Assessment of the safety of genetically modified soybean 40-3-2 for renewal authorisation under assimilated Regulation (EC) No. 1829/2003

Reference number RP212

Regulated Products Risk Assessment Unit

Science, Evidence and Research Division, FSA

Risk Assessment Team

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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
CLE	Crop Life Europe
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

Acronym	Definition
ORFs	Open reading frames
PMEM	Post-market environmental monitoring

Summary

Following the submission of application RP212 to the Food Standards Agency (FSA) under assimilated Regulation (EC) No. 1829/2003 from Bayer CropScience Ltd, FSA/FSS (Food Standards Scotland) have undertaken a safety assessment on genetically modified soybean 40-3-2. To support the safety assessment by FSA/FSS, the Advisory Committee on Novel Foods and Processes (ACNFP) provided advice to FSA/FSS on the data submitted for the renewal of authorisation for the genetically modified soybean 40-3-2, 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 soybean 40-3-2.

Soybean 40-3-2 is modified to express the CP4 EPSPS (5-enolpyruvylshikimate 3-phosphate synthase) protein from the CP4 strain of Agrobacterium tumefaciens, which has a lower binding affinity with glyphosate, conferring tolerance to glyphosate herbicides.

Soybean 40-3-2 has previously been authorised for food and feed uses and is most commonly used as a source of protein in 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 soybean 40-3-2. This also includes products other than food or feed. The application does not cover cultivation and therefore no soybean 40-3-2 will be grown in the UK.

In providing its advice on the safety of soybean 40-3-2 for food and feed, the ACNFP considered data provided as part of application RP212 (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 (or the first renewal in 2012).

FSA/FSS concludes, based on ACNFP advice, that there is no evidence in the renewal application RP212 for new hazards, modified exposures, or new scientific uncertainties that would change the conclusions of the original risk assessments on genetically modified soybean 40-3-2 (EFSA GMO Panel 2010, UK-ACNFP 1995).

1. Introduction

1.1 Background

On February 4th 2021, the Food Standards Agency (FSA) received application RP212 for the renewal of the authorisation of genetically modified soybean 40-3-2 (unique identifier: MON-Ø4Ø32-6), submitted by Bayer Agriculture BV (Antwerp, Belgium) on behalf of Bayer CropScience LP (Missouri, USA) (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 22nd February 2021, declared the application valid.

Following the submission of renewal application EFSA-GMO-RX-40-3-2 (and of the original application), and the publication of the EFSA (European Food Safety Authority) scientific opinions for both (EFSA GMO Panel 2010, UK-ACNFP 1995), the

placing on the market of genetically modified soybean 40-3-2 for products containing, consisting of, or produced from soybean 40-3-2, excluding cultivation in the EU, was authorised by Commission Implementing Decision 2012/82/EU (and previously by Commission Decision 96/281/EC). A copy of Commission Implementing Decision 2012/82/EU was provided by the applicant.

FSA and FSS would like to thank the following members of the ACNFP committee 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, the FSA /FSS were requested to carry out a scientific risk assessment of genetically modified soybean 40-3-2 for the renewal of authorisation for placing on the market of products containing, consisting of, or produced from soybean 40-3-2 in the context of its scope as defined in application RP212.

FSA/FSS sought safety advice from the Advisory Committee on Novel Foods and Processes (ACNFP) on soybean 40-3-2, which will inform the FSA/FSS safety assessment. The FSA/FSS safety assessment is to be seen as the opinion requested under Articles 6(6) and 18(6) of assimilated Regulation (EC) No. 1829/2003.

In addition to the present advice on the safety of genetically modified soybean 40-3-2, the ACNFP were also asked to report on the particulars listed under Articles 6(5) and 18(5) of Regulation (EC) No. 1829/2003.

2. Applicant details

Name: Bayer CropScience LP

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Missouri, 63167

USA

(represented by)

Name: Bayer CropScience Ltd

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3. Data and assessment

3.1 Data

The data for application RP212 submitted according to legal requirements contained in Regulation (EC) 1829/2003 and provided by the applicant at the time of submission are specified below. To inform the FSA/FSS safety assessment of the application for renewal of the authorisation of genetically modified soybean

40-3-2 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. They considered the requirements described in applicable guidance for the risk assessment of renewal applications of GM food and feed authorised under Regulation (EC) No. 1829/2003. The comments raised by the ACNFP were taken into consideration during the scientific risk assessment.

Contractors performed preparatory work and delivered reports on the methods applied by the applicant in performing sequencing and bioinformatic analyses.

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 assessments of genetically modified soybean 40-3-2 identified no potential adverse environmental effects, and the applications 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 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 against two electronic databases, SciSearch and CABA database covering 2010 to 2020, in accordance with the recommendations on literature searches outlined in EFSA guidance (2010, 2019). Searches in websites of relevant organisations were also performed.

Altogether, 74 publications were identified as relevant, however these publications did not have any implication on the risk assessment as no new hazards, modified exposures, or scientific uncertainties were reported.

The ACNFP assessed the applicant's literature searches on genetically modified soybean 40-3-2 and the newly expressed protein (CP4 EPSPS) 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 genetically modified soybean 40-3-2, 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 40-3-2 event (both insert and flanking sequences) to previously determined sequences for the 40-3-2 event. Re-examination of the original sequencing data showed that the DNA sequences of the insert and flanking DNA regions were identical to those sequences previously reported. The updated bioinformatics analyses found disruption of endogenous soybean genes at the 40-3-2 event insertion sites, but these disruptions had no significant impact on the plant or food safety. These disruptions were present since soybean 40-3-2 had been first developed, and are only identified now due to the availability of high-quality reference genomes.

The updated bioinformatics analyses for the 40-3-2 event found no DNA sequences that could provide sufficient length and identity to facilitate horizontal gene transfer.

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 amino acid sequence of the newly expressed protein. In addition, the amino acid sequence of the newly expressed protein 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 where the bioinformatics analyses performed using updated methodologies and tools identified new information, there was no change in the conclusions of the previous risk assessments, or change in the parameters of the previous authorisations.

4.4 Additional documents or studies provided by the applicant

The applicant stated that no prohibitions or restrictions have been placed on genetically modified soybean 40-3-2 in any country, and that no inconclusive scientific opinions have been issued by any regulatory agency.

Unpublished studies performed by, or on behalf of the applicant, since genetically modified soybean 40-3-2 was authorised were screened, and the relevance of the studies for molecular characterisation, human and animal safety, and the environment, was assessed by the applicant.

During the risk assessment, 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 previous risk assessment conclusions on genetically modified soybean 40-3-2.

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 (including independent peer-reviewed literature and updated bioinformatic analyses) provided in the application for renewal of authorisation of genetically modified soybean 40-3-2 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 previous risk assessment (EFSA GMO Panel 2010).

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 soybean 40-3-2.

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

The post-market environmental monitoring plan does not need to change, except the replacement of EuropaBio by Crop Life Europe (CLE).

Assessing any proposals to change the PMEM plan is within the remit of ACRE, and their assessment of forms part of the final safety assessment published by FSA/FSS.

ACRE's advice is available at 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 40-3-2 were validated. The methods and validation report are available via the following links: 40-3-2 documents | European Union Reference Laboratory for Genetically Modified Food and Feed (EURL GMFF) (europa.eu).

6. Overall conclusions and recommendations

FSA/FSS concludes, based on ACNFP advice, that there is no evidence in renewal application RP212 for new hazards, modified exposure, or scientific uncertainties that would change the conclusion of the original risk assessment on genetically modified soybean 40-3-2.

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 (2012/82/EU) of 10 February 2012 as regards the renewal of the authorisation for continued marketing of products containing, consisting of, or produced from genetically modified soybean 40-3-2 (MON-Ø4Ø32-6) pursuant to Regulation (EC) No. 1829/2003 of the European Parliament and of the Council. Official Journal of the European Union L 40/14 14/2/2012.

Commission Decision (96/281/EC) of 3 April 1996 concerning the placing on the market of genetically modified soya beans (Glycine max L.) with increased tolerance to the herbicide glyphosate, pursuant to Council Directive 90/220/EEC. Official Journal of the European Communities L 107/10 30/4/96.

EFSA Panel on Genetically Modified Organisms (GMO); Scientific Opinion of the Panel on Genetically Modified Organisms on applications (EFSA-GMO-RX-40-3-2) for the renewal of authorisation for the continued marketing of (1) food containing, consisting of, or produced from genetically modified soybean 40-3-2; (2) feed containing, consisting of, or produced from soybean 40-3-2; (3) other products containing or consisting of soybean 40-3-2 with the exception of cultivation, all under Regulation (EC) No 1829/2003 from Monsanto. EFSA Journal 2010;8(12):1908, [1-38]. https://doi.org/10.2903/j.efsa.2010.1908.

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), 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.

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