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Guidance for renewal applications of genetically modified food and feed authorised under Regulation (EC) No 1829/2003

Arpaia, Salvatore; Birch, Andrew Nicholas Edmund; Chesson, Andrew; du Jardin, Patrick; Gathmann, Achim; Gropp, Jürgen; Herman, Lieve; Hoen-Sorteberg, Hilde-Gunn Opsahl; Jones, Huw; Kiss, József; Kleter, Gijs ; Lovik, Martinus; Messéan, Antoine ; Naegeli, Hanspeter ; Nielsen, Kaare Magne; Ovesna, Jaroslava ; Perry, Joe ; Rostoks , Nils ; Tebbe, Christoph

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tel: +44 1970 62 2400
email: is@aber.ac.uk

SCIENTIFIC OPINION

Guidance for renewal applications of genetically modified food and feed authorised under Regulation (EC) No 1829/2003^{1,2}

EFSA Panel on Genetically Modified Organisms (GMO)^{3,4}

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

According to Articles 11(6) and 23(6) of Regulation (EC) No 1829/2003 on genetically modified food and feed, the European Food Safety Authority should publish detailed guidance to assist applicants in the preparation and presentation of their applications for the renewal of authorisations of that genetically modified food and feed. This guidance document describes the data requirements for renewal applications, which should contain a copy of the authorisation, post-market monitoring and post-market environmental monitoring reports, systematic search and evaluation of literature, updated bioinformatics and any additional documents or studies performed by or on behalf of the applicant during the authorisation period. The applicant is requested to assess the collected information and conclude whether the previous risk assessment remains valid. The applicant can also propose amending or complementing the original conditions of the authorisation, including the monitoring plan(s).

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KEY WORDS

renewal authorisation, GM food and feed, Regulation (EC) No 1829/2003, Articles 11 and 23

¹ On request from EFSA, Question No EFSA-Q-2013-00684, adopted on 27 May 2015.

² This guidance document provides guidance on data requirements for the assessment of renewal applications for GM food and feed for import and processing in the European Union, excluding cultivation.

³ Panel members: Salvatore Arpaia, Andrew Nicholas Edmund Birch, Andrew Chesson, Patrick du Jardin, Achim Gathmann, Jürgen Gropp, Lieve Herman, Hilde-Gunn Hoen-Sorteberg, Huw Jones, Jozsef Kiss, Gijs Kleter, Martinus Lovik, Antoine Messéan, Hanspeter Naegeli, Kaare Magne Nielsen, Jaroslava Ovesna, Joe Perry, Nils Rostoks and Christoph Tebbe. Correspondence: gmo@efsa.europa.eu

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SUMMARY

The European Food Safety Authority (EFSA) accepted a proposal from the EFSA Panel on Genetically Modified Organisms (GMO) to develop a guidance document for renewal applications of genetically modified (GM) food and feed authorised under Regulation (EC) No 1829/2003. Therefore, a working group with the aim of developing such guidance was established. This guidance document describes the data requirements for renewal applications for GM food and feed for import and processing in the European Union (EU), excluding cultivation. Applications should contain a copy of the authorisation, post-market monitoring and post-market environmental monitoring reports, systematic search and evaluation of literature, updated bioinformatics and any additional documents or studies performed by or on behalf of the applicant during the authorisation period. The collected information should be assessed to see whether the previous risk assessment remains valid. The applicant can also propose amending or complementing the original conditions of the authorisation, including the monitoring plan(s).

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BACKGROUND AS PROVIDED BY EFSA

According to Articles 11(6) and 23(6) of Regulation (EC) No 1829/2003⁵ on GM food and feed, EFSA should publish detailed guidance to assist applicants in the preparation and presentation of their applications for the renewal of authorisations of GM food and feed⁶ (hereafter referred to as 'renewal applications'). Previously, a guidance document was in place for the renewal of authorisations of existing GM products for food and feed uses lawfully placed on the market and notified according to Articles 8 and 20 of Regulation (EC) No 1829/2003 (EFSA, 2006). Since the renewal of the GM food and feed authorised under Regulation (EC) No 1829/2003 falls under Articles 11 and 23 of that same regulation, a new guidance document is needed to assist the applicant in the preparation and presentation of the renewal applications.⁷ The new guidance document for renewal applications of GM food and feed requires up-to-date data for the risk assessment of GM food and feed as laid down in EFSA guidance documents (EFSA GMO Panel, 2010a, b, 2011) and the Commission Implementing Regulation (EU) No 503/2013.⁸

On 18 July 2013, the EFSA GMO Panel proposed to EFSA to establish a self-tasking working group with the aim of developing a risk assessment guidance for renewal applications of GM food and feed authorised under Regulation (EC) No 1829/2003. On 26 July 2013, the proposal was accepted by EFSA and the renewal guidance working group had a first meeting on 9 December 2013.⁹

In accordance with the terms of reference, a draft version of the renewal guidance document was released for public consultation from 4 November 2014 until 4 January 2015. Through its dedicated working group, the EFSA GMO Panel assessed all comments received from interested parties and revised the guidance document, taking into account all relevant scientific comments that enhanced scientific quality and clarity. A technical report on the outcome of this public consultation has been published.

TERMS OF REFERENCE AS PROVIDED BY EFSA

The EFSA GMO Panel is asked:

- to prepare a guidance document for the renewal of applications for GM food and feed authorised under Regulation (EC) No 1829/2003;
- to consult the public in the frame of a public consultation;
- to review the draft guidance document considering the relevant comments gathered from the public consultation.

⁵ 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.

⁶ Articles 3 and 15 of 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.

⁷ 1. Authorisations under this Regulation shall be renewable for 10-year periods, on application to the Commission by the authorisation-holder at the latest one year before the expiry date of the authorisation. 2. The application shall be accompanied by the following: (a) a copy of the authorisation for placing the food/feed on the market; (b) a report on the results of the monitoring, if so specified in the authorisation; (c) any other new information which has become available with regard to the evaluation of the safety in use of the food/feed and the risks of the food/feed to the humans, animals or the environment; (d) where appropriate, a proposal for amending or complementing the conditions of the original authorisation, *inter alia* the conditions concerning future monitoring. 3. Articles 5(2), 6 and 7 shall apply *mutatis mutandis*. 4. Where, for reasons beyond the control of the authorisation-holder, no decision is taken on the renewal of an authorisation before its expiry date, the period of authorisation of the product shall automatically be extended until a decision is taken. 5. The Commission, having first consulted the Authority, may establish, in accordance with the procedure referred to in Article 35(2), implementing rules for the application of this Article, including rules concerning the preparation and the presentation of the application. 6. The Authority shall publish detailed guidance to assist the applicant in the preparation and the presentation of its application.

⁸ 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, p. 1–48.

⁹ <http://www.efsa.europa.eu/en/gmowgs/documents/renewalguidancecwg.pdf>

1. Introduction

In 2006, the first GM food and feed¹⁰ were authorised in the EU under Regulation (EC) No 1829/2003. This regulation foresees a 10-year authorisation period that is renewable following the provisions laid down in Articles 11 and 23.

According to these legal provisions, each renewal application for GM food and feed shall contain the following information:

1. a copy of the authorisation for placing the food/feed on the market;
2. a report on the results of the monitoring, if so specified in the authorisation;
3. any other new information, which has become available, with regard to the evaluation of the safety of the food/feed and the risks of the food/feed to humans, animals or the environment;
4. where appropriate, a proposal for amending or complementing the conditions of the original authorisation, *inter alia* the conditions concerning future monitoring.

Additional requirements for renewal applications are detailed in Article 8 of Commission Implementing Regulation (EU) No 503/2013, where the specifics for the methods of detection, identification and quantification of GM food or feed are laid down.

The EFSA GMO Panel provides guidance on data required for the assessment of renewal applications for GM food and feed for import and processing in the EU, excluding cultivation. Section 2 lists the data requirements that will be assessed in accordance with the principles described in Section 3. Under the assumption that the event(s) for renewal is identical in its sequence¹¹ to the originally assessed event(s), as determined by the complete nucleotide sequence (insert and flanking regions), the data requirements listed in Section 2 should allow the EFSA GMO Panel to examine whether the previous risk assessment of the EFSA GMO Panel still remains valid in light of current scientific information. In case this assumption is not verified by the available nucleotide sequence data for the complete event(s), it will be reflected in the EFSA scientific opinion.

2. Data requirements

On the basis of Regulation (EC) No 1829/2003, the EFSA GMO Panel establishes a set of data required for the risk assessment of renewal applications of GM food and feed authorised for import and processing in the EU. Any deviation from the hereunder listed requirements should be explained and justified.

2.1. Copy of authorisation for placing the food/feed on the market

The renewal application should contain a copy of the EU authorisation for the placing on the market of the GM food and/or feed.

2.2. Post-market monitoring and post-market environmental monitoring reports

Following the placing on the market of a GM plant in the EU, the applicant has a legal obligation to implement a post-market environmental monitoring (PMEM) plan and, when imposed as a condition of the authorisation, a post-market monitoring plan (PMM) in accordance with the conditions specified

¹⁰ That is GMOs for food/feed use, food/feed containing or consisting of GMOs and food/feed produced from or containing ingredients produced from GMOs (according to Articles 3 and 15 of Regulation (EC) No 1829/2003)

¹¹ Because naturally occurring mutations as well as meiotic recombination cause genomes to evolve, sequence identity of the event(s) cannot always be expected. Mutations occurring in seed lines containing this event(s) and giving rise to varieties imported to the EU close to the time of the renewal applications could be considered for further risk assessment (Section 3). The sequence identity of each event can most easily be ascertained by resequencing of relevant plant material. Event-specific detection methods, based on the use of a unique but limited sequence identity, are routinely used to detect event(s) in GM food or feed. However, because of the very limited sequence coverage, the use of these methods is not sufficient to confirm the complete sequence identity of the event(s).

in the authorisation.^{12,13} According to Articles 11 and 23 of Regulation (EC) No 1829/2003, the PMEM and, whenever available, the PMM reports should be provided by the applicant to support the assessment of renewal applications.

The applicant should consider and comment on the results of the PMEM and PMM reports, indicating whether their outcomes challenge or change in any way the conclusions of the original risk assessment, or require modifications to the implemented management or monitoring measures for the GM plant (see Section 3).

2.3. New information

2.3.1. Systematic search and evaluation of literature

As a tool to provide information on the safety of the GM food and feed for renewal, all scientific databases, relevant for the three main areas of the risk assessment (molecular characterisation, food and feed safety¹⁴ and the environment), should be searched for new scientific information in a comprehensive and structured manner.

The applicant should perform a literature search that ensures methodological rigour and coherence in the retrieval and selection of publications, transparency and reproducibility. The applicant should apply criteria for the search strategy as recommended in the EFSA guidance on the application of systematic review methodology to food and feed safety assessments (EFSA, 2010).

The databases examined, the search terms used, the total and relevant hits, and any restrictions used should be stated. The database searches should cover all literature on the GM food and feed for renewal, produced since the authorisation of that event(s). The results of the systematic search should be documented by a list of all hits with full references. Copies of the relevant papers should be provided.

All of the information retrieved from the systematic search and relevant for the molecular characterisation, the food and feed safety assessment and the environmental risk assessment of the GM food and feed for renewal should be evaluated and discussed in the context of the renewal application (see Section 3).

In case a systematic literature search was performed and documented in the frame of each of the yearly PMEM reports throughout the full duration of the authorisation period, consistently using the same search terms and databases, the applicant can, instead, provide a summary report of the outcome of these systematic literature searches.

2.3.2. Updated bioinformatics

The applicant is requested to provide updated bioinformatic analyses of the event(s) in the GM food and feed for renewal. The requirements are specified below:

- In order to assess any interruption of plant genes by the insert(s) in the GM food and feed, the applicant should perform similarity searches using up-to-date EST (Expressed Sequence Tag), general nucleotide and general protein databases (e.g. non-redundant nucleotide and protein databases) and, when publicly available, annotated genome databases of corresponding species.

¹² 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, 17.4.2001, p. 1–38.

¹³ 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.

¹⁴ All routes of exposure (oral, dermal and respiratory) should be considered.

- In order to identify whether the newly expressed proteins show significant amino acid sequence similarity to known toxic and/or allergenic proteins, the applicant is requested to perform such studies, using up-to-date databases.
- In order to identify whether open reading frames (ORFs) present within the insert(s) and spanning the junctions between the insert(s) and the flanking DNA potentially encode peptides with amino acid sequence similarity to known allergenic or toxic proteins, the applicant is requested to perform similarity searches using up-to-date databases for all ORFs between stop codons without applying a size limit.

For these searches, the applicant should follow relevant EFSA guidance documents for the risk assessment of food and feed from GM plants and the assessment of allergenicity (EFSA GMO Panel, 2010a, 2011).

Given that databases are regularly updated, bioinformatic analyses should be performed not earlier than one year prior to the submission of the renewal application. Based on the outcome of these analyses, further data and/or considerations may be necessary on a case-by-case basis (see Section 3).

In addition, the applicant should provide information on the similarities of DNA sequences inserted into the plant genome with microbial DNA sequences (including plasmid sequences). The applicant should assess whether this information would alter the outcome of the original assessment of the likelihood of gene transfer from plant material to microorganisms present in the receiving environment(s) (e.g. in the soil or the gastro-intestinal tract of humans or animals fed the GM food/feed). Where an increase in the likelihood of gene transfer from plant material to microorganisms is theoretically possible, the applicant should evaluate the consequences of horizontal gene transfer for human and animal health and the environment (see Section 3).

If relevant new sequence data on the event(s) for renewal have become available (see Section 2.3.3), the applicant should use these sequences to perform bioinformatic searches in updated databases.

Considering the average size of plant introns (Wu et al., 2013), a sequencing length of 1 kb on each side of the insert(s) is recommended for the characterisation of flanking sequences, in case the originally determined flanking regions did not allow to clearly determine whether known endogenous genes were interrupted (e.g. because the flanking sequences are too short, no suitable reference genome is available or the insertion site is not located in specific regions, such as transposon-rich regions).

2.3.3. Additional documents or studies performed by or on behalf of the applicant

The applicant is requested to give an overview of any prohibition or restriction imposed by the competent authority of any third country in which the food and/or feed is placed on the market. Inconclusive opinions should be included in this overview.

The applicant should list and summarise all unpublished studies produced, controlled or sponsored by the applicant or provided to the applicant by a third party and not previously submitted to the EU. The applicant should review and assess their relevance for molecular characterisation, human and animal safety and the environment. Amongst those studies, data on the sequence of the event(s) for renewal, derived from seed lines containing this event(s) and giving rise to varieties imported to the EU close to the time of the renewal application, should be included.

3. Overall assessment

The applicant is requested to evaluate whether the collected information leads to the identification of new hazards or modified exposure, or adds new scientific uncertainties and therefore challenges the previous risk assessment. It is the applicants' responsibility to make an overall assessment of all new information and to provide a scientific rationale for the need to further address any newly identified

hazards or uncertainties. If new hazards or modified exposure or uncertainties are identified that require new studies, these should be performed in accordance with current legislation and EFSA guidance documents.

4. Monitoring plan and proposal for improving the conditions of the original authorisation

Based on the conclusions of the overall assessment of the GM food and feed for renewal, the applicant might update the monitoring plan(s) and, where appropriate, propose changes to the existing restrictions and conditions of release/use as laid down in the initial authorisation.

DOCUMENTATION PROVIDED TO EFSA

1. Proposal by the GMO Panel for a self-tasking activity to develop a guidance document for the risk assessment of the renewal of GM plant products authorised under Regulation (EC) No 1829/2003. 18 July 2013. Submitted by the Chair of the EFSA GMO Panel.
2. Acceptance of the self-task mandate of the EFSA GMO panel to develop a guidance document for the risk assessment of the renewal of GM plant products authorised under Regulation (EC) No 1829/2003. 26 July 2013. Submitted by the EFSA Executive Director.
3. Legal interpretation of Articles 11 and 23 of Regulation (EC) No 1829/2003. 22 May 2014. Submitted by DG SANCO.
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