference EFSA-GMO-UK-2005-25) for the placing on the market of glufosinate-tolerant oilseed rape T45 for food and feed uses, import and processing and renewal of the authorisation of oilseed rapt T45 as existing products, both under Regulation (EC) 1829/2003 from Bayer CropScience. EFSA Journal 2008;6(3):635, 22 pp. https://doi.org/10.2903/j.efsa.2008.635

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 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 (European Food Safety Authority), Devos Y, Guajardo IM, Glanville J and Waigmann E, 2017a. 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 2017:EN-1207, 48 pp. https://doi.org/10.2903/sp.efsa.2017.EN-1207

EFSA (European Food Safety Authority), Gennaro A, Gomes A, Herman L, Nogue F, Papadopoulou N and Tebbe C, 2017b. 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 publications 2017:14(7):EN-1273, 11 pp. https://doi.org/10.2903/sp.efsa.2017.EN-1273

## Abbreviations

| | |
|---|---|
| ERA | environmental risk assessment |
| GM | genetically modified |
| GMO | genetically modified organisms |
| GMO Panel | EFSA Panel on Genetically Modified Organisms |
| HGT | horizontal gene transfer |
| ORFs | open reading frames |
| PAT | phosphinothricin *N*-acetyltransferase |
| PMEM | post-market environmental monitoring |

# Appendix A – List of relevant publications identified by the applicant through the systematic literature search (1/3/2009 – 30/9/2018)

| Reference |
|---|
| Fard NA, Minuchehr Z and Mousavi A, 2013. *In silico* allergenicity assessment of novel proteins derived from GMHR crops. Ortuno F and Rojas I [Eds.]. Proceedings IWBBIO. |
| Fard NA, Minuchehr Z and Mousavi A, 2013. Allergenicity study of genetically modified herbicide resistant crops (bioinformatics assessment). Bulletin of Environment, Pharmacology and Life Sciences, 2, 24–32. |
| Oh J, Mo K and Lee H, 2009. Evaluation for allergenicity for genetically modified organic foods. Journal of Allergy and Clinical Immunology, 123, S244. |
| Schafer BW, Embrey SK and Herman RA, 2016. Rapid simulated gastric fluid digestion of in-seed/grain proteins expressed in genetically engineered crops. Regulatory Toxicology and Pharmacology, 81, 106–112. |
| Verma AK, Misra A, Subash S, Das M and Dwivedi D, 2011. Computational allergenicity prediction of transgenic proteins expressed in genetically modified crops. Immunopharmacology and Immunotoxicology, 33, 410–422. |

# 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 oilseed rape T45

| Study identification | Title |
|---|---|
| M-475440-01-1 | PAT protein-acute toxicity by oral gavage in mice |
| M-500889-01-1 | The effect of temperature on microbially-produced PAT/pat as assessed by ELISA |
| M-517325-01-1 | Flanking sequence and inserted sequence for canola T45 |