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Scientific opinion on the renewal of the authorisation of Fumokomp (SF-009) as a smoke flavouring Primary Product

EFSA Panel name on Food Additives and Flavourings (FAF),
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Abstract

The EFSA Panel on Food Additives and Flavourings (FAF) was requested to evaluate the safety of the smoke flavouring Primary Product Fumokomp (SF-009), for which a renewal application was submitted in accordance with Article 12(1) of Regulation (EC) No 2065/2003 (in the renewal application the Primary Product is reported as 'Fumokomp Conc.'). This opinion refers to an assessment of data submitted on chemical characterisation, dietary exposure and genotoxicity of the Primary Product. Fumokomp Conc. is produced by pyrolysis of beech and hornbeam woods. Gas chromatography–mass spectrometry (GC–MS) was applied for both identification and quantification of the volatile constituents of the Primary Product. Given the limitations of the method, the Panel cannot judge with confidence whether the applied method meets the legal quality criterion that at least 80% of the volatile fraction shall be identified and quantified. Moreover, the Panel concluded that the absence of furan-2(5*H*)-one from the Primary Product was not convincingly demonstrated. At the maximum proposed use levels, dietary exposure estimates calculated with FAIM ranged from 0.04 to 0.9 mg/kg body weight (bw) per day at the mean and from 0.1 to 1.5 mg/kg bw per day at the 95th percentile. The information available on the 32 identified components of the Primary Product, although limited, did not indicate a concern for genotoxicity for any of these substances. However, whole mixture testing in an *in vitro* mouse lymphoma assay gave positive results which would require an adequate *in vivo* follow-up study. In addition, the potential for aneugenicity of the Primary Product has not been adequately investigated. Accordingly, the potential safety concern for genotoxicity of the Primary Product cannot be ruled out.

Keywords: Fumokomp, Fumokomp Conc., SF-009, smoke flavouring Primary Product, genotoxicity

Requestor: European Commission

Question number: EFSA-Q-2022-00414

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1. Introduction

1.1. Background and Terms of Reference as provided by the requestor

1.1.1. Background

Regulation (EC) No 2065/2003[1] establishes a procedure for the safety assessment and the authorisation of smoke flavouring primary products with a view to ensuring a high level of protection of human health and the effective functioning of the internal market. No smoke flavouring or any food where such a smoke flavouring is present (in or on) can be placed in the market if the smoke flavouring is not an authorised Primary Product or is not derived therefrom and if the conditions of use laid down in the authorisation in accordance with this Regulation are not adhered to (Article 4(2) of Regulation (EC) No 2065/2003).

Commission Implementing Regulation (EU) No 1321/2013[2] authorised 10 smoke flavouring primary products for a 10-year period, due to expire on 31 December 2023.

The European Commission has received an application for the renewal of the authorisation of the smoke flavouring primary product Fumokomp (SF-009) for a 10-year period, in accordance with Article 12 of Regulation (EC) No 2065/2003.

1.1.2. Terms of Reference

The European Commission requests the European Food Safety Authority (EFSA) to evaluate the safety of the smoke flavouring primary product Fumokomp (SF-009), for which a renewal application has been submitted, in accordance with Article 12(1) of Regulation (EC) No 2065/2003.

The safety assessment shall be carried-out in two steps. Firstly, EFSA shall give a scientific opinion on the data included in the renewal application dossier related to the chemical characterisation, the genotoxicity and the dietary exposure to Fumokomp (SF-009).

Secondly, provided that the genotoxic concern can be ruled out in the first part of the evaluation, EFSA shall complete the rest of the safety assessment without delay upon submission of the relevant pending data from the applicant.

1.2. Interpretation of the Terms of Reference

In line with the terms of reference (see Section 1.1.2), the safety of the Primary Product will be assessed in two steps.

The current (first) opinion will address the chemical characterisation, genotoxicity and dietary exposure to the smoke flavouring Primary Product.

If in the first opinion, no concern for genotoxicity is raised, EFSA will issue a second opinion assessing the toxicity other than genotoxicity data, as required by the EFSA guidance for the preparation of applications on smoke flavouring Primary Products (EFSA FAF Panel, 2021).

1.3. Additional information

EFSA issued two opinions on the safety of this smoke flavouring Primary Product Fumokomp in 2009 and in 2011 (EFSA CEF Panel, 2009, 2011a).

Following the safety assessment from EFSA, Fumokomp was authorised in the European Union and assigned the unique code 'SF-009', according to Commission Implementing Regulation (EU) No 1321/2013, establishing the Union list of authorised smoke flavouring Primary Products, for a 10-year period with effect from 1 January 2014.

The current opinion refers to an assessment of the data submitted by the authorisation holder for the renewal of the authorisation of Fumokomp (SF-009) as a smoke flavouring Primary Product, in line with Article 12(1) of Regulation (EC) No 2065/2003.

[1] 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, pp. 1–8.

[2] 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, pp. 54–67.

2. Data and methodologies

2.1. Data

The present evaluation is based on the data provided by the applicant in the form of a technical dossier, submitted according to Article 12(1) of Regulation (EC) No 2065/2003 for the renewal of the authorisation of the smoke flavouring Primary Product Fumokomp (SF-009). Since in the renewal application the Primary Product is reported as 'Fumokomp Conc.' by the applicant, this name is used throughout the current opinion.

In accordance with Article 38 of the Regulation (EC) No 178/2002[3] and taking into account the protection of confidential information and of personal data in accordance with Articles 39 to 39e of the same Regulation and of the Decision of the EFSA's Executive Director laying down practical arrangements concerning transparency and confidentiality,[4] the non-confidential version of the dossier is published on Open.EFSA.[5]

According to Art. 32c(2) of Regulation (EC) No 178/2002 and to the Decision of EFSA's Executive Director laying down the practical arrangements on pre-submission phase and public consultations, EFSA carried out a public consultation on the non-confidential version of the application from 15 November to 6 December 2022, for which no comments were received.

Additional information was sought from the applicant during the assessment process in response to requests from EFSA sent on 11 November 2022 and was subsequently provided (see Documentation provided to EFSA No. 2).

The Panel acknowledged the submission of data on toxicity other than genotoxicity by the applicant in the technical dossier (see Documentation provided to EFSA No. 1, No. 3 and No. 4). As indicated in Section 1.2, the assessment of these data is outside the scope of the present opinion.

2.2. Methodologies

The safety assessment of the Primary Product Fumokomp Conc. was conducted in line with the requirements laid down in Regulation (EC) No 2065/2003 and following the principles of the EFSA guidance for the preparation of applications on smoke flavouring Primary Products (EFSA FAF Panel, 2021).

The principles described in the EFSA Guidance on transparency with regard to scientific aspects of risk assessment (EFSA Scientific Committee, 2009) as well as the relevant cross-cutting guidance documents from the EFSA Scientific Committee published after the adoption of the guidance on smoke flavourings (EFSA FAF Panel, 2021), in particular the 'Guidance on technical requirements for regulated food and feed product applications to establish the presence of small particles including nanoparticles' (EFSA Scientific Committee, 2021a), were also considered during the risk assessment.

The uncertainty analysis was performed by checking whether standard and non-standard sources of uncertainties are present, as outlined in the standard procedure described in Section 4.2 of the EFSA guidance on smoke flavouring (EFSA FAF Panel, 2021). Standard uncertainties, as listed in Table G.1 of the above-mentioned EFSA guidance on smoke flavouring, were not discussed in detail in the present assessment. In case of the presence of non-standard uncertainties, these were reported in the relevant sections of the current opinion and their combined impact on the assessment was evaluated by the Panel (see Section 4).

[3] Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety. OJ L 31, 1.2.2002, pp. 1–48.

[4] Decision available online: https://www.efsa.europa.eu/en/corporate-pubs/transparency-regulation-practical-arrangements

[5] The non-confidential version of the dossier, following EFSA's assessment of the applicant's confidentiality requests, is published on Open.EFSA and is available at the following link: https://open.efsa.europa.eu/dossier/SFL-2022-5310

3. Assessment

3.1. Technical data

3.1.1. Manufacturing process

3.1.1.1. Source materials for the Primary Product

The source material of Fumokomp Conc. is hardwood from beech (*Fagus sylvatica* L.) (85–100%) and hornbeam (*Carpinus betulus* L.) (0–15%). According to the applicant, the trees from which the wood is used for manufacturing the Primary Product '*do not receive any chemical treatment in the period of 1 year before felling, or after*' (Documentation provided to EFSA No. 1). However, no respective certificate was submitted.

3.1.1.2. Method of manufacture of the Primary Product

The dried wood is pyrolysed in a continuously operated Lambiotte retort with automated gas-purging. The wood tar obtained by sedimentation is subsequently subjected to a series of fractional vacuum distillations. The Primary Product is obtained by combining appropriate distillates on the basis of the intended sensory properties of the final product. The resulting Primary Product is subjected to quality control (physico-chemical testing, analysis for polycyclic aromatic hydrocarbons (PAHs)).

The applicant submitted a description of the manufacturing process, with information on the drying step and the pyrolysis conditions.

According to the applicant, an HACCP system is implemented for quality assurance and production control.

3.1.2. Identity of the Primary Product

3.1.2.1. Trade name of the Primary Product

The trade name of the Primary Product is Fumokomp Conc.

3.1.2.2. Information on existing evaluation from other regulatory bodies

The applicant indicated that the smoke flavouring Fumokomp has not been evaluated by regulatory bodies other than EFSA. Regarding the existing authorisations in non-EU countries, no information was provided by the applicant (Documentation provided to EFSA No. 1).

3.1.2.3. Description of the physical state and sensory characteristics

The Primary Product is a viscous, oily, pale/intensive reddish-yellowish-brownish liquid, not miscible with water, and is described to have an odour of leafy woods. The Primary Product has an average density of 1100 g/L, a pH value ranging from 2 to 6, a refraction index (at 20°C) ranging from 1.485 to 1.550, and a viscosity (at 40°C) ranging from 7.06 to 12.6 centistokes (cSt).

3.1.2.4. Chemical composition of the Primary Product

The compositional data provided by the applicant for five batches of the Primary Product in the original dossier and in response to the EFSA request for additional information are summarised in Table 1 (Documentation provided to EFSA No. 1 and 2).

Table 1: Overview on the compositional data provided for five batches of Primary Product as reported by the applicant (Documentation provided to EFSA No. 1 and 2)

Batch no.	Density (g/L)	Total volatiles (wt%)	Identified volatiles		Unidentified volatiles		Total non-volatiles	Identified non-volatiles	Unidentified non-volatiles	Water (wt%)	Solvent-free fraction (wt%)[(1)]	Ident./quant. proportion of solvent-free fraction (wt%)[(3),(a)]	Ident./quant. proportion of volatile fraction (wt%)[(4),(b)]
			(area %)[(2)]	(wt%)	(area %)[(2)]	(wt%)							
7589	1,092	99.06	81.4	80.6	18.6	18.4	—	—	—	0.94	99.06	81.4	81.4
7665	1,106	98.53	80.0	78.8	20.0	19.7	—	—	—	1.47	98.53	80.0	80.0
7695	1,092	98.73	81.8	80.8	18.2	18.0	—	—	—	1.27	98.73	81.8	81.8
7709	1,104	98.71	81.7	80.6	18.3	18.1	—	—	—	1.29	98.71	81.7	81.7
7725	1,104	98.05	79.0	77.5	21.0	20.6	—	—	—	1.95	98.05	79.0	79.0
AVRG ± SD	1,100 ± 7	98.6 ± 0.4	80.8 ± 1.2	79.7 ± 1.5	19.2 ± 1.2	19.0 ± 1.1	—	—	—	1.38 ± 0.4	98.6 ± 0.4	80.8 ± 1.2	80.8 ± 1.2

wt: weight; SD: standard deviation.
(1): Calculated as: 100 − water (wt%).
(2): Area % in the gas chromatography–mass spectrometry (GC–MS) total ion chromatogram.
(3): Calculated as ((identified volatiles + identified non-volatiles)/solvent-free fraction) × 100.
(4): Calculated as (identified volatiles/total volatiles) × 100.
(a): Regulatory quality criterion for the applied method according to Regulation (EC) No 627/2006[6]: ≥ 50 (wt%).
(b): Regulatory quality criterion for the applied method according to Regulation (EC) No 627/2006: ≥ 80 (wt%).

[6] Commission Regulation (EC) No 627/2006 of 21 April 2006 implementing Regulation (EC) No 2065/2003 of the European Parliament and of the Council as regards quality criteria for validated analytical methods for sampling, identification and characterisation of primary smoke products. OJ L 109, 22.4.2006, pp. 3–6.

3.1.2.4.1. Chemical characterisation

The water content of the Primary Product was determined by the Karl Fischer titration method (Documentation provided to EFSA No. 2). In response to an additional data request from EFSA, the applicant provided data on the contents of the major chemical classes in the Primary Product, i.e. acids, carbonyls and phenols (Table 2). These data were calculated by summing up the areas of the respective peaks in the total ion chromatogram obtained for the volatile fraction, rather than by colorimetric methods or titration as requested by the Scientific Guidance (EFSA FAF Panel, 2021). Considering that the Primary Product does not contain a non-volatile fraction, and that the proportion of unidentified volatiles is below 20 wt%, the Panel considers this approach acceptable (Documentation provided to EFSA No. 2).

Table 2: Chemical compositions reported for five batches of the Primary Product

	Batch no.					Average	SD
	7589	7665	7695	7709	7725		
Acids wt% (as acetic acid)	5.1	4.3	4.4	4.7	4.6	4.6	0.3
Carbonyls wt% (as acetaldehyde)	14.2	13.6	11.1	14.1	14.1	13.4	1.3
Phenols wt% (as phenol)	47.5	47.6	50.9	47.1	46.3	47.9	1.8
Water wt%	0.9	1.5	1.3	1.3	1.9	1.4	0.4

SD: standard deviation; wt: weight.

Concentrations of arsenic, cadmium, lead and mercury were determined by inductively coupled plasma–mass spectrometry (ICP–MS) and were submitted to EFSA following an additional data request (Table 3) (Documentation provided to EFSA No. 2).

Table 3: Toxic elements reported for five batches of the Primary Product

	Batch no. (mg/L)					average (mg/L)	average (mg/kg)[a]
	7589	7665	7695	7709	7725		
Arsenic (As)	0.03	0.008	0.01	0.02	0.02	0.02 ± 0.01	0.02 ± 0.01
Cadmium (Cd)	0.001	0.001	0.001	0.001	< 0.001[b]	< 0.001	< 0.001
Lead (Pb)	0.08	0.06	0.06	0.05	0.04	0.06 ± 0.02	0.05 ± 0.01
Mercury (Hg)	0.002	0.004	0.001	0.002	0.003	0.002 ± 0.00	0.002 ± 0.001

(a): Average and standard deviation were calculated by the Panel from the values of the individual batches, taking into account their respective densities.
(b): Value below the corresponding limit of quantification (LOQ).

3.1.2.4.2. Identification and quantification of the volatile fraction

Gas chromatography–mass spectrometry (GC–MS) was applied for both identification and quantification of the volatile constituents of the Primary Product. Individual volatile constituents were considered as identified if their chromatographic (retention time) and their mass spectral data were in agreement with those of reference standards. Overall, using this approach, 32 constituents were identified and quantified in the Primary Product (Appendix A, Table A.1). The lowest concentration reported by the applicant was 0.08 wt% *trans*-crotonic acid (CAS-no.: 107-93-7). The 20 principal volatile constituents are presented in Table 4, which reflects the compositional data obtained for five batches of the Primary Product (for batch numbers see Table 1).

Quantification was based on the area% determined for the individual peaks in the total ion current (TIC) chromatogram. No substance-specific response factors were taken into consideration, which could have been done since the reference standards were in hand. This hampers the quantification, because depending on the effective split-ratio, the ionisation efficiency and the fragmentation patterns of the individual components, the areas determined on the basis of the total ions may result in over- or underestimations of the components' quantities. Therefore, the Panel considers the quantitative data provided for the individual volatile constituents reported in Table 4 and Appendix A as approximate only, and a non-standard source of uncertainty with respect to the chemical composition of the Primary Product (see Section 2.2 of this opinion and Table G.1 of the EFSA guidance on smoke flavourings (EFSA FAF Panel, 2021)).

Given the limitations of the quantification approach employed by the applicant, the Panel could not judge whether the applied method meets the legal quality criterion that at least 80% by mass of the volatile fraction shall be identified and quantified (Regulation (EC) No 627/2006).

Table 4: Twenty principal volatile constituents of the Primary Product reported by the applicant (Documentation provided to EFSA No. 1 and 2)

CAS-no	FL-no	Chemical name[a]	Average concentration (wt%)	
			Current application[b]	Former application[c]
91-10-1	04.036	2,6-dimethoxyphenol (syringol)	14.3	11.1
93-51-6	04.007	2-methoxy-4-methylphenol	9.1	6.6
2785-89-9	04.008	4-ethylguaiacol (2-methoxy-4-ethylphenol)	7.9	5.4
121-34-6	08.043	vanillic acid	6.9	7.6
765-70-8	07.056[d]	3-methylcyclopentan-1,2-dione (3-methyl-1,2-cyclopentanedione)	6.3	2.4
90-05-1	04.005	2-methoxyphenol (guajacol)	6.1	
106-44-5 108-39-4	04.028 04.026	4-/3-methylphenol (*p,m*-cresol)	4.4	5.1
105-67-9	04.066	2,4-dimethylphenol (2,4-xylenol)	2.6	
95-48-7	04.027	2-methylphenol (*o*-cresol)	2.0	1.7
108-95-2	04.041	phenol	2.0	4.9
2785-87-7	04.049	2-methoxy-4-propylphenol	2.0	
5857-25-0	–	2-ethyl-3-hydroxy-2-cyclopenten-1-one	1.8	
64-19-7	08.002	acetic acid	1.6	1.6
2896-67-5	–	6-methylguaiacol (2-methoxy-6-methylphenol)	1.5	
118-71-8	07.014	maltol (2-methyl-3-hydroxypyrone)	1.4	
111-55-7	–	ethylene glycol diacetate	1.2	
2758-18-1	07.112	3-methyl-2-cyclopenten-1-one	1.2	1.8
576-26-1	04.042	2,6-dimethylphenol (2,6-xylenol)	1.0	1.7
4463-33-6	–	2,3-dimethoxytoluene	1.0	
116-09-6	07.169	1-hydroxypropan-2-one (hydroxyacetone)	0.9	

CAS: Chemical Abstract Service; FL-no: FLAVIS number; wt: weight.
(a): In case a constituent of the Primary Product is an authorised flavouring substance (FL-no), the assigned chemical name corresponds to the respective entry in the EU Union List of flavourings. Deviating chemical names reported by the applicant in the dossier are given in brackets, if applicable.
(b): From the analysis of the batches presented in Table 1.
(c): from the data presented in the previous safety evaluation of the Primary Product (EFSA CEF Panel, 2009).
(d): [FL-no: 07.056] refers to the mixture of the tautomeric forms of 3-methylcyclopentan-1,2-dione.

Following an additional data request from EFSA, the applicant commented on the fact that the current list of identified volatile constituents does not fully match the list of identified volatile constituents provided at the time of the previous EFSA assessment of Fumokomp (EFSA CEF Panel, 2009). The applicant emphasised that there were no changes in the manufacturing process and explained that the observed differences are mainly due to the fact that in contrast to the previous application, volatiles were only considered as identified if their chromatographic and mass spectrometric data matched those of reference standards (Documentation provided to EFSA No. 2).

Moreover, in response to an additional data request from EFSA to confirm the absence of furan-2(5*H*)-one (CAS-no.: 497-23-4), the applicant searched the TIC chromatograms of five batches of the Primary Product (for batch numbers see Table 1) for the mass-to-charge ratio of m/z = 55, which constitutes the base peak in the mass spectrum of furan-2(5*H*)-one. Several peaks with this m/z were found, but according to the applicant, none corresponded to furan-2(5*H*)-one because the mass spectra patterns of peaks eluting in the retention region anticipated for furan-2(5*H*)-one did not match with the mass spectrum of furan-2(5*H*)-one from a library. The Panel noted as a severe limitation of this approach that no reference standard was used to reliably assign the retention time of potentially present furan-2(5*H*)-one. In addition, overlapping of the mass spectrum of furan-2(5*H*)-one by those

of co-eluting substances cannot be excluded, which would prevent the identification of the furan-2 (*5H*)-one mass spectrum.

In order to demonstrate the sensitivity of their approach to detect furan-2(5*H*)-one if it were present, the applicant determined the limit of quantification (LOQ) and the limit of detection (LOD) for the GC–MS determination (total ion count) of 2,3-dimethyl-2-cyclopenten-1-one, which was selected as a surrogate. Using solutions of this surrogate, an LOQ of 1.8 μg/mL and an LOD of 0.6 μg/mL were determined. The applicant considered this as valid for furan derivatives. The Panel noted that this approach had several limitations: (i) the LOQ and LOD were only determined using a pure solution of the chosen calibrant and thus do not necessarily reflect the sensitivity achievable when analysing the actual Primary Product matrix; (ii) in absence of relative response factors, the sensitivity of the method used to determine 2,3-dimethyl-2-cyclopenten-1-one cannot be extrapolated to other substances.

Overall, the Panel concluded that in light of the limitations outlined above, the additional data provided do not convincingly demonstrate that furan-2(5*H*)-one is absent in the Primary Product.

3.1.2.4.3. Characterisation of the non-volatile fraction

The Primary Product is completely volatile (98.6 wt%) with the remaining 1.4 wt% made up of water. The absence of a non-volatile fraction is in agreement with the fact that distillation and combination of distillate fractions are the final steps in manufacturing the Primary Product.

3.1.2.4.4. Unidentified fraction

According to the applicant, the unidentified fraction of the Primary Product amounts to approximately 19 wt%. However, the quantification of this unidentified fraction suffers from the same limitations as described above for the identified volatile constituents (see Section 3.1.2.4.2).

3.1.2.4.5. Overall composition of the Primary Product

Based on the average values (with limited reliability, see Section 3.1.2.4) reported for five batches of the Primary Product (Table 1), the overall composition of Fumokomp Conc. (wt% of Primary Product) is shown in Figure 1, and the composition (wt%) of the solvent-free fraction is shown in Figure 2.

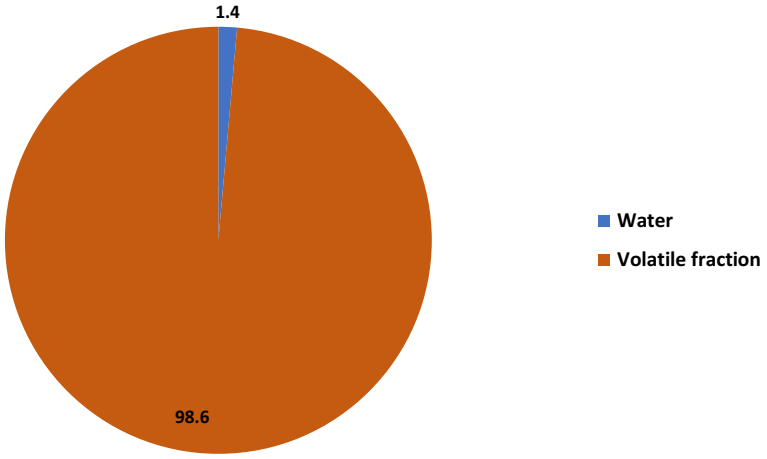

Figure 1: Overall composition of Fumokomp Conc. (wt% of Primary Product)

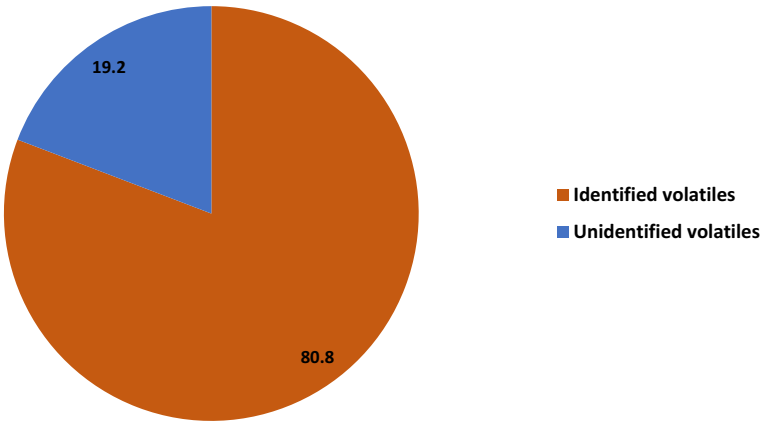

Figure 2: Composition (wt%) of the solvent-free fraction of Fumokomp Conc. as reported by the applicant

Despite the limitations in the quantification of the individual constituents, the Panel anticipates that for all five investigated batches of the Primary Product, the identified and quantified proportion of the solvent-free fraction is higher than 50%, thus meeting the legal quality criterion for the applied methods, i.e. at least 50% by mass (wt%) of the solvent-free fraction shall be identified and quantified (Regulation (EC) No 627/2006).

However, given the limitations of the quantification approach employed by the applicant (see Section 3.1.2.4.2), the Panel could not judge whether the applied method meets the legal quality criterion that at least 80% of the volatile fraction shall be identified and quantified (Regulation (EC) No 627/2006). This creates a non-standard uncertainty with respect to the chemical composition of the Primary Product (see Section 2.2 of this opinion and Table G.1 of the EFSA guidance document on smoke flavouring (EFSA FAF Panel, 2021)).

3.1.2.5. Polycyclic aromatic hydrocarbons (PAHs)

Analytical data on the contents of 16 PAHs were provided for one of the batches of the Primary Product (batch no. 7665). The analysis meets the performance criteria as set in Regulation (EC) No 627/2006. The levels reported for the individual PAHs (Table 5) are all below the minimum required limits of quantification according to Regulation (EC) No 627/2006.

The levels of benzo[a]pyrene and benzo[a]anthracene are below their respective limits of 10 and 20 μg/kg as laid down in the Regulation (EC) No 2065/2003.

The fact that data only for one batch have been submitted creates a non-standard uncertainty with respect to the PAHs levels (see Section 2.2 of this opinion and Table G.1 of the EFSA guidance document on smoke flavouring (EFSA FAF Panel, 2021)).

Table 5: Concentrations of PAHs in the Primary Product (Documentation provided to EFSA No. 1)

PAH	Conc. (μg/kg)
benzo[a]anthracene[(a)]	0.43
chrysene[(a)]	1.02
benzo[b]fluoranthene[(a)]	0.05
benzo[k]fluoranthene + benzo[j]fluoranthene	< 0.1[(b)]
benzo[a]pyrene[(a)]	< 0.03[(b)]
indeno[1,2,3-cd]pyrene	1.08
dibenzo[a,h]anthracene	< 0.90[(b)]
benzo[g,h,i]perylene	< 0.06[(b)]
dibenzo[a,l]pyrene	< 0.24[(b)]
dibenzo[a,i]pyrene	< 0.24[(b)]
dibenzo[a,h]pyrene	< 0.30[(b)]
dibenzo[a,e]pyrene	1.14

PAH	Conc. (μg/kg)
cyclopenta[cd]pyrene	0.95
5-methylchrysene	1.76
benzo[c]fluorene	1.79
PAH4	1.50–1.53

Data obtained from n = 1 sample, i.e. batch no. 7665.
PAH: polycyclic aromatic hydrocarbon.
(a): PAHs printed in bold are included in the calculation of 'PAH4', which is used for the evaluation of the exposure to these contaminants (see Section 3.3.3.2).
(b): Value below the corresponding the Limit of Quantification (LOQ).

3.1.2.6. Batch-to-batch variability

The batch-to-batch variability of the 20 principal volatile constituents of the batches presented in Table 1 was investigated by GC–MS and GC-FID. The absolute concentrations presented in Table 6 for each batch are subject to the same limitations as discussed in Section 3.1.2.4.2. However, the Panel considered the batch-to-batch variability of the five production batches (information on the production dates was not available) as acceptable, given that all batches were analysed using the same approach and the relative standard deviations are not affected by the limitations of the analytical technique (Table 6).

Table 6: Batch-to-batch variability of the Primary Product

CAS-no.	Chemical name	Batch no.					Average	SD	RSD (%)
		7665	7695	7589	7709	7725			
91-10-1	2,6-dimethoxyphenol (syringol)	13.9	19.1	14.0	13.5	11.0	14.3	2.6	18.5
93-51-6	2-methoxy-4-methylphenol	9.7	7.9	9.3	9.2	9.2	9.1	0.6	6.5
2785-89-9	4-ethylguaiacol (2-methoxy-4-ethylphenol)	8.0	10.8	7.0	6.9	6.7	7.9	1.5	19.4
121-34-6	vanillic acid	6.3	8.7	7.3	6.2	5.9	6.9	1.1	15.4
765-70-8	3-methylcyclopentan-1,2-dione (3-methyl-1,2-cyclopentanedione)	6.2	4.7	7.2	6.6	6.8	6.3	0.9	14.0
90-05-1	2-methoxyphenol (guajacol)	6.0	5.9	6.3	6.5	6.1	6.1	0.2	3.5
106-44-5 108-39-4	4-/3-methylphenol (*p,m*-cresol)	4.2	3.4	5.1	5.1	4.6	4.4	0.6	14.5
105-67-9	2,4-dimethylphenol (2,4-xylenol)	2.2	2.5	2.8	2.5	2.9	2.6	0.3	9.5
95-48-7	2-methylphenol (*o*-cresol)	2.6	1.7	1.7	1.5	2.7	2.0	0.5	24.4
108-95-2	phenol	2.2	1.1	2.4	2.2	2.1	2.0	0.5	24.1
2785-87-7	2-methoxy-4-propylphenol	2.0	2.1	1.4	2.8	1.5	2.0	0.5	25.3
5857-25-0	2-ethyl-3-hydroxy-2-cyclopentene-1-one	1.9	2.8	1.5	1.6	1.3	1.8	0.5	28.8
64-19-7	acetic acid	1.4	1.0	1.8	1.8	1.8	1.6	0.3	20.5
2896-67-5	6-methylguaiacol (2-methoxy-6-methylphenol)	1.0	1.7	1.6	1.6	1.7	1.5	0.3	16.6
118-71-8	maltol (2-methyl-3-hydroxypyrone)	1.9	1.2	1.2	1.5	1.0	1.4	0.3	24.1
111-55-7	ethylene glycol diacetate	0.8	0.7	1.6	1.5	1.4	1.2	0.4	30.1
2758-18-1	3-methyl-2-cyclopenten-1-one	1.3	0.5	1.4	1.4	1.4	1.2	0.3	29.3
576-26-1	2,6-dimethylphenol (2,6-xylenol)	1.4	0.2	0.4	1.8	1.4	1.0	0.6	61.8
4463-33-6	2,3-dimethoxytoluene	0.6	1.3	0.7	0.7	1.6	1.0	0.4	39.2
116-09-6	1-hydroxy-2-propanone (hydroxyacetone)	0.7	0.5	1.0	1.1	1.0	0.9	0.3	29.2

SD: standard deviation; RSD: relative standard deviation.

3.1.2.7. Solubility and particle size

The Primary Product is a viscous liquid which, according to the applicant, is not miscible with water. No experimental data on water solubility and on particle size of the Primary Product were provided. However, the Panel considered that owing to the final manufacturing steps, i.e. combination of the liquid fractions obtained by vacuum distillations, it is very unlikely that small particles including nanoparticles are present in the final Primary Product.

3.1.3. Specifications

The applicant provided the required product specification data and reported that the Primary Product Fumokomp Conc. is manufactured within its proposed specifications (Documentation provided to EFSA No. 1 and 2). Information on the parameters considered to be relevant for the specifications has been compiled by the Panel in Table 7.

Table 7: Relevant information for specifications of the Primary Product

	Specifications for Fumokomp Conc. as proposed by the applicant	**Specifications as reported in EFSA CEF Panel (2009)**	**Specifications as laid down in Reg. (EU) No 1321/2013**
Description	n.a.	Typically a viscous and oily, pale or intense yellow-brown liquid, not diluted by water, which is free of all extraneous smells and flavours and has a fragrance reminiscent of the smoke of deciduous trees	–
Source materials			
Woods	≥ 85% of beech (*Fagus sylvatica*), ≤ 15% of hornbeam (*Carpinus betulus*)		85% beech (*Fagus sylvatica*), 15% hornbeam (*Carpinus betulus*)
Identity parameters:			
Physico-chemical parameters			
– pH	2–6		
– Density	1,070–1,150 g/L	ρ = 1.070–1.130 g/cm^3	
– Refraction index	1.485–1.550	α = 1.485–1.525	
– Staining index	n.a.		
– Viscosity	6,00–20,00 cSt		
Chemical composition:			
Chemical classes:			
– Acids	1–8 wt%		1–8 wt% (as acetic acid)
– Carbonyls	12–30 wt%		25–30 wt %
– Phenols	15–60 wt%		15–60 wt%
– Water	≤ 2 wt%		< 2 wt%
20 principal constituents of the volatile fraction	see Table 4		
Purity:			
• benzo[a]pyrene	< 2 μg/kg	< 10 μg/kg	
• benzo[a]anthracene		< 20 μg/kg	

	Specifications for Fumokomp Conc. as proposed by the applicant	Specifications as reported in EFSA CEF Panel (2009)	Specifications as laid down in Reg. (EU) No 1321/2013
• PAH4[(a)]	< 10 μg/kg		
• Toxic elements			
– Lead	< 5 mg/kg		< 5 mg/kg
– Arsenic	< 3 mg/kg		< 3 mg/kg
– Cadmium	< 1 mg/kg		< 1 mg/kg
– Mercury	< 1 mg/kg		< 1 mg/kg

wt: weight; n.a.: not available.
(a): Sum of benzo[a]anthracene, benzo[a]pyrene, chrysene, benzo[b]fluoranthene.

The Panel noted that the analytical data for the batches analysed indicated that actual concentrations of toxic elements and PAHs (one batch only), reported in Tables 3 and 5, respectively, are lower than the currently proposed limits (Table 7), and the respective Regulations (i.e. Regulation (EU) No 1321/2013 for toxic elements and Regulation (EC) No 2065/2003 for benzo[a]pyrene).

Data for Staining Index has not been provided by the applicant. However, the Panel considered that this was not of relevance for the safety assessment.

Based on the newly provided data, the Panel considered that the proposed extension of the range of carbonyls (see Table 7) is justified by the newly provided compositional data.

3.1.4. Stability and fate in food

The applicant recommends storing the Primary Product in a cool place, protected from light and moisture (Documentation provided to EFSA No. 1).

The applicant performed a storage stability test based on GC–MS analysis of one batch (no. 7665) of the Primary Product stored under accelerated conditions (54 ± 2°C for 14 days). The applicant provided a visual comparison of the TIC chromatograms obtained from the volatile fraction of the Primary Product after different periods of storage (1, 5, 10 and 15 days). Under the applied storage conditions, the provided chromatograms looked similar. No quantitative data on individual constituents were provided. The applicant only compared the area sums and stated that the decrease observed over time was below 3%.

Although no quantitative data on the stability of the individual volatile constituents and major chemical classes were provided, the Panel considered that the data available indicate that there is no concern regarding the stability of the Primary Product under the conditions of storage as reported by the applicant.

No data on the stability of the Primary Product in commercial formulations or in the proposed food categories have been provided.

3.2. Proposed uses and use levels

The applicant applied for a renewal of authorisation of the Primary Product Fumokomp Conc. for use in food categories at the proposed maximum and expected typical use levels as presented in Table 8.

These proposed maximum and expected typical use levels were used to assess the dietary exposure to this Primary Product (see Section 3.3.2).

Table 8: Proposed maximum and expected typical use levels of the Primary Product (mg/kg) in food categories according to Annex II of Regulation (EC) No 1333/2008[7]

Food category number	Food category name	Proposed maximum use levels (mg/kg)[(a)]	Expected typical use levels (mg/kg)[(a)]
1.4	Flavoured fermented milk products including heat-treated products	8	2–6
1.6.3	Other creams	15	5–10
1.7	Cheese and cheese products	8	2–6
1.7.1	Unripened cheese excluding products falling in category 16	40	15–30
1.7.2	Ripened cheese	40	15–30
1.7.4	Whey cheese	40	15–30
1.7.5	Processed cheese	40	15–30
1.7.6	Cheese products (excluding products falling in category 16)	40	15–30
1.8	Dairy analogues, including beverage whiteners	40	15–30
2.1	Fats and oils essentially free from water (excluding anhydrous milkfat)	40	15–30
2.2.1	Butter and concentrated butter and butter oil and anhydrous milkfat	8	2–6
2.2.2	Other fat and oil emulsions including spreads as defined by Council Regulation (EC) No 1234/2007 and liquid emulsions	40	15–30
3	Edible ices	10	4–8
4.2.1	Dried fruit and vegetables	40	15–30
4.2.2	Fruit and vegetables in vinegar, oil or brine	40	15–30
4.2.3	Canned or bottled fruit and vegetables	40	15–30
4.2.4.1	Fruit and vegetable preparations excluding compote	40	15–30
4.2.4.2	Compote, excluding products covered by category 16	8	2–6
4.2.5.2	Jam, jellies and marmalades and sweetened chestnut puree as defined by Directive 2001/113/EC	40	15–30
4.2.5.3	Other similar fruit or vegetable spreads	8	2–6
4.2.5.4	Nut butters and nut spreads	40	15–30
4.2.6	Processed potato products	8	2–6
5.1	Cocoa and Chocolate products as covered by Directive 2000/36/EC	8	2–6
5.2.1	Other confectionery with added sugar	40	15–30
5.2.2	Other confectionery without added sugar	40	15–30
5.3	Chewing gum		
5.3.1	Chewing gum with added sugar	40	15–30
5.3.2	Chewing gum without added sugar	40	15–30
5.4	Decorations, coatings and fillings, except fruit-based filling covered by category 4.2.4	40	15–30
6.3	Breakfast cereals	8	2–6
6.4.1	Fresh pasta	8	2–6
6.4.2	Dry pasta	8	2–6
6.4.4	Potato gnocchi	8	2–6
6.5	Noodles	8	2–6
6.6	Batters	8	2–6
6.7	Pre-cooked or processed cereals	8	2–6
7.1	Breads and rolls	8	2–6

[7] 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, pp. 16–33.

Food category number	Food category name	Proposed maximum use levels (mg/kg)[(a)]	Expected typical use levels (mg/kg)[(a)]
7.2	Fine bakery wares	8	2–6
8.2	Meat preparations as defined by Regulation (EC) No 853/2004	40	15–30
8.3.1	Non-heat-treated meat products	40	15–30
8.3.2	Heat-treated meat products	40	15–30
9.2	Processed fish and fishery products including crustaceans and molluscs	20	15–20
9.3	Fish roe	40	15–30
10.2	Processed eggs and egg products	20	15–20
12.2.1	Herbs and spices	40	15–30
12.2.2	Seasonings and condiments	40	15–30
12.3	Vinegar	40	15–30
12.4	Mustard	40	15–30
12.5	Soups and broths	6	4–5
12.6	Sauces	40	15–30
12.7	Salads and savoury based sandwich spreads	40	15–30
12.9	Protein products, excluding products covered in category 1.8	40	15–30
13.3	Dietary foods for weight control diets intended to replace total daily food intake or an individual meal	40	15–30
14.1.4.1	Flavoured drinks with sugar	10	4–8
14.1.4.2	Flavoured drinks with sweetener	10	4–8
14.1.5.2	Other	10	4–8
14.2.1	Beer and malt beverages	40	15–30
14.2.2	Wine and other products defined by Regulation (EC) No 1234/2007, and alcohol-free counterparts	40	15–30
14.2.3	Cider and perry	40	15–30
14.2.4	Fruit wine and made wine	40	15–30
14.2.6	Spirit drinks as defined in Regulation (EC) No 110/2008	40	15–30
14.2.7.1	Aromatised wine	40	15–30
14.2.8	Other alcoholic drinks including mixtures of alcoholic drinks with non-alcoholic drinks and spirits with less than 15% of alcohol	40	15–30
15.1	Potato-, cereal-, flour- or starch based snacks	40	15–30
15.2	Processed nuts	40	15–30
16	Desserts excluding products covered in category 1, 3 and 4	40	15–30

(a): Use levels are provided for the foods as consumed.

3.3. Exposure

3.3.1. Food consumption data used for exposure assessment

The food consumption data used for the exposure assessment are from the EFSA Comprehensive European Food Consumption Database.[8] This database contains food consumption data at the level of the individual consumer from the most recent national dietary surveys carried out in EU countries and includes the currently best available food consumption data across the EU. These data cover infants (from 0 weeks of age), toddlers (1–2 years), children (3–9 years), adolescents (10–17 years), adults (18–64 years) and the elderly (65 years and older). As these data were collected by different

[8] https://www.efsa.europa.eu/en/data-report/food-consumption-data

methodologies, direct country-to-country comparisons of exposure estimates based on these data may not be appropriate.

The dietary exposure to the Primary Product was calculated by the applicant and EFSA using Food Additive Intake Model (FAIM, version 2.1). The food consumption data in FAIM (version 2.1) used in the exposure assessment were based on the version of the Comprehensive Database that was published in July 2021. These data covered 42 dietary surveys carried out in 22 EU countries (Table 9).

Table 9: Population groups and countries considered for the exposure estimates of the Primary Product with FAIM

Population	Age range	Countries with food consumption surveys covering more than 1 day
Infants	From 12 weeks up to and including 11 months of age	Bulgaria, Cyprus, Denmark, Estonia, Finland, France, Germany, Italy, Latvia, Portugal, Slovenia
Toddlers[(a)]	From 12 months up to and including 35 months of age	Belgium, Bulgaria, Cyprus, Denmark, Estonia, Finland, France, Germany, Hungary, Italy, Latvia, the Netherlands, Portugal, Slovenia, Spain
Children[(b)]	From 36 months up to and including 9 years of age	Austria, Belgium, Bulgaria, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Italy, Latvia, the Netherlands, Portugal, Spain, Sweden
Adolescents	From 10 years up to and including 17 years of age	Austria, Belgium, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Italy, Latvia, the Netherlands, Portugal, Romania, Slovenia, Spain, Sweden
Adults	From 18 years up to and including 64 years of age	Austria, Belgium, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, the Netherlands, Portugal, Romania, Slovenia, Spain, Sweden
The elderly[(b)]	From 65 years of age and older	Austria, Belgium, Cyprus, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, the Netherlands, Portugal, Romania, Slovenia, Spain, Sweden

(a): The term 'toddlers' in the Comprehensive Database (EFSA, 2011) corresponds to 'young children' (from 12 months up to and including 35 months of age) in Regulations (EC) No 1333/2008 and (EU) No 609/2013[9].
(b): In FAIM, the terms 'children' and 'the elderly' correspond, respectively, to 'other children' and the merge of 'elderly' and 'very elderly' in Comprehensive Database (EFSA, 2011).

The food consumption data from the Comprehensive Database in FAIM are codified according to the food categories as presented in Annex II, Part D, of Regulation (EC) No 1333/2008, which is the relevant regulation for the food categories of the smoke flavourings.

3.3.2. Exposure assessment to the Primary Product

Using FAIM, dietary exposure to the Primary Product was calculated by multiplying the relevant use level for each food category with its respective consumption amount for each individual. This was done for all individuals in the surveys (i.e. the estimates are not based on consumers only). The exposures per food category were subsequently added and divided by the individual body weight (bw) (as registered in the consumption survey) to derive an individual total exposure per day expressed per kilogram bw. These exposure estimates were averaged over the number of survey days in the survey, resulting in an individual average exposure per day. Dietary surveys with only 1 day per subject were excluded as they are not considered adequate to assess repeated exposure. The calculations resulted in distributions of individual exposure per survey and population group. Based on these distributions, the mean and the 95th percentile of exposure were calculated per survey and population group. The 95th percentile of exposure was only calculated for those population groups with a sufficiently large sample size to obtain a reliable estimate (EFSA, 2011).

[9] Regulation (EU) No 609/2013 of the European Parliament and of the Council of 12 June 2013 on food intended for infants and young children, food for special medical purposes and total diet replacement for weight control and repealing Council Directive 92/52/EEC, Commission Directives 96/8/EC, 1999/21/EC, 2006/125/EC and 2006/141/EC, Directive 2009/39/EC of the European Parliament and of the Council and Commission Regulations (EC) No 41/2009 and (EC) No 953/2009. OJ L 181, 29.6.2013, pp. 35–54.

3.3.2.1. Exposure assessment using FAIM

The applicant provided estimates of dietary exposure to the Primary Product using FAIM, based on the proposed maximum (proposed maximum use level exposure assessment scenario) and expected typical use levels (expected typical use level exposure assessment scenario) (Documentation provided to EFSA No. 1). These estimates were re-calculated by EFSA, because the applicant inserted the use levels in FAIM (Table 8) in an incorrect way (e.g. not applying a use level of a sub-category to its parent food category) (Documentation provided to EFSA No. 2).

In FAIM, use levels were linked to the corresponding food categories according to the instructions provided for its use.[10]

Exposure estimates using FAIM

In Table 10, the dietary exposure estimates of the Primary Product with FAIM are presented.

Table 10: Summary of dietary exposure to the Primary Product from its proposed maximum and expected typical use levels as a smoke flavouring in six population groups and estimated with FAIM (minimum-maximum across the dietary surveys in mg/kg body weight (bw) per day)

	Infants (12 weeks–11 months) (n = 11/9)	Toddlers (12–35 months) (n = 15/13)	Children (3–9 years) (n = 19/19)	Adolescents (10–17 years) (n = 21/20)	Adults (18–64 years) (n = 22/22)	The elderly (≥ 65 years) (n = 22/21)
Proposed maximum use level exposure assessment scenario						
Mean	0.04–0.4	0.2–0.9	0.3–0.7	0.2–0.4	0.2–0.4	0.1–0.3
95th percentile	0.1–1.5	0.5–1.5	0.5–1.3	0.3–0.7	0.4–1.2	0.3–0.7
Expected typical use level exposure assessment scenario						
Mean	0.03–0.3	0.2–0.7	0.2–0.5	0.1–0.3	0.1–0.3	0.1–0.2
95th percentile	0.1–1.1	0.4–1.1	0.4–1.0	0.2–0.6	0.3–0.9	0.2–0.5

n: number of surveys from which a mean/P95 could be calculated.

At the proposed maximum use levels, the mean exposure to the Primary Product from its use as a smoke flavouring ranged from 0.04 mg/kg bw per day in infants to 0.9 mg/kg bw per day in toddlers. The 95th percentile of exposure to the Primary Product ranged from 0.1 mg/kg bw per day in infants to 1.5 mg/kg bw per day in infants and toddlers.

At the expected typical use levels, the mean exposure to the Primary Product from its use as a smoke flavouring ranged from 0.03 mg/kg bw per day in infants to 0.7 mg/kg bw per day in toddlers. The 95th percentile of exposure to the Primary Product ranged from 0.1 mg/kg bw per day in infants to 1.1 mg/kg bw per day in infants and toddlers.

The Primary Product is requested for renewal of authorisation in 73 food categories (Table 8). For all these 73 food categories considered, it was assumed that 100% of the foods belonging to these food categories will contain the Primary Product at the proposed maximum or expected typical use levels. As it is unlikely that the Primary Product will be added to all foods categories (Table 8), the Panel considered that the calculated exposure to the Primary Product using FAIM is an overestimation of the expected exposure in EU countries if this Primary Product is used at the proposed maximum or expected typical use levels.

Additionally, overall sources of standard uncertainties (Annex A6) also contributed to an overestimation of the exposure.

Detailed results per population group and survey are presented in Annexes A2 (Proposed maximum use level exposure assessment scenario) and A3 (Expected typical use level exposure assessment scenario).

[10] Link to FAIM instructions: https://www.efsa.europa.eu/sites/default/files/applications/FAIM-instructions.pdf

Main food categories contributing to exposure to the Primary Product using FAIM

Under the conservative assumptions mentioned above, the main food categories contributing to the total mean exposure to the primary product for both exposure scenarios contributing to at least 30% to the total mean exposure in at least one population group in one survey, listed in order of the number of the FCs, are:

- FC 02.1 Fats and oils essentially free from water (excluding anhydrous milkfat).
- FC 04.2.4.1 Fruit and vegetable preparations excluding compote.
- FC 14.1.5.2. Other.
- FC 14.2.1 Beer and malt beverages.
- FC 14.2.2. Wine and other products defined by Regulation (EC) No 1234/2007, and alcohol-free counterparts.

Considering the conservative nature of the underlying assumption that 100% of the foods within the food categories (Table 8) contain the Primary Product, the Panel emphasises that the main food categories listed here may not reflect the food categories that contribute most to the exposure in real life.

Detailed results of the contributing food categories are presented in Annexes A4 (proposed maximum use level exposure assessment scenario) and A5 (expected typical use level exposure assessment scenario).

3.3.3. Anticipated exposure to impurities in the Primary Product

The potential exposure to the impurities arsenic, lead, cadmium, mercury and PAHs (as PAH4) from the use of the Primary Product can be calculated by assuming that they are present in the Primary Product up to a limit value and then by calculating pro-rata to the estimates of exposure to the Primary Product itself.

With regard to the dietary exposure to the Primary Product, the Panel considered the highest mean and the highest 95th percentile exposure estimates resulting from the exposure assessment using FAIM among the different population groups, i.e. 0.9 mg/kg bw per day for toddlers and 1.5 mg/kg bw per day for infants and toddlers, respectively (Table 10).

The level of the impurities in the Primary Product combined with the estimated exposure to the Primary Product (Table 10) can be used to estimate the exposure to these impurities. This exposure can then be compared with reference points (RP, i.e. lower limit of the benchmark dose (BMDL) for arsenic, lead and PAH4) or health-based guidance values (HBGV, i.e. tolerable weekly intake (TWI) for cadmium and mercury) for the undesirable impurities present in the Primary Product (Table 11).

Table 11: Reference points/health-based guidance values for the impurities present in the Primary Product

Impurity/constituent/ HBGV/RP	Basis/Reference
Arsenic (As)/0.3–8 μg/kg bw per day ($BMDL_{01}$)	The reference point is based on a range of benchmark dose lower confidence limit ($BMDL_{01}$) values between 0.3 and 8 μg/kg body weight (bw) per day identified for cancers of the lung, skin and bladder, as well as skin lesions. MOE should be at least 10,000 if the reference point is based on carcinogenicity in animal studies. However, as the BMDL for As is derived from human studies, an interspecies extrapolation factor (i.e. 10) is not needed, i.e. a MOE of 1,000 would be sufficient (EFSA CONTAM Panel, 2009a; EFSA Scientific Committee, 2012).
Cadmium (Cd)/2.5 μg/kg bw per week (TWI)	The derivation of the reference point is based on a meta-analysis to evaluate the dose –response relationship between selected urinary cadmium and urinary beta-2-microglobulin as the biomarker of tubular damage recognised as the most useful biomarker in relation to tubular effects. A group-based $BMDL_5$ of 4 μg Cd/g creatinine for humans was derived. A chemical specific adjustment factor of 3.9 was applied to account for human variability in urinary cadmium within each dose-subgroup in the analysis resulting in a reference point of 1.0 μg Cd per g creatinine. In order to remain below 1 μg Cd/g creatinine in urine in 95% of the population by age 50, the average daily dietary cadmium intake should not exceed 0.36 μg Cd/kg bw, corresponding to a weekly dietary intake of 2.5 μg Cd/kg bw (EFSA CONTAM Panel, 2009b).

Impurity/constituent/ HBGV/RP	Basis/Reference
Lead (Pb)/0.5 μg/kg bw per day ($BMDL_{01}$)	The reference point is based on a study demonstrating perturbation of intellectual development in children with the critical response size of 1 point reduction in IQ. The EFSA CONTAM Panel mentioned that a 1 point reduction in IQ is related to a 4.5% increase in the risk of failure to graduate from high school and that a 1 point reduction in IQ in children can be associated with a decrease of later productivity of about 2%. A risk cannot be excluded if the exposure exceeds the $BMDL_{01}$ (MOE lower than 1) (EFSA CONTAM Panel, 2010).
Mercury (Hg)/4 μg/kg bw per week (TWI)	The HBGV was set using kidney weight changes in male rats as the pivotal effect. Based on the $BMDL_{10}$ of 0.06 mg/kg bw per day, expressed as mercury, and an uncertainty factor of 100 to account for inter and intra species differences, with conversion to a weekly basis and rounding to one significant figure, a TWI for inorganic mercury of 4 μg/kg bw per week, expressed as mercury was established (EFSA CONTAM Panel, 2012).
PAH4/340 μg/kg bw per day ($BMDL_{10}$)	Polycyclic aromatic hydrocarbons (PAHs) are considered genotoxic and carcinogenic. The reference point is based on a carcinogenicity study by Culp et al. (1998), as reported by the EFSA CONTAM Panel (2008), who concluded that PAH4 (i.e. the sum of benz[a]anthracene, benzo[a]pyrene, benzo[b]fluoranthene and chrysene) is a suitable indicator for the occurrence and toxicity of PAHs in food. The MOE should be at least 10,000 (EFSA CONTAM Panel, 2008).

HBGV: health-based guidance value; RP: reference point; $BMDL_{01}$: lower confidence limit of the benchmark dose associated with a 1% extra risk for tumours (EFSA Scientific Committee, 2017a); $BMDL_{10}$: lower confidence limit of the benchmark dose associated with a 10% extra risk for tumours (EFSA Scientific Committee, 2017a) TWI: tolerable weekly intake; MOE: margin of exposure.

The risk assessment of the undesirable impurities helps to determine whether there could be a possible health concern if these impurities were present at their limit values in the Primary Product. The assessment is performed by calculating the MOE by dividing the reference point (i.e. BMDL, Table 11) by the exposure estimate for an impurity (Table 10), or by estimating the contribution of the exposure to an impurity due to the use of the Primary Product to the HBGV (expressed as percentage of the HBGV).

3.3.3.1. Toxic elements

The results of the analyses of arsenic, cadmium, lead and mercury in five batches of the Primary Product were reported (Table 3). The applicant proposed maximum limits for these toxic elements, which are the same as in the current EU specifications (Table 7). The Panel noted that the actual measured levels of the toxic elements in commercial samples of the Primary Product were substantially lower than these limits.

The Panel assessed the risk that would result if these toxic elements were present in the Primary Product according to two concentration scenarios: (i) at the current limits in the EU specifications and (ii) at the average measured levels multiplied by a factor of 5, to account for standard uncertainty in representativeness, homogeneity and analytical measurement.

The outcome of the risk assessment for the two concentration scenarios and for the highest mean and the highest 95th percentile exposure estimates among the different population groups (see Section 3.3.2) is presented in Table 12.

Table 12: Risk assessment for four toxic elements present in the Primary Product according to two concentration scenarios, using the reference points/health-based guidance values as provided in Table 11

Exposure to Fumokomp Conc. (mg/kg bw/day)	(i) Considering the presence of toxic elements at the current EU specifications limits for Fumokomp Conc.			
	MOE for As at 3 mg/kg	% of the TWI for Cd at 1 mg/kg	MOE for Pb at 5 mg/kg	% of the TWI for Hg at 1 mg/kg
0.9[(a)]	111–2,963	0.25	111	0.16
1.5[(b)]	67–1,778	0.42	67	0.26

	(ii) Considering the presence of toxic elements at their average measured levels in Fumokomp Conc. multiplied by a factor of 5			
	MOE for As at 0.1 mg/kg	**% of the TWI for Cd at 0.005 mg/kg**	**MOE for Pb at 0.25 mg/kg**	**% of the TWI for Hg at 0.01 mg/kg**
0.9[(a)]	3,333–88,889	0.0013	2,222	0.0016
1.5[(b)]	2,000–53,333	0.0021	1,333	0.0026

bw: body weight; MOE: margin of exposure; TWI: tolerable week intake.
(a): Highest mean exposure level among the different population groups (proposed maximum use level exposure assessment scenario – toddlers (Table 10)).
(b): Highest 95th percentile exposure level among the different population groups (proposed maximum use level exposure assessment scenario – infants and toddlers (Table 10)).

When considering the current limits in the EU specifications (scenario (i) in Table 12), the Panel concluded that for arsenic the lower end of the ranges of the calculated MOE values was insufficient, i.e. below the target value of 1,000 (Table 11). For the other three toxic elements (cadmium, lead, mercury), the EU current specifications limit values do not give rise to safety concerns.

When considering the average reported levels multiplied by a factor of 5 (scenario (ii) in Table 12), the presence of these toxic elements in the Primary Product does not give rise to concern.

Overall, the Panel considered that the limits in the EU specifications for arsenic, cadmium, lead and mercury should be established based on actual levels in the commercial Primary Product. If the European Commission decides to revise the current limits in the EU specifications, the estimated exposure to the toxic elements as described above could be considered.

3.3.3.2. Polycyclic aromatic hydrocarbons (PAHs)

The results of the analysis for 16 PAHs were reported by the applicant for one batch of the Primary Product (Table 5).

The proposed limit for one of these PAHs (i.e. benzo[a]pyrene) is below its limit of 10 μg/kg, as laid down in Regulation (EC) No 2065/2003. However, the Panel noted that the actual measured level for benzo[a]pyrene in the Primary Product (Table 5) is substantially lower than the limit proposed by the applicant. The measured level for benzo[a]anthracene (Table 5) is substantially lower than the current limit in Regulation (EC) No 2065/2003.

According to the data submitted by the applicant, the Panel considered the maximum reported level of PAH4 in the Primary Product, i.e. 1.53 μg/kg (Table 5). Based on this level, the Panel assessed the risk that would result if PAH4 were present in the Primary Product: (i) at the specifications limits for PAH4 in the Primary Product as proposed by the applicant (Table 7) and (ii) at the maximum reported level of PAH4 from one batch of the Primary Product (Table 5). The outcome of the risk assessment for the two concentration scenarios and for the highest mean and the highest 95th percentile FAIM exposure estimates among the different population groups (see Section 3.3.2) is presented in Table 13.

Table 13: Risk assessment for PAH4, i.e. benzo[a]anthracene, benzo[a]pyrene, benzo[b]fluoranthene and chrysene in the Primary Product according to two concentration scenarios, using the reference points/health-based guidance values as provided in Table 11

Exposure to Fumokomp Conc. (mg/kg bw/day)	**MOE for PAH4**
	(i) Considering the presence of PAH4 at the specifications limits for PAH4 as proposed by the applicant in Fumokomp Conc. (10 μg/kg)
0.9[(a)]	37.8×10^6
1.5[(b)]	22.7×10^6
	(ii) Considering the presence of PAH4 at their maximum reported level in Fumokomp Conc. (1.53 μg/kg)
0.9[(a)]	247×10^6
1.5[(b)]	148×10^6

bw: body weight; MOE: margin of exposure.

(a): Highest mean exposure level among the different population groups (proposed maximum use level exposure assessment scenario – toddlers (Table 10)).
(b): Highest 95th percentile exposure level among the different population groups (proposed maximum use level exposure assessment scenario – infants and toddlers (Table 10)).

The Panel concluded that the resulting MOEs for PAH4 were far above the target value of 10,000 for both concentration scenarios and both exposure estimates of the Primary Product (EFSA Scientific Committee, 2012) (Table 11).

Furthermore, the Panel noted that at the highest proposed maximum use level of the Primary Product in any of the food categories, i.e. 40 mg/kg food (Table 8), and the maximum reported level of PAH4 in the Primary Product, i.e. 1.53 μg/kg Primary Product, the concentration of PAH4 in food would be 61×10^{-6} μg/kg food, which is far below the lowest maximum level (ML) of these contaminants in any of the foods listed in Regulation (EU) 2023/915[11] (i.e. 1 μg PAH4/kg food).

3.4. Genotoxicity data

The present evaluation is conducted in line with the applicable EFSA guidance on smoke flavourings (EFSA FAF Panel, 2021) which encompasses all the EFSA guidance documents on genotoxicity (EFSA Scientific Committee, 2011, 2017b, 2019, 2021b). These documents were not available at the time when the smoke flavourings were evaluated previously by the CEF Panel. In addition, for the assessment of the renewal applications, the reliability and relevance of all submitted genotoxicity studies (see Section 3.4.2) were evaluated by the FAF Panel based on the criteria described in Appendix B.

3.4.1. Genotoxicity assessment of the individual components

The 32 identified and quantified components of Fumokomp Conc. were evaluated individually for genotoxicity considering first the data available from the literature as provided by the applicant and then, in the absence of relevant information from the literature, considering the *in silico* information/data submitted by the applicant, when available, supplemented by *in silico* data generated by EFSA (see Annex B).

The applicant submitted literature data on 25 identified components and performed *in silico* analysis for 15 components, using the VEGA quantitative structure–activity relationship (QSAR) platform (version 1.1.5),[12] applying the following models (Documentation provided to EFSA No. 1):

- Mutagenicity CONSENSUS Model version 1.0.3.
- Mutagenicity CAESAR Model version 2.1.13.
- Mutagenicity SarPy/IRFMN Model version 1.0.7.
- Mutagenicity ISS Model version 1.0.2.
- Mutagenicity KNN/Read-Across Model version 1.0.0.
- *In vitro* Micronucleus Activity (IRFMN/VERMEER) Version 1.0.0.
- Cramer Classification (TOXTREE) Version 1.0.0.

In case of equivocal or highly uncertain predictions with VEGA QSAR models or contradictory results in the literature, the Organisation for Economic Co-operation and Development (OECD) QSAR Toolbox v. 4.4.1[13] was used by the applicant for tentative read-across evaluations. If equivocal or uncertain predictions could not be resolved, the Danish (Q)SAR database[14] was also used.

A short summary of the data available from the literature as submitted by the applicant and of the overall conclusions from the applicant on the genotoxicity potential of the individual components, including the *in silico* analysis, when available, is reported in Annex B of this opinion (see columns 'G' and 'I'). The complete set of information from the applicant is available under the section 'Genotoxicity' of the technical dossier (see Documentation provided to EFSA No. 1).

[11] Commission Regulation (EU) 2023/915 of 25 April 2023 on maximum levels for certain contaminants in food and repealing Regulation (EC) No 1881/2006. OJ L 119, 5.5.2023, pp. 103–157.
[12] https://www.vegahub.eu/portfolio-item/vega-qsar/
[13] https://www.oecd.org/chemicalsafety/oecd-qsar-toolbox.htm
[14] Danish (Q)SAR Database, Division of Diet, Disease Prevention and Toxicology, National Food Institute, Technical University of Denmark, http://qsar.food.dtu.dk

In line with the EFSA guidance on smoke flavourings (EFSA FAF Panel, 2021), the Panel conducted a (Q)SAR analysis for all the 32 identified components of the Primary Product using the following six profilers as available in the OECD QSAR Toolbox v. 4.5:

- DNA alerts for AMES, Chromosomal Aberrations (CA) and Micronucleus (MN) by OASIS;
- DNA binding by OASIS;
- DNA binding by OECD;
- Protein binding alerts for chromosomal aberration by OASIS;
- *In vitro* mutagenicity (Ames test) alerts by ISS;
- *In vivo* mutagenicity (Micronucleus) alerts by ISS.

As described in column 'K' of Annex B, reporting the '*EFSA's conclusion on the genotoxicity of the components of the Primary Product based on the available data*', the individual structural alerts identified by the six profilers may have different positive predictivity (i.e. rate of positives to the total number of substances with the alert) for the genotoxic potential of the target substance. The predictivities of the individual alerts are documented by Benigni et al. (2008, 2009), based on the concepts of the alerts and predictivity indices as described by the European Chemicals Agency (ECHA, 2008). Alerts with low positive predictivity, which were counterbalanced by additional data were not taken into consideration for the conclusion on the individual components of this Primary Product. When necessary, the application of profilers was followed by an expert review (e.g. check of close analogues/structurally related substances).

In conclusion, the Panel noted that for all the 32 identified constituents of the Primary Product genotoxicity data were available from the literature, either on the substance or on structurally related substances, that were assessed previously by EFSA as chemically defined flavouring substances. The Panel noted that in many cases these data were limited. However, supported by the results of the (Q) SAR analyses, they did not indicate a concern for genotoxicity for any of the 32 components.

3.4.2. Genotoxicity assessment of the Primary Product (whole mixture)

The applicant resubmitted the genotoxicity studies on the Primary Product (whole mixture) that were already evaluated by the CEF Panel in 2009, to investigate the genotoxicity of the unidentified fraction of the Primary Product, in line with the EFSA Scientific Committee statement on genotoxicity assessment of chemical mixtures (EFSA Scientific Committee, 2019): a bacterial reverse mutation test (Lab International Research Centre, 2005a), an *in vitro* mammalian cell gene mutation assay in mouse lymphoma cells (Lab International Research Centre, 2005b), an *in vitro* mammalian chromosomal aberration test (Lab International Research Centre, 2005c), an *in vivo* micronucleus assay in mouse bone marrow (Toxi-Coop Kkt, 2008a) and an *in vivo* rat liver unscheduled DNA synthesis (UDS) assay (Toxi-Coop Kkt, 2008b). No new genotoxicity studies, addressing the genotoxic potential of the whole mixture were provided.

The evaluation of these studies as described in the scientific opinion 'Safety of smoke flavour Primary Product – Fumokomp' (EFSA CEF Panel, 2009) is reported below. For each study, comments and evaluation by the FAF Panel are reported. The studies are summarised in Tables C.1 and C.2 (Appendix C), where the evaluation of reliability and relevance are reported according to the approach described in Appendix B.

The Panel noted that the general compositional data of the product evaluated in 2009 do not fundamentally deviate from the product assessed in the current opinion. In addition, as stated by the applicant, the manufacturing process has not changed and the batch-to-batch variability was low both in the previous evaluation (EFSA CEF Panel, 2009) and in the current opinion (see Table 6 in Section 3.1.2.6). Therefore, the Panel considered the Primary Product that was evaluated in 2009 similar to the Primary Product evaluated in this opinion and that the batch used for the genotoxicity testing in the past can still be considered representative for the current product.

3.4.2.1. Bacterial reverse mutation test (Lab International Research Centre, 2005a)

'*The bacterial reverse mutation assay was performed in accordance with OECD Guideline 471, using* Salmonella Typhimurium *TA98, TA100, TA1535, TA1537 and Escherichia coli WP2 uvrA and dose levels of Fumokomp of 5000, 4000, 2000, 800, 320 and 128 μg/plate and in the presence and absence of S9 metabolic activation, using both a plate incorporation method and a pre-incubation method. Cytotoxicity was primarily evident in the plate incorporation method at dose levels of 4000–5000 μg, and also in the pre-incubation method in the presence of S9. In the absence of S9 in the*

pre-incubation method toxicity was apparent at dose levels down to 800 μg/plate. No evidence of increased revertants was seen with any of the bacterial strains, either with or without S9, under the conditions of this test. Positive control substances gave the expected responses'. (EFSA CEF Panel, 2009).

The FAF Panel agreed with this evaluation and considered the study to be reliable without restrictions and its result of high relevance.

3.4.2.2. *In vitro* mammalian cell gene mutation assay in mouse lymphoma cells (Lab International Research Centre, 2005b)

'*A mammalian cell mutation assay in mouse lymphoma cells (L5478Y TK+/− 3.7.2C cells) was performed with Fumokomp in accordance with OECD Guideline 476. Cells were treated with concentrations of 100, 75, 50, 25 and 10 μg/ml test material for 3 hours in the presence and absence of S9 metabolic activation, and with concentrations of 40, 30, 20 and 10 μg/ml test material for 24 hours in the absence of S9. Statistically significant increases in mutation frequencies were seen at concentrations of 100, 75 and 50 μg/ml after the 3-hours treatment, both in the presence and absence of S9 metabolic activation. Both large and small colonies were increased. After the 24-hours treatment without S9, statistically significant increases in mutation frequencies were seen at concentrations of 40, 30 and 20 μg/ml. The test material was cytotoxic at concentrations of 50 μg/ml in the presence of S9 and at 20–25 μg/ml in its absence. It is concluded that the Primary Product gave a clearly positive result in the mouse lymphoma tk-assay, with and without S9, with increases of both large and small colonies, thus indicating the ability of the test material to induce genotoxic effects both at gene and chromosome level'*. (EFSA CEF Panel, 2009).

The FAF Panel agreed with the previous evaluation of the CEF Panel that the Primary Product gave clearly positive results in the absence of S9-mix (3 h treatment). However, based on the most recent OECD TG 490 (OECD, 2016a) according to which the global evaluation factor has to be taken into account as an additional criterion, the FAF Panel considered the results in the presence of S9-mix at 3 h, and in the absence of S9-mix at 24 h as equivocal. Historical controls were not reported. Therefore, the Panel considered the study to be reliable with restrictions and its results of limited relevance.

3.4.2.3. *In vitro* mammalian chromosomal aberration test (Lab International Research Centre, 2005c)

'*Fumokomp was tested in an in vitro mammalian chromosome aberration test in Chinese hamster ovary cells (line CHO-KI) in accordance with OECD Guideline 473. Two independent assays were carried out. In study 1, concentrations of 75, 25 and 5 μg/ml were incubated for 4 hours in the presence and absence of metabolic activation, whilst in study 2, concentrations of 50, 25 and 5 μg/ml were incubated for 20 hours in the absence of metabolic activation and concentrations of 75, 25 and 5 μg/ml were incubated for 4 hours in the presence of metabolic activation. Dose levels were selected based on a preliminary cytotoxicity assay, in which mitotic index was reduced to approximately 50% of control at 25–50 μg/ml. There was no significant increase in cells showing chromosomal aberrations or polyploid or endoreplicated metaphases in either study, in the presence or absence of metabolic activation, and it was concluded that the Primary Product did not show evidence of clastogenic activity in this test*'. (EFSA CEF Panel, 2009).

The FAF Panel agreed that the Primary Product did not show evidence of clastogenic activity, polyploidy or endoreduplication in this test. However, based on the most recent OECD TG 473 (OECD, 2016b) the study has some limitations (only 200 metaphases/concentration instead of 300 were scored and historical controls were not provided). Therefore, the Panel considered the study to be reliable with restrictions and its negative result of limited relevance.

3.4.2.4. *In vivo* bone marrow mouse micronucleus test (Toxi-Coop Kkt, 2008a)

'*Fumokomp was examined for its genotoxic potential in an in vivo bone marrow mouse micronucleus test in NMRI BR mice in accordance with OECD Guideline 474. Following a dose-range study, in the main study groups of five male and five female mice received a single dose of 500, 1000 or 2000 mg/kg bw test substance in polyethylene glycol 400 by gavage, while a positive control group (five males and five females) received a single dose of 60 mg/kg bw cyclophosphamide intraperitoneally. The study included both untreated and vehicle controls. Test animals and positive and untreated and vehicle controls were killed 24 hours after dosing for sampling of bone marrow, and additional groups of five male and five female mice receiving either 0 or 2000 mg/kg bw Fumokomp*

were included to allow a second sampling period at 48 hours after treatment. In both the dose-range study and the main study, evidence of clinical toxicity was seen in Fumokomp-treated animals at levels of 1000 and 2000 mg/kg bw. These consisted of decreased activity, hunchbacked posture, piloerection and (at 2000 mg/kg bw only) loss of coordination and increased respiration persisting for up to 4 hours after dosing. The PCE/NCE ratio was reduced at 48 hours (with a slight reduction also at 24 hours) in both males and females receiving 2000 mg/kg bw Fumokomp compared with vehicle controls. There was no significant increase in the frequency of micronucleated polychromatic erythrocytes (MNCPE)[15] *in male or female mice at either 24 hours or 48 hours after treatment with Fumokomp compared to the vehicle or untreated controls, while the positive control showed the anticipated increases in MPCE*[15]*'*. (EFSA CEF Panel, 2009).

The FAF Panel concluded that the study did not show any increase in the frequency of MNPCE. The Panel considered that the high dose tested was the maximum tolerated dose and that bone marrow toxicity (reduction in polychromatic erythrocytes (PCE)/normochromatic erythrocytes (NCE) ratio) provided evidence of bone marrow exposure.

It should also be noted that, according to the statement on genotoxicity assessment of chemical mixtures (EFSA Scientific Committee, 2019), even in the case of bone marrow exposure, the assessment of genotoxicity of mixtures in the bone marrow is limited by the fact that target tissue exposure to all potential genotoxic components cannot be demonstrated unequivocally.

Therefore, the Panel considered the study reliable without restriction and the negative result of limited relevance.

3.4.2.5. *In vivo* rat liver UDS assay (Toxi-Coop Kkt, 2008b)

'An in vivo rat liver UDS test was also performed with Fumokomp. DNA repair in hepatocytes was measured following administration by gavage of 500, 1000 or 2000 mg/kg bw Fumokomp in PEG 400 to groups of male Wistar rats (Crl:[WI]BR). The negative control group were dosed with PEG alone, while positive control groups (n=3 for each substance) received either 2-acetylaminofluorene (late sampling period) or N, N'-dimethylhydrazine dihydrochloride (DMH) (early sampling period). Hepatocytes were isolated at 4 or 12 hours after treatment of the rats with 0, 500, 1000 or 2000 mg/ kg bw Fumokomp (n=3 per group) or with the positive control DMH (at 4 hours) or 2-AAF (at 12 hours). Unscheduled DNA synthesis was measured by autoradiography, following a 4 hour incubation of the hepatocyte cultures with [methyl-3H]- thymidine. Fumokomp did not cause an increase in net nuclear grain count at either sampling time, while positive controls gave expected increases. It can be concluded that under the conditions of this study, Fumokomp did not induce unscheduled DNA synthesis in the rat liver'. (EFSA CEF Panel, 2009).

The FAF Panel agreed with the previous evaluation of the CEF Panel. However, based on the low adequacy of the UDS assay to follow-up positive *in vitro* results, as explained in the EFSA Scientific Committee Opinion (EFSA Scientific Committee, 2017b), the Panel considered that the results of a negative UDS study are of low relevance and, accordingly, do not contribute to the overall assessment of genotoxicity.

Overall, the Panel noted that since the Primary Product induced gene mutations *in vitro* in a mouse lymphoma assay, an *in vivo* gene mutation assay in transgenic rodents or an *in vivo* comet assay would be needed with the Primary Product, according to the recommendation given in the EFSA Scientific Committee Guidance (EFSA Scientific Committee, 2011). At least duodenum and liver should be analysed. In addition, the potential aneugenicity has not been fully investigated. The results of the *in vivo* MN assay have limited relevance and can also not rule out a possible aneugenic potential. In order to clarify the potential of the mixture to induce micronuclei, an *in vitro* MN study would be needed. If this study were positive the mechanism of MN formation should be investigated (with fluorescence in situ hybridisation (FISH) analysis). If aneugenicity can be excluded, an *in vivo* Comet assay (OECD TG 489 (2016c)) at the site of contact and in the liver would be appropriate, with oral exposure, which could be done in the same animals studied for gene mutations.

4. Discussion

The European Commission has requested the European Food Safety Authority (EFSA) to evaluate the safety of the smoke flavouring Primary Product Fumokomp Conc. (SF-009), for which a renewal application has been submitted, in accordance with Article 12(1) of Regulation (EC) No 2065/2003.

[15] MCPE and MPCE are erroneous abbreviations; they should read MNPCE.

The Primary Product is produced from hardwood made of beech (*F. sylvatica* L.) (85–100%) and hornbeam (*C. betulus* L.) (0–15%).

The production of the Primary Product occurs in three main stages: (i) wood is subjected to pyrolysis; (ii) the resulting tar is processed by vacuum distillation; (iii) the distillates are organoleptically classified and combined to obtain the Primary Product. The Panel considered the information provided on the manufacturing process as sufficient. The data demonstrated that the Primary Product is produced in the same way as the product evaluated formerly (EFSA CEF Panel, 2009).

The applicant provided compositional data for five batches of the Primary Product. Despite the limitations in the quantification of individual constituents, the Panel concluded that the applied methods meet the legal quality criterion that at least 50% by mass of the solvent-free fraction shall be identified and quantified (Regulation (EC) No 627/2006).

Regarding the identified and quantified proportion of the volatile fraction, given the limitations of the quantification method employed by the applicant (see Section 3.1.2.4.2), the Panel could not judge whether the applied methods meet the legal quality criterion that at least 80% of the volatile fraction shall be identified and quantified (Regulation (EC) No 627/2006).

Furan-2(5*H*)-one is a genotoxic substance which can be anticipated to be generated in the course of the pyrolysis of wood. Therefore, the Panel requested the applicant to confirm the absence of this substance in the Primary Product. The Panel noted several limitations in the analytical procedure applied by the applicant in reply to this request (see Section 3.1.2.4.2 Identification and quantification of the volatile fraction). Therefore, the Panel concluded that the additional data provided do not convincingly demonstrate that furan-2(5*H*)-one is absent in the Primary Product.

Data provided for five batches of the Primary Product demonstrated that their batch-to-batch variability was sufficiently low (i.e. the observed relative standard deviations for the individual constituents was on average below 20%), based on the analytical data for the 20 principal volatile constituents and the chemical classes. However, PAHs information was submitted only for one of the batches of the Primary Product. Nevertheless, taking into account that the batch-to-batch variability for the 20 principal volatile constituents and the chemical classes is sufficiently low, the Panel noted that the applicant has adequate control over the relevant steps of the production process (pyrolysis and distillation), and thus anticipated that the data on PAHs concentrations in this one batch are representative for the Primary Product.

The Panel considered that owing to the final manufacturing steps, i.e. combination of the liquid fractions obtained by vacuum distillations, it is very unlikely that small particles including nanoparticles are present in the final Primary Product.

The analytical procedure for the determination of 16 PAHs meets the performance criteria as set in Regulation (EC) No 627/2006. The levels of benzo[a]pyrene and benzo[a]anthracene were below the current limits in Regulation (EC) No 2065/2003. Based on the estimated exposure to the Primary Product and the maximum reported level of the PAH4 in the Primary Product (i.e. 1.53 μg/kg), an MOE of at least 148×10^6 could be calculated for the exposure to PAHs, which would be of low concern from a public health point of view and might be reasonably considered as a low priority for risk management actions (see EFSA Scientific Committee, 2012). The Panel noted that including a limit for PAH4 in the EU specifications would take better account of the presence of other PAHs than only the two PAHs benzo[a]pyrene and benzo[a]anthracene.

The applicant proposed limits for toxic elements (As, Cd, Pb, Hg), which are the same as in the current EU specifications (Table 7). The Panel noted that the actual measured levels for arsenic, cadmium, lead and mercury in five batches of the Primary Product (Table 3) were substantially lower than these limits.

The Panel performed a risk assessment on the presence of these toxic elements in the Primary Product and concluded that, when considering the current limits in the EU specifications (scenario (i) in Table 12), the lower end of the range of the calculated MOE values for arsenic was insufficient, below the target value of 1,000. For the other three toxic elements (cadmium, mercury, lead), their presence up to the current limits in the EU specifications does not give rise to safety concern. When considering the average reported levels multiplied by a factor of 5 (scenario (ii) in Table 12), the presence of these toxic elements in the Primary Product would not give rise to concern.

Overall, the Panel considered that the limits in the EU specifications for the four toxic elements and PAH4 should be established based on actual levels in the commercial Primary Product. If the European Commission decides to revise the limits already present and to include a limit for PAH4, the estimated

exposure to toxic elements and PAH4 as presented in Sections 3.3.3.1 and 3.3.3.2 could be considered.

The Primary Product is requested to be authorised for use in 73 food categories. The Panel performed an exposure assessment for this Primary Product based on proposed maximum and expected typical use levels in these food categories using FAIM. At the maximum proposed use levels, mean exposure estimates to the Primary Product ranged from 0.04 mg/kg bw per day in infants to 0.9 mg/kg bw per day in toddlers (Table 10). The 95th percentile of exposure to the Primary Product ranged from 0.1 mg/kg bw per day in infants to 1.5 mg/kg bw per day in infants and toddlers. At the expected typical use levels, the mean dietary exposure to the Primary Product estimates ranged from 0.03 mg/kg bw per day in infants to 0.7 mg/kg bw per day in toddlers (Table 10). At the 95th percentile the exposure to t the Primary Product ranged from 0.1 mg/kg bw per day in infants to 1.1 mg/kg bw per day in infants and toddlers (Table 10).

For all food categories considered, it was assumed that 100% of the foods belonging to these food categories will contain Fumokomp Conc. at the proposed maximum use levels or the upper level of the range of expected typical use levels. As it is unlikely that the Primary Product will be added to all foods belonging to these food categories, the Panel considered that the calculated exposure to Fumokomp Conc. is an overestimation of the expected exposure in EU countries, even if this Primary Product is used at the proposed maximum use levels or upper level of the range of expected typical use levels.

The Panel noted that for all the 32 identified components of the Primary Product genotoxicity data were available from the literature, either on the substance or on structurally related substances, that were assessed previously by EFSA as chemically defined flavouring substances. The Panel noted that in many cases these data were limited. However, supported by the results of the (Q)SAR analyses, the Panel concluded that these data did not indicate a concern for genotoxicity for any of the 32 components.

The applicant provided *in vitro* and *in vivo* genotoxicity studies on the Fumokomp Conc. (whole mixture) that were already evaluated by the CEF Panel (EFSA CEF Panel, 2009).

The testing of the whole mixture in *in vitro* genotoxicity studies indicated that it did not induce gene mutations in bacterial cells and it did not show evidence of clastogenic activity, polyploidy or endoreduplication in the chromosomal aberration test. The results of these two test systems have high and limited relevance, respectively. The Panel noted that the Primary Product was not tested in an *in vitro* micronucleus study, therefore the potential aneugenicity was not sufficiently investigated.

The Primary Product tested in an *in vitro* gene mutation test in mammalian cells gave clearly positive results in the absence of S9-mix (3 h treatment). The Panel considered that the results of the study have limited relevance due to the absence of historical control data. The Primary Product did not induce unscheduled DNA synthesis in the liver of rats. The Panel considered that the results are of low relevance and, accordingly, do not contribute to the overall assessment of genotoxicity.

Accordingly, the Panel considered that these results require an appropriate *in vivo* follow-up according to the recommendations of the EFSA Scientific Committee (2011).

The testing of the Primary Product in an *in vivo* micronucleus assay in bone marrow did not show any increase in the frequency of MNPCE. Bone marrow toxicity (reduction in PCE/NCE ratio) provided evidence of bone marrow exposure. Considering that the high dose tested was the maximum tolerated dose, the Panel considered the study to be reliable without restrictions. However, the Panel considered that according to the EFSA Scientific Committee statement on genotoxicity assessment of chemical mixtures (EFSA Scientific Committee, 2019), even in the case of bone marrow exposure, the assessment of genotoxicity of mixtures in the bone marrow is limited by the fact that target tissue exposure to all potential genotoxic components cannot be demonstrated unequivocally. Therefore, the Panel considered the negative result of limited relevance.

Overall, the whole mixture induced gene mutations *in vitro* that would require an appropriate *in vivo* follow-up according to the recommendations of the EFSA Scientific Committee (2011). In addition, the potential for aneugenicity has not been adequately investigated. Accordingly, the available data are not sufficient to rule out a potential concern for genotoxicity for the whole mixture.

5. Conclusions

In line with the ToR as provided by the European Commission, in the current opinion EFSA assessed the chemical characterisation, the genotoxicity and the dietary exposure Fumokomp Conc. (SF-009).

From all data available on characterisation, the Panel concluded that the Primary Product considered in this opinion is representative for the one authorised in Commission Implementing

Regulation (EU) No 1321/2013 under the code name SF-009. The Panel concluded that the compositional data provided on the Primary Product were not fully adequate. More specifically, given the limitations of the method employed by the applicant to quantify the volatile constituents, the Panel cannot judge whether the applied method meets the legal quality criterion that at least 80% by mass of the volatile fraction shall be identified and quantified, as set in Regulation (EC) 627/2006. The Panel concluded that the applicant has adequate control over the production process and that the Primary product is sufficiently stable upon storage.

Considering the different purification steps during the manufacturing process, the Panel concluded that it is unlikely that small particles including nanoparticles are present in the final Primary Product and therefore the conventional risk assessment is sufficient.

Among the identified constituents in the Primary Product, there were none that raised a (potential) concern for genotoxicity. Following a request for additional information to substantiate the absence of furan-2(5*H*)-one, the Panel concluded that the submitted data do not convincingly demonstrate the absence of this substance from the Primary Product because of several limitations in the analytical method applied by the applicant. Because furan-2(5*H*)-one is a substance that can be anticipated to be formed during the pyrolysis of wood, and because this substance is known to be genotoxic *in vivo* via the oral route, it is essential that its absence is convincingly demonstrated.

Since no new data on genotoxicity testing of the whole mixture were submitted, the Panel re-examined the data which were already available in the past and concluded that the whole mixture induced gene mutations *in vitro* that would require an appropriate *in vivo* follow-up according to the recommendations of the EFSA Scientific Committee (2011, 2017b, 2021b). In addition, the potential for aneugenicity of the Primary Product has not been adequately investigated.

Overall, according to the EFSA guidance on smoke flavourings (EFSA FAF Panel, 2021), the safety of the smoke flavouring Primary Product Fumokomp Conc. has not been sufficiently demonstrated.

6. Documentation as provided to EFSA

1) Dossier "Application for renewal of an already authorised smoke flavouring - FUMOKOMP CONC smoke flavour". Dossier number: SFL-2022-5310. June 2022. Submitted by Kompozíció Kft.[5]
2) Additional data received on 10 January 2023, submitted by Kompozíció Kft in response to additional data request from EFSA sent on 11 November 2022.
3) Additional data received on 6 March 2023, submitted by Kompozíció Kft as spontaneous submission.
4) Additional data received on 16 March 2023, submitted by Kompozíció Kft as spontaneous submission.
5) Lab International Research Centre, 2005a. The Testing of "Fumokomp" Smoke Flavour with bacterial reverse mutation assay. Lab International Research Centre Hungary Ltd. Study Code 05/069-007M. November 2005. Submitted by Kompozíció Kft.
6) Lab International Research Centre, 2005b. Testing of mutagenic effect of test item "Fumokomp" Smoke Flavour by Mouse Lymphoma Assay. Lab International Research Centre Hungary Ltd. Study Code 05/069-033EL. December 2005. Submitted by Kompozíció Kft.
7) Lab International Research Centre, 2005c. Testing of "Fumokomp" Smoke Flavour with *in vitro* mammalian chromosome aberration test. Lab International Research Centre Hungary Ltd. Study Code 05/069-020C. December 2005. Submitted by Kompozíció Kft.
8) Toxi-Coop Kkt, 2008a. Testing of Mutagenic Effect of test item "Fumokomp" Smoke Flavour by mouse micronucleus test. Study Code 07/030-008E. January 2008. Submitted by Kompozíció Kft.
9) Toxi-Coop Kkt, 2008b. Test of "Fumokomp" in Unscheduled DNA Synthesis (UDS) Assay with rat liver cells *in vivo*. Study Number 421.738.1525. November 2008. Submitted by Kompozíció Kft.

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Abbreviations

BMDL	benchmark dose lower limit
bw	body weight
CA	chromosomal aberration
CAS	Chemical Abstract Service
CEF	Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids
CONTAM	Panel on Contaminants in the Food Chain
cST	centistokes
ECHA	European Chemicals Agency
FAF	Panel on Food Additives and Flavourings
FAIM	Food Additive Intake Model
FC	food category
FISH	fluorescence in situ hybridisation
FL-no	FLAVIS number
GC–MS	gas chromatography–mass spectrometry
GLP	good laboratory practices
HACCP	Hazard Analysis Critical Control Point
HBVG	health-based guidance values
ICP–MS	inductively coupled plasma–mass spectrometry
IQ	intelligence quotient
ISS	Istituto Superiore di Sanità
LOD	limit of detection
LOQ	limit of quantification
MN	micronucleus
MNPCE	micronucleated polychromatic erythrocytes
MOE	margin of exposure
NCE	normochromatic erythrocytes
OECD	Organisation for Economic Co-operation and Development
P95	95th percentile
PAHs	polycyclic aromatic hydrocarbons
PCE	polychromatic erythrocytes
PEG	polyethylene glycol
PPM	parts per million
QSAR	quantitative structure–activity relationship
RP	reference points
RSD	relative standard deviation
SD	standard deviation
SF	smoke flavouring
TICs	total ion current
TK	thymidine kinase
TOR	terms of reference

TR	technical requirements
TG	test guideline
TWI	tolerable weekly intake
UDS	unscheduled DNA synthesis
wt	weight

Appendix A – Full list of identified and quantified constituents of smoke flavouring Primary Product (SF-009)

Table A.1: Compilation of the 32 identified and quantified volatile constituents in the Primary Product (Documentation provided to EFSA No. 1 and 2)

CAS-no	FL-no	Chemical name[a]	Average[b] (wt%)
91-10-1	04.036	2,6-dimethoxyphenol (syringol)	14.3
93-51-6	04.007	2-methoxy-4-methylphenol	9.1
2785-89-9	04.008	4-ethylguaiacol (2-methoxy-4-ethylphenol)	7.9
121-34-6	08.043	vanillic acid	6.9
765-70-8	07.056[c]	3-methylcyclopentan-1,2-dione (3-methyl-1,2-cyclopentanedione)	6.3
90-05-1	04.005	2-methoxyphenol (guajacol)	6.1
106-44-5 108-39-4	04.028 04.026	4–/3-methylphenol (*p,m*-cresol)	4.4
105-67-9	04.066	2,4-dimethylphenol (2,4-xylenol)	2.6
95-48-7	04.027	2-methylphenol (*o*-cresol)	2.0
108-95-2	04.041	phenol	2.0
2785-87-7	04.049	2-methoxy-4-propylphenol	2.0
5857-25-0	–	2-ethyl-3-hydroxy-2-cyclopenten-1-one	1.8
64-19-7	08.002	acetic acid	1.6
2896-67-5	–	6-methylguaiacol (2-methoxy-6-methylphenol)	1.5
118-71-8	07.014	maltol (2-methyl-3-hydroxypyrone)	1.4
111-55-7	–	ethylene glycol diacetate	1.2
2758-18-1	07.112	3-methyl-2-cyclopenten-1-one	1.2
576-26-1	04.042	2,6-dimethylphenol (2,6-xylenol)	1.0
4463-33-6	–	2,3-dimethoxytoluene	1.0
116-09-6	07.169	1-hydroxypropan-2-one (hydroxyacetone)	0.9
97-54-1[d]	04.004	isoeugenol (2-methoxy-4-propenylphenol)	0.85
1121-05-7	–	2,3-dimethyl-2-cyclopenten-1-one	0.76
6443-69-2	–	3,4,5-trimethoxy-toluene	0.74
79-09-4	08.003	propionic acid	0.71
98-01-1	13.018	furfural	0.62
91-57-6	former 01.051[e]	2-methylnaphthalene	0.47
90-12-0	former 01.014[e]	1-methylnaphthalene	0.43
150-76-5	04.077	4-methoxyphenol (mequinol)	0.37
95-65-8	04.048	3,4-dimethylphenol (3,4-xylenol)	0.32
1120-73-6	–	2-methyl-2-cyclopenten-1-one	0.32

CAS-no	FL-no	Chemical name[a]	Average[b] (wt%)
107-93-7	08.072[f]	but-2-enoic acid (*cis* and *trans*) (crotonic acid)	0.08

wt: weight.

(a): In case a constituent of the Primary Product is an authorised flavouring substance (FL-no), the assigned chemical name corresponds to the respective entry in the EU Union List of flavourings. Deviating chemical names reported by the applicant in the dossier are given in brackets, if applicable.

(b): From the analysis of the five batches presented in Table 1.

(c): [FL-no: 07.056] refers to the mixture of the tautomeric forms of 3-methylcyclopentan-1,2-dione.

(d): The Panel noted that at the GC peak corresponding to this compound, two different CAS numbers were attributed by the applicant in the technical dossier (see Documentation provided to EFSA No. 1). More specifically, CAS number 97-53-0 (i.e. eugenol) and CAS number 97-54-1 (i.e. isoeugenol) were reported in dossier's sections 'Information on the identity of the Primary Product' and 'Genotoxicity', respectively. Based on the available experimental data considered by EFSA for both substances in existing FGE opinions (i.e. FGE.60 (EFSA AFC Panel, 2009) for eugenol; FGE.30Rev1 (EFSA CEF Panel, 2011b); FGE.81 (EFSA CEF Panel, 2010) for isoeugenol), the Panel did not identify concern for genotoxicity for any of these substances. Therefore, the conflicting information provided by the applicant related to the identity of this component does not affect the conclusions reached by the Panel for the Primary Product (see Sections 5 and 6).

(e): 'Former FL-number' refers to substances that were initially included in the evaluation programme but were not included or were removed/withdrawn from the Union List.

(f): [FL-no: 08.072] refers to the mixture of *E*/*Z* isomers.

Appendix B – Approach for assessing reliability and relevance of genotoxicity studies

Evaluation of data quality for hazard/risk assessment includes evaluation of reliability of studies and relevance of study results (Klimisch et al., 1997; ECHA, 2011; EFSA Scientific Committee, 2011, 2017b, 2021b). Reliability is assessed using a scoring system based on published criteria (Klimisch et al., 1997) described in the following Section. In a second step, the relevance (high, limited or low) of study results is assessed based on several aspects (genetic endpoint, route of administration, status of validation of the assay, etc.) discussed in Section B.2, and also taking into account the assessment of the reliability of the study.

Only studies with acceptable relevance (high or limited) are considered in the weight of evidence approach (WoE). Genotoxicity studies evaluated as of low relevance are not further considered in the WoE.

B.1. Evaluation of reliability of results of genotoxicity studies – general considerations

The scoring system for reliability is based on the scoring system of Klimisch et al. (1997). Reliability is defined by Klimisch as 'evaluating the inherent quality of a test report or publication relating to preferably standardised methodology and the way that the experimental procedure and results are described to give evidence of the clarity and plausibility of the findings'. In assigning the reliability score, the compliance with the OECD Test Guidelines (TGs) or standardised methodology and the completeness of the reporting should be considered.

The reliability scores are:

1) reliable without restriction;
2) reliable with restrictions;
3) reliability insufficient;
4) reliability cannot be evaluated.

1. Reliable without Restriction 'This includes studies or data from the literature or reports which were carried out or generated according to generally valid and/or internationally accepted testing guidelines (preferably performed according to GLP) or in which the test parameters documented are based on a specific (national) testing guideline (preferably performed according to GLP) or in which all parameters described are closely related/comparable to a guideline method'.

2. Reliable with Restrictions 'This includes studies or data from the literature, reports (mostly not performed according to GLP), in which the test parameters documented do not totally comply with the specific testing guideline, but are sufficient to accept the data or in which investigations are described which cannot be subsumed under a testing guideline, but which are nevertheless well documented and scientifically acceptable'.

3. Reliability Insufficient[16] 'This includes studies or data from the literature/reports in which there are interferences between the measuring system and the test substance or in which organisms/test systems were used which are not relevant in relation to the exposure (...) or which were carried out or generated according to a method which is not acceptable, the documentation of which is not sufficient for an assessment and which is not convincing for an expert judgment'.

4. Reliability cannot be evaluated[17] 'This includes studies or data from the literature, which do not give sufficient experimental details, and which are only listed in short abstracts or secondary literature (books, reviews, etc.)'.

B.2. Evaluation of relevance of results of individual genotoxicity studies – general considerations

The relevance of the test system and test results are reported separately.

The relevance of the test systems (high, limited, low) is principally based on the following criteria:

[16] Klimisch et al. (1997) used the term 'Not reliable' however, 'Reliability Insufficient' was considered more appropriate.
[17] Klimisch et al. (1997) used the term 'Not assignable' however, 'Reliability cannot be evaluated' was considered more appropriate.

- Genetic endpoint: higher relevance is given to studies providing information on apical endpoints, i.e. gene mutations, structural and numerical chromosomal alterations. Supporting information may be obtained from indicator assays; exception is the *in vivo* Comet assay that is considered with high relevance when applied as follow-up to a positive *in vitro* result (as recommended by the EFSA Scientific Committee (2011)).
- Status of validation of the test system (e.g. (in order of decreasing relevance) availability of an OECD TG consolidated or in the course of development or internationally recommended protocol, validation at national level only).

The relevance of the study results (high, limited, low) are principally based on the following criteria:

- Reliability of studies: the results of studies with reliability that are insufficient or which cannot be evaluated (see points 3–4 in Section B.1) are considered of low relevance.
- Relevance of the test system.
- Route of administration: higher relevance is given to oral vs. intravenous or subcutaneous injection and inhalation exposure in case of *in vivo* studies. Lower relevance is given to studies using the intraperitoneal route, which is not physiological and not recommended by OECD TGs.
- Biological relevance of the test results, considering: purity of the test substance; the metabolic capabilities of the test system; the bioavailability of the test substance, with particular consideration of the evidence of target tissue exposure in tests *in vivo* (negative results without evidence of target tissue exposure are considered as inconclusive and their relevance low); the interference of high cytotoxicity; the reproducibility of test results.

Appendix C – Genotoxicity studies on the Primary Product (whole mixture) evaluated by the CEF Panel (EFSA CEF Panel, 2009)

Table C.1: Summary of *in vitro* genotoxicity studies on Fumokomp (SF-009) including re-evaluation of reliability and relevance by the FAF Panel (approach described in Appendix B)

Name	Test system *in vitro*	Test object	Concentrations and test conditions	Result	Reliability/comments	Relevance of test system/ relevance of the result	Reference
Fumokomp	Bacterial Reverse Mutation test	*S. Typhimurium* TA98, TA100, TA1535, TA1537 *E. Coli* WP2 uvrA	Experiment 1: 128–5000 μg/plate (plate incorporation, +/−S9) Expriment 2: 128–5000 μg/plate (pre-incubation, +/−S9)	Negative	Reliable without restrictions. Study performed according to OECD TG 471 and in compliance with GLP.	High/High	LAB International Research Centre, 2005a
	In vitro mammalian cell gene mutation test in mouse lymphoma cells	L5178Y $TK^{+/-}$ mouse lymphoma cells	Experiment 1: 10–100 μg/mL (3 + 21 h, +/−S9) Experiment 2: 10–100 μg/mL (3 + 21 h, +S9) 10–40 μg/mL (24 h −S9)	Positive (3 + 21 h, −S9) Equivocal (3 + 21 h, +S9; 24 h -S9)	Reliable with restrictions (historical controls not provided). Study performed according to OECD TG 476 (applicable at that time, now OECD TG 490) and in compliance with GLP.	High/Limited	LAB International Research Centre, 2005b
	In vitro mammalian chromosomal aberration test	Chinese hamster ovary cells (CHO-KI cell line)	Experiment 1: 5, 25, 75 μg/mL (4 + 20 h, +/−S9) Experiment 2: 5, 25, 50 μg/mL (20 + 28 h, −S9) 5, 25, 75 μg/mL (4 + 28 h, +S9)	Negative	Reliable with restrictions (only 200 metaphases/ concentration instead of 300 were scored and historical controls not provided). Study performed according to OECD TG 473 and in compliance with GLP.	High/Limited	LAB International Research Centre, 2005c

Table C.2: Summary of *in vivo* genotoxicity studies on Fumokomp (SF-009) including re-evaluation of reliability and relevance by the FAF Panel (approach described in Appendix B)

Name	Test system *in vivo*	Test object route	Doses (mg/kg bw per day)	Result	Reliability/comments	Relevance of test system/ relevance of the result	Reference
Fumokomp	Micronucleus assay in bone marrow	NMRI BR mice; M and F Oral	500, 1,000 and 2,000[(a)]	Negative	Reliable without restrictions. Study performed according to OECD TG 474 and in compliance with GLP	High/Limited[(b)]	TOXI-COOP KKT, 2008a
	UDS test in liver	Wistar rats; M Gavage	500, 1,000 and 2,000	Negative	Reliable without restrictions. Study performed according to OECD TG 486 and in compliance with GLP	Low/Low	TOXI-COOP KKT, 2008b

bw: body weight; M: males; F: females.
(a): One administration with sampling at: 24 h in the low and mid dose groups; 24 h and 48 h in the high dose and vehicle groups.
(b): The reason for the limitation of the relevance is that, according to the statement on genotoxicity assessment of chemical mixtures (EFSA Scientific Committee, 2019), even in the case of bone marrow exposure, the assessment of genotoxicity of mixtures in the bone marrow is limited by the fact that target tissue exposure to all potential genotoxic components cannot be demonstrated unequivocally.

Annex A – Exposure assessment results

- Annex A1: Occurrence data per food category considered in FAIM, (mg/kg).
- Annex A2: Total estimated exposure of Fumokomp Conc. (SF-009) from its proposed maximum level exposure scenario per population group and survey: mean and 95th percentile (mg/kg bw per day).
- Annex A3: Total estimated exposure of Fumokomp Conc. (SF-009) from its expected typical exposure assessment scenario per population group and survey: mean and 95th percentile (mg/kg bw per day).
- Annex A4: Main food categories contributing to exposure to Fumokomp Conc. (SF-009) using the maximum level exposure assessment scenario (> 5% to the total mean exposure).
- Annex A5: Main food categories contributing to exposure to Fumokomp Conc. (SF-009) using the expected typical level exposure assessment scenario (> 5% to the total mean exposure).
- Annex A6: Qualitative evaluation of the influence of standard uncertainties on the dietary exposure estimates of the Primary Product.

Annex A can be found in the online version of this output, in the 'Supporting information' section.

Annex B – Genotoxicity assessment of the identified constituents in the Primary Product

Annex B can be found in the online version of this output, in the 'Supporting information' section.