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## Scientific Opinion on Flavouring Group Evaluation 72, Revision 2 (FGE.72Rev2): consideration of aliphatic, branched-chain saturated and unsaturated alcohols, aldehydes, acids and related esters evaluated by JECFA (61st, 68th and 69th meetings) and structurally related to flavouring substances in FGE.05Rev3

EFSA Panel on Food Additives and Flavourings (FAF),  
Maged Younes, Gabriele Aquilina, Laurence Castle, Karl-Heinz Engel, Paul Fowler,  
Maria Jose Frutos Fernandez, Peter Fürst, Ursula Gundert-Remy, Rainer Gürtler, Trine Husøy,  
Peter Moldeus, Agneta Oskarsson\*, Romina Shah, Ine Waalkens-Berendsen, Detlef Wölfle,  
Romualdo Benigni, Claudia Bolognesi, Kevin Chipman, Eugenia Cordelli, Gisela Degen,  
Daniel Marzin, Camilla Svendsen, Giorgia Vianello and Wim Mennes

### Abstract

The EFSA Panel on Food Additives and Flavourings was requested to evaluate 31 flavouring substances assigned to the Flavouring Group Evaluation 72 (FGE.72), using the Procedure as outlined in the Commission Regulation (EC) No 1565/2000. Twenty-three substances have already been considered in FGE.72 and FGE.72Rev1 ([FL-no: 02.011, 02.012, 02.027, 02.029, 02.058, 02.076, 02.109, 05.020, 05.021, 05.124, 05.148, 05.169, 08.036, 08.044, 08.047, 08.055, 08.064, 08.070, 08.079, 09.273, 09.408, 09.931 and 16.001]). The remaining eight flavouring substances have been cleared with respect to genotoxicity in FGE.200Rev1 ([FL-no: 05.114]) and FGE.201Rev2 ([FL-no: 02.174, 05.033, 05.090, 05.095, 05.105, 05.107 and 05.126]) and they are considered in this revision 2 of FGE.72. The substances were evaluated through a stepwise approach that integrates information on the structure–activity relationships, intake from current uses, toxicological threshold of concern (TTC), and available data on metabolism and toxicity. The Panel concluded that none of these 31 substances gives rise to safety concerns at their levels of dietary intake, estimated on the basis of the ‘Maximised Survey-derived Daily Intake’ (MSDI) approach. Besides the safety assessment of the flavouring substances, the specifications for the materials of commerce have also been considered and found adequate for all 31 flavouring substances. For 21 substances, evaluated through the Procedure in the previous revision (FGE.72Rev1), no normal and maximum use levels are available. For four substances, the modified Theoretical Added Maximum Daily Intake (mTAMDI) intake estimates are equal to ([FL-no: 05.090]) or above ([FL-no: 05.107, 05.105, 05.033]) the TTC for their structural class. Therefore, for these 25 substances more detailed data on uses and use levels should be provided in order to refine their exposure assessments and to finalise their safety evaluations.

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**Correspondence:** [fip@efsa.europa.eu](mailto:fip@efsa.europa.eu)

\*: Member of the EFSA Panel on Food Additives and Flavourings (FAF) and of its Working Group on Flavourings until 31st December 2019.

**Panel members:** Gabriele Aquilina, Laurence Castle, Karl-Heinz Engel, Paul Fowler, Maria Jose Frutos Fernandez, Peter Fürst, Ursula Gundert-Remy, Rainer Gürtler, Trine Husøy, Wim Mennes, Peter Moldeus, Agneta Oskarsson, Romina Shah, Ine Waalkens-Berendsen, Detlef Wölfle and Maged Younes.

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## 1. Introduction

The present revision of this Flavouring Group Evaluation (FGE) concerns the inclusion of eight aliphatic, branched-chain  $\alpha,\beta$ -unsaturated alcohols and aldehydes (i.e. [FL-no: 02.174, 05.033, 05.090, 05.095, 05.105, 05.107, 05.114 and 05.126]) which have been evaluated with respect to genotoxicity in FGE.200Rev1 ([FL-no: 05.114]) and FGE.201Rev2 ([FL-no: 02.174, 05.033, 05.090, 05.095, 05.105, 05.107 and 05.126]). According to the Mandates and Terms of Reference of these FGEs, when for a flavouring substance the concern for genotoxicity is ruled out, the European Food Safety Authority (EFSA) proceeds to the full evaluation of these flavouring substances, taking into account the requirements of the Commission Regulation (EC) No 1565/2000<sup>1</sup> and of Regulation (EU) No 1334/2008<sup>2</sup>.

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

#### 1.1.1. Background to Mandate from FGE.200Rev1 (M-2018-0041)

The Union list of flavourings and source materials was established by Commission Implementing Regulation (EC) No 872/2012<sup>3</sup>. The list includes a number of flavouring substances for which the safety evaluation should be completed in accordance with Commission Regulation (EC) No 1565/2000.<sup>1</sup>

In February 2011, the EFSA Panel had evaluated a first dossier submitted by Industry in response to the requested data for representative substances in FGE. 200. These data were not considered adequate to alleviate the genotoxicity concern for the substance in subgroup 1.1.1 and the Panel recommended at that time 'to perform *in vivo* dietary Comet assays (in drinking water or in feed, not by gavage) for the three linear representatives of subgroup 1.1.1 [FL-no: 05.073, 05.058 and 05.060]'

Additional data were submitted in February and June 2013 by Industry related to one representative substance of subgroup 1.1.1, hex-2(trans)-enal [FL-no: 05.073] and two other substances of the group.

On 21 May 2014 the EFSA CEF Panel adopted an opinion on this Flavouring Group Evaluation 200 (FGE.200). The Panel confirmed the need for an *in vivo* Comet assay performed in duodenum and liver for hex-2(trans)-enal [FL-no: 05.073]. For the two representative substances of subgroup 1.1.1 (nona-2 (trans), 6(cis)-dial [FL-no: 05.058] and oct-2-enal [FL-no: 05.060]), a combined *in vivo* Comet assay and micronucleus assay would be required and evidence of bone marrow exposure should be provided.

New data concerning the three representative substances of this group addressing the EFSA opinion have been submitted during 2017. The data also included updated poundage and use levels concerning these substances.

The list of the substances referred to in this letter is included in Annex II.<sup>4</sup>

#### 1.1.2. Terms of Reference of Mandate from FGE.200Rev1 (M-2018-0041)

The European Commission requests the European Food Safety Authority (EFSA) to evaluate the new information submitted and, depending on the outcome, proceed to full evaluation of the substances in this group in accordance with Commission Regulation (EC) No 1565/2000<sup>1</sup>. In accordance with the usual practice by the CEF panel, the first step (assessment of the genotoxicity) should be completed within 9 months. An additional 9 months if necessary is also established for the second step (evaluation through the CEF Procedure). In case the genotoxic potential cannot be ruled out or the procedure cannot be applied in the first step, EFSA is asked to quantify the exposure.

#### 1.1.3. Background to Mandate from FGE.201Rev2 (M-2017-0048)

The use of flavourings is regulated under Regulation (EC) No 1334/2008<sup>2</sup> of the European Parliament and Council of 16 December 2008 on flavourings and certain food ingredients with flavouring properties for use in and on foods. On the basis of Article 9(a) of this Regulation, an evaluation and approval are required for flavouring substances.

<sup>1</sup> Commission Regulation (EC) No 1565/2000 of 18 July 2000 laying down the measures necessary for the adoption of an evaluation programme in application of Regulation (EC) No 2232/96. OJ L 180, 19.7.2000, p. 8–16.

<sup>2</sup> Regulation (EC) No 1334/2008 of the European Parliament and of the Council of 16 December 2008 on flavourings and certain food ingredients with flavouring properties for use in and on foods and amending Council Regulation (EEC) No 1601/91, Regulations (EC) No 2232/96 and (EC) No 110/2008 and Directive 2000/13/EC. OJ L 354, 31.12.2008, p. 34–50.

<sup>3</sup> Commission implementing Regulation (EU) No 872/2012 of 1 October 2012 adopting the list of flavouring substances provided for by Regulation (EC) No 2232/96 of the European Parliament and of the Council, introducing it in Annex I to Regulation (EC) No 1334/2008 of the European Parliament and of the Council and repealing Commission Regulation (EC) No 1565/2000 and Commission Decision 1999/217/EC. OJ L 267, 2.10.2012, p. 1–161.

<sup>4</sup> Annex II refers here to the annex of the mandate letter from the EC to EFSA related to FGE.200Rev1.

The Union List of flavourings and source materials was established by Commission Implementing Regulation (EC) No 872/2012<sup>3</sup>. The list includes a number of flavouring substances for which the safety evaluation should be completed in accordance with Commission Regulation (EC) No 1565/2000<sup>1</sup>. The substances in this group were included in the Union list with a footnote 1 (under evaluation by EFSA).

In its opinion about this subgroup of 2012, the EFSA Panel considered that the mutagenicity hazard could not be cleared by the endpoints evaluated in the *in vivo* micronucleus assay submitted. The Panel therefore conclude that further data were required in order to clarify the genotoxic potential of this subgroup. The Panel considered the Comet assay with [FL-no: 05.095] as test material and performed on liver, blood and first site of contact, as a preferred option to further investigate the genotoxicity *in vivo*.

The additional data submitted by the applicant consist essentially of:

- a transgenic mutation assay in combination with an *in vivo* micronucleus assay for the substance 2-methylcrotonaldehyde [FL-no: 05.095];
- a combination of a Comet/micronucleus assay for the substance 2-methylpent-2-enal [FL-no: 05.090].

The Panel also considered in this opinion on FGE.201 rev.1 that the additional data on 2-methylcrotonaldehyde [FL-no: 05.095] could also be considered representative for the following substances: 2,8-dithianon-4-en-4-carboxaldehyde [FL-no: 12.065] and 2-(methylthiomethyl)but-2-enal [FL-no: 12.079].

#### 1.1.4. Terms of Reference of Mandate from FGE.201Rev1 (M-2017-0048)

The European Commission requests the European Food Safety Authority (EFSA) to evaluate the new information submitted on 2-methylpent-2-enal [FL-no: 05.090] and 2-methylcrotonaldehyde [FL-no: 05.095] including also 2,8-dithianon-4-en-4-carboxaldehyde [FL-no: 12.065] and 2-(methylthiomethyl) but-2-enal [FL-no: 12.079] and, depending on the outcome, proceed to the full evaluation of the substances of this group listed in the table below, in accordance with Commission Regulation (EC) No 1565/2000, within 9 months.

In case the genotoxic potential cannot be ruled out or the procedure cannot be applied, EFSA is asked to characterise the hazards and also quantify the exposure.

As regards the substance 2,6-dimethyl-2,5,7-octatriene-1-ol acetate ([FL-no: 09.931] CAS no 999999-91-4) the applicant indicate that it is included in this subgroup 1.1.2 of FGE19 (FGE.201). However, this substance has been already evaluated by EFSA in FGE 207 and FGE 72 Rev.1 of 2013.

As regards substance 4-methyl-3-hepten-5-one ([FL-no: 07.261] CAS no 22319-31-9) EFSA indicated in its opinion FGE.204 that 'the 2-methyl substituted alpha, beta-unsaturated aldehydes in FGE.201Rev1 can be considered as structurally related to it [FL-no: 07.261]. Thus, the final conclusion on [FL-no: 07.261] will be drawn based on the outcome of the evaluation of FGE.201Rev1'.

## 1.2. Interpretation of the Terms of Reference

Flavouring substances [FL-no: 02.174, 05.033, 05.090, 05.095, 05.105, 05.107 and 05.126] were first allocated to FGE.201Rev2 and [FL-no: 05.114] to FGE.200Rev1 for evaluation with respect to genotoxicity. Based on new genotoxicity data submitted, the Panel concluded that these eight flavouring substances do not give rise to concern with respect to genotoxicity and can accordingly be evaluated through the Procedure in the present revision of FGE.72 (FGE.72Rev2), in accordance with Commission Regulation (EC) No 1565/2000.

In addition, use levels for two substances, previously evaluated in FGE.72Rev1 ([FL-no: 05.169 and 09.931]) have been provided by industry and accordingly their modified Theoretical Added Maximum Daily Intake (mTAMDI) value estimates will be calculated and included in the current revision 2 of this FGE.

The methodology for the evaluation of these substances is clarified in Appendix A.

## 2. Data and methodologies

### 2.1. Data

The present opinion is based on the data presented in Table 1.

**Table 1:** Data considered in the current revision 2 of FGE.72 (FGE.72Rev2)

FL-no	Chemical name	Data provided for the current revision 2 of FGE.72	Appendix (Table nr) and relevant section of the opinion	Documentation provided to EFSA nr:
02.174	2-Methylbut-2-en-1-ol	Specifications, EU poundage data (MSDI), Use levels (mTAMDI)	Appendix B (Table B.1) Appendix C (Tables C.1 and C.4)	Documentation provided to EFSA nr: 1, 2, 3
05.033	2-Ethylhept-2-enal			
05.090	2-Methylpent-2-enal			
05.095	2-Methylcrotonaldehyde			
05.107	2-Isopropyl-5-methylhex-2-enal			
05.114	4-Methylpent-2-enal			
05.126	2-Methyloct-2-enal			
05.105	2-Butylbut-2-enal			
05.169	12-Methyltridecanal	Use levels (mTAMDI)	Appendix C (Tables C.1 and C.4)	Documentation provided to EFSA nr: 1, 4
09.931	2,6-Dimethyl-2,5,7-octatriene-1-ol acetate			

MSDI: Maximised Survey-derived Daily Intake; mTAMDI: modified Theoretical Added Maximum Daily Intake.

In addition, the following data have been used in FGE.72Rev2:

- JECFA specifications for the eight candidate substances [FL-no: 02.174, 05.033, 05.090, 05.095, 05.105, 05.107, 05.144 and 05.126] (JECFA, 2003);
- Genotoxicity data evaluated in FGE.200Rev1 and FGE.201Rev2 (EFSA FAF Panel, 2018a,b);
- 61st, 68th and 69th JECFA reports and 61st JECFA toxicology monograph (JECFA, 2004a,b, 2007, 2008);
- EFSA Scientific Opinion on FGE.72 (EFSA CEF Panel, 2010a);
- EFSA Scientific Opinion on FGE.72Rev1 (EFSA CEF Panel, 2013b);
- EFSA Scientific Opinion on FGE.05Rev3 ((EFSA FAF Panel, 2019).

### 2.1.1. History of the evaluation of the substances in FGE.72

In the first version of Flavouring Group Evaluation 72 (FGE.72), EFSA considered a group of 22 aliphatic branched-chain saturated and unsaturated alcohols, aldehydes, acids and related esters which had been evaluated by JECFA at their 61st meeting (JECFA, 2004a).

The revision 1 of FGE.72 was prepared due to inclusion of one additional substance, 2,6-dimethyl-2,5,7-octatriene-1-ol acetate [FL-no: 09.931]. Furthermore, European poundage data for two substances [FL-no: 05.148 and 08.079] as well as information on the stereoisomeric composition for 12 substances [FL-no: 02.011, 02.012, 02.027, 02.029, 05.020, 05.021, 05.148, 08.036, 08.044, 08.055, 08.079 and 09.273] had been provided since the first publication of FGE.72.

The CEF Panel concluded that the 23 candidate substances in FGE.72Rev1 are structurally related to the group of branched- and straight-chain unsaturated carboxylic acids and esters of these with aliphatic saturated alcohols evaluated by EFSA in the FGE.05Rev2 (EFSA CEF Panel, 2010b). The concern with respect to genotoxicity for all 23 candidate substances was ruled out in FGE.202 (EFSA CEF Panel, 2009) and FGE.207 (EFSA CEF Panel, 2013a), based on the genotoxicity data available for candidate substances [FL-no: 05.020, 05.124 and 09.931] and structurally related substances in FGE.05Rev2. The CEF Panel agreed with the way the application of the Procedure has been performed by JECFA for the 23 substances considered in FGE.72Rev1 (EFSA CEF Panel, 2013b). Adequate specifications including complete purity criteria and identity are available for all 23 JECFA-evaluated substances. Overall, for all 23 JECFA-evaluated aliphatic branched-chain saturated and unsaturated alcohols, aldehydes, acids and related esters [FL-no: 02.011, 02.012, 02.027, 02.029, 02.058, 02.076, 02.109, 05.020, 05.021, 05.124, 05.148, 05.169, 08.036, 08.044, 08.047, 08.055, 08.064, 08.070, 08.079, 09.273, 09.408, 09.931 and 16.001], the Panel agreed with the JECFA conclusion 'No safety concern at estimated levels of intake as flavouring substances' based on the 'Maximised Survey-derived Daily Intake' (MSDI) approach.

For all 23 substances in revision 1, use levels were needed to calculate the 'modified Theoretical Added Maximum Daily Intake' (mTAMDI) estimates in order to identify those flavouring substances that need more refined exposure assessment and to finalise the evaluation.

From the substances considered in the present revision 2 of FGE.72 (FGE.72Rev.2), six flavouring substances [FL-no: 05.033, 05.090, 05.095, 05.105, 05.107, 05.126 and 05.178] were evaluated by JECFA in its 61st meeting (JECFA, 2004a) and one of these substances [FL-no: 05.126] was re-evaluated by JECFA in its 69th meeting (JECFA, 2008). Five candidate substances ([FL-no: 02.174, 05.033, 05.090, 05.095, 05.105, 05.107 and 05.126]) were evaluated by EFSA in FGE.201Rev2 (EFSA FAF Panel, 2018a) and one substance ([FL-no: 05.114]) in FGE.200Rev1 (EFSA FAF Panel, 2018b), where it was concluded that the concern for genotoxicity for these substances could be ruled out. Therefore, they could be evaluated through the Procedure.

In addition, FGE.72Rev2 also deals with two additional flavouring substances [FL-no: 02.174 and 05.114] evaluated by JECFA in its 68th (JECFA 2007) and 61st meeting (JECFA, 2004a), respectively. By expert judgement, they have been included in FGE.72Rev2 on the basis of their structural similarities with the substances considered in this group. These flavouring substances were considered of no genotoxic concern in FGE.201Rev1 (EFSA FAF Panel, 2018a). Therefore, they can be evaluated through the Procedure. In addition, for two substances ([FL-no: 05.169 and 09.931]), previously evaluated in FGE.72Rev1, use levels have been provided and accordingly their mTAMDI value estimates can be calculated and included in the current revision 2 of this FGE.

Together with the 23 substances that were already considered in FGE.72Rev1, the current revision comprises 31 substances. The 23 flavouring substances, for which the evaluation was finalised in FGE.72Rev1, will not be further discussed. Nevertheless, for the sake of completion the information for all the 31 substances is maintained in the various tables in this FGE.

FGE	Adopted by EFSA	Link	No of substances
FGE.72	25 November 2009	<a href="http://www.efsa.europa.eu/efsajournal/pub/1402">http://www.efsa.europa.eu/efsajournal/pub/1402</a>	22
FGE.72Rev1	25 September 2013	<a href="http://www.efsa.europa.eu/efsajournal/pub/3392">http://www.efsa.europa.eu/efsajournal/pub/3392</a>	23
FGE.72Rev2	28 January 2020	<a href="http://www.efsa.europa.eu/efsajournal/pub/">http://www.efsa.europa.eu/efsajournal/pub/</a>	31

FGE: Flavouring Group Evaluation.

## 2.2. Methodologies

This opinion was elaborated following the principles described in the EFSA Guidance on transparency with regard to scientific aspects of risk assessment (EFSA Scientific Committee, 2009) and following the relevant existing guidance documents from the EFSA Scientific Committee. The assessment strategy applied for the evaluation programme of flavouring substances, as laid down in Commission Regulation (EC) No 1565/2000, is based on the Opinion on a Programme for the Evaluation of Flavouring substances of the Scientific Committee on Food (SCF, 1999).

### 2.2.1. Procedure for the safety evaluation of flavouring substances

The approach for safety evaluation of chemically defined flavouring substances as referred to in Commission Regulation (EC) No 1565/2000, named the 'Procedure', is described in Appendix A.

### 2.2.2. Approach used for the calculation of exposure

The approach used for calculation of the intake of the flavouring substances is described in Appendix A (point 'a') *Intake*) and in Appendix C (Section C.2 'mTAMDI calculation').

## 3. Assessment

### 3.1. Specifications



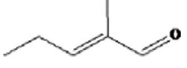
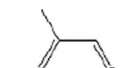
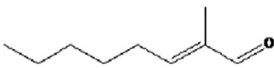
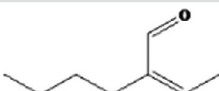
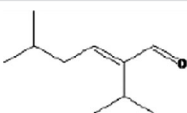

#### *JECFA status*

JECFA specifications are available for all the flavouring substances in FGE.72Rev2, including the eight newly included flavouring substances [FL-no: 02.174, 05.033, 05.090, 05.095, 05.105, 05.107, 05.114 and 05.126] (JECFA, 2003).

#### *EFSA considerations*

Table 2 shows the chemical structures of the candidate substances which are considered in this revision of FGE.72 (FGE.72Rev2).

**Table 2:** Flavouring substances under evaluation in FGE.72Rev2

FL-no	Chemical name	Structural formula	Structural class*
02.174	2-Methylbut-2-en-1-ol		Class I
05.114	4-Methylpent-2-enal		Class I
05.090	2-Methylpent-2-enal		Class I
05.095	2-Methylcrotonaldehyde		Class I
05.126	2-Methyloct-2-enal		Class I
05.105	2-Butylbut-2-enal		Class III
05.107	2-Isopropyl-5-methylhex-2-enal		Class III
05.033	2-Ethylhept-2-enal		Class III

FGE: Flavouring Group Evaluation; FL-no: FLAVIS number.

\*: Determined with OECD Toolbox (version 4.3.1 available at <https://www.oecd.org/chemicalsafety/risk-assessment/oecd-qsar-toolbox.htm>).

The newly included flavouring substances in FGE.72Rev2 can exist as geometrical stereoisomers due to the presence of a double bond.

With regard to composition of the stereoisomeric mixtures, adequate information to describe the materials of commerce for these flavouring substances has been submitted by industry (Documentation provided to EFSA nr: 1). Based on this information on stereoisomerism, the chemical names and/or the CAS numbers for flavouring substances [FL-no: 02.174, 05.033, 05.090, 05.095, 05.105, 05.107 and 05.126] should be changed in the Union List (UL) to reflect their stereochemical configuration (see 'EFSA comments' column in Table B.1 – Appendix B).

The purity requirements for flavouring substances [FL-no: 05.090 and 05.126] should be updated as outlined in Table B.1 – Appendix B in accordance with the information provided by industry (Documentation provided to EFSA nr: 1).

In addition, the Panel noted that the CAS number for flavouring substance [FL-no: 09.931], previously considered in FGE.72Rev1, has still to be changed to 197098-61-6. The CAS number currently reported in the UL (999999-91-4) does not exist.

The most recent specifications data for all 31 substances in FGE.72Rev2 are summarised in Table B.1 – Appendix B.

### 3.2. Estimation of intake

#### JECFA status

For 30 flavouring substances in FGE.72Rev2, including seven newly allocated flavouring substances [FL-no: 02.174, 05.033, 05.090, 05.095, 05.107, 05.114 and 05.126], intake data are available for the EU (JECFA, 2004a, 2007, 2008). In the JECFA report (JECFA, 2004a), for one candidate substance [FL-no: 05.105] (JECFA-no: 1214), production figures are only available for the USA.



### *EFSA considerations*

For all eight candidate substances [FL-no: 02.174, 05.033, 05.090, 05.095, 05.105, 05.107, 05.114 and 05.126] updated EU production figures have been submitted by industry (Documentation provided to EFSA nr. 2 and 3). The MSDI values range from 0.012 to 11.93  $\mu\text{g}/\text{capita}$  per day (Table C.4 – Appendix C).

For the eight newly included flavouring substances [FL-no: 02.174, 05.033, 05.090, 05.095, 05.105, 05.107, 05.114 and 05.126] and for two substances previously considered in FGE.72Rev1 ([FL-no: 05.169 and 09.931]), normal and maximum use levels have been submitted (Documentation provided to EFSA nr. 1 and 4) and mTAMDI intake values can be calculated. The mTAMDI intake estimates calculated from these data for six substances are below ([FL-no: 02.174, 05.095, 05.114, 05.126, 05.169 and 09.931]) the toxicological threshold of concern (TTC) for their structural class I. For four substances, the mTAMDI intake estimates are equal to ([FL-no: 05.090]) or above ([FL-no: 05.107, 05.105, 05.033]) the TTC for their structural class (I and III). Therefore, for these four substances, more detailed data on uses and use levels should be provided in order to refine the exposure assessment and to finalise their safety evaluation.

No normal and maximum use levels have been provided for the 21 remaining flavouring substances [FL-no: 02.011, 02.012, 02.027, 02.029, 02.058, 02.076, 02.109, 05.020, 05.021, 05.124, 05.148, 08.036, 08.044, 08.04, 08.055, 08.064, 08.070, 08.079, 09.273, 09.408 and 16.001], previously considered in FGE.72Rev1.

The MSDI values for the 31 flavouring substances and the mTAMDI intake estimates for [FL-no: 02.174, 05.033, 05.090, 05.095, 05.105, 05.107, 05.114, 05.126, 02.076, 05.169 and 09.931], are shown in Table C.4 – Appendix C.

## **3.3. Biological and toxicological data**

### **3.3.1. ADME data**

According to JECFA (2004b), the eight  $\alpha,\beta$ -unsaturated alcohols and aldehydes [FL-no: 02.174, 05.033, 05.090, 05.095, 05.105, 05.107, 05.114 and 05.126] would be expected to be absorbed from the gastrointestinal tract and then distributed rapidly throughout the body, metabolised, and excreted as polar metabolites in the urine, faeces and expired air. No accumulation in the body is expected. Particularly, compounds with shorter branched-chain would undergo  $\beta$ -oxidative cleavage to yield intermediates of the amino acid and/or fatty acid metabolic pathways. The resulting intermediates are completely oxidised to carbon dioxide ( $\text{CO}_2$ ) via the tricarboxylic acid cycle. For alcohols and aldehydes with longer chain lengths, and with more chain substitutions, formation of polar metabolites would be expected via oxidation and hydration reactions. Overall, JECFA concluded that these flavouring substances can be evaluated along the A-side of the Procedure scheme, since they are expected to be completely oxidised, or oxidised to polar metabolites, and then excreted primarily in the urine.

### *EFSA considerations*

Based on the information provided by JECFA (2004b) and taking into account the outcome of the evaluation of genotoxicity, as described in Section 3.3.2, the Panel agrees with JECFA and considers that these flavouring substances would be expected to be metabolised to innocuous products and thus that candidate substances [FL-no: 02.174, 05.033, 05.090, 05.095, 05.105, 05.107, 05.114 and 05.126] in FGE.72Rev2 can be evaluated along the A-side. For the structurally related substances in FGE.05Rev3 (EFSA FAF Panel, 2019), EFSA also decided to evaluate these compounds through the A-side of the Procedure.

### **3.3.2. Genotoxicity data**

This revision involves the inclusion of eight flavouring substances, for which in FGE.19 a concern for genotoxicity had been identified based on the presence of a structural alert (i.e.  $\alpha,\beta$ -unsaturated carbonyl substance or precursor for that), preventing their evaluation through the Procedure (see also Appendix A). Therefore, these substances were evaluated in FGE.201Rev2 ([FL-no: 02.174, 05.033, 05.090, 05.095, 05.105, 05.107 and 05.126]) and in FGE.200Rev1 ([FL-no: 05.114]) where their genotoxic potential has been assessed and ruled out (EFSA FAF Panel, 2018a,b). Therefore, the safety evaluation through the Procedure can be performed for these eight flavouring substances.

### 3.3.3. Toxicological data

Studies of oral acute toxicity with candidate substances 2-methyl-2-pentenal and 2-isopropyl-5-methyl-2-hexenal [FL-no: 05.090 and 05.107] are available in the JECFA toxicology monograph (JECFA, 2004b). An oral median lethal dose (LD<sub>50</sub>) of 4,290 mg/kg bw for [FL-no: 05.090] and > 5,000 mg/kg bw for [FL-no: 05.107] in rats has been reported by Smyth et al. (1954) and by Moreno (1973),<sup>5</sup> respectively.

No subacute, subchronic/chronic toxicity and carcinogenicity studies are available on the candidate substances.

### 3.4. Application of the Procedure

*Application of the Procedure to eight aliphatic, branched-chain  $\alpha,\beta$  unsaturated alcohols and aldehydes by JECFA (2004 and 2008)*

JECFA allocated the eight candidate flavouring substances [FL-no: 02.174, 05.033, 05.090, 05.095, 05.105, 05.107, 05.114 and 05.126], currently under evaluation in FGE.72Rev2, to structural class I according to the decision tree approach presented by Cramer et al. (1978).

JECFA considered that these flavouring substances can be anticipated to be metabolised to innocuous products (step 2). The intakes, based on MSDI approach, for all substances are below the toxicological threshold of concern (TTC) for structural class I (1,800  $\mu\text{g}/\text{person}$  per day) (step A3). Therefore, JECFA concluded that these eight substances would pose no safety concern at their estimated level of use, based on the MSDI approach.

The JECFA safety evaluations of the flavouring substances in FGE.72Rev2 are summarised in Table D.1 – Appendix D.

#### *EFSA considerations*

The FAF Panel partially agrees with JECFA with respect to the allocation of the eight candidate flavouring substances to structural class I. According to the predictions run in OECD (Q)SAR Toolbox (version 4.3.1), three out of the eight candidate substances ([FL-no: 05.033, 05.105 and 05.107]) are assigned to structural class III. For the remaining substances the Panel agrees with JECFA to assign them to structural class I.

The Panel agrees with the way of the application of the Procedure that has been performed by JECFA for all candidate flavouring substances. The MSDI exposure estimates for the all candidate flavouring substances are below the TTC for their structural classes (I and III) (see Table C.4 – Appendix C). Therefore, the FAF Panel concludes, at step A3 of the Procedure scheme, that the flavouring substances [FL-no: 02.174, 05.033, 05.090, 05.095, 05.105, 05.107, 05.114, 05.126] do not raise a safety concern when used as flavouring substances at the current levels of use, based on the MSDI approach.

For all eight flavouring substances, use levels are available and mTAMDI values have been calculated (see Table C.4 – Appendix C). For four substances, the mTAMDI intake estimates are below ([FL- no: 02.174, 05.095, 05.114 and 05.126]) the TTC for their structural class. For four substances, the mTAMDI intake estimates are equal to ([FL-no: 05.090]) or above ([FL-no: 05.107, 05.105, 05.033]) the TTC for their structural class. Therefore, for these four substances, more detailed data on uses and use levels should be provided in order to refine the exposure assessment and to finalise their safety evaluation.

## 4. Discussion

This revision 2 of FGE.72 comprises in total 31 JECFA-evaluated flavouring substances, 23 of which have already been considered in FGE.72 and FGE.72Rev1. The remaining eight substances [FL-no: 02.174, 05.033, 05.090, 05.095, 05.105, 05.107, 05.114 and 05.126] have been included in this revision, following evaluation in FGE.200Rev1 and FGE.201Rev2 of their genotoxic potential due to the presence of a structural alert for genotoxicity (i.e.  $\alpha,\beta$ -unsaturated carbonyl or precursors for that).

Based on consideration of structural class, metabolism data, the absence of genotoxic potential *in vivo* and the MSDI exposure estimates, the FAF Panel concludes that the flavouring substances considered in this revision of FGE.72 (FGE.72Rev2) do not raise a safety concern at step A3 of the Procedure.

<sup>5</sup> As cited in JECFA toxicology monograph (JECFA, 2004b).

For 10 substances, including the eight newly included flavouring substances in FGE.72Rev2 and two substances from the previous revision ([FL-no: 05.169 and 09.931]), normal and maximum use levels have been provided. For six substances [FL- no: 02.174, 05.095, 05.114, 05.126, 05.169 and 09.931], the mTAMDI intake estimates are below the TTC for their structural class. For four substances, the mTAMDI intake estimates are equal to ([FL-no: 05.090]) or above ([FL-no: 05.107, 05.105, 05.033]) the TTC for their structural class. Therefore, for these four substances, more detailed data on uses and use levels should be provided in order to refine the exposure assessment and to finalise their safety evaluation.

No normal and maximum use levels have been provided for the remaining 21 flavouring substances [FL-no: 02.011, 02.012, 02.027, 02.029, 02.058, 02.076, 02.109, 05.020, 05.021, 05.124, 05.148, 08.036, 08.044, 08.047, 08.055, 08.064, 08.070, 08.079, 09.273, 09.408 and 16.001], previously considered in FGE.72Rev1. Therefore, for these 21 substances, normal and maximum use levels are needed to calculate the mTAMDI estimates in order to identify those flavouring substances that need more refined exposure assessment and to finalise the evaluation accordingly.

To determine whether the conclusions for the 31 JECFA-evaluated substances can be applied to the materials of commerce, it is necessary to consider the available specifications. Adequate specifications, including complete purity criteria and identity, are available for all the 31 flavouring substances in FGE.72Rev2.

## 5. Conclusions

In conclusion, for all 31 flavouring substances in FGE.72Rev2, the Panel agrees with JECFA conclusions 'No safety concern at estimated levels of intake as flavouring substances' based on the MSDI approach. For 21 substances, use levels are still needed to calculate the mTAMDI estimates. For four substances, the mTAMDI intake estimates are equal to ([FL-no: 05.090]) or above ([FL-no: 05.107, 05.105, 05.033]) the TTC for their structural class. Therefore, for these 25 flavouring substances more detailed data on uses and use levels should be provided in order to finalise their safety evaluations.

## 6. Recommendation

The Panel recommends the European Commission to consider:

- to request normal and maximum use levels for [FL-no: 02.011, 02.012, 02.027, 02.029, 02.058, 02.076, 02.109, 05.020, 05.021, 05.124, 05.148, 08.036, 08.044, 08.047, 08.055, 08.064, 08.070, 08.079, 09.273, 09.408 and 16.001];
- to request more detailed data on uses and use levels for substances [FL-no: 05.033, 05.090, 05.105, and 05.107]. When these data are received, the assessment for these flavouring substances should be updated accordingly and expanded if necessary (i.e. request of additional toxicology data);
- in accordance with the latest specifications for the materials of commerce provided by industry:
  - a) to change the chemical names and/or the CAS numbers in the Union List for flavouring substance [FL-no: 02.174, 05.033, 05.090, 05.095, 05.105, 05.107 and 05.126] to reflect their stereochemical configuration (see Table B.1 of Appendix B);
  - b) to update the purity requirements in the Union List for flavouring substances [FL-no: 05.090 and 05.126] (see Table B.1 of Appendix B).
- to change the CAS number in the Union List for flavouring substance [FL-no: 09.931], previously considered in FGE.72Rev1, to 197098-61-6 as the currently reported CAS number is not existing. (see Table B.1 of Appendix B)

## 7. Documentation provided to EFSA

- 1) EFFA (European Flavour Association), 2019. Submission of additional information on isomeric composition and refined use levels of substances of FGE.201 Rev2 (FGE.19 Subgroup 1.1.2) and FGE.200 Rev1 (SG 1.1.1) for evaluation in FGE.72 Rev2.
- 2) EFFA (European Flavour Association), 2018. EFFA 2015 poundage information for 74 substances from FGE.19 subgroup 1.1.1 corresponding to FGE.200. Unpublished data submitted from EFFA to EFSA. Dated August 2018.

- 3) EFFA (European Flavour Association), 2019. Submission of additional information on EU poundage data of substances of FGE.201 Rev2 (FGE.19 Subgroup 1.1.2) for evaluation in FGE.72 Rev2.
- 4) EFFA (European Flavour and Fragrance Association), 2000. Assessment of 19 flavouring substances (candidate chemicals) of the chemical groups 1 and 2 (Annex I of 1565/2000/EC), structurally related to esters of aliphatic acyclic primary alcohols and branched-chain aliphatic acyclic carboxylic acids from TRS 884; FAO/JECFA 49/52. December 10, 2000. SCOOP/FLAV/8.1 rev.1. European inquiry on volume of use. IOFI, International Organization of the Flavor Industry, 1995. Private communication to FEMA. Unpublished report submitted by EFFA to SCF.
- 5) EFFA (European Flavour Association), 2002. Letter from EFFA to Dr. Joern Gry, Danish Veterinary and Food Administration. Dated 31 October 2002. Re.: Second group of questions. FLAVIS/8.26.

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## Abbreviations

ADME	absorption, distribution, metabolism and excretion
CAS	Chemical Abstracts Service
CEF	EFSA panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids
CoE	Council of Europe
FAF	EFSA Panel on Food Additives and Flavourings
FEMA	Flavor and Extract Manufacturers Association
FGE	Flavouring Group Evaluation
FL-no	FLAVIS number
ID	identity
IR	infrared spectrometry
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LD <sub>50</sub>	median lethal dose
mTAMDI	modified Theoretical Added Maximum Daily Intake
MSDI	Maximised Survey-derived Daily Intake
MS	mass spectrometry
NMR	nuclear magnetic resonance
OECD	Organisation for Economic Co-operation and Development
SC	secondary components
SCF	Scientific Committee on Food

TAMDI Theoretical Added Maximum Daily Intake  
TTC toxicological threshold of concern  
UL Union List

## Appendix A – Procedure of the safety evaluation

The approach for a safety evaluation of chemically defined flavouring substances as referred to in Commission Regulation (EC) No 1565/2000, named the 'Procedure', is shown in schematic form in Figure A.1. The Procedure is based on the Opinion of the Scientific Committee on Food expressed on 2 December 1999 (SCF, 1999), which is derived from the evaluation Procedure developed by the Joint FAO/WHO Expert Committee on Food Additives at its 44th, 46th and 49th meetings (JECFA, 1995, 1996, 1997, 1999), hereafter named the 'JECFA Procedure'.<sup>6</sup>

The Procedure is a stepwise approach that integrates information on intake from current uses, structure–activity relationships, metabolism and, when needed, toxicity. One of the key elements in the Procedure is the subdivision of flavourings into three structural classes (I, II and III) for which toxicological thresholds of concern (TTCs) (human exposure thresholds) have been specified. Exposures below these TTCs are not considered to present a safety concern.

Class I contains flavourings that have simple chemical structures and efficient modes of metabolism, which would suggest a low order of oral toxicity. Class II contains flavourings that have structural features that are less innocuous but are not suggestive of toxicity. Class III comprises flavourings that have structural features that permit no strong initial presumption of safety, or may even suggest significant toxicity (Cramer et al., 1978). The TTCs for these structural classes of 1,800, 540 or 90 µg/person per day, respectively, are derived from a large database containing data on subchronic and chronic animal studies (JECFA, 1996).

In step 1 of the Procedure, the flavourings are assigned to one of the structural classes. The further steps address the following questions:

- Can the flavourings be predicted to be metabolised to innocuous products<sup>7</sup> (step 2)?
- Do their exposures exceed the TTC for the structural class (steps A3 and B3)?
- Are the flavourings or their metabolites endogenous<sup>8</sup> (step A4)?
- Does a NOAEL exist on the flavourings or on structurally related substances (steps A5 and B4)?

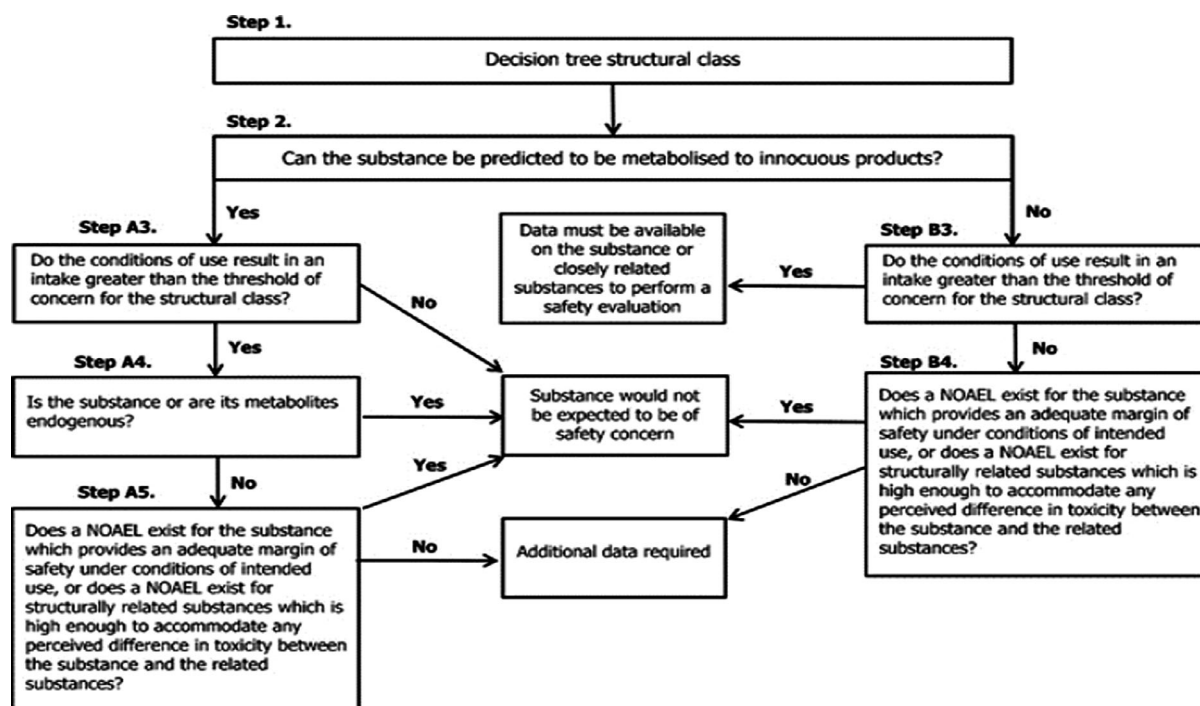
In addition to the data provided for the flavouring substances to be evaluated (candidate substances), toxicological background information available for compounds structurally related to the candidate substances is considered (supporting substances), in order to assure that these data are consistent with the results obtained after application of the Procedure. The Procedure is not to be applied to flavourings with existing unresolved problems of toxicity. Therefore, the right is reserved to use alternative approaches if data on specific flavourings warranted such actions.

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<sup>6</sup> The FAF Panel is aware that a revised Procedure for the Safety Evaluation of Flavouring agents has been agreed by JECFA (JECFA, 2016). The EFSA Scientific Committee has developed a modified procedure for evaluation of substances based on the TTC approach (EFSA Scientific Committee, 2019). However, these developments have no impact on the present evaluation, which should follow the requirements as set out in Commission Regulation (EC) No 1565/2000.

<sup>7</sup> Innocuous products: products that are known or readily predicted to be harmless to humans at the estimated intake of the flavouring agent (JECFA, 1997).

<sup>8</sup> Endogenous substances: intermediary metabolites normally present in human tissues and fluids, whether free or conjugated; hormones and other substances with biochemical or physiological regulatory functions are not included (JECFA, 1997).



**Figure A.1:** Procedure for the safety evaluation of chemically defined flavouring substances

For the flavouring substances considered in this Flavouring Group Evaluation (FGE), the EFSA Panel on Food Additives and Flavourings (FAF) compares the JECFA evaluation of structurally related substances with the result of a corresponding EFSA evaluation, focussing on specifications, intake estimations and toxicity data, especially genotoxicity data. The considerations by EFSA will conclude whether the flavouring substances are of no safety concern at their estimated levels of intake, whether additional data are required or whether certain substances should not be evaluated through the EFSA Procedure.

The following issues are of special importance:

a) *Intake*

In its evaluation, the Panel as a default uses the 'maximised survey-derived daily intake' (MSDI)<sup>9</sup> approach to estimate the per capita intakes of the flavouring substances in Europe.

In its evaluation, JECFA includes intake estimates based on the MSDI approach derived from both European and USA production figures. The highest of the two MSDI figures is used in the evaluation by JECFA. It is noted that in several cases, only the MSDI figures from the USA were available, meaning that certain flavouring substances have been evaluated by JECFA only on the basis of these figures. For substances in the Union List<sup>3</sup> of flavouring substances for which this is the case, the Panel will need European Union (EU) production figures in order to finalise the evaluation.

When the Panel examined the information provided by the European Flavour Industry on the use levels in various foods, it appeared obvious that the MSDI approach in a number of cases would grossly underestimate the intake by regular consumers of products flavoured at the use levels reported by the Industry, especially in those cases where the annual production values were reported to be small. In consequence, the Panel had reservations about the data on use and use levels provided and the intake estimates obtained by the MSDI approach. It is noted that JECFA, at its 65th meeting, considered 'how to improve the identification and assessment of flavouring agents, for which the MSDI estimates may be substantially lower than the dietary exposures that would be estimated from the anticipated average use levels in foods' (JECFA, 2006).

In the absence of more accurate information that would enable the Panel to make a more realistic estimate of the intakes of the flavouring substances, the Panel has decided also to perform an

<sup>9</sup> EU MSDI: Amount added to food as flavour in (kg/year) × 10<sup>9</sup> / (0.1 × population in Europe (= 375 × 10<sup>6</sup>) × 0.6 × 365) = µg/capita per day.



estimate of the daily intakes per person using a modified Theoretical Added Maximum Daily Intake (mTAMDI) approach based on the normal use levels reported by Industry (see Appendix C.2).

As information on use levels for the flavouring substances has not been requested by JECFA or has not otherwise been provided to the Panel, it is not possible to estimate the daily intakes using the mTAMDI approach for many of the substances evaluated by JECFA. The Panel will need information on use levels in order to finalise the evaluation.

*b) Threshold of 1.5 µg/person per day (step B5) used by JECFA*

JECFA uses the threshold of concern of 1.5 µg/person per day as part of the evaluation procedure:

'The Committee noted that this value was based on a risk analysis of known carcinogens which involved several conservative assumptions. The use of this value was supported by additional information on developmental toxicity, neurotoxicity and immunotoxicity. In the judgement of the Committee, flavouring substances for which insufficient data are available for them to be evaluated using earlier steps in the Procedure, but for which the intake would not exceed 1.5 µg/person per day would not be expected to present a safety concern. The Committee recommended that the Procedure for the Safety Evaluation of Flavouring Agents, used at the forty-sixth meeting, should be amended to include the last step on the right-hand side of the original procedure ('Do the conditions of use result in an intake greater than 1.5 µg per day?')' (JECFA, 1999).

In line with the opinion expressed by the Scientific Committee on Food (SCF, 1999), the Panel does not make use of this threshold of 1.5 µg per person per day.

*c) Genotoxicity*

As reflected in the opinion of SCF (1999), the Panel has in its evaluation focussed on a possible genotoxic potential of the flavouring substances or of structurally related substances. Generally, substances for which the Panel has concluded that there is an indication of genotoxic potential *in vitro*, will not be evaluated using the EFSA Procedure until further genotoxicity data are provided. Substances for which a genotoxic potential *in vivo* has been concluded, will not be evaluated through the Procedure.

*d) Specifications*

Regarding specifications, the evaluation by the Panel could lead to a different opinion than that of JECFA, since the Panel requests information on e.g. isomerism.

*e) Structural Relationship*

In the consideration of the JECFA evaluated substances, the Panel will examine the structural relationship and metabolism features of the substances within the flavouring group and compare this with the corresponding FGE.

## Appendix B – Specifications

**Table B.1:** Summary table on specifications data for flavouring substances in FGE.72Rev2, for chemical structures see Appendix D

Information included in the EU Union list Regulation No (EU) 1334/2008 as amended			Most recent available specifications data <sup>(a)</sup>				EFSA comments
FL-no JECFA-no FEMA no CoE no CAS no	Chemical name	Purity of the named compound	Phys. form Mol. formula Mol. weight	Solubility <sup>(c)</sup> Solubility in ethanol <sup>(d)</sup>	Boiling point, °C <sup>(e)</sup> Melting point, °C ID test Assay minimum (isomers distribution/SC <sup>(h)</sup> )	Refrac. Index <sup>(f)</sup> Spec. gravity <sup>(g)</sup>	
02.011 1219 2309 59 106-22-9	Citronellol	90%	Liquid C <sub>10</sub> H <sub>20</sub> O 156.27	Slightly soluble Soluble	225  IR 90% (racemate) Other constituents: di-unsaturated and saturated C <sub>10</sub> alcohols, citronellyl acetate, citronellal	1.454–1.462 0.850–0.860	
02.012 1223 2507 60 106-24-1	Geraniol	88%	Liquid C <sub>10</sub> H <sub>18</sub> O 154.25	Slightly soluble Soluble	230  IR 88% ((total alcohols as C <sub>10</sub> H <sub>18</sub> O) SC: citronellyl, neryl, and geranyl acetate esters	1.469–1.478 0.870–0.885	
02.027 1222 2980 76 6812-78-8	(-)-Rhodinol	82%	Liquid C <sub>10</sub> H <sub>20</sub> O 156.27	Insoluble Soluble	132–135 (5 hPa)  IR 82% (total alcohols as C <sub>10</sub> H <sub>20</sub> O) SC: naturally occurring terpenoid esters – citronellyl, neryl and geranyl acetate esters	1.463–1.473 0.860–0.880	
02.029 1230 2478 78 4602-84-0	3,7,11-Trimethyldodeca-2,6,10-trien-1-ol	(b)	Liquid C <sub>15</sub> H <sub>26</sub> O 222.37	Insoluble Soluble	263  IR 96% (mixture of <i>Z</i> - and <i>E</i> -isomers: 10–15% <i>2Z,6Z</i> ; 20–25% <i>2E,6Z</i> ; 20–25% <i>2Z,6E</i> ; 40–50% <i>2E,6E</i> )	1.487–1.492 0.884–0.889	

Information included in the EU Union list Regulation No (EU) 1334/2008 as amended			Most recent available specifications data <sup>(a)</sup>				EFSA comments
FL-no JECFA-no FEMA no CoE no CAS no	Chemical name	Purity of the named compound	Phys. form Mol. formula Mol. weight	Solubility <sup>(c)</sup> Solubility in ethanol <sup>(d)</sup>	Boiling point, °C <sup>(e)</sup> Melting point, °C ID test Assay minimum (isomers distribution/SC <sup>(h)</sup> )	Refrac. Index <sup>(f)</sup> Spec. gravity <sup>(g)</sup>	
02.058 1224 2770 2018 106-25-2	(Z)-Nerol	(b)	Liquid C <sub>10</sub> H <sub>18</sub> O 154.25	Insoluble Soluble	227  IR 95% (total alcohols as C <sub>10</sub> H <sub>18</sub> O)	1.467–1.478 0.875–0.880	
02.076 1199 3998 2346 137-32-6	2-Methylbutan-1-ol	(b)	Liquid C <sub>5</sub> H <sub>12</sub> O 88.15	Very slightly soluble Soluble	130  IR NMR MS 99% (racemate)	1.409–1.412 0.815–0.820	
02.109 1200 3647 11795 556-82-1	3-Methylbut-2-en-1-ol	(b)	Liquid C <sub>5</sub> H <sub>10</sub> O 86.10	Insoluble Soluble	140  IR NMR MS 99%	1.438–1.448 0.844–0.852	
02.174 1617 – 10258 4675-87-0	2-Methylbut-2-en-1-ol	(b)	Liquid C <sub>5</sub> H <sub>10</sub> O 86.13	Freely soluble	137  MS 90% ( <i>E</i> )-isomer 5% ( <i>Z</i> )-isomer	1.439–1.445 0.863–0.869	The chemical name should be changed to 2-methylbut-(2 <i>E</i> )-en-1-ol and the CAS number to 497-02-9, according to the specifications provided (Documentation provided to EFSA nr: 1)
05.020 1225 2303 109 5392-40-5	Citral	(b)	Liquid C <sub>10</sub> H <sub>16</sub> O 152.24	Very slightly soluble Soluble	228  IR 96% (mixture of ( <i>Z</i> )- and ( <i>E</i> )-isomer)	1.486–1.490 0.885–0.891	Citral is a nearly equimolar mixture of ( <i>E</i> ) and ( <i>Z</i> ) stereoisomers

Information included in the EU Union list Regulation No (EU) 1334/2008 as amended			Most recent available specifications data <sup>(a)</sup>				EFSA comments
FL-no JECFA-no FEMA no CoE no CAS no	Chemical name	Purity of the named compound	Phys. form Mol. formula Mol. weight	Solubility <sup>(c)</sup> Solubility in ethanol <sup>(d)</sup>	Boiling point, °C <sup>(e)</sup> Melting point, °C ID test Assay minimum (isomers distribution/SC <sup>(h)</sup> )	Refrac. Index <sup>(f)</sup> Spec. gravity <sup>(g)</sup>	
05.021 1220 2307 110 106-23-0	Citronellal	85%	Liquid C <sub>10</sub> H <sub>18</sub> O 154.25	Insoluble Soluble	206  IR 85% (racemate) SC: 1,8-cineole, 2-isopropylidene-5-methylcyclohexanol, linalool and citronellyl acetate	1.446–1.456 0.850–0.860	
05.033 1216 2438 120 10031-88-6	2-Ethylhept-2-enal	(b)	Liquid C <sub>9</sub> H <sub>16</sub> O 140.23	Insoluble Soluble	55–60 (5 hPa)  NMR 90% ( <i>E</i> )-isomer 5% ( <i>Z</i> )-isomer	1.460–1.466 0.891–0.898	The chemical name should be changed to 2-ethylhept-(2 <i>E</i> )-enal and the CAS number to 34210-19-0, according to the specifications provided (Documentation provided to EFSA nr: 1)
05.090 1209 3194 2129 23-36-9	2-Methylpent-2-enal	At least 92%; secondary components 1.5–2.5% propionaldehyde and 3.5–4.5% propionic acid	Liquid C <sub>6</sub> H <sub>10</sub> O 98.15	Insoluble Soluble	137  IR MS 90% ( <i>E</i> ) isomer 5% ( <i>Z</i> )- isomer SC: 2-methyl-2-pentenoic acid up to 1%	1.445–1.453 0.855–0.865	The chemical name should be changed to 2-methylpent-(2 <i>E</i> )-enal and the CAS number to 14250-96-5; the purity requirement for the named compound [FL-no: 05.090] should be updated to 'at least 95%', according to the specifications provided (Documentation provided to EFSA nr: 1)

Information included in the EU Union list Regulation No (EU) 1334/2008 as amended			Most recent available specifications data <sup>(a)</sup>				EFSA comments
FL-no JECFA-no FEMA no CoE no CAS no	Chemical name	Purity of the named compound	Phys. form Mol. formula Mol. weight	Solubility <sup>(c)</sup> Solubility in ethanol <sup>(d)</sup>	Boiling point, °C <sup>(e)</sup> Melting point, °C ID test Assay minimum (isomers distribution/SC <sup>(h)</sup> )	Refrac. Index <sup>(f)</sup> Spec. gravity <sup>(g)</sup>	
05.095 1201 3407 2281 497-03-0	2-Methylcrotonaldehyde	(b)	Liquid C <sub>5</sub> H <sub>8</sub> O 84.12	Slightly soluble Soluble	117–118  IR NMR 96% ( <i>E</i> )-isomer 2–3% ( <i>Z</i> )-isomer SC: acetic acid (up to 0.1%), tiglic acid (up to 0.5%) and paraldehyde (up to 1%)	1.445–1.450 0.868–0.873 (20°)	The chemical name should be changed to 2-methylbut-(2 <i>E</i> )-enal in accordance with the CAS number and the specifications provided (Documentation provided to EFSA nr: 1)
05.105 1214 3392 10324 25409-08-9	2-Butylbut-2-enal	(b)	Liquid C <sub>8</sub> H <sub>14</sub> O 126.20	Insoluble Soluble	50 (18 hPa)  NMR 90% ( <i>E</i> )-isomer 5% ( <i>Z</i> )-isomer	1.447–1.453 1.449–1.459 (20°)	The chemical name should be changed to 2-butylbut-(2 <i>E</i> )-enal and the CAS number to 87745-65-1, according to the specifications provided (Documentation provided to EFSA nr: 1)
05.107 1215 3406 10361 35158-25-9	2-Isopropyl-5-methylhex-2-enal	(b)	Liquid C <sub>10</sub> H <sub>18</sub> O 154.25	Insoluble Soluble	189  NMR Mixture of 60% ( <i>E</i> )-isomer and 40% ( <i>Z</i> )-isomer	1.448–1.454 0.840–0.846	(Documentation provided to EFSA nr: 1)
05.114 1208 3510 10364 5362-56-1	4-Methylpent-2-enal	(b)	Liquid C <sub>6</sub> H <sub>10</sub> O 98.14	Slightly soluble Soluble	126–130  IR NMR 94% ( <i>E</i> ) isomer 1% ( <i>Z</i> ) isomer	1.435–1.445 0.858–0.866	The chemical name should be changed to 4-methylpent-(2 <i>E</i> )-enal and the CAS number to 24502-08-7, according to the specifications provided (Documentation provided to EFSA nr: 1)

Information included in the EU Union list Regulation No (EU) 1334/2008 as amended			Most recent available specifications data <sup>(a)</sup>				EFSA comments
FL-no JECFA-no FEMA no CoE no CAS no	Chemical name	Purity of the named compound	Phys. form Mol. formula Mol. weight	Solubility <sup>(c)</sup> Solubility in ethanol <sup>(d)</sup>	Boiling point, °C <sup>(e)</sup> Melting point, °C ID test Assay minimum (isomers distribution/SC <sup>(h)</sup> )	Refrac. Index <sup>(f)</sup> Spec. gravity <sup>(g)</sup>	
05.124 1202 3646 10354 107-86-8	3-Methylcrotonaldehyde	(b)	Liquid C <sub>5</sub> H <sub>8</sub> O 84.11	Slightly soluble Soluble	133–135  IR NMR 99%	1.458–1.464 0.870–0.875	
05.126 1217 3711 10363 49576-57-0	2-Methyloct-2-enal	(b)	Liquid C <sub>9</sub> H <sub>16</sub> O 140.23	Insoluble Soluble	7–75 (10 hPa) IR 90% ( <i>E</i> )-isomer SC: 10% ( <i>E</i> )-2-methyloct-2-enoic acid methyl ester	1.449-1.459 0.872-0.882	The chemical name should be changed to 2-methyloct-(2 <i>E</i> )-enal in accordance with the CAS number; the purity requirement for the named compound [FL-no: 05.126] should be updated to '90% ( <i>E</i> -isomer) SC: 10% ( <i>E</i> )-2-methyloct-2-enoic acid methyl ester', according to the specifications provided. (Documentation provided to EFSA nr: 1)
05.148 1228 4019 – 19317-11-4	Farnesal	(b)	Liquid C <sub>15</sub> H <sub>24</sub> O 220.36	Insoluble Soluble	198–201 (10 hPa) IR NMR MS 99% (mixture of <i>Z</i> - and <i>E</i> -isomer: 10–15% 2 <i>Z</i> ,6 <i>Z</i> ; 20–25% 2 <i>E</i> ,6 <i>Z</i> ; 20–25% 2 <i>Z</i> ,6 <i>E</i> ; 40–50% 2 <i>E</i> ,2 <i>E</i> )	1.494–1.504 0.890–0.900	

Information included in the EU Union list Regulation No (EU) 1334/2008 as amended			Most recent available specifications data <sup>(a)</sup>				EFSA comments
FL-no JECFA-no FEMA no CoE no CAS no	Chemical name	Purity of the named compound	Phys. form Mol. formula Mol. weight	Solubility <sup>(c)</sup> Solubility in ethanol <sup>(d)</sup>	Boiling point, °C <sup>(e)</sup> Melting point, °C ID test Assay minimum (isomers distribution/SC <sup>(h)</sup> )	Refrac. Index <sup>(f)</sup> Spec. gravity <sup>(g)</sup>	
05.169 1229 4005 – 75853-49-5	12-Methyltridecanal	(b)	Liquid C <sub>14</sub> H <sub>28</sub> O 212.38	Insoluble Soluble	141–143 (5 hPa) IR NMR MS 97%	1.445–1.455 0.930–0.941	
08.036 1221 3142 616 502-47-6	Citronellic acid	90%	Liquid C <sub>10</sub> H <sub>18</sub> O <sub>2</sub> 170.25	Insoluble Soluble	121–122 (1 hPa)  NMR 90% (racemate) Other main constituents: citronellal; citronellyl acetate, nerol and geraniol	1.455–1.462 0.920–0.926 (20°)	
08.044 1211 3143 744 21016-46-6	(2E),4-Dimethylpent-2-enoic acid	92%	Liquid C <sub>7</sub> H <sub>12</sub> O <sub>2</sub> 128.17	Very slightly soluble Soluble	133–134 (20 hPa)  NMR 92% (E)-isomer SC: 4-methyl-2-methylenevaleric acid	1.459–1.467 0.991–0.999	
08.047 1212 2706 2003 1188-02-9	2-Methylheptanoic acid	(b)	Liquid C <sub>8</sub> H <sub>16</sub> O <sub>2</sub> 144.21	Very slightly soluble Soluble	121–122 (17 hPa)  NMR 97% (racemate)	1.420–1.427 0.899–0.905	
08.055 1210 3195 11680 3142-72-1	2-Methyl-2-pentenoic acid	(b)	Liquid C <sub>6</sub> H <sub>10</sub> O <sub>2</sub> 114.14	Slightly soluble Soluble	123–125 (39 hPa)  IR 98% (mixture of Z- and (E)-isomer: 60–75% (E) and 20–30% (Z))	1.450–1.460 0.976–0.982	CAS number in UL does not specify stereoisomeric composition
08.064 1205 3599 10168 80-59-1	(2E)-Methylcrotonic acid	(b)	Solid C <sub>5</sub> H <sub>8</sub> O <sub>2</sub> 100.10	Slightly soluble Soluble	n.a. 61–67 MS 99%	n.a. n.a.	

Information included in the EU Union list Regulation No (EU) 1334/2008 as amended			Most recent available specifications data <sup>(a)</sup>				EFSA comments
FL-no JECFA-no FEMA no CoE no CAS no	Chemical name	Purity of the named compound	Phys. form Mol. formula Mol. weight	Solubility <sup>(c)</sup> Solubility in ethanol <sup>(d)</sup>	Boiling point, °C <sup>(e)</sup> Melting point, °C ID test Assay minimum (isomers distribution/SC <sup>(h)</sup> )	Refrac. Index <sup>(f)</sup> Spec. gravity <sup>(g)</sup>	
08.070 1204 3187 10138 541-47-9	3-Methylcrotonic acid	(b)	Solid C <sub>5</sub> H <sub>8</sub> O <sub>2</sub> 100.12	– Soluble	70 MS 98%	n.a. n.a.	
08.079 1218 3800 – 16493-80-4	4-Ethyl octanoic acid	(b)	Liquid C <sub>10</sub> H <sub>20</sub> O <sub>2</sub> 172.27	Slightly soluble Soluble	110 (1 hPa)  IR NMR 99% (racemate)	1.430–1.439 0.898–0.908	
09.273 1206 3432 10706 589-66-2	Isobutyl crotonate	(b)	Liquid C <sub>8</sub> H <sub>14</sub> O <sub>2</sub> 142.20	Slightly soluble Soluble	171  IR 95% (mixture of <i>Z</i> - and <i>E</i> -isomer: 70– 85% ( <i>E</i> ) and 10–35% ( <i>Z</i> ))	1.426–1.430 0.880–0.900	CAS number in UL does not specify stereoisomeric composition
09.408 1213 2180 247 7779-81-9	Isobutyl 2-methylbut-2 ( <i>cis</i> )-enoate	(b)	Liquid C <sub>9</sub> H <sub>16</sub> O <sub>2</sub> 156.23	Insoluble Soluble	176–177  IR NMR 98%	1.438–1.446 0.874–0.880	



Information included in the EU Union list Regulation No (EU) 1334/2008 as amended			Most recent available specifications data <sup>(a)</sup>				EFSA comments
FL-no JECFA-no FEMA no CoE no CAS no	Chemical name	Purity of the named compound	Phys. form Mol. formula Mol. weight	Solubility <sup>(c)</sup> Solubility in ethanol <sup>(d)</sup>	Boiling point, °C <sup>(e)</sup> Melting point, °C ID test Assay minimum (isomers distribution/SC <sup>(h)</sup> )	Refrac. Index <sup>(f)</sup> Spec. gravity <sup>(g)</sup>	
09.931 1226 3886 – 999999-91-4	2,6-Dimethyl-2,5,7-octatriene-1-ol acetate	(b)	Liquid C <sub>12</sub> H <sub>18</sub> O <sub>2</sub> 194.28	Insoluble Soluble	70 (3 hPa)  MS 95% (mixture of <i>Z</i> - and <i>E</i> -isomers: 14–20% <i>2Z,5Z</i> ; 33–40% <i>2Z,5E</i> ; 14–19% <i>2E,5Z</i> ; 26–33% <i>2E,5E</i> )	1.490–1.500 0.937–0.947	CAS number to be changed to 197098-61-6
16.001 1203 2054 464 7563-33-9	Ammonium isovalerate	(b)	Solid C <sub>5</sub> H <sub>13</sub> O <sub>2</sub> N 119.16	Soluble Soluble	n.a. 72 NMR 98%	n.a. n.a.	

FL-no: FLAVIS number; JECFA: Joint FAO/WHO Expert Committee on Food Additives; FEMA: Flavor and Extract Manufacturers Association; CoE: Council of Europe; CAS: Chemical Abstracts Service; ID: identity; IR: infrared spectrometry; NMR: nuclear magnetic resonance; MS: mass spectrometry; UL: Union List.

(a): JECFA 2003; EFSA CEF Opinion, 2013; Documentation provided to EFSA nr: 1.

(b): At least 95% unless otherwise specified.

(c): Solubility in water, if not otherwise stated.

(d): Solubility in 95% ethanol, if not otherwise stated.

(e): At 1,013.25 hPa, if not otherwise stated.

(f): At 20°C, if not otherwise stated.

(g): At 25°C, if not otherwise stated.

(h): Secondary components.

## Appendix C – Exposure estimates

### C.1. Normal and Maximum Use Levels

**Table C.1:** Normal and maximum use levels (mg/kg) of JECFA evaluated flavouring substances in FGE.72Rev2 in food categories listed in Annex III of Reg. (EC) 1565/2000 (Documentation provided to EFSA n. 1 and 4)

FL-no	Food Categories																		
	Normal use levels <sup>(a)</sup> (mg/kg)																		
	Maximum use levels (mg/kg)																		
	01.0	02.0	03.0	04.1	04.2	05.0	05.3 <sup>(b)</sup>	06.0	07.0	08.0	09.0	10.0	11.0	12.0	13.0	14.1	14.2	15.0	16.0
02.174	5.03 11.86	0.5 4	0.5 2.75	– –	4.78 5	5 14.22	2.2 9.56	3.79 11.4	6.2 17.17	0.79 3.5	0.5 1.75	0.01 3	0.51 4.38	1.75 5	0.01 5.01	2 4.43	1 2	2 3	0.5 0.5
05.033	7 8	7 8	7 8	– –	7 8	33 37	– –	7 8	21 29	7 8	7 8	7 8	7 8	1 2	– –	5 6	1 2	1 2	7 8
05.090	3.33 6	3 5	– –	3 5	3 5	5 9	– –	3 5	6.5 15.33	7 10	3 5	3 5	3 5	1 2	– –	2 4	1 2	1 2	3 5
05.095	5.03 11.86	0.5 4	0.5 2.75	– –	4.78 5	5 14.22	2.2 9.56	3.79 11.4	6.2 17.17	0.79 3.5	0.5 1.75	0.01 3	0.51 4.38	1.75 5	0.01 5.01	2 4.43	1 2	2 3	0.5 0.5
05.105	5.03 11.86	0.5 4	0.5 2.75	– –	4.78 5	5 14.22	2.2 9.56	3.79 11.4	6.2 17.17	0.79 3.5	0.5 1.75	0.01 3	0.51 4.38	1.75 5	0.01 5.01	2 4.43	1 2	2 3	0.5 0.5
05.107	5.03 11.86	0.5 4	0.5 2.75	– –	4.78 5	5 14.22	2.2 9.56	3.79 11.4	6.2 17.17	0.79 3.5	0.5 1.75	0.01 3	0.51 4.38	1.75 5	0.01 5.01	2 4.43	1 2	2 3	0.5 0.5
05.114	5.7 12	1.5 14.25	0 0	– –	5 5.03	5.5 14.46	5.3 20.87	4.8 11.5	6.3 19.07	0.9 2.98	– –	– –	– –	2 5	– –	2 4.43	1 2	2.5 4.5	– –
05.126	5.03 11.86	0.5 4	0.5 2.75	– –	4.78 5	5 14.22	2.2 9.56	3.79 11.4	6.2 17.17	0.79 3.5	0.5 1.75	0.01 3	0.51 4.38	1.75 5	0.01 5.01	2 4.43	1 2	2 3	0.5 0.5
05.169	3 15	2 10	3 15	2 10	– –	4 20	– –	2 10	5 25	1 5	1 5	– –	– –	2 10	3 15	– –	4 20	5 25	2 10
09.931	5.03 11.86	0.5 4	0.5 2.75	– –	4.78 5	5 14.22	2.2 9.56	3.79 11.4	6.2 17.17	0.79 3.5	0.5 1.75	0.01 3	0.51 4.38	1.75 5	0.01 5.01	2 4.43	1 2	2 3	0.5 0.5

(a): 'Normal use' is defined as the average of reported usages and 'maximum use' is defined as the 95th percentile of reported usages (Documentation provided to EFSA n.5).

(b): Additional food category 05.3 (chewing-gum as per Annex II part D of Reg. (EC) 1333/2008) for which EFTA submitted use levels (Documentation provided to EFSA n. 1). These data have been considered in the calculation of mTAMDI.

## C.2. mTAMDI calculations

The method for calculation of modified Theoretical Added Maximum Daily Intake (mTAMDI) values is based on the approach used by the SCF up to 1995 (SCF, 1995). The assumption is that a person may consume the amount of flavourable foods and beverages listed in Table C.2. These consumption estimates are then multiplied by the reported use levels in the different food categories and summed up.

**Table C.2:** Estimated amount of flavourable foods, beverages, and exceptions assumed to be consumed per person per day (SCF, 1995)

Class of product category	Intake estimate (g/day)
Beverages (non-alcoholic)	324.0
Foods	133.4
Exception a: Candy, confectionery	27.0
Exception b: Condiments, seasonings	20.0
Exception c: Alcoholic beverages	20.0
Exception d: Soups, savouries	20.0
Exception e: Others, e.g. chewing gum	E.g. 2.0 (chewing gum)

The mTAMDI calculations are based on the normal use levels reported by Industry. The seven food categories used in the SCF TAMDI approach (SCF, 1995) correspond to the 18 food categories as outlined in Commission Regulation (EC) No 1565/2000 and reported by the Flavour Industry in the following way (see

- Beverages (SCF, 1995) correspond to food Table C.3): category 14.1
- Foods (SCF, 1995) correspond to the food categories 1, 2, 3, 4.1, 4.2, 6, 7, 8, 9, 10, 13, and/or 16
- Exception a (SCF, 1995) corresponds to food category 5 and 11
- Exception b (SCF, 1995) corresponds to food category 15
- Exception c (SCF, 1995) corresponds to food category 14.2
- Exception d (SCF, 1995) corresponds to food category 12
- Exception e (SCF, 1995) corresponds to others, e.g. chewing gum.

**Table C.3:** Distribution of the 18 food categories listed in Commission Regulation (EC) No 1565/2000 into the seven SCF food categories used for mTAMDI calculations (SCF, 1995)

Key	Food categories according to Commission Regulation 1565/2000 Food category	Distribution of the seven SCF food categories		
		Foods	Beverages	Exceptions
01.0	Dairy products, excluding products of category 02.0	Foods		
02.0	Fats and oils, and fat emulsions (type water-in-oil)	Foods		
03.0	Edible ices, including sherbet and sorbet	Foods		
04.1	Processed fruit	Foods		
04.2	Processed vegetables (incl. mushrooms & fungi, roots & tubers, pulses and legumes), and nuts & seeds	Foods		
05.0	Confectionery			Exception a
06.0	Cereals and cereal products, incl. flours & starches from roots & tubers, pulses & legumes, excluding bakery	Foods		
07.0	Bakery wares	Foods		
08.0	Meat and meat products, including poultry and game	Foods		
09.0	Fish and fish products, including molluscs, crustaceans and echinoderms	Foods		
10.0	Eggs and egg products	Foods		
11.0	Sweeteners, including honey			Exception a
12.0	Salts, spices, soups, sauces, salads, protein products, etc.			Exception d
13.0	Foodstuffs intended for particular nutritional uses	Foods		
14.1	Non-alcoholic ('soft') beverages, excl. dairy products		Beverages	
14.2	Alcoholic beverages, incl. alcohol-free and low-alcoholic counterparts			Exception c
15.0	Ready-to-eat savouries			Exception b
16.0	Composite foods (e.g. casseroles, meat pies, mincemeat) – foods that could not be placed in categories 01.0–15.0	Foods		

mTAMDI: modified Theoretical Added Maximum Daily Intake.

**Table C.4:** Estimated intakes based on the MSDI approach and the mTAMDI approach for substances in FGE.72Rev2

Estimated intakes based on the MSDI approach and the mTAMDI approach						
FL-no	EU Union List name	MSDI – EU <sup>(a)</sup> (µg/capita per day)	MSDI – USA <sup>(b)</sup> (µg/capita per day)	mTAMDI <sup>(c)</sup> (µg/person per day)	Structural class	TTC (µg/person per day)
02.011	Citronellol	320	0.5	NA	Class I	1,800
02.012	Geraniol	550	315	NA	Class I	1,800
02.027	(-)-Rhodinol	13	8.4	NA	Class I	1,800
02.029	3,7,11-Trimethyldodeca-2,6,10-trien-1-ol	7.7	2.6	NA	Class I	1,800
02.058	(Z)-Nerol	250	171	NA	Class I	1,800
02.076	2-Methylbutan-1-ol	0.73	35	NA	Class I	1,800
02.109	3-Methylbut-2-en-1-ol	4.6	3.8	NA	Class I	1,800
02.174	2-Methylbut-2-en-1-ol	0.12	NA	1700	Class I	1,800
05.020	Citral	5844	6990	NA	Class I	1,800
05.021	Citronellal	810	324	NA	Class I	1,800
05.033	2-Ethylhept-2-enal	0.12	0.1	5400	Class III	90
05.090	2-Methylpent-2-enal	11.93	0.2	1800	Class I	1,800
05.095	2-Methylcrotonaldehyde	0.24	0.2	1700	Class I	1,800
05.105	2-Butylbut-2-enal	0.02	0.01	1700	Class III	90
05.107	2-Isopropyl-5-methylhex-2-enal	3.90	0.01	1700	Class III	90
05.114	4-Methylpent-2-enal	0.012	0.2	1700	Class I	1,800
05.124	3-Methylcrotonaldehyde	3.3	0.5	NA	Class I	1,800
05.126	2-Methyloct-2-enal	0.06	7.9	1700	Class I	1,800
05.148	Farnesal	0.49	0.2	NA	Class I	1,800
05.169	12-Methyltridecanal	0.24	0.5	1000	Class I	1,800
08.036	Citronellic acid	2.7	0.2	NA	Class I	1,800
08.044	(2E),4-Dimethylpent-2-enoic acid	0.12	0.1	NA	Class I	1,800
08.047	2-Methylheptanoic acid	14	6	NA	Class I	1,800
08.055	2-Methyl-2-pentenoic acid	36	20	NA	Class I	1,800
08.064	(2E)-Methylcrotonic acid	4.1	1.6	NA	Class I	1,800
08.070	3-Methylcrotonic acid	0.012	0.01	NA	Class I	1,800
08.079	4-Ethyl-octanoic acid	0.73	4	NA	Class I	1,800
09.273	Isobutyl crotonate	0.46	45	NA	Class I	1,800
09.408	Isobutyl 2-methylbut-2(cis)-enoate	0.12	0.1	NA	Class I	1,800

**Estimated intakes based on the MSDI approach and the mTAMDI approach**

FL-no	EU Union List name	MSDI – EU <sup>(a)</sup> (µg/capita per day)	MSDI – USA <sup>(b)</sup> (µg/capita per day)	mTAMDI <sup>(c)</sup> (µg/person per day)	Structural class	TTC (µg/person per day)
09.931	2,6-Dimethyl-2,5,7-octatriene-1-ol acetate	1.2	7.7	1700	Class I	1,800
16.001	Ammonium isovalerate	15	16	NA	Class I	1,800

mTAMDI: modified Theoretical Added Maximum Daily Intake; MSDI: Maximised Survey-derived Daily Intake; TTC: toxicological threshold of concern.

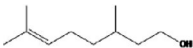
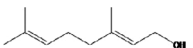
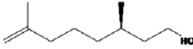
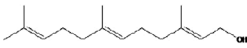
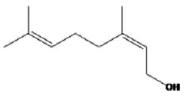
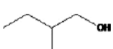
(a): Based on EU production figures from JECFA (JECFA 2004a, 2007, 2008) and submitted by industry (Documentation provided to EFSA nr. 2 and 3).



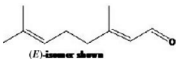
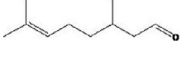
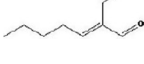
(b): Based on US production figures from JECFA (JECFA 2004a, 2007, 2008).

(c): Based on use levels submitted by industry (Documentation provided to EFSA nr. 1 and 4).

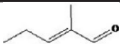

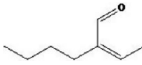
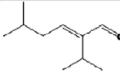
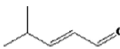

## Appendix D – Summary of safety evaluations

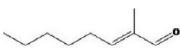
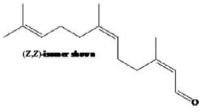
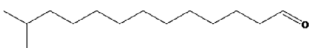
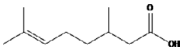
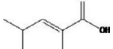
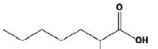
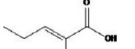
**Table D.1:** Summary of safety evaluations performed by JECFA (2004a, 2007, 2008) and EFSA conclusions on flavouring substances in FGE.72 and its revisions

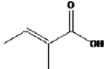
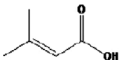
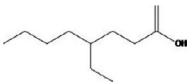
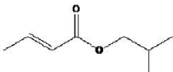
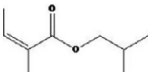
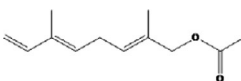
FL-no JECFA-no	EU Union List chemical name	Structural formula	JECFA conclusions	EFSA conclusions
			<b>Class<sup>(a)</sup></b> <b>Evaluation procedure path<sup>(b)</sup></b> <b>Outcome on the named compound based on the MSDI<sup>(c)</sup> approach</b>	<b>Procedural path if different from JECFA, Conclusion based on the MSDI<sup>(d)</sup> approach on the named compound and on the material of commerce</b>
02.011 1219	Citronellol		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. Concluded in FGE.72
02.012 1223	Geraniol		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. Concluded in FGE.72
02.027 1222	(-)-Rhodinol		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. Concluded in FGE.72
02.029 1230	3,7,11-Trimethyldodeca-2,6,10-trien-1-ol		Class I A3: Intake below threshold	No safety concern at the estimated level of intake. Concluded in FGE.72
02.058 1224	(Z)-Nerol		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. Concluded in FGE.72
02.076 1199	2-Methylbutan-1-ol		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. Concluded in FGE.72

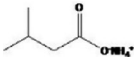
FL-no JECFA-no	EU Union List chemical name	Structural formula	JECFA conclusions Class <sup>(a)</sup> Evaluation procedure path <sup>(b)</sup> Outcome on the named compound based on the MSDI <sup>(c)</sup> approach	EFSA conclusions Procedural path if different from JECFA, Conclusion based on the MSDI <sup>(d)</sup> approach on the named compound and on the material of commerce
02.109 1200	3-Methylbut-2-en-1-ol		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. Concluded in FGE.72
02.174 1617	2-Methylbut-2-en-1-ol		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. The chemical name should be changed to 2-Methylbut-(2E)-en-1-ol and the CAS number to 497-02-9, Concluded in FGE.72Rev2
05.020 1225	Citral		Class I A3: Intake above threshold A4: Not endogenous A5: Adequate NOAEL exists No safety concern	No safety concern at the estimated level of intake. Concluded in FGE.72
05.021 1220	Citronellal		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. Concluded in FGE.72
05.033 1216	2-Ethylhept-2-enal		Class I A3: Intake below threshold No safety concern	Class III A3: Intake below threshold No safety concern at the estimated level of intake. The chemical name should be changed to 2-Ethylhept-(2E)-enal and the CAS number to 34210-19-0, Concluded in FGE.72Rev2



FL-no JECFA-no	EU Union List chemical name	Structural formula	JECFA conclusions Class <sup>(a)</sup> Evaluation procedure path <sup>(b)</sup> Outcome on the named compound based on the MSDI <sup>(c)</sup> approach	EFSA conclusions Procedural path if different from JECFA, Conclusion based on the MSDI <sup>(d)</sup> approach on the named compound and on the material of commerce
05.090 1209	2-Methylpent-2-enal		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. The chemical name should be changed to 2-Methylpent-(2 <i>E</i> )-enal and the CAS number to 14250-96-5. The purity requirement for the named compound [FL-no: 05.090] should be updated. (see Table B.1 – Appendix B). Concluded in FGE.72Rev2
05.095 1201	2-Methylcrotonaldehyde		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. The chemical name should be changed to 2-methylbut-(2 <i>E</i> )-enal. Concluded in FGE.72Rev2
05.105 1214	2-Butylbut-2-enal		Class I A3: Intake below threshold No safety concern	Class III A3: Intake below threshold No safety concern at the estimated level of intake. The chemical name should be changed to 2-butylbut- (2 <i>E</i> )-enal and the CAS number to 87745-65-1. Concluded in FGE.72Rev2
05.107 1215	2-Isopropyl-5-methylhex-2-enal		Class I A3: Intake below threshold No safety concern	Class III A3: Intake below threshold No safety concern at the estimated level of intake. Concluded in FGE.72Rev2
05.114 1208	4-Methylpent-2-enal		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. The chemical name should be changed to 4-methylpent-(2 <i>E</i> )-enal and the CAS number to 24502-08-7. Concluded in FGE.72Rev2
05.124 1202	3-Methylcrotonaldehyde		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. Concluded in FGE.72

FL-no JECFA-no	EU Union List chemical name	Structural formula	JECFA conclusions Class <sup>(a)</sup> Evaluation procedure path <sup>(b)</sup> Outcome on the named compound based on the MSDI <sup>(c)</sup> approach	EFSA conclusions Procedural path if different from JECFA, Conclusion based on the MSDI <sup>(d)</sup> approach on the named compound and on the material of commerce
05.126 1217	2-Methyloct-2-enal		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. The chemical name should be changed to 2- methyloct-(2E)-enal. The purity requirement for the named compound [FL-no: 05.126] should be updated (see Table B.1 – Appendix B). Concluded in FGE.72Rev2
05.148 1228	Farnesal		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. Concluded in FGE.72
05.169 1229	12-Methyltridecanal		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. Concluded in FGE.72
08.036 1221	Citronellic acid		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. Concluded in FGE.72
08.044 1211	(2E),4-Dimethylpent-2-enoic acid		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. Concluded in FGE.72
08.047 1212	2-Methylheptanoic acid		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. Concluded in FGE.72
08.055 1210	2-Methyl-2-pentenoic acid		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. Concluded in FGE.72

FL-no JECFA-no	EU Union List chemical name	Structural formula	JECFA conclusions Class <sup>(a)</sup> Evaluation procedure path <sup>(b)</sup> Outcome on the named compound based on the MSDI <sup>(c)</sup> approach	EFSA conclusions Procedural path if different from JECFA, Conclusion based on the MSDI <sup>(d)</sup> approach on the named compound and on the material of commerce
08.064 1205	(2E)-Methylcrotonic acid		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. Concluded in FGE.72
08.070 1204	3-Methylcrotonic acid		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. Concluded in FGE.72
08.079 1218	4-Ethylcrotonic acid		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. Concluded in FGE.72
09.273 1206	Isobutyl crotonate		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. Concluded in FGE.72
09.408 1213	Isobutyl 2-methylbut-2(cis)-enoate		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. Concluded in FGE.72
09.931 1226	2,6-Dimethyl-2,5,7-octatriene-1-ol acetate		Class I A3: Intake below threshold No safety concern	No safety concern at the estimated level of intake. Concluded in FGE.72Rev1

FL-no JECFA-no	EU Union List chemical name	Structural formula	JECFA conclusions	EFSA conclusions
16.001 1203	Ammonium isovalerate		Class I A3: Intake below threshold No safety concern	Procedural path if different from JECFA, Conclusion based on the MSDI <sup>(d)</sup> approach on the named compound and on the material of commerce  No safety concern at the estimated level of intake. Concluded in FGE.72

JECFA: Joint FAO/WHO Expert Committee on Food Additives; MSDI: Maximised Survey-derived Daily Intake; FGE: Flavouring Group Evaluation.

(a): Thresholds of concern: Class I = 1,800 µg/person per day, Class II = 540 µg/person per day, Class III = 90 µg/person per day.

(b): Procedure path A substances can be predicted to be metabolised to innocuous products. Procedure path B substances cannot.

(c): EU MSDI: Amount added to food as flavour in (kg/year) × 10<sup>9</sup> / (0.1 × population in Europe (= 375 × 10<sup>6</sup>) × 0.6 × 365) = µg/capita per day.

(d): Refer to Appendix C for MSDI values considered by EFSA based on EU production figures submitted by industry (Documentation provided to EFSA n.: 3 and 4).