SCIENTIFIC OPINION

Draft Guidance for Renewal Applications of Genetically Modified Food and Feed authorised under Regulation (EC) No. 1829/2003[1]

EFSA Panel on Genetically Modified Organisms (GMO)[2, 3]

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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 GM food and feed. This Guidance document describes the mandatory requirements for renewal applications, which should contain the identification of the transformation event(s), 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 on the GM food and feed. Applicants are requested to assess the collected information and conclude whether the assumptions made during the previous risk assessment remain valid. The applicants should also make a proposal, if appropriate, for amending or complementing the conditions of the original authorisation, *inter alia* the conditions concerning future monitoring.

KEY WORDS

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

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SUMMARY

This Guidance document describes the mandatory requirements for renewal applications, which should contain the identification of the transformation event(s), 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 on the GM food and feed. The collected information should be assessed to see whether the assumptions made during the previous risk assessment remain valid. If appropriate, the applicants should also make a proposal, for amending or complementing the conditions of the original authorisation, *inter alia* the conditions concerning future monitoring.

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BACKGROUND AS PROVIDED BY EFSA

According to Articles 11(6) and 23(6) of Regulation (EC) No 1829/2003[4] on genetically modified (GM) food and feed, the European Food Safety Authority (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 feed[5] (hereafter referred to as 'renewal applications'). Currently, a Guidance Document is 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 GMO Panel, 2006). Since the renewal of the GM food and feed authorised directly 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 applicants in the preparation and presentation of the renewal applications.

The first renewals of GM food and feed authorised under Regulation (EC) No 1829/2003 are expected in 2016. The new Guidance Document on the risk assessment of renewal applications of GM food and feed should consider the highest scientific standards and up-to-date data requirements for the risk assessment of GM food and feed as laid down in EFSA Guidance documents.

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 Genetically Modified 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[6].

[4] 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, 1-23.
[5] 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, 1-23.
[6] http://www.efsa.europa.eu/en/gmowgs/documents/guidanceRAofGM1829-2003.pdf

TERMS OF REFERENCE AS PROVIDED BY EFSA

The EFSA GMO Panel is asked:

- To prepare a Guidance Document for the risk assessment of GM food and feed already authorised under Regulation (EC) No 1829/2003 in the frame of the renewal of authorisations,
- 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.

ASSESSMENT

1. INTRODUCTION

In 2006, the first GM food and feed[7] were authorised in the European Union under Regulation (EC) No 1829/2003. This Regulation foresees a ten year authorisation period that is renewable following the provisions laid down in Articles 11 and 23.

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

(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 animals, humans or the environment; and
(d) 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 the Commission Implementing Regulation (EU) No 503/2013[8] where the specifics for the methods of detection, identification and quantification of GM food or feed are laid down.

This document provides guidance on data requirements and assessment of renewal applications of GM food and feed for import and processing in the European Union (EU). Section 2 lists the mandatory data requirements that need to be assessed according to the principles described in Section 3.

2. MANDATORY DATA REQUIREMENTS

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

2.1. Identification of the transformation event(s)

Since naturally occurring mutations cause genomes to evolve, a GM event(s) for renewal may not always have sequences identical to those originally assessed. Furthermore, detection of the event(s) with the method provided in the original application cannot be used as evidence of sequence identity, since mutations in either the insert, or flanking regions, or both do not necessarily result in a loss of detection capacity.

Therefore, applicants are requested to confirm the identity of the event(s) for renewal authorisation by sequencing. In addition, the characterisation of the flanking sequences should provide updated sequence data for subsequent bioinformatic analyses (see Section 2.4.2). Unless the insertion site is located in specific regions (e.g. transposon rich regions), and taking into consideration the average size of plant introns (Wu et al., 2013), a length of 1kb on each side of the insert is normally considered the minimum requirement for the characterisation of flanking sequences.

[7] i.e. 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)
[8] 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, 1-48.

In case the sequence is not identical to the one of the initially authorised event(s) the genetic changes (SNPs, insertions or deletions) should be further considered, discussed and risk assessed (see Sections 2.4.2 and 3). In some cases it may be necessary to extend the sequence analysis further into the plant genomic DNA (see Section 3).The material used for sequencing should be selected from GM plants only containing the event(s) for which renewal is sought. The data should be generated from a representative number of current varieties of GM plants from different geographical areas that typically export to the European Union. Applicants should justify the choice of varieties and geographical areas.

For commercialised GM food and feed, sequence data should be collected from the latest grown generation, or from the last generated batch of homozygous parental lines for those crops typically marketed as hybrids (e.g. maize, oilseed rape). For single events that are not or no longer commercialised, sequence data should also be collected. Applicants are requested to explain the rationale applied for selecting the GM plant material.

2.2. 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.

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

Following the placing on the market of a GMO in the EU, applicants have the legal obligation to propose and implement a post-market environmental monitoring (PMEM) plan, according to the conditions specified in the authorisation[9] [10]. Applicants are requested to report on the PMEM in accordance with the standard reporting formats established by the European Commission Decision 2009/770/EC[11]. In addition, where requested, reports for the post-market monitoring (PMM) activities for that GMO should be included.

According to Articles 11 and 23 of Regulation (EC) No 1829/2003, the PMEM and, whenever available, PMM reports should be provided by applicants to support the assessment of renewal applications.

Applicants should consider and comment the results of the PMEM and PMM reports, indicating whether their outcomes change in any way the conclusions of the original risk assessment or require modifications to the implemented management or monitoring measures of the GMO (see Section 3). Applicants need to describe any unintended environmental exposure and adverse impacts observed during the PMEM.

2.4. New information

2.4.1. Systematic search and evaluation of literature.

As a tool to provide information on the safety of the GM food and feed for renewal, all relevant scientific databases should be searched for new scientific information in a comprehensive and structured manner.

[9] 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 106/1-38

[10] 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, 1-23.

[11] Commission decision of 13 October 2009 establishing standard reporting formats for presenting the monitoring results of the deliberate release into the environment of genetically modified organisms, as or in products, for the purpose of placing on the market, pursuant to Directive 2001/18/EC of the European Parliament and of the Council. OJ L 275, 9-27.

Applicants should perform a literature search that ensures methodological rigour and coherence in the retrieval and selection of publications, transparency, and reproducibility. Applicants 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.

The databases examined, search terms used, total and relevant hit rate 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 publication of the most recent EFSA scientific opinion. Results of the systematic search should be documented. Copies of the relevant papers should be provided.

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

2.4.2. Updated bioinformatics

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

- In order to assess any interruption of plant genes by the insert(s) in GM food and feed, applicants are requested to provide bioinformatic analyses of the regions flanking the insert and an analysis of inter- and intra-species sequence similarities. The similarity searches should be performed using up-to-date EST, general nucleotide and general protein databases (e.g. non-redundant nucleotide and protein).

- In order to identify whether the newly expressed proteins show relevant similarity with known toxic and/or allergenic proteins, applicants are requested to perform such a study, using up-to-date databases.

- In order to identify whether ORFs present within the inserts and spanning the junctions between the inserts and the flanking DNA, potentially encode peptides with similarity to known allergenic or toxic proteins, applicants are requested to perform a similarity search using up-to-date databases for all open reading frames between stop codons without applying a size limit.

For these searches, applicants should follow relevant EFSA Guidance Documents for the risk assessment of food and feed from GM plants and the assessment of allergenicity.

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, applicants should provide information on the similarities of inserted plant DNA sequences with microbial DNA sequences. Applicants should assess whether this information would alter the assessment of the likelihood of gene transfer from plant material to the microorganisms present in the receiving environment(s) (e.g. into soil, or inside the gastro-intestinal tract of human or animals fed GM food/feed), and should evaluate the consequences of horizontal gene transfer for human and animal health and the environment (see Section 3).

Applicants should use the sequences obtained from the identity confirmation of the event(s) presented in the renewal application (see Section 2.1), as these are considered the most appropriate and relevant sequences for the bioinformatic searches in updated databases.

2.5. Additional documents or studies performed by the applicant or third party

Applicants are requested to report any authorisations for the GM food and feed granted by third countries. Information on any conditions for release/use and specific restrictions attached to the authorisations should also be included.

In addition, applicants should list all applications either under assessment, or pending authorisation submitted within or outside the EU that include the event(s) for renewal, for example in the context of stacked event applications. This list should also mention unsuccessful applications, providing the reasons for such negative or inconclusive opinion(s).

Applicants should consider relevant documents or studies on the GM food and feed for renewal, produced since the publication of the most recent EFSA scientific opinion. In particular, applicants are requested to provide any relevant information gained from the introduction of the event into other varieties, such as protein expression levels or agronomic and compositional characteristics which could further support the evaluation of the GM food and feed.

3. RISK ASSESSMENT

Applicants are requested to evaluate if the collected information leads to the identification of new hazards or modified exposure or adds new scientific uncertainties and therefore challenges assumptions made during the previous risk assessment. It is the applicants' responsibility to make an initial assessment of all new information and to provide a scientific rationale for the need to further address any newly characterised hazards or uncertainties. When new hazards or uncertainties are identified, the risk assessment may require that new studies are performed in accordance with current legislation and the most recent EFSA guidance documents.

4. MONITORING PLAN AND PROPOSAL FOR IMPROVING THE CONDITIONS OF THE ORIGINAL AUTHORISATION.

If new or additional risks and/or critical uncertainties linked to the GM food/feed or the environment are identified, there may be the need to revise the management and/or monitoring measures proposed and conducted by applicants. Based on the conclusions of the overall assessment of the GM food and feed for renewal, applicants will update their monitoring plan 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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EFSA GMO Panel (EFSA Panel on Genetically Modified Organisms), 2006. Guidance document of the Scientific Panel on Genetically Modified Organisms for renewal of authorisations of existing GMO products lawfully placed on the market, notified according to Articles 8 and 20 of Regulation (EC) No 1829/2003. EFSA Journal 435, 1-4.

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