

## COVER PAGE

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# Scientific Guidance for the preparation of applications on smoke flavouring primary products

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## Abstract

Following a request from the European Commission, EFSA developed updated scientific guidance to assist applicants in the preparation of applications on smoke flavouring primary products. This guidance describes the scientific data to be included the applications for the authorisation of new smoke flavouring primary products, as well as for the modification or for the renewal of existing authorisations, submitted under Articles 7, 11 and 12 of Regulation (EC) No 2065/2003. Information to be provided in all applications relates to: the characterisation of the primary product, including the description of the source materials, manufacturing process, chemical composition, specifications and stability; the proposed uses and use levels and the assessment of the dietary exposure; the safety data, including information on the genotoxic potential of the identified components and of the uncharacterised fraction of the primary product, toxicological data other than genotoxicity and information on the safety for the environment. For the toxicological studies, a tiered approach is devised in the guidance consisting of two tiers, for which the testing requirements, key issues and triggers are described. A description of the standard uncertainties relevant for the evaluation of primary products and how these are considered in the standardised risk assessment procedure is also included. The applicant should generate the data requested in each section to support the safety assessment of the smoke flavouring primary product. On the basis of the submitted data, EFSA will assess the safety of the primary product and conclude whether or not it presents risks to human health and to the environment under the proposed conditions of use.

## Keywords

Smoke flavourings, primary products, guidance, renewal, mixtures.

## 36 Summary

37 The European Commission asked the European Food Safety Authority (EFSA) to develop  
38 updated consolidated guidance for submission of applications on smoke flavouring primary  
39 products under Regulations (EC) No 2065/2003 and No 1321/2013.

40 This document provides guidance to applicants on the data to be included in applications for  
41 the authorisation of new smoke flavouring primary product, as well as for the modification or  
42 for the renewal of existing authorisations, submitted respectively under Articles 7, 11 and 12  
43 of Regulation (EC) No 2065/2003.

44 This document is also intended to outline the type and quality of information required by EFSA  
45 to carry out the evaluation of a smoke flavouring primary product and to conclude whether it  
46 is safe under the proposed conditions of use.

47 Chapters 1–3 of the guidance document reflect the structure that should be followed by  
48 applicants when preparing the dossier to support such an application:

- 49 – Chapter 1 – *Characterisation of the Primary Product*, containing the information  
50 specific to the production process, compositional data, specification and stability of the  
51 smoke flavouring primary product.
- 52 – Chapter 2 – *Proposed uses and exposure assessment*, including the information  
53 specific to the proposed uses and use levels and the anticipated intake of the primary  
54 product.
- 55 – Chapter 3 – *Safety data*, describing the type of toxicity studies needed to demonstrate  
56 the safety of the primary product for human health and for the environment. It includes  
57 the data requirements needed to assess the genotoxic and toxicity potential of the  
58 primary product and the potential impact of its use on the environment.

59 Chapter 4 on *Uncertainty* includes the characterisation of the standard uncertainties relevant  
60 to the safety assessment of smoke flavouring primary products together with a description of  
61 how they are expected to influence the outcome of the risk assessment.

62 The applicant should generate the data requested in each section to support the safety  
63 assessment of the smoke flavouring primary product. Based on the submitted data, EFSA will  
64 assess the safety of the primary product and conclude whether or not it presents risks to  
65 human health and to the environment under the proposed conditions of use.

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## 129 **Introduction**

130 Background as provided by the requestor

131 Smoke flavourings are a specific category of flavourings and are subject to the general  
132 Regulation (EC) No 1334/2008<sup>1</sup> on flavourings and certain food ingredients with flavouring  
133 properties for use in/on foods. This Regulation lays down the general requirements for safe  
134 use of flavourings, provides definitions for different types of flavourings and sets out flavouring  
135 substances for which an evaluation and approval is required.

136 Smoke flavourings are specifically regulated by Regulation (EC) No 2065/2003<sup>2</sup> of the  
137 European Parliament and of the Council on smoke flavourings used or intended for use in or  
138 on foods. This Regulation establishes a Community procedure for the safety assessment and  
139 the authorisation of smoke flavourings intended for use in or on foods on the basis of a high  
140 level of protection of human health and protection of consumers' interests, as well as to ensure  
141 fair trade practices.

142 Regulation (EU) No 1321/2013<sup>3</sup> establishing the Union list of authorised smoke flavouring  
143 primary products for use as such in or on foods and/or for the production of derived smoke  
144 flavourings, was published on 12 December 2013. This Regulation lists the 10 authorised  
145 smoke flavouring primary products for use in or on foods and their conditions of use. This list  
146 was established on the basis of the applications submitted under Article 20 of the Regulation  
147 (EC) No 2065/2003<sup>2</sup> and after evaluation by EFSA.

148 As provided for under Article 7, paragraph 4 of Regulation (EC) No 2065/2003<sup>2</sup>, EFSA  
149 developed the existing current guidance for the submissions of applications intended to  
150 establish the list of authorised smoke flavourings in view of their evaluation under the same  
151 Regulation.

152 The guidance is applicable to new applications on smoke flavourings primary products and for  
153 the renewal of the existing authorisations.

154 The current guidance is essentially based on a set of EFSA documents mentioned below:

- 155 – Guidance on the submission of a dossier on a smoke flavouring primary product (EFSA  
156 AFC Panel, 2005)

157 This lays down the information required by applicants to be included in the application. It lays  
158 down requirements in terms of administrative, technical and toxicological data necessary to  
159 enable EFSA to carry out the safety assessment of a smoke flavouring primary product.

160 This document is supplemented by the following additional documents:

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<sup>1</sup> Regulation (EC) No 1334/2008 of the European Parliament and of the Council of 16 December 2008 on flavourings and certain food ingredients with flavouring properties for use in and on foods and amending Council Regulation (EEC) No 1601/91, Regulations (EC) No 2232/96 and (EC) No 110/2008 and Directive 2000/13/EC. OJ L 354, 31.12.2008, p. 34–50

<sup>2</sup> Regulation (EC) No 2065/2003 of the European Parliament and of the Council of 10 November 2003 on smoke flavourings used or intended for use in or on foods. OJ L 309, 26.11.2003, p. 1–8.

<sup>3</sup> Commission Implementing Regulation (EU) No 1321/2013 of 10 December 2013 establishing the Union list of authorised smoke flavouring primary products for use as such in or on foods and/or for the production of derived smoke flavourings. OJ L 333, 12.12.2013, p. 54–67.

161 – Dietary exposure assessment methods for smoke flavouring primary products (EFSA  
162 CEF Panel, 2009)

163 Dietary exposure for smoke flavourings is assessed using specifically developed methods, the  
164 SMK-TAMDI and SMK-EPIC methods.

165 – Statement on the interpretation of the Margin of Safety for Smoke Flavourings Primary  
166 Products (EFSA, 2010)

167 This statement clarifies the use of the margin of safety for smoke flavouring primary products  
168 on the basis of the available toxicological data.

169 EFSA is asked to update the above-mentioned documents and compile them in a single  
170 comprehensive document taking into account cross-sectional guidance documents, such as:

171 – Opinion on genotoxicity testing strategies applicable to food and feed safety  
172 assessment (EFSA Scientific Committee, 2011);

173 – Opinion on the clarification of some aspects related to genotoxicity assessment (EFSA  
174 Scientific Committee, 2017);

175 – Statement on the genotoxicity assessment of chemical mixtures (EFSA Scientific  
176 Committee, 2019);

177 – Harmonised methodologies for human and animal health and ecological risk  
178 assessment of combined exposure to multiple chemicals (EFSA Scientific Committee,  
179 2019);

180 – Guidance on the use of the Threshold of Toxicological Concern approach in food  
181 safety assessment (EFSA, Scientific Committee, 2019).

182 In addition, in the preparation of the new guidance, EFSA should also consider the latest  
183 updated version of the relevant OECD Test Guidelines (TG), such as:

184 – OECD TG 488 (OECD, 2020) Transgenic Rodent Somatic and Germ Cell Gene Mutation  
185 Assays;

186 – OECD TG 474 (OECD, 2016a) *In vivo* mammalian erythrocyte micronucleus test OECD  
187 TG 489 (OECD, 2016b) *In vivo* Mammalian Alkaline Comet Assay.

188 As regards the exposure assessment, EFSA should take into account that the food categories  
189 used for regulatory purposes in flavourings are the food categories mentioned in Part D of  
190 Annex II of Regulation (EC) No 1333/2008<sup>4</sup> on food additives. A more refined exposure  
191 assessment could also be considered, based on actual use levels and on detailed food  
192 consumption data across different population groups and scenarios.

193 Besides the safety aspects derived from the general requirements for flavourings, the  
194 protection of the environment should be considered, where appropriate.

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<sup>4</sup> Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives. OJ L 354, 31.12.2008, p. 16–33.

195 Furthermore, the relevant provisions arising from the recently published transparency  
196 Regulation<sup>5</sup> should also be taken into account in the preparation of this updated guidance and  
197 consistency should be ensured with other sectors where similar updates will be done.

198 While recognizing a connection with the general guidance and requirements for flavourings  
199 which may need also to be revised, the Commission considers that it is desirable, in view of  
200 the specific conditions of smoke flavourings, to consider this update of the guidance on smoke  
201 flavouring primary products separately.

## 202 Terms of Reference as provided by the requestor

203 The Commission requests EFSA to prepare an updated consolidated guidance for the  
204 submission of applications on smoke flavouring primary products under Regulations (EC) No  
205 2065/2003<sup>2</sup> and No 1321/2013<sup>3</sup>, taking into account the experience gained with the  
206 assessment and the regulation of the currently authorised and assessed smoke flavouring  
207 products in the EU and, notably, the numerous other relevant scientific and technical  
208 documents published by EFSA since the adoption of the current guidance related to the safety  
209 of smoke flavourings.

210 The guidance should be updated taking into account applications on new smoke flavourings  
211 and the renewals of the existing authorisations.

212 EFSA should take into account the relevant provisions of Regulation (EU) 2019/1381<sup>5</sup> of the  
213 European Parliament and of the Council on the transparency and sustainability of the EU risk  
214 assessment in the food chain in the preparation of this updated guidance and should ensure  
215 consistency with other sectors where similar updates will be done.

216 The Commission requests EFSA to carry out this updating within 18 months from the receipt  
217 of this letter.

## 218 Interpretation of the Terms of Reference

219 In accordance with the Terms of Reference as provided by the European Commission, the  
220 comparison between smoke flavouring primary products (see 'Definitions') and conventional  
221 methods of smoking with respect to their respective impact on human health and the  
222 environment is not considered in this guidance document, as it is outside the scope of the  
223 request.

224 All administrative information related to the preparation and submission of an application for  
225 a new authorisation, or for a modification, or a renewal of an existing authorisation of smoke  
226 flavouring primary products is addressed in a separate EFSA document, 'Administrative  
227 guidance for the preparation of applications on smoke flavouring primary products' (EFSA,  
228 2020), which is applicable to applications submitted as of 27 March 2021.

229 As indicated in the Terms of Reference, this document is mainly intended to provide guidance  
230 to applicants for the preparation of applications:

- 231 – for the authorisations of new smoke flavouring primary products submitted under  
232 Article 7 of Regulation (EC) No 2065/2003 and

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<sup>5</sup> Regulation (EU) 2019/1381 of the European Parliament and of the Council on the transparency and sustainability of the EU risk assessment in the food chain. OJ L 231 of 6/9/2019 p.1



















































































