EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF); Scientific Opinion on Flavouring Group Evaluation 96 (FGE.96): Consideration of 88 flavouring substances considered by EFSA for which EU production volumes / anticipated production volumes have been submitted on request by DG SANCO. Addendum to FGE. 51, 52, 53, 54, 56, 58, 61, 62, 63, 64, 68, 69, 70, 71, 73, 76, 77, 79, 80, 83, 84, 85 and 87

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SCIENTIFIC OPINION

Scientific Opinion on Flavouring Group Evaluation 96 (FGE.96):

Consideration of 88 flavouring substances considered by EFSA for which EU production volumes / anticipated production volumes have been submitted on request by DG SANCO[1]

Addendum to FGE. 51, 52, 53, 54, 56, 58, 61, 62, 63, 64, 68, 69, 70, 71, 73, 76, 77, 79, 80, 83, 84, 85 and 87.

EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF)[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

The Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids of the European Food Safety Authority was requested to consider evaluations of flavouring substances assessed since 2000 by the Joint FAO/WHO Expert Committee on Food Additives (the JECFA), and to decide whether further evaluation is necessary, as laid down in Commission Regulation (EC) No 1565/2000. The present FGE.96 concerns 88 JECFA-evaluated substances from different FGEs. Common for all the 88 substances was that for none of them European production volumes were available at the time for the first consideration of the FGEs in question. As a consequence, no MSDI could be calculated for EU and accordingly the substances could not be considered by EFSA using the evaluation Procedure. Industry has now provided production volumes for these substances. Based on these newly provided production figures, MSDI values for EU have been calculated and based on these MSDI values the substances have been re-considered by the stepwise approach (the Procedure) that integrates information on structure-activity relationships, intake from current uses, toxicological threshold of concern, and available data on metabolism and toxicity. In the FGEs in question, genotoxicity of the

1 On request from the Commission, Question No EFSA-Q-2010-01246, adopted on 25 November 2010.

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3 Acknowledgement: The Panel wishes to thank the members of the Working Groups on Flavourings for the preparation of this Opinion: Ulla Beckman Sundh, Vibe Beltoft, Wilfried Bursch, Angelo Carere, Karl-Heinz Engel, Henrik Frandsen, Rainer Gürtler, Frances Hill, Trine Husøy, John Christian Larsen, Pia Lund, Wim Mennes, Gerard Mulder, Karin Nørby, Gerard Pascal, Iona Pratt, Gerrit Speijers, Harriet Wallin and EFSA's staff member Kim Rygaard Nielsen for the preparatory work on this scientific Opinion.

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substances considered in FGE.96 has already been addressed. For none of the substances a concern for genotoxicity was identified. The Panel concluded that 87 of the substances do not give rise to safety concerns at the levels of dietary intake, estimated on the basis of the MSDI approach. However, for the substance 2-acetyl-1-ethylpyrrole [FL-no: 14.045], the Panel could not identify an appropriate NOAEL and accordingly additional data are required. Besides the safety assessment of these flavouring substances, the specifications for the materials of commerce have also been considered and for eight stereoisomeric substances [FL-no: 06.040, 08.073, 09.371, 09.780, 10.050, 13.060, 13.161 and 16.039], the stereoisomeric composition has to be specified further.

KEY WORDS

Footnote 8, European anticipated production volume, MSDI.

SUMMARY

The European Food Safety Authority (EFSA) asked the Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (the Panel) to provide scientific advice to the Commission on the implications for human health of chemically defined flavouring substances used in or on foodstuffs in the Member States. In particular, the Panel was requested to consider the Joint FAO/WHO Expert Committee on Food Additives (the JECFA) evaluations of flavouring substances assessed since 2000, and to decide whether no further evaluation is necessary, as laid down in Commission Regulation (EC) No 1565/2000. These flavouring substances are listed in the Register, which was adopted by Commission Decision 1999/217/EC and its consecutive amendments.

The present FGE.96 concerns 88 JECFA-evaluated substances from different groups. These groups have been previously considered by EFSA in FGE.51, 52, 53, 54, 56, 58, 61, 62, 63, 64, 68, 69, 70, 71, 73, 76, 77, 79, 80, 83, 84, 85 and 87. Common for all the 88 substances was that for none of them European production volumes were available at the time for the first consideration in the above-mentioned FGEs. As a consequence, no MSDI could be calculated for EU and accordingly the substances could not be considered by EFSA using the Procedure.

By February/April 2010 Industry provided production volumes for these substances. Based on these newly provided (anticipated) production figures, MSDI values for EU have been calculated (see Table 1.1 and Table 2), and based on these MSDI values the substances have been re-considered by EFSA in the current FGE.96. For the flavouring substances for which the production volumes are anticipated figures, the present evaluation will have to be reconsidered when actual production volumes become available.

In the FGEs mentioned above, genotoxicity of the substances considered in FGE.96 has already been addressed. For none of the substances a concern for genotoxicity was identified.

The Panel has considered 87 of the JECFA evaluated substances to be of no safety concern when used at the estimated intake based on the MSDI approach. For the remaining substance, 2-acetyl-1-ethylpyrrole [FL-no: 14.045] the Panel could not identify an appropriate NOAEL and accordingly additional data are required.

In order to determine whether the conclusion for the 88 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 tests are available for 79 of the JECFA-evaluated substances. For [FL-no: 15.008], the solubility in water is missing. Otherwise the specifications for this substance are appropriate. For eight stereoisomeric substances [FL-no: 06.040,

08.073, 09.371, 09.780, 10.050, 16.039, 13.060 and 13.161], the stereoisomeric composition has to be specified further.

Thus, for 79 of the 88 substances, the Panel concluded that they would be of no safety concern when used at their estimated levels of intake as flavouring substances based on the MSDI approach. For eight of the remaining nine substances, additional data on stereochemical composition are required to finalise their evaluation as material of commerce. For [FL-no: 14.045] additional toxicity data are required to finalise the evaluation.

The Panel noted that amino acids [FL-no: 16.056, 17.001, 17.003, 17.015 and 17.026] may react with other food constituents upon heating. The reaction mixtures formed are commonly referred to as "process flavours" which have not been evaluated by the Panel. The present evaluation is therefore on the basis that the present flavouring substances are in an unchanged form when they are consumed, thus in food that is not intended to be heated

TABLE OF CONTENTS

BACKGROUND

Regulation (EC) No 2232/96 of the European Parliament and the Council (EC, 1996a) lays down a Procedure for the establishment of a list of flavouring substances, the use of which will be authorised to the exclusion of all other substances in the EU. In application of that Regulation, a Register of flavouring substances used in or on foodstuffs in the Member States was adopted by Commission Decision 1999/217/EC (EC, 1999a), as last amended by Commission Decision 2009/163/EC (EC, 2009a). Each flavouring substance is attributed a FLAVIS-number (FL-number) and all substances are divided into 34 chemical groups. Substances within a group should have some metabolic and biological behaviour in common.

Substances which are listed in the Register are to be evaluated according to the evaluation programme laid down in Commission Regulation (EC) No 1565/2000 (EC, 2000a), which is broadly based on the Opinion of the Scientific Committee on Food (SCF, 1999a).

Commission Regulation (EC) No 1565/2000 lays down that substances that are contained in the Register and will be classified in the future by the Joint FAO/WHO Expert Committee on Food Additives (the JECFA) so as to present no safety concern at current levels of intake will be considered by the European Food Safety Authority (EFSA), who may then decide that no further evaluation is necessary.

In the period 2000 – 2008, during its 55th, 57th, 59th, 61st, 63rd, 65th, 68th and 69th meetings, the JECFA evaluated about 1000 substances, which are in the EU Register.

TERMS OF REFERENCE

The European Food Safety Authority (EFSA) is requested to consider the JECFA evaluations of flavouring substances assessed since 2000, and to decide whether no further evaluation is necessary, as laid down in Commission Regulation (EC) No 1565/2000 (EC, 2000a). These flavouring substances are listed in the Register which was adopted by Commission Decision 1999/217 EC (EC, 1999a) and its consecutive amendments.

ASSESSMENT

The approach used by EFSA for safety evaluation of flavouring substances is referred to in Commission Regulation (EC) No 1565/2000 (EC, 2000a), hereafter named the "EFSA Procedure". This Procedure is based on the Opinion of the Scientific Committee on Food (SCF, 1999a), which has been derived from the evaluation Procedure developed by the Joint FAO/WHO Expert Committee on Food Additives (JECFA, 1995; JECFA, 1996a; JECFA, 1997a; JECFA, 1999b), hereafter named the "JECFA Procedure". The Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (the Panel) 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 evaluations 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 put through the EFSA Procedure.

The following issues are of special importance.

Intake

In its evaluation, the Panel as a default uses the "Maximised Survey-derived Daily Intake" (MSDI) approach to estimate the *per capita* intakes of the flavouring substances in Europe.

In its evaluation, the 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 the 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 the JECFA only on the basis of these figures. For Register substances for which this is the case the Panel will need 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 level 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 the 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, 2006c).

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 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.

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

Threshold of 1.5 Microgram/Person/Day (Step B5) Used by the JECFA

The JECFA uses the threshold of concern of 1.5 microgram/person/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 microgram per 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 be amended to include the last step on the right-hand side of the original procedure ("Do the condition of use result in an intake greater than 1.5 microgram per day?") (JECFA, 1999b).

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 microgram per person per day.

Genotoxicity

As reflected in the Opinion of SCF (SCF, 1999a), 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.

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.

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.

HISTORY OF THE EVALUATION OF THE SUBSTANCES IN THE PRESENT FGE

The present FGE.96 concerns 88 JECFA-evaluated substances evaluated in different JECFA groups and former been considered by EFSA in FGE. 51, 52, 53, 54, 56, 58, 61, 62, 63, 64, 68, 69, 70, 71, 73, 76, 77, 79, 80, 83, 84, 85 and 87.

In the FGEs mentioned above, genotoxicity of the substances considered in FGE.96 has been addressed. For none of the substances a concern for genotoxicity was identified.

Common for all 88 substances considered by EFSA in the above mentioned FGEs was that no European production volumes were available at the time for the first consideration of the FGEs. As no European production volumes were available no MSDI could be calculated for EU and accordingly the substances could not be considered by EFSA using the Procedure.

By February 2010 Industry provided production volumes for these 88 substances. For 27 of the substances the provided production figure origins from the EFFA European survey conducted in 2004 and for 55 of the provided production volumes the figure is anticipated (EFFA, 2010c). For the remaining six substances it has not been stated if the figures are from an European survey or anticipated production volumes (EFFA, 2010a) (see Table 1.1).

Based on the provided (anticipated) production figures MSDI for EU have been calculated (see Table 1.1), and based on these MSDI values the 88 substances will be re-considered by EFSA along the Procedure scheme. For the 55 flavouring substances for which the production volumes are anticipated figures, the present evaluation will have to be reconsidered when actual production volumes become available.

The conclusions of FGE.96 were published in the minutes of the 17th CEF Panel meeting of 23-25 November 2010. Since, some of the FGEs included in FGE.96 have been revised. It has therefore been decided in November 2011 to publish FGE.96, including only the JECFA-evaluated substances from FGEs which have not yet been revised.

1. Presentation of the substances in the JECFA Flavouring Group

1.1. Description

1.1.1. JECFA Status

The 107 flavouring substances considered in the present FGE have all been evaluated by JECFA in the period 2000 (53rd meeting) to 2008 (69th meeting). They have been evaluated through the Procedure based on the MSDI approach where the MSDI figures have all been based on US production volumes as no production volumes were available for Europe.

1.1.2. EFSA Considerations

As no EU production volumes were available for the 107 flavouring substances no EU MSDI could be calculated and accordingly these substances could not be considered using the Procedure.

EU Production volume / anticipated production volumes have now been provided for the 107 substances (reference).

In Table 1.1 the distribution of the 107 JECFA-evaluated substances into the corresponding EFSA FGE (1st column) have been listed. For each substance the Procedure evaluation step on which the substance has been approved by JECFA has been indicated (6th column) as well as the US MSDI value on which the evaluation was based (5th column). Based on the newly submitted EU production volumes / anticipated production volumes (7th column) EU MSDI values have been calculated (8th column). Based on the EU MSDI values the Panel concluded that the 107 can be considered using the Procedure. The outcome of this evaluation (Procedure step) is shown in the 9th column.

Table 1.1 Distribution of 88 JECFA-evaluated substances into their respective FGEs

FGE	FL-no JECFA-no	Register name	Struct class	US-MSDI µg/cap/d	Evaluated by JECFA based on US-MSDI At step (6)(7)	EU Production volumes (kg/year)	EU-MSDI µg/cap/d	Evaluated by EFSA based on EU-MSDI At step (6)(8)
FGE.51	09.230 1094	Cyclohexyl butyrate	I	0.1	A3: No (59th)	7.31[3]	0.89	A3: No[1]
FGE.52	04.093 888	Butyl vanillyl ether	II	0.1	A3: No (57th)	11.3[3]	1.4	A3: No[1]
FGE.52	08.071 883	p-Anisic acid	I	0.1	A3: No (57th)	13.59[3]	1.7	A3: No[1]
FGE.52	08.076 908	2,4-Dihydroxybenzoic acid	I	6	A3: No (57th)	45[4]	5.5	A3: No[1]
FGE.52	08.092 882	3-Methoxybenzoic acid	I	0.01	A3: No (57th)	0.1[4]	0.012	A3: No[1]
FGE.52	09.145 874	p-Anisyl propionate	I	5	A3: No (57th)	3.46[3]	0.42	A3: No[1]
FGE.52	09.807 907	o-Tolyl salicylate	I	30	A3: No (57th)	230[4]	28	A3: No[1]
FGE.52	16.075 892	Ethyl vanillin beta-D-glucopyranoside	II	30	A3: No (57th)	230[4]	28	A3: No[1]
FGE.53	06.027 1005	4,5-Dimethyl-2-benzyl-1,3-dioxolan	I	1	A3: No (59th)	1.0[3]	0.12	A3: No[1]
FGE.53	09.702 1010	Propyl phenylacetate	I	0.3	A3: No (59th)	1.1[3]	0.13	A3: No[1]
FGE.53	09.783 1008	Methyl phenylacetate	I	20	A3: No (59th)	778.4[3]	95	A3: No[1]
FGE.53	16.041 1029	Sodium 2-(4-methoxyphenoxy)propionate	III	6	A3: No (59th)	0.1[3]	0.012	A3: No[1]
FGE.54	06.019 840	1-Benzyloxy-1-(2-methoxyethoxy)ethane	I	1	B4: Yes (57th)	10[4]	1.2	B4: Yes[1]
FGE.54	09.294 863	2-Methylbenzyl acetate	I	3	A3: No (57th)	20[4]	2.4	A3: No[1]
FGE.54	09.803 862	Propylene glycol dibenzoate	I	14	A3: No (57th)	110[4]	13	A3: No[1]
FGE.54	09.812 861	Glyceryl tribenzoate	I	49	A3: No (57th)	370[4]	45	A3: No[1]
FGE.56	02.224 1408	3-(1-Menthoxy)propane-1,2-diol	I	789	A3: No (63rd)	33.7[3]	4.1	A3: No[1]
FGE.56	02.246 1416	p-Menthane-3,8-diol	I	18	A3: No (63rd)	321.8[4]	39	A3: No[1]
FGE.56	02.254 1411	3-Menthoxy-2-methylpropane-1,2-diol	I	500	A3: No (63rd)	500[4]	61	A3: No[1]
FGE.58	04.037 720	4-Ethoxyphenol	I	0.4	A3: No (55th)	3[4]	0.37	A3: No[1]
FGE.58	04.052 723	4-Ethyl-2,6-dimethoxyphenol	I	1	A3: No (55th)	11[4]	1.3	A3: No[1]
FGE.58	04.053 722	4-Methyl-2,6-dimethoxyphenol	I	0.04	A3: No (55th)	0.44[4]	0.054	A3: No[1]
FGE.58	04.056 724	2,6-Dimethoxy-4-propylphenol	I	0.1	A3: No (55th)	0.5[4]	0.061	A3: No[1]
FGE.58	09.036 699	p-Tolyl acetate	I	70	A3: No (55th)	0.39[3]	0.047	A3: No[1]
FGE.58	09.102 704	p-Tolyl dodecanoate	I	0.3	A3: No (55th)	2[4]	0.24	A3: No[1]
FGE.58	09.288 731	4-(4-Acetoxyphenyl)butan-2-one	I	0.1	A3: No (55th)	0.97[3]	0.12	A3: No[1]

Table 1.1 Distribution of 88 JECFA-evaluated substances into their respective FGEs

FGE	FL-no JECFA-no	Register name	Struct class	US-MSDI µg/cap/d	Evaluated by JECFA based on US-MSDI At step (6)(7)	EU Production volumes (kg/year)	EU-MSDI µg/cap/d	Evaluated by EFSA based on EU-MSDI At step (6)(8)
FGE.61	06.081 943	1-Ethoxy-1-(3-hexenyloxy)ethane	I	0	A3: No (57th)	37.69[3]	4.6	A3: No[1]
FGE.62	02.189 1283	Nona-3,6-dien-1-ol	I	0.9	A3: No (61st)	1.07[3]	0.13	A3: No[1]
FGE.62	02.243 1284	(E,Z)-3,6-Nonadien-1-ol	I	0.9	A3: No (61st)	5[4]	0.61	A3: No[1]
FGE.63	07.069 1121	Tetrahydro-pseudo-ionone	II	0.01	A3: No (59th)	0.1[4]	0.012	A3: No[1]
FGE.63	07.100 1119	5-Methylhex-5-en-2-one	II	0.3	A3: No (59th)	2[4]	0.24	A3: No[1]
FGE.63	09.658 1142	1-Methylbutyl butyrate	I	1	A3: No (59th)	3.82[3]	0.47	A3: No[1]
FGE.64	06.040 913	1,2,3-Tris([1'-ethoxy]-ethoxy)propane	I	140	A3: No (57th)	1	0.12	A3: No[1]
FGE.64	08.004 930	Lactic acid	I	47000	A4: Yes (57th)	156280[3]	19000	No safety concern[8]
FGE.64	09.443 939	Isopentyl pyruvate	I	0	A3: No (57th)	143	17	A3: No[1]
FGE.64	09.552 914	3-Oxodecanoic acid glyceride	III	270	A4: Yes (57th)	429	52	A3: No[2]
FGE.64	09.555 910	3-Oxohexanoic acid glyceride	III	270	A4: Yes (57th)	0.5	0.061	A3: No[2]
FGE.64	09.557 916	3-Oxotetradecanoic acid glyceride	III	270	A4: Yes (57th)	0.1	0.012	A3: No[2]
FGE.64	16.039 933	Potassium 2-(1'-ethoxy)ethoxypropanoate	I	1400	A3: No (57th)	10000[4]	1200	A3: No[1]
FGE.68	02.051 675	5-Phenylpentan-1-ol	I	0.1	A3: No (55th)	10[4]	1.2	A3: No[1]
FGE.68	05.094 680	3-(4-Isopropylphenyl)propionaldehyde	I	0.1	A3: No (55th)	0.1[4]	0.012	A3: No[1]
FGE.68	09.071 642	3-Phenylpropyl hexanoate	I	0.4	A3: No (55th)	2[4]	0.24	A3: No[1]
FGE.68	09.084 637	3-Phenylpropyl formate	I	0.8	A3: No (55th)	0.1[4]	0.012	A3: No[1]
FGE.68	09.746 643	Methyl 3-phenylpropionate	I	3	A3: No (55th)	1[4]	0.12	A3: No[1]
FGE.68	09.780 760	Cinnamyl benzoate	I	1	A3: No (55th)	10[4]	1.2	A3: No[1]
FGE.69	07.070 830	3-Benzylheptan-4-one	II	1	A3: No (57th)	0.41[3]	0.05	A3: No[1]
FGE.69	09.189 823	1-Phenylpropyl butyrate	I	0.3	A3: No (57th)	2[4]	0.24	A3: No[1]
FGE.69	09.200 816	1-Methyl-3-phenylpropyl acetate	I	7	A3: No (57th)	50[4]	6.1	A3: No[1]
FGE.69	09.501 835	Ethyl 2-acetyl-3-phenylpropionate	I	0.4	A3: No (57th)	3[4]	0.37	A3: No[1]
FGE.70	08.085 1176	Hexa-2,4-dienoic acid	I	6	A3: No (57th)	500[4]	61	No safety concern[8]
FGE.70	09.371 1193	Ethyl deca-2,4,7-trienoate	I	0.4	A3: No (61st)	0.2[4]	0.024	A3: No[1]
FGE.70	09.639 1191	Methyl deca-2,4-dienoate	I	1	A3: No (61st)	0.8[4]	0.097	A3: No[1]
FGE.71	08.073 1372	Dec-2-enoic acid	I	4	A3: No (63rd)	0.1[4]	0.012	A3: No[1]
FGE.71	08.123 1373	trans-2-Heptenoic acid	I	4	A3: No (63rd)	39[4]	4.7	A3: No[1]
FGE.71	09.157 1352	Ethyl 2-nonynoate	I	0.9	A3: No (63rd)	9[4]	1.1	A3: No[1]
FGE.71	09.239 1358	Methyl 2-undecynoate	I	0.04	A3: No (63rd)	0.1[4]	0.012	A3: No[1]
FGE.73	02.141 986	2-(6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl)ethan-1-ol	I	0.01	A3: No (59th)	270[4]	33	A3: No[1]
FGE.73	09.488 966	Ethyl cyclohexanepropionate	I	0.1	A3: No (59th)	1[4]	0.12	A3: No[1]
FGE.73	09.534 963	Ethyl cyclohexanecarboxylate	I	0.1	A3: No (59th)	2[4]	0.24	A3: No[1]
FGE.75	13.060 1447	Tetrahydrofurfuryl cinnamate	III	0.01	A3: No (63rd)	0.1[4]	0.012	A3: No[1]
FGE.76	15.002 1057	2-Methyl-5-methoxythiazole	III	0.01	B4: Yes (59th)	0.1[4]	0.012	B4: Yes[1]
FGE.76	15.008 1053	2-Thienyl disulfide	III	0.07	B4: Yes (59th)	0.5[4]	0.061	B4: Yes[1]
FGE.76	15.027 1042	2-Propionylthiazole	II	0.2	B4: Yes (59th)	0.46[3]	0.056	B4: Yes[1]

Table 1.1 Distribution of 88 JECFA-evaluated substances into their respective FGEs

FGE	FL-no JECFA-no	Register name	Struct class	US-MSDI µg/cap/d	Evaluated by JECFA based on US-MSDI At step (6)(7)	EU Production volumes (kg/year)	EU-MSDI µg/cap/d	Evaluated by EFSA based on EU-MSDI At step (6)(8)
FGE.77	14.045 1305	2-Acetyl-1-ethylpyrrole	II	0.009	A3: No (63rd)	1	0.12	B4: No[2]
FGE.77	14.058 1311	2-Isobutylpyridine	III	0.9	A3: No (63rd)	0.05[3]	0.0061	B4: Yes[2]
FGE.77	14.059 1312	3-Isobutylpyridine	II	0.07	A3: No (63rd)	0.4[4]	0.049	B4: Yes[2]
FGE.77	14.164 1322	2-Propylpyridine	II	0.9	A3: No (63rd)	5[4]	0.61	B4: Yes[2]
FGE.79	17.001 1418	beta-Alanine	I	13	A3: No (63rd)	2924[3]	360	A3: No[1]
FGE.79	17.003 1438	l-Arginine	I	57	No safety concern (63rd)	8266[3]	1000	No safety concern[8]
FGE.79	17.015 1427	S-Methylmethioninesulponium chloride	III[5]	75	A3: No (63rd)	2858[3]	350	B4: Yes[1]
FGE.79	17.026 1439	l-Lysine	I	57	No safety concern (63rd)	8600 [3]	1000	No safety concern[8]
FGE.79	16.056 1435	Taurine	I	217	A3: No (63rd)	6317[3]	770	A3: No[1]
FGE.80	10.050 1161	Hexahydro-3,6-dimethyl-2(3H)-benzofuranone	III	12	A3: No (61st)	66[4]	8.0	A3: No[1]
FGE.80	10.061 1159	cis-5-Hexenyldihydro-5-methylfuran-2(3H)-one	I	13	A3: No (61st)	829[4]	100	A3: No[1]
FGE.80	10.069 1158	3-Methyl gamma-decalactone	I	5	A3: No (61st)	37[4]	4.5	A3: No[1]
FGE.80	10.070 1157	4-Methyl-5-hexen-1,4-olide	I	3	A3: No (61st)	18[4]	2.2	A3: No[1]
FGE.80	10.072 1167	Dimethyl-3,6-benzo-2(3H)-furanone	III	2	B4: Yes (61st)	6.92[3]	0.84	B4: Yes[1]
FGE.80	13.161 1166	Octahydrocoumarin	III	0.07	A3: No (61st)	10.3[3]	1.3	A3: No[1]
FGE.83	13.027 1485	2-Pentyl-5 or 6-keto-1,4-dioxane	III	0.2	A3: No (65th)	1[4]	0.12	A3: No[1]
FGE.83	13.028 1484	2-Butyl-5 or 6-keto-1,4-dioxane	III	0.5	A3: No (65th)	3.5[4]	0.43	A3: No[1]
FGE.84	09.561 1538	Hex-3(cis)-enyl anthranilate	I	53	A3: No (65th)	0.1[3]	0.012	A3: No[1]
FGE.84	09.722 1541	Cyclohexyl anthranilate	I	0.007	A3: No (65th)	0.06[4]	0.0073	A3: No[1]
FGE.84	09.801 1544	2-Naphthyl anthranilate	I	2	A3: No (65th)	11[4]	1.3	A3: No[1]
FGE.85	14.014 1566	5,7-Dihydro-2-methylthieno(3,4-d)pyrimidine	III	0.4	B4: Yes (65th)	0.1[3]	0.012	B4: Yes[1]
FGE.85	14.029 1568	1-Phenyl-(3 or 5)-propylpyrazole	III	0.2	B4: Yes (65th)	1.4[4]	0.17	B4: Yes[1]
FGE.85	14.070 1565	4-Acetyl-2-methylpyrimidine	II	0.01	B4: Yes (65th)	0.09[4]	0.011	B4: Yes[1]
FGE.87	09.153 1392	Bornyl valerate	I	5	A3: No (63rd)	30[4]	3.7	A3: No[1]
FGE.87	09.319 1412	Bornyl butyrate	I	9	A3: No (63rd)	50[4]	6.1	A3: No[1]

1 EFSA agrees with the way JECFA has applied the Procedure when based on the US MSDI.
2 EFSA does not agree with the JECFA application of the Procedure but concluded the substance at another Procedure step (see text).
3 Newly provided EU production volume. EFFA survey conduction in 2004, the EU MSDI has been calculated using the EU population size in this year.
4 Newly provided EU production volume. EFFA anticipated production volumes 2010, the EU MSDI has been calculated using the EU population size in this year.
5 EFSA has allocated this substance to structural class I (see text).
6 For the Procedure steps – see Annex I.
7 No of JECFA meeting evaluated at.
8 Not evaluated through the Procedure for various reasons (see text).

1.2. Isomers

1.2.1. JECFA Status

Of the 88 JECFA-evaluated substances 36 [FL-no: 02.141, 02.224, 02.246, 02.254, 06.019, 06.027, 06.040, 06.081, 07.069, 07.070, 08.004, 09.153, 09.189, 09.200, 09.319, 09.501, 09.552, 09,555, 09.557, 09.658, 09.803, 10.050, 10.061, 10.069, 10.070, 10.072, 13.027, 13.028, 13.060, 13.161,

16.039, 16.041, 16.075, 17.003, 17.015, 17.026] possess one or more chiral centres and 12 [FL-no: 02.189, 02.243, 06.081, 08.073, 08.085, 08.123, 09.371, 09.561, 09.639, 09.780, 10.061 and 13.060] can exist as geometric isomers due to one or more double-bonds. Furthermore, six substances are mixtures of structural isomers.

1.2.2. EFSA Considerations

For one substance [FL-no: 06.040], in the present FGE.96, the stereoisomeric composition has to be specified. For seven of the stereoisomeric substances, the Industry (EFFA, 2010a) has informed that the commercial products are mixtures of stereoisomers, but no information on the ratio of the stereoisomers in the cases of mixtures has been given [FL-no: 08.073, 09.371, 09.780, 10.050, 13.060, 13.161 and 16.039]. The composition of stereoisomeric mixtures has to be specified.

1.3. Specifications

1.3.1. JECFA Status

The JECFA specifications are available for all substances in the present FGE.

1.3.2. EFSA Considerations

For one of the JECFA-evaluated substances the specifications are incomplete, as the solubility in water is missing for [FL-no: 09.807].

2. Intake Estimations

2.1. JECFA Status

By February/April 2010 Industry provided production volumes for these 107 substances. For 37 of the substances the provided production figure origins from the EFFA European survey conducted in 2004, for 64 of the provided production volumes the figure is anticipated (see Table 1.1).

2.2. EFSA Considerations

Based on these newly provided (anticipated) production figures MSDI for EU have been calculated (see Table 1.1).

3. Application of the Procedure

3.1. EFSA Considerations to the application of the Procedure as performed by JECFA in FGE.51, 52, 53, 54, 56, 58, 61, 62, 63, 64, 68, 69, 70, 71, 73, 76, 77, 79, 80, 83, 84, 85 and 87.

3.1.1. FGE.51 Alicyclic ketones and secondary alcohols and related esters (EFSA, 2008aj)

http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902162890.htm

“The Panel agrees with the application of the Procedure as performed by the JECFA for the 13 substances in the group of alicyclic ketones, secondary alcohols and related esters.

However, for one substance [FL-no: 09.230] no European production figure was available and consequently no European exposure estimates could be calculated. Accordingly, the safety in use could not be assessed using the Procedure for the substance".

3.1.1.1. EFSA considerations based on new information on production volumes

Based on the newly submitted EU production volume for [FL-no: 09.230] the MSDI is 0.89 microgram/*capita*/day, which is below the threshold for a structural class I substance of 1800 microgram/person/day.

The Panel concluded at step A3 that [FL-no: 09.230] would be of no safety concern at the estimated level of intake based on the MSDI approach.

3.1.2. FGE.52 Hydroxy- and alkoxy-substituted benzyl derivatives (EFSA, 2008y)

http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178692189524.htm

"The Panel agrees with the application of the Procedure as performed by the JECFA at its 57th meeting (JECFA, 2002a) for 43 of the 44 substances in the group of hydroxy- and alkoxy-substituted benzyl derivatives.

More recent studies on butyl 4-hydroxybenzoate [FL-no: 09.754] considered in the EFSA Opinion on methyl, ethyl and propyl 4-hydroxybenzoates, evaluated as food additives, have demonstrated that in juvenile rats given dietary doses of approximately 10, 100 or 1000 mg/kg body weight (bw) per day for eight weeks, effects were observed on male reproductive organs, sperm parameters or sex hormones at all doses (EFSA, 2004b; JECFA, 2007b). In juvenile mice given dietary doses of butyl 4-hydroxybenzoate of 15-1500 mg/kg bw per day for ten weeks, effects on sperm counts and serum concentrations of testosterone were observed (JECFA, 2007b). As no NOAEL could be demonstrated for these effects on male reproductive parameters in rodents the Panel concluded that additional data would be required before butyl 4-hydroxybenzoate [FL-no: 09.754] can be evaluated as a flavouring substance using the Procedure".

For seven substances [FL-no: 04.093, 08.071, 08.076, 08.092, 09.145, 09.807 and 16.075] the evaluation could not be finalised due to missing EU production volumes.

3.1.2.1. EFSA considerations based on new information on production volumes

Based on the newly submitted EU production volumes for the seven JECFA-evaluated substances [FL-no: 04.093, 08.071, 08.076, 08.092, 09.145, 09.807 and 16.075] the MSDIs range from 0.012 to 28 microgram/*capita*/day, which are all below the threshold for their respective structural class.

For all seven substances [FL-no: 04.093, 08.071, 08.076, 08.092, 09.145, 09.807 and 16.075], the Panel concluded at step A3 that these substances would be of no safety concern at their estimated level of intake based on the MSDI approach.

3.1.3. FGE.53Rev1 Phenethyl alcohol, aldehyde, acid and related acetals and esters (EFSA, 2009aq)

http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902882405.htm

"The Panel agrees with the way the application of the Procedure has been performed by the JECFA for all the 42 substances in the group of phenylethyl alcohol, aldehyde, acid and related acetals and esters and related substances.

However, for four substances [FL-no: 06.027, 09.702, 09.783 and 16.041] no European production figures were available and consequently no European exposure estimate could be calculated. Accordingly, the safety in use in Europe could not be assessed using the Procedure for these four substances".

3.1.3.1. EFSA considerations based on new information on production volumes

Based on the newly submitted EU production volumes for the four JECFA-evaluated substances [FL-no: 06.027, 09.702, 09.783 and 16.041] the MSDIs range from 0.012 to 95 microgram/*capita*/day, which are all below the threshold for their respective structural class.

For all four substances [FL-no: 06.027, 09.702, 09.783 and 16.041], the Panel concluded at step A3 that these substances would be of no safety concern at their estimated level of intake based on the MSDI approach.

3.1.4. FGE.54Rev1 Benzyl derivatives (EFSA, 2009af)

http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902524149.htm

"The Panel agrees with the way the application of the Procedure has been performed by the JECFA for all the 37 substances in the group of benzyl derivatives performed.

However, for four substances [FL-no: 06.019, 09.294, 09.803 and 09.812] no European production volumes were available and consequently no European exposure estimate could be calculated. Accordingly, the safety in use in Europe could not be assessed using the Procedure for these four substances."

3.1.4.1. EFSA considerations based on new information on production volumes

Based on the newly submitted EU production volumes for the four JECFA-evaluated substances [FL-no: 06.019, 09.294, 09.803 and 09.812] the MSDIs range from 1.2 to 45 microgram/*capita*/day, which are below the threshold for their structural class.

For three substances [FL-no: 09.294, 09.803 and 09.812], the Panel concluded at step A3 that these substances would be of no safety concern at their estimated level of intake based on the MSDI approach.

For [FL-no: 06.019], which was evaluated via the B-side of the Procedure, an NOAEL for a structurally related substance was not available. However, the Panel noted that upon ingestion, this substance will be hydrolysed to yield benzyl alcohol [FL-no: 02.010], acetaldehyde [FL-no: 05.001] and methoxyethanol (not in register). Benzyl alcohol [FL-no: 02.010] and acetaldehyde [FL-no: 05.001] were considered of no safety concern by EFSA in FGE.54Rev1 and by the JECFA in 1999. When ingested at the level of the MSDI (1.2 microgram/*capita*/day), substance [FL-no: 06.019] will release 0.43 microgram/*capita*/day of methoxyethanol. For this substance a NOAEL of 6 mg/kg bw/day has been identified in a multi-generation study (Gulati et al., 1990a; Gulati et al., 1990b), as cited by JECFA 2002a). When the estimated exposure to methoxyethanol released from [FL-no: 06.019] is compared to this NOAEL an adequate margin of safety of 8.3×10^5 can be calculated.

Therefore the Panel concluded that this substance would be of no safety concern at the estimated level of intake based on the MSDI approach at step B4 of the Procedure.

3.1.5. FGE.56 Monocyclic secondary alcohols, ketones and related esters (EFSA, 2009i)

http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902255809.htm

"The Panel agrees with the application of the Procedure as performed by the JECFA for four out of the six monocyclic secondary alcohols, ketones and related esters [FL-no: 02.224, 02.246, 02.254 and 09.521]. However, for three substances [FL-no: 02.224, 02.246 and 02.254] no European production figures were available and consequently no European exposure estimates could be calculated. Accordingly, the safety in use could not be assessed using the Procedure for these three substances. For [FL-no: 07.110 and 07.111] the Panel concluded in line with the conclusion on cyclotetradecanone [FL-no: 07.207] evaluated in FGE.09Rev1, that the substances could not be anticipated to be metabolised to innocuous products and should therefore be evaluated via the B-side of the EFSA Procedure. As no adequate NOAELs were available for [FL-no: 07.110 and 07.111], additional data were required for these substances."

3.1.5.1. EFSA considerations based on new information on production volumes

Based on the newly submitted EU production volumes for the three JECFA-evaluated substances [FL-no: 02.224, 02.246 and 02.254] the MSDIs range from 4.1 to 61 microgram/*capita*/day, which are below the threshold for their structural class.

For three substances [FL-no: 02.224, 02.246 and 02.254], the Panel concluded at step A3 that these substances would be of no safety concern at their estimated level of intake based on the MSDI approach.

3.1.6. FGE.58 Phenol derivatives (EFSA, 2008ab)

http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178710472028.htm

The Panel agrees with the application of the Procedure as performed by the JECFA for 43 of the 44 substances in the group of phenol derivatives.

The Panel has transferred one substance [FL-no: 07.046], which contain an alpha,beta-unsaturated ketone, to subgroup 3.2 of FGE.19, for further evaluation of possible genotoxic potential.

For seven substances [FL-no: 04.037, 04.052, 04.053, 04.056, 09.036, 09.102 and 09.288] no European production figures were available and consequently no European exposure estimate could be calculated. Accordingly, the safety in use in Europe could not be assessed using the Procedure for these substances.

3.1.6.1. EFSA considerations based on new information on production volumes

Based on the newly submitted EU production volumes for the seven JECFA-evaluated substances [FL-no: 04.037, 04.052, 04.053, 04.056, 09.036, 09.102 and 09.288] the MSDIs range from 0.047 to 1.3 microgram/*capita*/day, which are below the threshold for their structural class.

For all seven substances the Panel concluded at step A3 that these substances would be of no safety concern at their estimated level of intake based on the MSDI approach.

3.1.7. FGE.61Rev1 Aliphatic acyclic acetals (EFSA, 2009aj)

http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902722375.htm

"The Panel agrees with the way the application of the Procedure has been performed by the JECFA for all nine substances in the group of aliphatic acyclic acetals.

However, for one substance [FL-no: 06.081] no European production figure was available and consequently no European exposure estimate could be calculated. Accordingly, the safety in use in Europe could not be assessed using the Procedure for this substance."

3.1.7.1. EFSA considerations based on new information on production volumes

Based on the newly submitted EU production volumes for the [FL-no: 06.081] the MSDI is 4.6 microgram/*capita*/day, which is below the threshold for a structural class I substance.

For [FL-no: 06.081] the Panel concluded at step A3 that this substance would be of no safety concern at the estimated level of intake based on the MSDI approach.

3.1.8. FGE.62Rev1 Linear and branched-chain aliphatic unsaturated, unconjugated alcohols, aldehydes, acids, and related esters (EFSA, 2008aq)

http://www.efsa.europa.eu/en/scdocs/scdoc/1407.htm

"The Panel agrees with the way the application of the Procedure has been performed by the JECFA for the 22 substances in the group of linear and branched-chain aliphatic unsaturated, unconjugated alcohols, aldehydes, acids, and related esters. The Panel considered the study by Cox et al., 1978 on ethyl-2-methyl-3,4-pentadienoate [FL-no: 09.540] valid to provide a NOAEL and agree with JECFA that the decrease in body weight seen in female rats was not considered relevant.

For two substances [FL-no: 02.189 and 02.243] no European production figures were available and consequently no European exposure estimates could be calculated. Accordingly, the safety in use in Europe could not be assessed using the Procedure for these substances".

3.1.8.1. EFSA considerations based on new information on production volumes

Based on the newly submitted EU production volumes for the two JECFA-evaluated substances [FL-no: 02.189 and 02.243] the MSDIs are 0.13 and 0.61 microgram/*capita*/day, respectively, which are below the threshold for a structural class I substance.

For the two substances the Panel concluded at step A3 that these substances would be of no safety concern at their estimated level of intake based on the MSDI approach.

3.1.9. FGE.63 Aliphatic secondary alcohols, ketones and related esters (EFSA, 2008ae)

http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178706503680.htm

"The Panel agrees with the application of the Procedure as performed by the JECFA for the 13 substances in the group of aliphatic secondary alcohols, ketones and related esters."

For three substances [FL-no: 07.069, 07.100 and 09.658] no European production figures were available and consequently no European exposure estimates could be calculated. Accordingly, the safety in use in Europe could not be assessed using the Procedure for these substances.

3.1.9.1. EFSA considerations based on new information on production volumes

Based on the newly submitted EU production volumes for the three JECFA-evaluated substances [FL-no: 07.069, 07.100 and 09.658] the MSDIs range from 0.012 to 0.47 microgram/*capita*/day, which are all below the threshold for their respective structural class.

For the three substances the Panel concluded at step A3 that these three substances would be of no safety concern at their estimated level of intake based on the MSDI approach.

3.1.10. FGE.64 Aliphatic acyclic diols, triols, and related substances (EFSA, 2009p)

http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902322349.htm

"The Panel agrees with the application of the Procedure as performed by the JECFA for the 25 aliphatic acyclic diols, triols and related substances. However, for seven substances [FL-no: 06.040, 08.004, 09.443, 09.552, 09.555, 09.557 and 16.039] no European production figures were available and consequently no European exposure estimate could be calculated. Accordingly the safety in use could not be assessed using the Procedure for these seven substances".

3.1.10.1. EFSA considerations based on new information on production volumes

Based on newly submitted EU production volumes for the seven JECFA-evaluated substances [FL-no: 06.040, 08.004, 09.443, 09.552, 09.555, 09.557 and 16.039], for which EU production volumes were missing, the MSDIs range from 0.012 to 19000 microgram/*capita*/day. The MSDI for lactic acid [FL-no: 08.004] is 19000 microgram/*capita*/day, which is above the threshold of toxicological concern for the structural class for lactic acid of 1800 microgram/person/day. However, the human exposure of the candidate substance lactic acid [FL-no: 08.004] through food is orders of magnitude higher than the anticipated levels of exposure from the use of the flavouring substances. Therefore this substance is not taken through the Procedure. In addition, in 1973 JECFA derived an ADI "not limited" for lactate and several salts (JECFA, 1974d). In 1991, this view was also supported by the SCF (SCF, 1991); ADI "not specified" and later iterated in the evaluation of lactate and sodium lactate for poultry carcass treatment (EFSA, 2006l). Therefore, the Panel concluded that the substance was not of safety concern at the estimated level of intake as flavouring substance.

For [FL-no: 06.040, 09.443 and 16.039] the MSDI is below the threshold of 1800 microgram/person/day for a structural class I substance. Thus, for the three substances the Panel concluded at step A3 that these substances would be of no safety concern at the estimated level of intake based on the MSDI approach.

For [FL-no: 09.552, 09.555 and 09.557] from structural class III the JECFA concluded these substances at step A4: the US MSDI were above the threshold of structural class III of 90 microgram/person/day, but the substances are endogenous. As the EU MSDIs are below the threshold of the structural class for all three substances, the Panel could conclude the three substances at step A3.

Thus the Panel concluded that all seven substances would be of no safety concern at their estimated level of intake based on the MSDI approach.

3.1.11. FGE.68 Cinnamyl alcohol and related flavouring (EFSA, 2009ak)

http://www.efsa.europa.eu/en/efsajournal/pub/1032.htm

"The Panel agrees with the way the application of the Procedure has been performed by the JECFA for all 54 substances in the group of cinnamyl alcohol and related substances.

However, the structural class have, based on EFSA considerations, been changed for the following flavouring substances:

- [FL-no: 06.013, 09.026 and 09.090 and 09.468] from structural class I to class II,
- [FL-no: 02.051] from structural class II to class I,
- [FL-no: 06.014] from structural class II to class III.

These changes in structural classes do not give rise to change in the outcome of the application of the Procedure.

For six substances [FL-no: 02.051, 05.094, 09.071, 09.084, 09.746 and 09.780] no European production figures were available and consequently no European exposure estimates could be calculated. Accordingly, the safety in use in Europe could not be assessed using the Procedure for these six substances."

3.1.11.1. EFSA considerations based on new information on production volumes

Based on the newly submitted EU production volumes for the six JECFA-evaluated substances [FL-no: 02.051, 05.094, 09.071, 09.084, 09.746 and 09.780] the MSDIs range from 0.012 to 1.2 microgram/*capita*/day, which are all below the threshold for their respective structural class.

For all six substances the Panel concluded at step A3 that these substances would be of no safety concern at their estimated levels of intake based on the MSDI approach.

3.1.12. FGE.69 Aromatic substituted secondary alcohols, ketones, and related esters (EFSA, 2008am)

http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902172504.htm

"The Panel agrees with the application of the Procedure as performed by the JECFA for all the 33 substances in the group of aromatic substituted secondary alcohols, ketones and related esters.

However, for four substances [FL-no: 07.070, 09.189, 09.200 and 09.501] no European production figures are available and consequently no European exposure estimates could be calculated. Accordingly, the safety in use in Europe could not be assessed using the Procedure for these four substances."

3.1.12.1. EFSA considerations based on new information on production volumes

Based on the newly submitted EU production volumes for the four JECFA-evaluated substances [FL-no: 07.070, 09.189, 09.200 and 09.501] the MSDIs range from 0.05 to 6.1 microgram/*capita*/day, which are all below the threshold for their respective structural class I and II.

For all four substances the Panel concluded at step A3 that these substances would be of no safety concern at their estimated level of intake based on the MSDI approach.

3.1.13. FGE.70 Aliphatic, alicyclic, linear, alpha,beta-unsaturated, di- and tri-enals and related alcohols, acids and esters (EFSA, 2009at)

http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902866033.htm

"Following hydrolysis of the esters in the gastrointestinal tract, the resulting carboxylic acids will participate in normal fatty acid metabolism including beta-oxidation and citric acid cycle, which finally leads to the total oxidation of these substances as described for the mono-unsaturated, shorter chain carboxylic acids evaluated in FGE.05 Revision 1 (Annex III of FGE.05Rev.1 (EFSA, 2008j). The Panel therefore agrees with the conclusion of the JECFA, that the substances in this FGE will be metabolised to innocuous products and can be evaluated via the A-side of the Procedure.

The Panel agrees with the way that the application of the Procedure has been performed by the JECFA for all seven substances. However, for three substances [FL-no: 08.085, 09.371 and 09.639] no European production figures were available and consequently no European exposure estimates could be calculated. Accordingly, the safety in use in Europe could not be assessed using the Procedure for these three substances.

The Panel notes that one of these substances hexa-2,4-dienoic acid [FL-no: 08.085] (synonyms: 2,4-hexadienoic acid and sorbic acid), together with its calcium, sodium and potassium salts, has been allocated a group ADI of 25 mg/kg body weight (expressed as sorbate) by the JECFA (JECFA, 1986a)."

3.1.13.1. EFSA considerations based on new information on production volumes

Based on the newly submitted EU production volumes for the three JECFA-evaluated substances [FL-no: 08.085, 09.371 and 09.639] the MSDIs range from 0.024 to 61 microgram/*capita*/day. For the two substances [FL-no: 09.371 and 09.639] the MSDI values are below the threshold for their structural class.

For the remaining substance [FL-no: 08.085], the MSDI (61 microgram/*capita*/day; 1 microgram/kg bw/day) is also below the threshold for its structural class. However, as an ADI of 25 mg/kg bw/day (sorbic acid) has been derived by the JECFA (JECFA, 1986a) and by the EU-SCF in 1996 (EC, 1996b), the Panel considers it more appropriate to evaluate the exposure to this substance when used as a flavouring substance with this ADI. The ADI is not exceeded.

Thus for these three substances [FL-no: 08.085, 09.371 and 09.639] the Panel concluded that these substances would be of no safety concern at their estimated level of intake based on the MSDI approach. For two of these substances, this decision was reached at step A3 of the Procedure. For the third one, this decision was reached by comparison of the exposure estimate (MSDI) with the ADI available for this substance.

3.1.14. FGE.71 Aliphatic, linear, alpha,beta-unsaturated carboxylic acids and related esters (EFSA, 2010a)

http://www.efsa.europa.eu/en/scdocs/scdoc/1401.htm

"The Panel agrees with the way the application of the Procedure has been performed by the JECFA for all nine substances in the group of aliphatic alpha,beta-unsaturated aldehydes, acids and related alcohols, acetals and esters.

However, for four substances, [FL-no: 08.073, 08.123, 09.157 and 09.239] no European production volumes were available and consequently no European exposure estimates could be calculated. Accordingly, the safety in use in Europe could not be assessed using the Procedure for these four substances."

3.1.14.1. EFSA considerations based on new information on production volumes

Based on the newly submitted EU production volumes for the four JECFA-evaluated substances [FL-no: 08.073, 08.123, 09.157 and 09.239] the MSDIs range from 0.012 to 4.7 microgram/*capita*/day, which are below the threshold for their structural class.

For the four substances the Panel concluded at step A3 that these substances would be of no safety concern at their estimated level of intake based on the MSDI approach.

3.1.15. FGE.73 Alicyclic primary alcohols, aldehydes, acids and related esters (EFSA, 2008an)

http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902172436.htm

"The Panel agrees with the application of the Procedure as performed by the JECFA for the 15 substances in the group of alicyclic primary alcohols, aldehydes, acids and related esters.

The Panel noted that one substance [FL-no: 05.123] has a terminal double bond. Although theoretically, the double bond may be oxidised to give reactive epoxides, it is expected that for this substance, the metabolism via this pathway is negligible. The terminal double bond is present in a molecule that has aldehyde function at the end distal from the double bond. The aldehyde function is expected to be readily attacked by oxidation processes, ultimately yielding unsaturated carboxylic acids. Biochemical attack of these carboxylic acids via e.g. beta-oxidation or conjugation with glucuronic acid is expected to be much more efficient and rapid than microsomal oxidation.

However, for three substances [FL-no: 02.141, 09.488 and 09.534] no European production figures were available and consequently no European exposure estimates could be calculated. Accordingly, the safety in use could not be assessed using the Procedure for these three substances."

3.1.15.1. EFSA considerations based on new information on production volumes

Based on the newly submitted EU production volumes for the three JECFA-evaluated substances [FL-no: 02.141, 09.488 and 09.534] the MSDIs range from 0.12 to 33 microgram/*capita*/day, which are below the threshold for their structural class.

For the three substances the Panel concluded at step A3 that these substances would be of no safety concern at their estimated level of intake based on the MSDI approach.

3.1.16. FGE.75 Tetrahydrofuran and furanone derivatives (EFSA, 2008aw)

http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902219579.htm

"The JECFA concluded all the 11 tetrahydrofuran derivatives at step A3. The Panel agrees with the application of the Procedure as performed by the JECFA for 10 of the 11 substances. For the remaining substance [FL-no: 13.097] the Panel did not find that the substance could be metabolized to innocuous products and should accordingly be evaluated via the B-side of the Procedure scheme. A NOAEL could not be identified for the substance or for structurally related substances and accordingly, additional data are required for this substance.

For one substance [FL-no: 13.060] no European production figures were available and consequently no European exposure estimate could be calculated. Accordingly, the safety in use in Europe could not be assessed using the Procedure for this substance."

3.1.16.1. EFSA considerations based on new information on production volumes

Based on the newly submitted EU production volume for the JECFA-evaluated substance [FL-no: 13.060] the MSDI is 0.012 microgram/*capita*/day, which is below the threshold for a structural class III substance of 90 microgram/person/day.

For [FL-no: 13.060] the Panel concluded at step A3 that this substance would be of no safety concern at the estimated level of intake based on the MSDI approach.

3.1.17. FGE.76 Sulfur-containing heterocyclic substances (EFSA, 2008ap)

http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902192133.htm

"The Panel agrees with the application of the Procedure, as performed by the JECFA, for 20 of the 26 substances in the group of sulphur-containing heterocyclic compounds. Four of the 26 substances evaluated by the JECFA, thiazole [FL-no: 15.028], 2-(sec-butyl)-4,5-dimethyl-3-thiazoline [FL-no:

15.029], 4,5-dimethyl-2-ethyl-3-thiazoline [FL-no: 15.030] and 4,5-dimethyl-2-isobutyl-3-thiazoline [FL-no: 15.032] were considered by the Panel to have genotoxic potential *in vitro*, and therefore the Panel concluded that the Procedure should not be applied to these four flavouring substances until adequate *in vivo* genotoxicity data become available. Additionally, the Panel noted the presence of a terminal conjugated double bond in the substances 2,4-dimethyl-5-vinylthiazole [FL-no: 15.005] and 4-methyl-5-vinylthiazole [FL-no: 15.018], which raised concern for genotoxicity. The Panel concluded, contrary to the JECFA, that the Procedure should not be applied to these two substances either until genotoxicity data become available.

For the three substances [FL-no: 15.014, 15.015 and 16.027], expected to be metabolised to innocuous products (A-side), the Panel agrees with the JECFA-evaluation.

For 17 of the remaining 20 substances the Panel agreed with the JECFA that they cannot be expected to be metabolised to innocuous products. The 17 substances were allocated to one of the 10 structural subgroups identified in FGE.21 (for description and explanation, see FGE.21). Taking these substances through the Procedure, it can be estimated that the intakes (MSDI) are below the thresholds for their structural classes II and III, and as the JECFA concluded that adequate NOAELs provides a sufficient safety margin, these substances were concluded at step B4 in the Procedure to be of no safety concern by the JECFA. For 15 of these 17 substances, from the structural subgroups A-Ic (thiophenes with thiol-containing ring substituents [FL-no: 15.001 and 15.008]) and A-II (thiazoles [FL-no: 15.002, 15.011, 15.013, 15.017, 15.019, 15.020, 15.021, 15.022, 15.026, 15.027, 15.033 and 15.035]), as summarized in Table 3.1, including benzothiazole [FL-no: 15.016] which is not supported by the substances in FGE.21, the Panel agrees with the JECFA conclusion that these substances are not expected to be of safety concern when used as flavouring substances. For the remaining two of the 17 substances, both from the structural subgroup B-IV (dithiazines [FL-no: 15.109 and 15.113]), the Panel concluded at step B4 in line with its previous evaluation of this subgroup in FGE.21 that there are no adequate NOAEL available to provide sufficient margins of safety from their use as flavouring substances and that additional toxicity data are needed.

However, for eight substances [FL-no: 15.002, 15.005, 15.008, 15.027, 15.029, 15.030, 15.109 and 15.113] no European production figures were available and consequently no European exposure estimates could be calculated. Accordingly, the safety in use in Europe could not be assessed using the Procedure for these eight substances."

3.1.17.1. EFSA considerations based on new information on production volumes

Based on the newly submitted EU production volumes for three of the eight JECFA-evaluated substances [FL-no: 15.002, 15.008 and 15.027], for which EU production volumes were missing, the MSDIs range from 0.012 to 0.061 microgram/*capita*/day, which are all below the threshold for their respective structural class II and III. For the remaining five substances no production volume has been submitted.

All three substances were evaluated via the B-side of the Procedure.

For the substance 2-methyl-5-methoxythiazole [FL-no: 15.002], an NOAEL of 8.6 mg/kg bw/day was identified from a 90-day toxicity study (Posternak et al., 1975). Comparison of the exposure estimate (MSDI) of 0.012 microgram/*capital*/day for Europe with this NOAEL provides an adequate margin of safety of 4.3×10^7.

For the substance 2-thienyl disulphide [FL-no: 15.008], an NOAEL of 0.29 mg/kg bw/day was identified from a 90-day toxicity study (Morgareidge and Oser, 1970g). Comparison of the exposure estimate (MSDI) of 0.061 microgram/*capital*/day for Europe with this NOAEL provides an adequate margin of safety of 2.9×10^5.

For the substance 2-propionylthiazole [FL-no: 15.027], no NOAEL was available for the substance itself, but a NOAEL of 50 mg/kg bw/day was identified from a 90-day toxicity study with the structurally related substance 2-acetylthiazole [FL-no: 15.020] (Wheldon et al., 1970). Comparison of the exposure estimate (MSDI) of 0.056 microgram/*capital*/day for Europe with this NOAEL provides an adequate margin of safety of 5.4×10^7.

Therefore the Panel concluded at step B4 of the Procedure that these three substances would be of no safety concern at their estimated levels of intake based on the MSDI approach.

3.1.18. FGE.77 Pyridine, pyrrole and quinoline derivatives (EFSA, 2009q)

http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902297025.htm

"The Panel agrees with the application of the Procedure as performed by the JECFA for five of the 22 substances. Methyl nicotinate [FL-no: 14.071], indole [FL-no: 14.007] and 3-methylindole [FL-no: 14.004] were evaluated on the A-side of the Procedure as they were anticipated to be metabolised to innocuous products. 1-Furfurylpyrrole [FL-no: 13.134] and 2-pyridine methanethiol [FL-no: 14.030] were the only two substances evaluated through the B-side of the Procedure as the substances were not anticipated to be metabolised to innocuous products by JECFA.

For 6-methylquinoline [FL-no: 14.042], the Panel concluded, in line with the conclusions for 2-methylquinoline, 4-methylquinoline and 4-butylquinoline in FGE.24Rev1 [FL-no: 14.138, 14.002, 14.094] (EFSA, 2008t), that this substance should not be evaluated using the Procedure until adequate *in vivo* genotoxicity data become available.

For the remaining 16 substances the Panel, in contrast to the JECFA, did not anticipate that they will be metabolised to innocuous products due to concern with respect to N-oxidation of pyridines and for the pyrroles concerns about N-oxidation and epoxidation and accordingly concluded that they should be evaluated along the B-side.

For pyrrole and the five pyrrole derivatives and for isoquinoline [FL-no: 14.041, 13.134, 14.045, 14.046, 14.047, 14.068 and 14.001] NOAELs could not be derived as such or for structurally related substances. Accordingly, additional toxicological data are required for these seven substances (step B4).

For 10 substances [FL-no: 14.038, 14.039, 14.058, 14.059, 14.060, 14.061, 14.065, 14.066, 14.072 and 14.164] NOAELs could be derived to provide adequate margins of safety to the estimated level of intakes as flavouring substance (step B4).

A 90-day oral feeding study in rats is available for 2-acetylpyridine [FL-no: 14.038]. The NOAEL derived is 37 mg/kg bw/day (Til and van der Meulen, 1971). The MSDI values for the 10 pyridine derivatives in this FGE are between 0.06 and 50 microgram/*capita*/day. The combined estimated daily per *capita* intake of the 10 pyridine derivatives evaluated through the B-side is 57 microgram corresponding to 0.95 microgram/kg bw/day. Thus, a margin of safety of approximately 39000 can be calculated using the NOAEL of 37 mg/kg bw/day. The 10 pyridine derivatives in this flavouring group evaluated through the B-side are accordingly not expected to be of safety concern at the estimated levels of intake.

However, for four substances [FL-no: 14.045, 14.058, 14.059 and 14.164] no European production figures were available for use as flavouring substances and consequently no European exposure estimates could be calculated. Accordingly, the safety in use in Europe could not be assessed using the Procedure for these four substances."

3.1.18.1. EFSA considerations based on new information on production volumes

Based on the newly submitted EU production volumes the four JECFA-evaluated substances [FL-no: 14.045, 14.058, 14.059 and 14.164], for which EU production volumes were missing, the MSDIs range from 0.0061 to 0.61 microgram/*capita*/day, which are all below the threshold for their respective structural class II and III.

For three of the four substances, which were evaluated via the B-side of the Procedure, an adequate margin of safety could be calculated using the NOAEL of 37 mg/kg bw/day from the structurally related substance 2-acetylpyridine [FL-no: 14.038] (Til and van der Meulen, 1971). Comparison of the exposure estimates (MSDIs) for these three substances with this NOAEL provides adequate margins of safety ranging from 3.6×10^6 to 3.6×10^8.

For [FL-no: 14.045] a NOAEL could not be derived as such or for structurally related substances. Accordingly, additional toxicological data are required for this substance.

Therefore the Panel concluded that [FL-no: 14.058, 14.059 and 14.164] would be of no safety concern at step B4 of the Procedure at their estimated levels of intake based on the MSDI approach but for [FL-no: 14.045] additional toxicological data are required.

3.1.19. FGE.79 Amino acids and related substances (EFSA, 2008bm)

http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902181544.htm

"The Panel agrees with the evaluation as performed by the JECFA for the 19 substances in the group of amino acids and related substances.

The Panel noted that amino acids may react with other food constituents upon heating. The reaction mixtures formed are commonly referred to as "process flavours" which have not been evaluated by the Panel. The present evaluation is therefore on the basis that the present flavouring substances are in an unchanged form when they are consumed, thus in food that is not intended to be heated.

However, for five substances [FL-no: 16.056, 17.001, 17.003, 17.015 and 17.026] no European production figures were available for use as flavouring substances and consequently no European exposure estimates could be calculated. Accordingly, the safety in use in Europe could not be assessed using the Procedure for these five substances."

3.1.19.1. EFSA considerations based on new information on production volumes

Based on the newly submitted EU production volumes for the five JECFA-evaluated substances [FL-no: 16.056, 17.001, 17.003, 17.015 and 17.026], for which EU production volumes were missing, the estimated MSDIs range from 350 to 1000 microgram/*capita*/day.

For two of these substances [FL-no: 17.001 and 16.056], from structural class I and evaluated via the A-side of the Procedure, the EU MSDI is below the threshold of concern for the structural class I. Therefore, these substances would not be expected to be of safety concern at step A3 of the Procedure when used as flavouring substances.

For the substances [FL-no: 17.015], in addition to the newly submitted data on use, the Panel considered additional information of metabolism. From this information, the Panel can no longer agree with JECFA with respect to the way this substance was evaluated through the Procedure by JECFA. For [FL-no: 17.015] two metabolic options have been described in literature. It can act as a methyl donor in the formation of methionine from homocysteine, catalyzed by the enzyme betaine homocysteine methyltransferase, in which process ultimately two methionine molecules are formed. In the other metabolic route the substance is hydrolytically cleaved to yield dimethyl sulphide and

homoserine (Gessler et al., 1991). Since dimethyl sulphide was evaluated by the JECFA via the B-side of the Procedure (JECFA, 2000b) and since dimethyl sulphide [FL-no: 12.006] is a structural analogue of a number of substances evaluated in FGE.08 via the B-side of the Procedure, it would be consistent to evaluate [FL-no: 17.015] also via the B-side, rather than via the A-side. The methionine or homoserine formed in the metabolic processes mentioned above are endogenous substances which are important intermediates in protein and amino acid metabolism and not of toxicological concern, similar to other amino acids (Voet and Voet, 2004; Karlsson, 1963). The dimethyl sulphide could theoretically be formed to a maximum level of 1.8 μg/kg bw, if [FL-no: 17.015] were ingested at the level of its MSDI (350 μg *per capita* per day), assuming complete hydrolysis and no demethylation by methyl transferase. If the dimethyl sulphide thus formed is evaluated through the Procedure at step B4, this exposure estimate could be compared to a NOAEL of 250 mg/kg bw/day obtained in a 90-day study in rats (Butterworth et al., 1975b). From this comparison an adequate Margin of Safety of 1.4×10^5 can be calculated. Based on these considerations, the use of [FL-no: 17.015] as a flavouring substance is not of safety concern at the estimated level of exposure.

The two substances [FL-no: 17.003 and 17.026] are macronutrients and normal components of proteins. The human exposure through food is orders of magnitude higher than the anticipated level of exposure from their use as a flavouring substances. These two substances will not be evaluated using the Procedure. The Panel concluded that these two substances would not be of safety concern at the estimated level of exposure.

3.1.20. FGE.80Rev1 Alicyclic, alicyclic-fused and aromatic-fused ring lactones (EFSA, 2009au)

http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902878576.htm

"The Panel agrees with the way the application of the Procedure has been performed by the JECFA for all 13 substances in the group of alicyclic, alicyclic-fused and aromatic-fused ring lactones.

However, for six of these 13 substances [FL-no: 10.050, 10.061, 10.069, 10.070, 10.072 and 13.161] no European production figure was available and consequently no European exposure estimate could be calculated. Accordingly, the safety in use in Europe could not be assessed using the Procedure for these substances."

3.1.20.1. EFSA considerations based on new information on production volumes

Based on the newly submitted EU production volumes for the six JECFA-evaluated substances [FL-no: 10.050, 10.061, 10.069, 10.070, 10.072 and 13.161] the MSDIs range from 0.84 to 100 microgram/*capita*/day, which are below the threshold for their respective structural class I and III.

For five substances [FL-no: 10.050, 10.061, 10.069, 10.070 and 13.161], the Panel concluded at step A3 that these substances would be of no safety concern at their estimated level of intake based on the MSDI approach.

Candidate substance [FL-no: 10.072] was evaluated via the B-side of the Procedure and as no NOAEL for the substance itself could be found, its assessment should rely on the NOAEL of 5.42 mg/kg bw/day for the structurally related substance 3-propylidenephthalide [FL-no: 10.005] as derived in a 90-day study by Posternak et al. (Posternak et al., 1969). Based on this NOAEL and the estimated exposure (MSDI) for Europe, of 0.84 microgram/*capita*/day, an adequate margin of safety of 3.9×10^5 can be calculated. Therefore the Panel concluded that this substance would be of no safety concern at the estimated level of intake based on the MSDI approach.

3.1.21. FGE.83Rev1 Ethyl maltol and two 6-keto-1,4-dioxane derivatives (EFSA, 2010b)

http://www.efsa.europa.eu/en/scdocs/scdoc/1409.htm

"The Panel agrees with the way the application of the Procedure has been performed by the JECFA for the three substances in the group of ethyl maltol and 5- or 6-keto-1,4-dioxane derivatives.

However, for the two substances [FL-no: 13.027 and 13.028] no European production figures were available and consequently no European exposure estimates could be calculated. Accordingly, the safety in use in Europe could not be assessed using the Procedure for the substances."

3.1.21.1. EFSA considerations based on new information on production volumes

Based on the newly submitted EU production volumes for the two JECFA-evaluated substances [FL-no: 13.027 and 13.028] the MSDIs are 0.12 to 0.43 microgram/*capita*/day, respectively, which are below the threshold for a structural class III substance.

For the two substances the Panel concluded at step A3 that these substances would be of no safety concern at their estimated levels of intake based on the MSDI approach.

3.1.22. FGE.84 Anthranilate derivatives (EFSA, 2008ao)

http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902168053.htm

"The Panel agrees with the application of the Procedure as performed by the JECFA for 17 of the 18 substances in the group of anthranilate derivatives.

For methyl anthranilate [FL-no: 09.715] the estimated daily exposure for Europe from its use as a flavouring substance is 686 microgram per person, which is below the threshold of 1800 microgram per person for class I substances. Therefore, the evaluation of methyl anthranilate as a flavouring substance in Europe could be concluded to be of no safety concern already at step A3 of the Procedure scheme, while the JECFA concluded "no safety concern" for this substance at step A5 (based on the US MSDI of 3764 microgram/person/day).

However, for three substances [FL-no: 09.561, 09.722 and 09.801] no European production figures were available and consequently no European exposure estimates could be calculated. Accordingly, the safety in use in Europe could not be assessed using the Procedure for these three substances.

The Panel considered further the possible consequences of nitrosation after ingestion of the secondary and tertiary amine and secondary amide candidate substances according to the approach described in the Annex to the minutes of the 30th AFC Panel meeting, May 2008 (EFSA, 2008e). From these considerations, the Panel concluded that extremely large margins of exposure could be calculated (>> 10^9) for nitrosated products possibly formed from amines used as flavouring substances in foods. Such large margins of exposure indicate that a risk of carcinogenicity resulting from such possible nitrosation products is virtually absent.

The Panel also notes that this conclusion is not applicable for foods preserved with nitrites, because for such foods the conditions for nitrosation, either in the foods themselves or after consumption in the stomach, may differ substantially from the worst-case conditions on which the calculations in the above mentioned Annex were based."

3.1.22.1. EFSA considerations based on new information on production volumes

Based on the newly submitted EU production volumes for the three JECFA-evaluated substances [FL-no: 09.561, 09.722 and 09.801] the MSDIs range from 0.0073 to 1.3 microgram/*capita*/day, which are below the threshold for their structural class.

For all three substances the Panel concluded at step A3 that these substances would be of no safety concern at their estimated levels of intake based on the MSDI approach.

3.1.23. FGE.85 Miscellaneous nitrogen containing flavouring substances (EFSA, 2008af)

http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902092610.htm

"The Panel agrees with the application of the Procedure as performed by the JECFA for the 16 substances in the group of miscellaneous nitrogen-containing substances.

However, for three substances [FL-no: 14.014, 14.029 and 14.070] no European production figures were available and consequently no European exposure estimates could be calculated. Accordingly, the safety in use could not be assessed using the Procedure for these three substances."

3.1.23.1. EFSA considerations based on new information on production volumes

Based on the newly submitted EU production volumes for the three JECFA-evaluated substances [FL-no: 14.014, 14.029 and 14.070] the MSDIs range from 0.011 to 0.17 microgram/*capita*/day, which are below the threshold for their respective structural class.

All three substances were evaluated via the B-side of the Procedure.

For the substance 5,7-dihydro-2-methylthieno(3,4-d)pyrimidine [FL-no: 14.014], an NOAEL of 6.6 mg/kg bw/day was identified from a 90-day toxicity study (Shellenberger, 1970g); as cited by the JECFA (JECFA, 2006d). Comparison of the exposure estimate (MSDI) of 0.012 microgram/*capital*/day for Europe with this NOAEL provides an adequate margin of safety of 3.3×10^7.

For the substance 1-phenyl-(3- or 5)-propylpyrazole [FL-no: 14.029], an NOAEL of 25 mg/kg bw/day was identified from a 90-day toxicity study (Posternak et al., 1969). Comparison of the exposure estimate (MSDI) of 0.17 microgram/*capital*/day for Europe with this NOAEL provides an adequate margin of safety of 8.8×10^6.

For the substance 4-acetyl-2-methylpyrimidine [FL-no: 14.070] an NOAEL of 1 mg/kg bw/day was identified from a 90-day toxicity study (Peano, 1981); as cited by JECFA (JECFA, 2006d). Comparison of the exposure estimate (MSDI) of 0.011 microgram/*capital*/day for Europe with this NOAEL provides an adequate margin of safety of 5.5×10^6.

Therefore the Panel concluded at step B4 of the Procedure that these three substances would be of no safety concern at their estimated levels of intake based on the MSDI approach.

3.1.24. FGE.87 Bicyclic secondary alcohols, ketones and related esters (EFSA, 2008az)

http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902222183.htm

"The Panel agrees with the application of the Procedure as performed by the JECFA for the 15 bicyclic secondary alcohols, ketones and related esters. However, for two substances [FL-no: 09.153 and 09.319] no European production figures were available and consequently no European exposure estimates could be calculated. Accordingly, the safety in use could not be assessed using the Procedure for these two substances."

3.1.24.1. EFSA considerations based on new information on production volumes

Based on the newly submitted EU production volumes for the two JECFA-evaluated substances [FL-no: 09.153 and 09.319] the MSDIs are 3.7 and 6.1 microgram/*capita*/day, which are below the threshold for a structural class I substance.

For the two substances the Panel concluded at step A3 that these substances would be of no safety concern at their estimated level of intake based on the MSDI approach.

4. Conclusion

The present FGE.96 concerns 88 JECFA-evaluated substances from different groups. These groups have been previously considered by EFSA in FGE.51, 52, 53, 54, 56, 58, 61, 62, 63, 64, 68, 69, 70, 71, 73, 76, 77, 79, 80, 83, 84, 85 and 87. Common for all the 88 substances was that for none of them European production volumes were available at the time for the first consideration in the above-mentioned FGEs. As a consequence, no MSDI could be calculated for EU and accordingly the substances could not be considered by EFSA using the Procedure.

By February/April 2010 Industry provided production volumes for these substances. For 27 of the substances the provided production figure origins from the EFFA European survey conducted in 2004 and for 55 of the provided production volumes, the figure is anticipated (EFFA, 2010c). For the remaining six substances it has not been stated if the figures are from an European survey or anticipated production volumes (see Table 1.1). Based on these newly provided (anticipated) production figures, MSDI values for EU have been calculated (see Table 1.1 and Table 2), and based on these MSDI values the substances have been re-considered by EFSA in the current FGE.96. For the flavouring substances for which the production volumes are anticipated figures, the present evaluation will have to be reconsidered when actual production volumes become available.

In the FGEs mentioned above, genotoxicity of the substances considered in FGE.96 has already been addressed. For none of the substances a concern for genotoxicity was identified.

Seventy-one of the 88 substances were considered to be of no concern at step A3 of the Procedure and 12 substances were considered to be of no concern at step B4. Four substances were not evaluated through the Procedure. Two of these four are macronutrients [FL-no: 17.003 and 17.026] for which the Procedure is not applicable, and one [FL-no: 08.004] is a very common constituent of food, for which an ADI ”non-specified” has been derived in the past. For the fourth substance (sorbic acid [FL-no: 08.085]), an ADI has been derived. Based on the estimated exposure on the basis of the MSDI approach the Panel concluded no safety concern for these four substances. For the remaining substance, 2-acetyl-1-ethylpyrrole [FL-no: 14.045], the Panel could not identify an appropriate NOAEL and accordingly additional data are required.

For five substances [FL-no: 14.045, 14.058, 14.059, 14.164 and 17.015] the Panel concluded that these should be evaluated via the B-side of the Procedure, where JECFA evaluated these substances via the A-side. However, based on the data available, the Panel concluded that four substances were not of safety concern at step B4 of the Procedure. For the remaining substance, 2-acetyl-1-ethylpyrrole [FL-no: 14.045], as mentioned above, the Panel could not identify an appropriate NOAEL and accordingly additional data are required. For three substances [FL-no: 09.552, 09.555 and 09.557] the Panel concluded at step A3 (where the JECFA concluded at step A4) as the EU MSDI were below the threshold of concern for the structural class.

In order to determine whether the conclusion for the 88 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 tests are available for 79 of the JECFA-evaluated substances. For [FL-no: 15.008], the solubility in water is missing. Otherwise the specifications for this substance are appropriate. For eight stereoisomeric substances [FL-no: 06.040, 08.073, 09.371, 09.780, 10.050, 16.039, 13.060 and 13.161], the stereoisomeric composition has to be specified further.

Thus, for 79 of the 88 substances, the Panel concluded that they would be of no safety concern when used at their estimated levels of intake as flavouring substances based on the MSDI approach. For eight of the remaining nine substances, additional data on stereochemical composition are required to finalise their evaluation as material of commerce. For [FL-no: 14.045] additional toxicity data are required to finalise the evaluation.

The Panel noted that amino acids [FL-no: 16.056, 17.001, 17.003, 17.015 and 17.026] may react with other food constituents upon heating. The reaction mixtures formed are commonly referred to as “process flavours” which have not been evaluated by the Panel. The present evaluation is therefore on the basis that the present flavouring substances are in an unchanged form when they are consumed, thus in food that is not intended to be heated.

TABLE 1: SPECIFICATION SUMMARY

Table 1: specifications summary for the JECFA-evaluated substances in the present group

Table 1: Specification Summary of the Substances in the present group

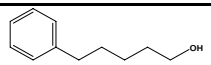
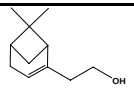
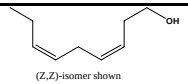
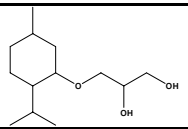
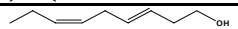
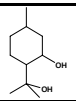
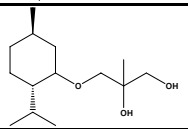
FL-no JECFA-no	EU Register name	Structural formula	FEMA no CoE no CAS no	Phys.form Mol.formula Mol.weight	Solubility 1) Solubility in ethanol 2)	Boiling point, °C 3) Melting point, °C ID test Assay minimum	Refrac. Index 4) Spec.gravity 5)	EFSA comments
02.051 675	5-Phenylpentan-1-ol		3618 674 10521-91-2	Liquid $C_{11}H_{16}O$ 164.25	Insoluble Miscible	155 (26 hPa) IR 98 %	1.514-1.521 0.970-0.977	
02.141 986	2-(6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl)ethan-1-ol		3938 128-50-7	Liquid $C_{11}H_{18}O$ 166.26	Insoluble Miscible	230 IR NMR 95 %	1.490-1.500 0.965-0.973	Racemate (EFFA, 2010a).
02.189 1283	Nona-3,6-dien-1-ol	 (Z,Z)-isomer shown	3885 10289 76649-25-7	Liquid $C_9H_{16}O$ 140.23	Slightly soluble Soluble	70 (3 hPa) IR NMR 97 %	1.462-1.469 0.863-0.871	CASrn in Register does not specify stereoisomeric composition. According to JECFA: Min. Assay value is "97 % Z,Z , 1 % E,Z isomer; 1 % Z,E isomer; 0.5 % E,E isomer". Register name to be changed to (Z,Z)-3,6-nonadien-1-ol.
02.224 1408	3-(1-Menthoxy)propane-1,2-diol		3784 87061-04-9	Liquid $C_{13}H_{26}O_3$ 230.35	Very slightly soluble Soluble	121-125(0.3hPa) NMR 99 %	1.472-1.476 0.989-0.999	Racemate.
02.243 1284	(E,Z)-3,6-Nonadien-1-ol		3884 56805-23-3	Liquid $C_9H_{16}O$ 140.23	Slightly soluble Soluble	73 (20 hPa) IR NMR 92 %	1.462-1.469 0.863-0.871	According to JECFA: Min. assay value is "92 %" and secondary component "(E,E)-3,6-nonadien-1-ol".
02.246 1416	p-Menthane-3,8-diol		4053 42822-86-6	Solid $C_{10}H_{20}O_2$ 172.27	Slightly soluble Soluble	105 (0.05 hPa) 34.5 IR 99 %	0.976-0.982	Racemate.
02.254 1411	3-Menthoxy-2-methylpropane-1,2-diol		3849 195863-84-4	Liquid $C_{14}H_{28}O_5$ 244.36	Slightly soluble Soluble	124 (0.53 hPa) NMR 99%	1.468-1.474 0.978-0.984	CASrn in Register refers to the (1R, 2S, 5S) isomer. Register name to be changed to (1R,2S,5S)-3-Menthoxy-

Table 1: Specification Summary of the Substances in the present group

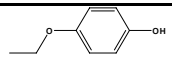
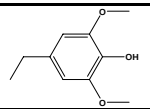
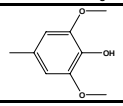
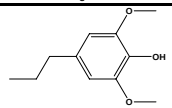
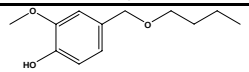
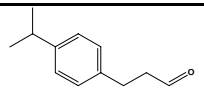
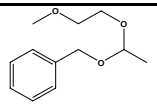
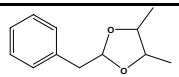
FL-no JECFA-no	EU Register name	Structural formula	FEMA no CoE no CAS no	Phys.form Mol.formula Mol.weight	Solubility 1) Solubility in ethanol 2)	Boiling point, °C 3) Melting point, °C ID test Assay minimum	Refrac. Index 4) Spec.gravity 5)	EFSA comments
								2-methylpropane-1,2-diol.
04.037 720	4-Ethoxyphenol		3695 2258 622-62-8	Solid $C_8H_{10}O_2$ 138.17	Slightly soluble Moderately soluble	246-247 64 IR 95 %	n.a. n.a.	According to JECFA: Melting point is "64° (minimum)".
04.052 723	4-Ethyl-2,6-dimethoxyphenol		3671 11231 14059-92-8	Liquid $C_{10}H_{14}O_3$ 182.22	Insoluble Miscible	106 (0.3 hPa) MS 98 %	1.536-1.537 1.075-1.080	
04.053 722	4-Methyl-2,6-dimethoxyphenol		3704 6638-05-7	Solid $C_9H_{12}O_3$ 168.19	Insoluble Moderately soluble	145-146 (16hPa) 37-42 IR 97 %	n.a. n.a.	
04.056 724	2,6-Dimethoxy-4-propylphenol		3729 6766-82-1	Liquid $C_{11}H_{16}O_3$ 196.25	Insoluble Miscible	115 (0.5 hPa) IR NMR 98 %	1.529-1.530 1.071-1.076	
04.093 888	Butyl vanillyl ether		3796 82654-98-6	Liquid $C_{12}H_{18}O_3$ 210.27	Insoluble Miscible	241 IR 95 %	1.511-1.521 1.048-1.068	
05.094 680	3-(4-Isopropylphenyl)propionaldehyde		2957 2261 7775-00-0	Liquid $C_{12}H_{16}O$ 176.26	Insoluble Miscible	270 MS 90 %	1.503-1.508 0.946-0.952	Minimum 95 % combined o- and p-isomers (EFFA, 2010a).
06.019 840	1-Benzyloxy-1-(2-methoxyethoxy)ethane		2148 523 7492-39-9	Liquid $C_{12}H_{18}O_3$ 210.27	Insoluble Miscible	161-162 (13hPa) IR 98 %	1.479-1.489 1.019-1.025	Racemate. Min. assay value: 98 % (sum of parent compound and starting materials). The “starting materials” are methoxyethanol, acetaldehyde and benzyl alcohol which make up less than 10 % combined of the mixture under anhydrous conditions (EFFA, 2010a).
06.027 1005	4,5-Dimethyl-2-benzyl-1,3-dioxolan		2875 669 5468-06-4	Liquid $C_{12}H_{16}O_2$ 192.26	Insoluble Miscible	118 (13 hPa) NMR 93 %	1.496-1.512 1.030-1.040	Racemate. Secondary component: butane-2,3-diol (2-3 %) (EFFA, 2010a).

Table 1: Specification Summary of the Substances in the present group

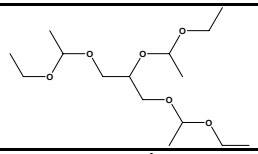
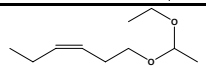
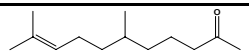
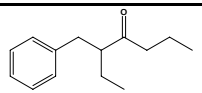
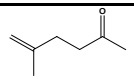
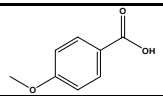
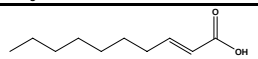
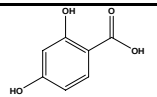
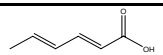
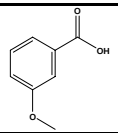
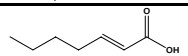
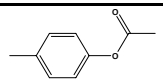
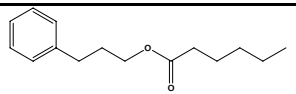
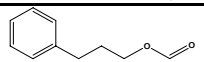
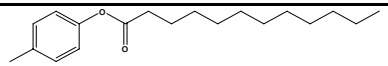
FL-no JECFA-no	EU Register name	Structural formula	FEMA no CoE no CAS no	Phys.form Mol.formula Mol.weight	Solubility 1) Solubility in ethanol 2)	Boiling point, °C 3) Melting point, °C ID test Assay minimum	Refrac. Index 4) Spec.gravity 5)	EFSA comments
06.040 913	1,2,3-Tris([1'-ethoxy]-ethoxy)propane 6)		3593 11930 67715-82-6	Liquid $C_{15}H_{32}O_6$ 308.42	Insoluble Miscible	117 (1.3 hPa) NMR 97.5 %	1.419-1.425 0.952-0.958	
06.081 943	1-Ethoxy-1-(3-hexenyloxy)ethane		3775 10034 28069-74-1	Liquid $C_{10}H_{20}O_2$ 172.27	Insoluble Miscible	85 (9 hPa) IR 97 %	1.430-1.435 0.846-0.856	Register name to be changed to 1-Ethoxy-1-(3Z-hexenyloxy)ethane. Racemate of 1-Ethoxy-1-(3Z-hexenyloxy)ethane (EFFA, 2010a).
07.069 1121	Tetrahydro-pseudo-ionone		3059 2053 4433-36-7	Liquid $C_{13}H_{24}O$ 196.33	Insoluble Miscible	234 NMR 95 %	1.449-1.455 0.865-0.875	Racemate (EFFA, 2010a).
07.070 830	3-Benzylheptan-4-one		2146 2140 7492-37-7	Liquid $C_{14}H_{20}O$ 204.31	Insoluble Miscible	158-160 (13hPa) IR 99 %	1.490-1.495 0.931-0.937	Racemate (EFFA, 2010a).
07.100 1119	5-Methylhex-5-en-2-one		3365 11150 3240-09-3	Liquid $C_7H_{12}O$ 112.17	Insoluble Miscible	148-149 NMR 97 %	1.428-1.433 0.862-0.868	
08.004 930	Lactic acid		2611 4 598-82-3	Liquid $C_3H_6O_3$ 90.08	Miscible Miscible	122 (20 hPa) 17 IR 95 %	1.413-1.429 1.200-1.209	Racemate (EFFA, 2010a). According to JECFA: Min. Assay value is "95 by chemical analysis (acid/base titration)".
08.071 883	p-Anisic acid		3945 10077 100-09-4	Solid $C_8H_8O_3$ 152.15	Soluble Freely soluble	275-280 184 IR 98 %	n.a. n.a.	
08.073 1372	Dec-2-enoic acid	 (E)-isomer shown	3913 10087 3913-85-7	Liquid $C_{10}H_{18}O_2$ 170.25	n.a. Soluble	161-162 (20hPa) IR NMR MS 97 %	1.456-1.466 0.923-0.933	Mixture of (Z)- and (E)-isomers (EFFA, 2010a). Composition of stereoisomeric mixture to be specified.

Table 1: Specification Summary of the Substances in the present group

FL-no JECFA-no	EU Register name	Structural formula	FEMA no CoE no CAS no	Phys.form Mol.formula Mol.weight	Solubility 1) Solubility in ethanol 2)	Boiling point, °C 3) Melting point, °C ID test Assay minimum	Refrac. Index 4) Spec.gravity 5)	EFSA comments
08.076 908	2,4-Dihydroxybenzoic acid		3798 89-86-1	Solid $C_7H_6O_4$ 154.12	Soluble Soluble	n.a. 225 IR 97 %	n.a. n.a.	According to JECFA: Melting point is "225° (decomposes, rapid heating required)".
08.085 1176	Hexa-2,4-dienoic acid		3921 110-44-1	Solid $C_6H_8O_2$ 112.13	Slightly soluble Soluble	n.a. 132-135 IR NMR 99 %	n.a. n.a.	JECFA evaluated (E,E)-2,4-hexadienoic acid (CASrn as in Register). CASrn in Register refers to the (E,E)-isomer. Register name to be changed to (E,E)-hexa-2,4-dienoic acid.
08.092 882	3-Methoxybenzoic acid		3944 586-38-9	Solid $C_8H_8O_3$ 152.15	Soluble Freely soluble	170-172 107-109 IR 98 %	n.a. n.a.	
08.123 1373	trans-2-Heptenoic acid		3920 10352-88-2	Liquid $C_7H_{12}O_2$ 128.18	n.a. Soluble	224-228 IR NMR MS 97 %	1.447-1.157 0.968-0.978	CASrn in Register refers to (E)-isomer.
09.036 699	p-Tolyl acetate		3073 226 140-39-6	Liquid $C_9H_{10}O_2$ 150.18	Slightly soluble Miscible	208-212 IR 98 %	1.499-1.503 1.044-1.052	
09.071 642	3-Phenylpropyl hexanoate		2896 321 6281-40-9	Liquid $C_{15}H_{22}O_2$ 234.34	Insoluble Miscible	292 IR 99 %	1.482-1.488 0.947-0.960	
09.084 637	3-Phenylpropyl formate		2895 351 104-64-3	Liquid $C_{10}H_{12}O_2$ 164.20	Insoluble Miscible	238 MS 97 %	1.494-1.499 1.012-1.019	
09.102 704	p-Tolyl dodecanoate		3076 378 10024-57-4	Liquid $C_{19}H_{30}O_2$ 290.45	Insoluble	208-210 (13hPa) NMR 90 %	1.494-1.500 0.946-0.952	Mixture of p-tolyl dodecanoate (min. 90 %), p-tolyl tetradecanoate (3-6 %), p-tolyl decanoate (2-5 %), p-tolyl hexadecanoate(1-2 %) (EFFA, 2010a).

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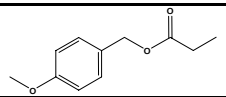
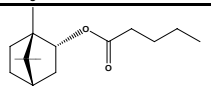
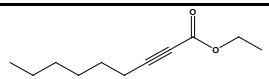
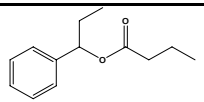
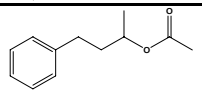
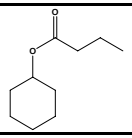
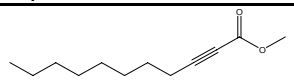
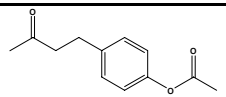
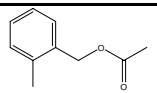
FL-no JECFA-no	EU Register name	Structural formula	FEMA no CoE no CAS no	Phys.form Mol.formula Mol.weight	Solubility 1) Solubility in ethanol 2)	Boiling point, °C 3) Melting point, °C ID test Assay minimum	Refrac. Index 4) Spec.gravity 5)	EFSA comments
09.145 874	p-Anisyl propionate		2102 426 7549-33-9	Liquid $C_{11}H_{14}O_3$ 194.23	Insoluble Miscible	100-103(0.7hPa) IR 97 %	1.505-1.510 1.070-1.086	
09.153 1392	Bornyl valerate		2164 471 7549-41-9	Liquid $C_{15}H_{26}O_2$ 238.37	Insoluble Soluble	136-137 (16hPa) NMR 96 %	1.459-1.465 0.957-0.963	Racemate (±) = DL-bornyl valerate (EFFA, 2010a). CASrn in Register refers to (1R,2S,4R)-stereoisomer. Register CASrn to be changed.
09.157 1352	Ethyl 2-nonynoate		2448 480 10031-92-2	Liquid $C_{11}H_{18}O_2$ 182.26	Insoluble Soluble	226-227 NMR 96 %	1.450-1.456 0.901-0.907	
09.189 823	1-Phenylpropyl butyrate		2424 628 10031-86-4	Liquid $C_{13}H_{18}O_2$ 206.28	Insoluble Miscible	282 IR 97 %	1.486-1.491 0.986-0.992	Racemate (EFFA, 2010a).
09.200 816	1-Methyl-3-phenylpropyl acetate		2882 671 10415-88-0	Liquid $C_{12}H_{16}O_2$ 192.26	Insoluble Miscible	72-74 (0.7 hPa) NMR MS 98 %	1.498-1.505 0.975-0.980	Racemate.
09.230 1094	Cyclohexyl butyrate		2351 2082 1551-44-6	Liquid $C_{10}H_{18}O_2$ 170.25	Practically insoluble Miscible	212 NMR 98 %	1.439-1.451 0.953-0.959	
09.239 1358	Methyl 2-undecynoate		2751 2111 10522-18-6	Liquid $C_{12}H_{20}O_2$ 196.29	Insoluble Soluble	230 NMR 97 %	1.443-1.449 0.915-0.921 (20°)	
09.288 731	4-(4-Acetoxyphenyl)butan-2-one		3652 3572-06-3	Liquid $C_{12}H_{14}O_3$ 206.24	Insoluble Miscible	155 (3 hPa) IR 93 %	1.506-1.512 1.096-1.100	According to JECFA: Min. assay value is "93 (min. 95 % combined o- and p-isomers)" and "contains 2-5 % ortho isomer".
09.294 863	2-Methylbenzyl acetate		3702 17373-93-2	Liquid $C_{10}H_{12}O_2$ 164.20	Insoluble Miscible	215-222 IR 98 %	1.500-1.510 1.024-1.040	CAS-nr refers to: 2-methyl (= ortho-) isomer. Min. assay value is 98 % (sum of positional isomers: relative

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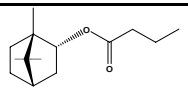
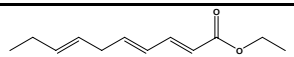
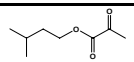
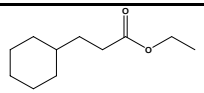
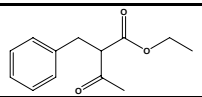
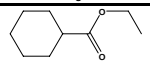
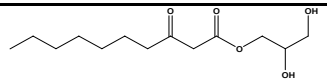
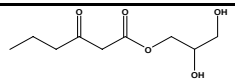
								ratio of o-, m- and p-isomers 31-33 % of each isomer, respectively) (EFFA, 2010a).
09.319 1412	Bornyl butyrate		3907 13109-70-1	Liquid $C_{14}H_{24}O_2$ 224.34	Slightly soluble Soluble	247 MS 97 %	1.462-1.469 0.981-0.991	CASrn in Register refers to (1R,2S,4R)-stereoisomer. Register name to be changed accordingly.
09.371 1193	Ethyl deca-2,4,7-trienoate		3832 10576 78417-28-4	Liquid $C_{12}H_{18}O_2$ 194.28	Soluble Soluble	134 (18 hPa) IR NMR 95 %	1.547-1.554 0.933-0.939	Mixture of (Z)- and (E)-isomer for all three C=C double bonds (EFFA, 2010a). CASrn in Register does not specify stereoisomeric composition. Composition of stereoisomeric mixture to be specified.
09.443 939	Isopentyl pyruvate		2083 431 7779-72-8	Liquid $C_8H_{14}O_3$ 158.20	Insoluble Miscible	185 IR 97 %	1.417-1.424 0.972-0.980	
09.488 966	Ethyl cyclohexanepropionate		2431 2095 10094-36-7	Liquid $C_{11}H_{20}O_2$ 184.28	Insoluble Miscible	91 (10 hPa) NMR 98 %	1.444-1.452 0.926-0.932	
09.501 835	Ethyl 2-acetyl-3-phenylpropionate		2416 2241 620-79-1	Liquid $C_{13}H_{16}O_3$ 220.27	Insoluble Miscible	276 IR 97 %	1.498-1.502 1.033-1.037	Racemate (EFFA, 2010a).
09.534 963	Ethyl cyclohexanecarboxylate		3544 11916 3289-28-9	Liquid $C_9H_{16}O_2$ 156.22	Insoluble Miscible	82 (16 hPa) IR NMR 99 %	1.447-1.454 0.966-0.978 (20°)	
09.552 914	3-Oxodecanoic acid glyceride		3767 10650 91052-69-6	Solid $C_{13}H_{24}O_5$ 260.33	Insoluble Slightly soluble	n.a. 57-60 NMR 95 %	n.a. n.a.	Racemate (EFFA, 2010a). According to JECFA: Min. Assay value is "95 by ester determination".
09.555 910	3-Oxohexanoic acid glyceride		3770 10653 91052-72-1	Solid $C_9H_{16}O_5$ 316.36	Insoluble Slightly soluble	n.a. 41-44 NMR 95 %	n.a. n.a.	Racemate (EFFA, 2010a). According to JECFA: Min. Assay value is "95 by ester

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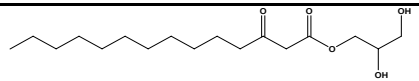
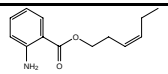
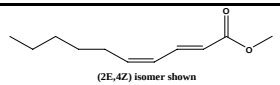
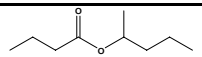
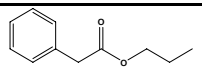
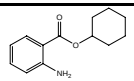
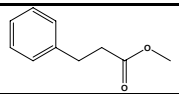
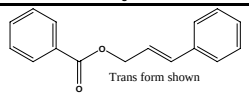
FL-no JECFA-no	EU Register name	Structural formula	FEMA no CoE no CAS no	Phys.form Mol.formula Mol.weight	Solubility 1) Solubility in ethanol 2)	Boiling point, °C 3) Melting point, °C ID test Assay minimum	Refrac. Index 4) Spec.gravity 5)	EFSA comments
								determination".
09.557 916	3-Oxotetradecanoic acid glyceride		3772 10655 91052-73-2	Solid $C_{17}H_{32}O_5$ 316.44	Insoluble n.a.	n.a. 73-75 NMR 95 %	n.a. n.a.	Racemate (EFFA, 2010a). According to JECFA: Min. Assay value is "95 by ester determination".
09.561 1538	Hex-3(cis)-enyl anthranilate		3925 10676 65405-76-7	Liquid $C_{13}H_{17}O_2N$ 219.29	Insoluble Soluble	160 (7 hPa) IR NMR 98 %	1.545-1.554 1.047-1.054	
09.639 1191	Methyl deca-2,4-dienoate	 (2E,4Z) isomer shown	3859 4493-42-9	Liquid $C_{11}H_{18}O_2$ 182.26	Insoluble Soluble	67 (1 hPa) IR NMR 93 5	1.488-1.494 0.917-0.923	CASrn refers to (2E, 4Z)-isomer. Material in commerce is min. 93 % pure (2E,4Z)-isomer. Min. Purity > 95 % (sum of isomers: other isomer mainly (2E,4E)-isomer (< 5 %))(EFFA, 2010a). Registed name to ge changed to Methyl (E,Z)-deca-2,4-dienoate.
09.658 1142	1-Methylbutyl butyrate		3893 10763 60415-61-4	Liquid $C_9H_{18}O_2$ 158.24	Insoluble 50% Soluble	185-186 IR NMR MS 99 %	1.409-1.415 0.862-0.868	Racemate (EFFA, 2010a).
09.702 1010	Propyl phenylacetate		2955 229 4606-15-9	Liquid $C_{11}H_{14}O_2$ 178.23	Insoluble Miscible	253 NMR 97 %	1.489-1.497 0.985-0.995 (15.5°)	
09.722 1541	Cyclohexyl anthranilate		2350 257 7779-16-0	Liquid $C_{13}H_{17}O_2N$ 219.29	Insoluble Soluble	318 NMR 97 %	1.571-1.577 1.015-1.021	
09.746 643	Methyl 3-phenylpropionate		2741 427 103-25-3	Liquid $C_{10}H_{12}O_2$ 164.20	Insoluble Miscible	238-239 IR 98 %	1.499-1.505 1.037-1.045	
09.780 760	Cinnamyl benzoate	 Trans form shown	4703 743 5320-75-2	Solid $C_{16}H_{14}O_2$ 238.29	Insoluble Miscible	335 31 IR 98 %	n.a. n.a.	Mixture of (Z)- and (E)-isomers (EFFA, 2010a). Composition of stereoisomeric mixture to be specified.

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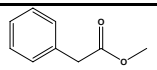
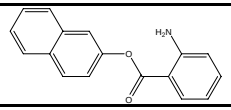
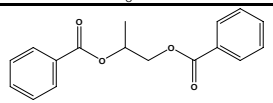
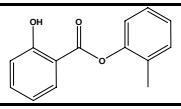
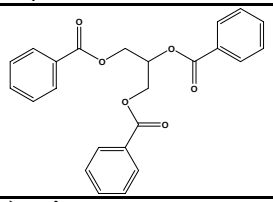
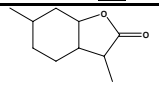
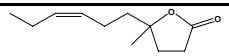
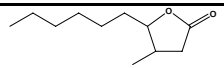
FL-no JECFA-no	EU Register name	Structural formula	FEMA no CoE no CAS no	Phys.form Mol.formula Mol.weight	Solubility 1) Solubility in ethanol 2)	Boiling point, °C 3) Melting point, °C ID test Assay minimum	Refrac. Index 4) Spec.gravity 5)	EFSA comments
09.783 1008	Methyl phenylacetate		2733 2155 101-41-7	Liquid $C_9H_{10}O_2$ 150.18	Insoluble 1 ml in 6 ml 60% ethanol	215 IR 97 %	1.504-1.510 1.061-1.067	
09.801 1544	2-Naphthyl anthranilate		2767 11862 63449-68-3	Liquid $C_{17}H_{13}O_2N$ 263.30	Insoluble Soluble	340 NMR 98 %	1.531-1.539 1.300-1.308	
09.803 862	Propylene glycol dibenzoate		3419 10890 19224-26-1	Liquid $C_{17}H_{16}O_4$ 284.31	Insoluble Miscible	232 (16 hPa) IR 96 %	1.542-1.547 1.157-1.163	Racemate.
09.807 907	o-Tolyl salicylate		3734 617-01-6	Solid $C_{14}H_{12}O_3$ 228.25	Insoluble Soluble	180 (3 hPa) 25 NMR 99 %	1.576-1.584 1.164-1.174	
09.812 861	Glyceryl tribenzoate		3398 10656 614-33-5	Solid $C_{24}H_{20}O_6$ 404.42	Insoluble Slightly soluble	n.a. 68-72 IR 95 %	n.a. n.a.	
10.050 1161	Hexahydro-3,6-dimethyl-2(3H)-benzofuranone		4032 92015-65-1	Liquid $C_{10}H_{16}O_2$ 168.24	Soluble Soluble	274-276 (17hPa) IR NMR 99.4 %	1.464-1.470 1.016-1.022 (20°)	Mixture of optical isomers (diastereoisomers) (EFFA, 2010a). CASrn in Register does not specify stereoisomeric composition. Composition of stereoisomeric mixture to be specified.
10.061 1159	cis-5-Hexenyldihydro-5-methylfuran-2(3H)-one		3937 70851-61-5	Liquid $C_{11}H_{18}O_2$ 182.26	Insoluble Soluble	150 (8 hPa) IR NMR 97 %	1.463-1.468 0.960-0.967	Racemate of (Z)-isomer (EFFFA, 2010a). CASrn in Register does not specify stereoisomeric composition.
10.069 1158	3-Methyl gamma-decalactone		3999 67663-01-8	Liquid $C_{11}H_{20}O_2$ 184.28	Insoluble Soluble	110-115 (5 hPa) NMR	1.446-1.452 0.938-0.944	Composition: cis-3-methyl-gamma-decalactone (40-54

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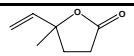
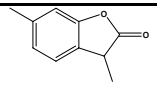
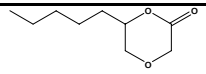
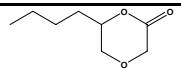
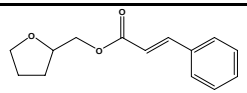
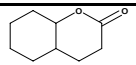
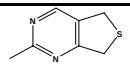
FL-no JECFA-no	EU Register name	Structural formula	FEMA no CoE no CAS no	Phys.form Mol.formula Mol.weight	Solubility 1) Solubility in ethanol 2)	Boiling point, °C 3) Melting point, °C ID test Assay minimum	Refrac. Index 4) Spec.gravity 5)	EFSA comments
						94 %		%), trans-3-methyl-gamma-decalactone (40-54 %) and Heptan-1-ol (1-2 %) (EFFA, 2010a).
10.070 1157	4-Methyl-5-hexen-1,4-olide		4051 1073-11-6	Liquid $C_7H_{10}O_2$ 126.15	Insoluble Soluble	219 IR NMR 97 %	1.457-1.462 1.015-1.025 (20°)	Racemate (EFFA, 2010a).
10.072 1167	Dimethyl-3,6-benzo-2(3H)-furanone		3863 65817-24-5	Liquid $C_{10}H_{10}O_2$ 162.19	Insoluble Soluble	64 (0.1 hPa) IR NMR 98 %	1.518-1.524 1.099-1.104	Racemate (EFFA, 2010a).
13.027 1485	2-Pentyl-5 or 6-keto-1,4-dioxane		2076 2205 65504-96-3	Liquid $C_9H_{16}O_3$ 172.22	Slightly soluble Soluble	101-103 (20hPa) NMR 97 %	1.480-1.486 1.288-1.294	Mixture of 5-pentyl- and 6-pentyl-1,4-dioxane-2-one 68 % 5- & 29 % 6-isomer (sum isomers > 95 %). Racemate (EFFA, 2010).
13.028 1484	2-Butyl-5 or 6-keto-1,4-dioxane		2204 2206 65504-45-2	Liquid $C_8H_{14}O_3$ 158.20	Slightly soluble Soluble	98-99 (17 hPa) NMR 97 %	1.472-1.478 1.292-1.296	Mixture of 5-butyl- and 6-butyl-1,4-dioxane-2-one: 65 % 5- and 32 % 6-isomer (sum isomers > 95%). Racemate (EFFA, 2010a). Change CASrn to 65504-95-2.
13.060 1447	Tetrahydrofurfuryl cinnamate		3320 11821 65505-25-1	Liquid $C_{14}H_{16}O_3$ 232.28	Insoluble Soluble	>300 NMR 95 %	1.593-1.600 1.107-1.113	Racemate of mixture of (Z)- and (E)-isomer (EFFA, 2010a). Composition of stereoisomeric mixture to be specified.
13.161 1166	Octahydrocoumarin		3791 4430-31-3	Liquid $C_9H_{14}O_2$ 154.21	Insoluble Soluble	293-298 NMR 99 %	1.489-1.493 1.090-1.096	Mixture of optical isomers (diastereoisomers) (EFFA, 2010a). Composition of stereoisomeric mixture to be specified.
14.014 1566	5,7-Dihydro-2-methylthieno(3,4-d)pyrimidine		3338 720 36267-71-7	Solid $C_7H_8N_2S$ 152.22	Very slightly soluble Soluble	 64 NMR 98 %	n.a. n.a.	

Table 1: Specification Summary of the Substances in the present group

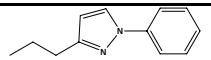
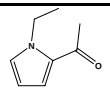
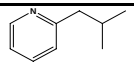
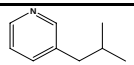
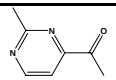
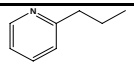
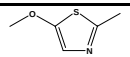
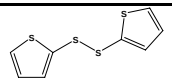
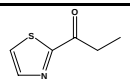
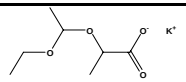
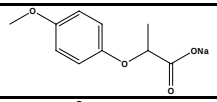
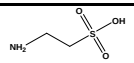
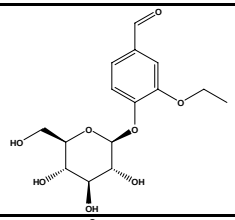
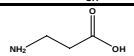
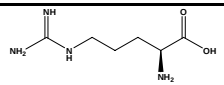
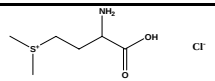
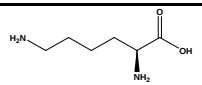
FL-no JECFA-no	EU Register name	Structural formula	FEMA no CoE no CAS no	Phys.form Mol.formula Mol.weight	Solubility 1) Solubility in ethanol 2)	Boiling point, °C 3) Melting point, °C ID test Assay minimum	Refrac. Index 4) Spec.gravity 5)	EFSA comments
14.029 1568	1-Phenyl-(3 or 5)-propylpyrazole	 1-Phenyl-3-propylpyrazole shown	3727 2277 65504-93-0	Liquid $C_{12}H_{14}O_2$ 190.24	Insoluble Soluble	182-193 NMR 96 %	1.428-1.436 1.078-1.081	CASrn in Register corresponds to an incompletely defined structure.
14.045 1305	2-Acetyl-1-ethylpyrrole		3147 11371 39741-41-8	Liquid $C_8H_{11}ON$ 137.18	Slightly soluble Soluble	209-211 NMR 98 %	1.550-1.556 1.052-1.058	Slightly soluble in water (EFSA, 2010a).
14.058 1311	2-Isobutylpyridine		3370 11395 6304-24-1	Liquid $C_9H_{13}N$ 135.21	Insoluble Soluble	181 NMR 97 %	1.480-1.486 0.894-0.900	
14.059 1312	3-Isobutylpyridine		3371 11396 14159-61-6	Liquid $C_9H_{13}N$ 135.21	Insoluble Soluble	68-68.5 (10hPa) NMR 97 %	1.488-1.494 0.898-0.904	
14.070 1565	4-Acetyl-2-methylpyrimidine		3654 67860-38-2	Liquid $C_7H_8ON_2$ 136.15	Slightly soluble Soluble	87-89 (13 hPa) NMR 99 %	1.501-1.507 1.096-1.102	
14.164 1322	2-Propylpyridine		 622-39-9	Liquid $C_8H_{11}N$ 121.20	Slightly soluble Soluble	169-171 NMR 98 %	1.490-1.496 0.907-0.917	
15.002 1057	2-Methyl-5-methoxythiazole		3192 736 38205-64-0	Liquid C_5H_7ONS 129.18	Insoluble Miscible	117 (44 hPa) MS 98 %	1.515-1.520 1.146-1.154	
15.008 1053	2-Thienyl disulfide		3323 2333 6911-51-9	Solid $C_8H_6S_4$ 230.39	Soluble	n.a. 55-60 NMR 98 %	n.a. n.a.	SW 7).
15.027 1042	2-Propionylthiazole		3611 43039-98-1	Liquid C_6H_7ONS 141.19	Insoluble Miscible	95 (1 hPa) IR NMR MS 98 %	1.528-1.533 1.205-1.210	
16.039 933	Potassium 2-(1'-ethoxy)ethoxypropanoate		3752	Solid $C_7H_{13}KO_4$ 200.28	Freely soluble Slightly soluble	n.a. n.a. NMR 98 %	n.a. n.a.	Mixture of diastereomeric isomers (EFFA, 2010a). Composition of stereoisomeric mixture to be specified. According to JECFA: Min. Assay value is "98 by acid/base titration".

Table 1: Specification Summary of the Substances in the present group

FL-no JECFA-no	EU Register name	Structural formula	FEMA no CoE no CAS no	Phys.form Mol.formula Mol.weight	Solubility 1) Solubility in ethanol 2)	Boiling point, °C 3) Melting point, °C ID test Assay minimum	Refrac. Index 4) Spec.gravity 5)	EFSA comments
								CASrn to be introduced into the Register.
16.041 1029	Sodium 2-(4-methoxyphenoxy)propionate		3773 13794-15-5	Solid $C_{10}H_{11}O_4,Na$ + 218.19	Soluble Miscible	n.a. 190 IR 98 %	n.a. n.a.	Racemate.
16.056 1435	Taurine		3813 107-35-7	Solid $C_2H_7O_3NS$ 125.15	Soluble Soluble	 >300° NMR 98 %	n.a. n.a.	
16.075 892	Ethyl vanillin beta-D-glucopyranoside		3801	Solid $C_{15}H_{20}O_8$ 328.32	Slightly soluble Slightly soluble	n.a. 199-200 NMR 99 %	n.a. n.a.	CASrn to be included in the Register: 122397-96-0. According to JECFA: Boiling point is "n/a (decomposes on heating)".
17.001 1418	beta-Alanine		3252 107-95-9	Solid $C_3H_7O_2N$ 89.09	Soluble Slightly soluble	 202-207 NMR 97 %	n.a. n.a.	
17.003 1438	l-Arginine		3819 11890 74-79-3	Solid $C_6H_{14}O_2N_4$ 174.20	Soluble Slightly soluble	 222 MS 98 %	n.a. n.a.	According to JECFA: "Sp rotation = +15 to +17° (20°, 6N HCl)". Register name to be changed to L-Arginine.
17.015 1427	S-Methylmethioninesulphonium chloride		3445 761 1115-84-0	Solid $C_6H_{14}O_2NS$ 199.70	Soluble Soluble	 139 NMR 98 %	n.a. n.a.	Register name to be changed to L-Methylmethioninesulpho-nium chloride.
17.026 1439	l-Lysine		3847 11947 56-87-1	Solid $C_6H_{14}O_2N_2$ 146.19	Soluble Slightly soluble	 215 MS 97 %	n.a. n.a.	According to JECFA: "Sp.rotation = +12.5 to +13.5° (23°, 6N HCl)". Register name to be changed to L-Lysine.

1) Solubility in water, if not otherwise stated.
2) Solubility in 95 % ethanol, if not otherwise stated.
3) At 1013.25 hPa, if not otherwise stated.
4) At 20°C, if not otherwise stated.
5) At 25°C, if not otherwise stated.

6) Stereoisomeric composition not specified.
7) SW: Missing data on solubility.

TABLE 2: SUMMARY OF SAFETY EVALUATIONS

Table 2: Summary of Safety Evaluation of the JECFA substances in the present group

Table 2: Summary of Safety Evaluation of the JECFA substances in the present group

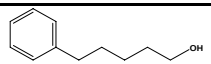
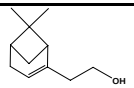
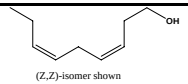
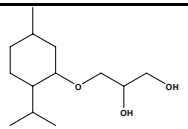
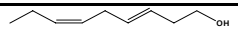
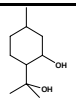
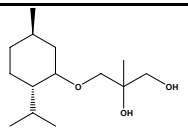
FL-no JECFA-no	EU Register name	Structural formula	EU MSDI 1) US MSDI (µg/*capita*/day)	Class 2) Evaluation procedure path 3)	Outcome on the named compound [4) or 5)]	EFSA conclusion on the named compound (Procedure steps, intake estimates, NOAEL, genotoxicity)	EFSA conclusion on the material of commerce
02.051 675	5-Phenylpentan-1-ol		1.2 0.1	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
02.141 986	2-(6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl)ethan-1-ol		33 0.01	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
02.189 1283	Nona-3,6-dien-1-ol	 (Z,Z)-isomer shown	0.13 0.9	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	Register name to be changed to (Z,Z)-Nona-3,6-dien-1-ol. No safety concern at the estimated level of intake based on the MSDI approach
02.224 1408	3-(1-Menthoxy)propane-1,2-diol		4.1 789	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	Racemate. No safety concern at the estimated level of intake based on the MSDI approach.
02.243 1284	(E,Z)-3,6-Nonadien-1-ol		0.61 0.9	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
02.246 1416	p-Menthane-3,8-diol		39 18	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	Racemate. No safety concern at the estimated level of intake based on the MSDI approach.
02.254 1411	3-Menthoxy-2-methylpropane-1,2-diol		61 500	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	Register name to be changed to (1R,2S,5S)-3-Menthoxy-2-methylpropane-1,2-diol. No safety concern at the estimated level of intake

Table 2: Summary of Safety Evaluation of the JECFA substances in the present group

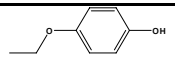
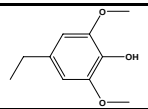
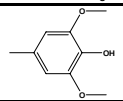
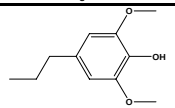
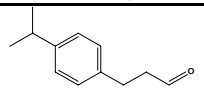
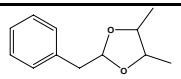
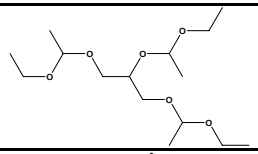
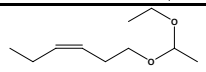
FL-no JECFA-no	EU Register name	Structural formula	EU MSDI 1) US MSDI (µg/*capita*/day)	Class 2) Evaluation procedure path 3)	Outcome on the named compound [4) or 5)]	EFSA conclusion on the named compound (Procedure steps, intake estimates, NOAEL, genotoxicity)	EFSA conclusion on the material of commerce
							based on the MSDI approach.
04.037 720	4-Ethoxyphenol		0.37 0.4	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
04.052 723	4-Ethyl-2,6-dimethoxyphenol		1.3 1	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
04.053 722	4-Methyl-2,6-dimethoxyphenol		0.054 0.04	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
04.056 724	2,6-Dimethoxy-4-propylphenol		0.061 0.1	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
05.094 680	3-(4-Isopropylphenyl)propionaldehyde		0.012 0.1	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
06.027 1005	4,5-Dimethyl-2-benzyl-1,3-dioxolan		0.12 1	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	Racemate (EFFA, 2010a). No safety concern at the estimated level of intake based on the MSDI approach.
06.040 913	1,2,3-Tris([1'-ethoxy]-ethoxy)propane		0.12 140	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	Stereoisomeric composition to be specified.
06.081 943	1-Ethoxy-1-(3-hexenyloxy)ethane		4.6 0	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.

Table 2: Summary of Safety Evaluation of the JECFA substances in the present group

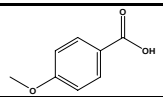
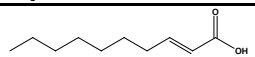
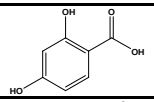
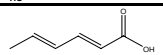
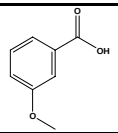
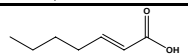
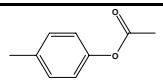
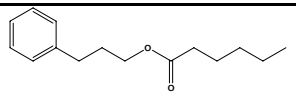
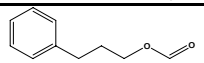
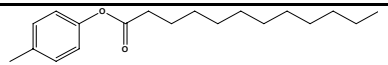
FL-no JECFA-no	EU Register name	Structural formula	EU MSDI 1) US MSDI (µg/*capita*/day)	Class 2) Evaluation procedure path 3)	Outcome on the named compound [4) or 5)]	EFSA conclusion on the named compound (Procedure steps, intake estimates, NOAEL, genotoxicity)	EFSA conclusion on the material of commerce
08.071 883	p-Anisic acid		1.7 0.1	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
08.073 1372	Dec-2-enoic acid	 (E)-isomer shown	0.012 4	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	Composition of stereoisomeric mixture to be specified.
08.076 908	2,4-Dihydroxybenzoic acid		5.5 6	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
08.085 1176	Hexa-2,4-dienoic acid		61 6	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	Register name to be changed to (E,E)-2,4-hexadienoic acid. No safety concern at the estimated level of intake based on the MSDI approach.
08.092 882	3-Methoxybenzoic acid		0.012 0.01	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
08.123 1373	trans-2-Heptenoic acid		4.7 4	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	Stereoisomeric composition to be specified.
09.036 699	p-Tolyl acetate		0.047 70	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
09.071 642	3-Phenylpropyl hexanoate		0.24 0.4	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
09.084 637	3-Phenylpropyl formate		0.012 0.8	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
09.102 704	p-Tolyl dodecanoate		0.24 0.3	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI	No safety concern at the estimated level of intake based on the MSDI

Table 2: Summary of Safety Evaluation of the JECFA substances in the present group

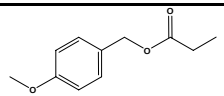
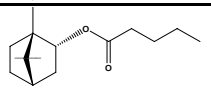
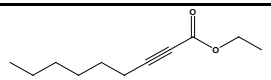
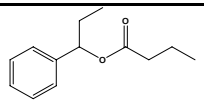
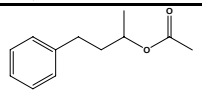
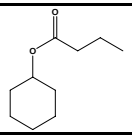
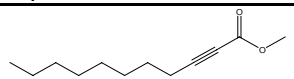
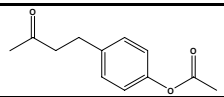
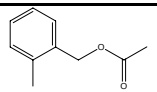
FL-no JECFA-no	EU Register name	Structural formula	EU MSDI 1) US MSDI (µg/*capita*/day)	Class 2) Evaluation procedure path 3)	Outcome on the named compound [4) or 5)]	EFSA conclusion on the named compound (Procedure steps, intake estimates, NOAEL, genotoxicity)	EFSA conclusion on the material of commerce
						approach	approach.
09.145 874	p-Anisyl propionate		0.42 5	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
09.153 1392	Bornyl valerate		3.7 5	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	Racemate (EFFA, 2010a). No safety concern at the estimated level of intake based on the MSDI approach.
09.157 1352	Ethyl 2-nonynoate		1.1 0.9	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
09.189 823	1-Phenylpropyl butyrate		0.24 0.3	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
09.200 816	1-Methyl-3-phenylpropyl acetate		6.1 7	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
09.230 1094	Cyclohexyl butyrate		0.89 0.1	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
09.239 1358	Methyl 2-undecynoate		0.012 0.04	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
09.288 731	4-(4-Acetoxyphenyl)butan-2-one		0.12 0.1	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
09.294 863	2-Methylbenzyl acetate		2.4 3	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.

Table 2: Summary of Safety Evaluation of the JECFA substances in the present group

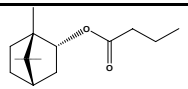
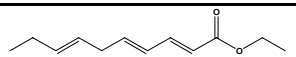
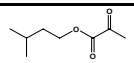
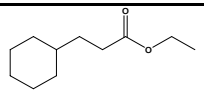
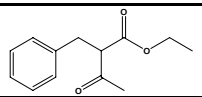
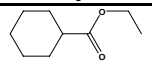
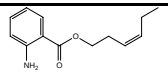
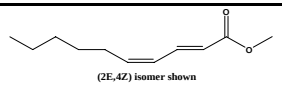
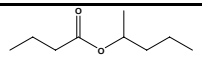
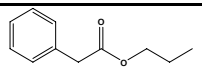
FL-no JECFA-no	EU Register name	Structural formula	EU MSDI 1) US MSDI (µg/*capita*/day)	Class 2) Evaluation procedure path 3)	Outcome on the named compound [4) or 5)]	EFSA conclusion on the named compound (Procedure steps, intake estimates, NOAEL, genotoxicity)	EFSA conclusion on the material of commerce
09.319 1412	Bornyl butyrate		6.1 9	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	CASrn refers to (1R,2S,4R)-stereoisomer. No safety concern at the estimated level of intake based on the MSDI approach.
09.371 1193	Ethyl deca-2,4,7-trienoate		0.024 0.4	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	Composition of stereoisomeric mixture to be specified.
09.443 939	Isopentyl pyruvate		17 0	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
09.488 966	Ethyl cyclohexanepropionate		0.12 0.1	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
09.501 835	Ethyl 2-acetyl-3-phenylpropionate		0.37 0.4	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
09.534 963	Ethyl cyclohexanecarboxylate		0.24 0.1	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
09.561 1538	Hex-3(cis)-enyl anthranilate		0.012 53	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
09.639 1191	Methyl deca-2,4-dienoate	 (2E,4Z) isomer shown	0.097 1	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
09.658 1142	1-Methylbutyl butyrate		0.47 1	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	Racemate. No safety concern at the estimated level of intake based on the MSDI approach.
09.702 1010	Propyl phenylacetate		0.13 0.3	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.

Table 2: Summary of Safety Evaluation of the JECFA substances in the present group

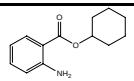
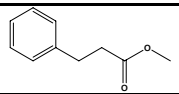
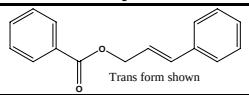
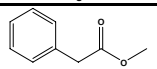
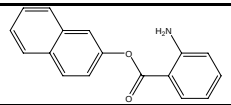
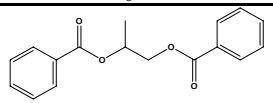
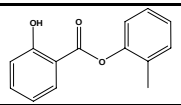
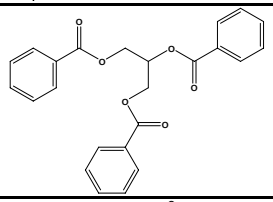
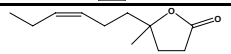
FL-no JECFA-no	EU Register name	Structural formula	EU MSDI 1) US MSDI (µg/*capita*/day)	Class 2) Evaluation procedure path 3)	Outcome on the named compound [4) or 5)]	EFSA conclusion on the named compound (Procedure steps, intake estimates, NOAEL, genotoxicity)	EFSA conclusion on the material of commerce
09.722 1541	Cyclohexyl anthranilate		0.0073 0.007	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
09.746 643	Methyl 3-phenylpropionate		0.12 3	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
09.780 760	Cinnamyl benzoate		1.2 1	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	Composition of stereoisomeric mixture to be specified.
09.783 1008	Methyl phenylacetate		95 20	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
09.801 1544	2-Naphthyl anthranilate		1.3 2	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
09.803 862	Propylene glycol dibenzoate		13 14	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	Racemate. No safety concern at the estimated level of intake based on the MSDI approach.
09.807 907	o-Tolyl salicylate		28 30	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
09.812 861	Glyceryl tribenzoate		45 49	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
10.061 1159	cis-5-Hexenyldihydro-5-methylfuran-2(3H)-one		100 13	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.

Table 2: Summary of Safety Evaluation of the JECFA substances in the present group

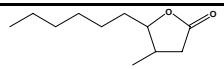
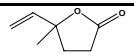
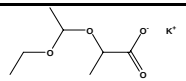
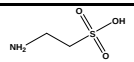
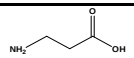
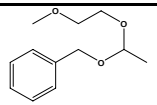
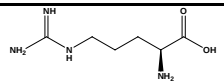
FL-no JECFA-no	EU Register name	Structural formula	EU MSDI 1) US MSDI (µg/*capita*/day)	Class 2) Evaluation procedure path 3)	Outcome on the named compound [4) or 5)]	EFSA conclusion on the named compound (Procedure steps, intake estimates, NOAEL, genotoxicity)	EFSA conclusion on the material of commerce
10.069 1158	3-Methyl gamma-decalactone		4.5 5	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
10.070 1157	4-Methyl-5-hexen-1,4-olide		2.2 3	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
16.039 933	Potassium 2-(1'-ethoxy)ethoxypropanoate		1200 1400	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	Composition of stereoisomeric mixture to be specified.
16.056 1435	Taurine		770 217	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at estimated level of intake based on the MSDI approach.
17.001 1418	beta-Alanine		360 13	Class I A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at estimated level of intake based on the MSDI approach.
06.019 840	1-Benzyloxy-1-(2-methoxyethoxy)ethane		1.2 1	Class I B3: Intake below threshold, B4: Adequate NOAEL exists	4)	No safety concern at the estimated level of intake based on the MSDI approach. EFSA based the safety evaluation on NOAELs derived from studies performed with the hydrolysis products.	No safety concern at the estimated level of intake based on the MSDI approach.
08.004 930	Lactic acid		19000 47000	Class I A3: Intake above threshold, A4: Endogenous	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
17.003 1438	l-Arginine		1000 57	Class I No evaluation		The substance is a macronutrient which is a normal component of food protein and, as such, human exposure through food is orders of magnitude higher than the anticipated level of exposure from use as a flavouring substance.	No safety concern at estimated level of intake based on the MSDI approach.

Table 2: Summary of Safety Evaluation of the JECFA substances in the present group

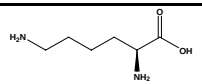
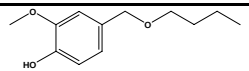
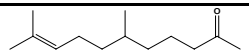
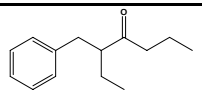
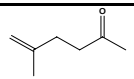
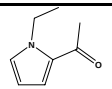
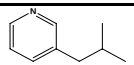
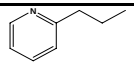
FL-no JECFA-no	EU Register name	Structural formula	EU MSDI 1) US MSDI (µg/*capita*/day)	Class 2) Evaluation procedure path 3)	Outcome on the named compound [4) or 5)]	EFSA conclusion on the named compound (Procedure steps, intake estimates, NOAEL, genotoxicity)	EFSA conclusion on the material of commerce
17.026 1439	l-Lysine		1000 57	Class I No evaluation		The substance is a macronutrient which is a normal component of food protein and, as such, human exposure through food is orders of magnitude higher than the anticipated level of exposure from use as a flavouring substance.	No safety concern at estimated level of intake based on the MSDI approach.
04.093 888	Butyl vanillyl ether		1.4 0.1	Class II A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
07.069 1121	Tetrahydro-pseudo-ionone		0.012 0.01	Class II A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
07.070 830	3-Benzylheptan-4-one		0.05 1	Class II A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
07.100 1119	5-Methylhex-5-en-2-one		0.24 0.3	Class II A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
14.045 1305	2-Acetyl-1-ethylpyrrole		0.12 0.009	Class II A3: Intake below threshold	4)	Not metabolised to innocouos products - EFSA evaluated at step B4: No, no adequate NOAEL could be established	
14.059 1312	3-Isobutylpyridine		0.049 0.07	Class II A3: Intake below threshold	4)	Concluded at step B4 to be of no safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
14.164 1322	2-Propylpyridine		0.61 0.9	Class II A3: Intake below threshold	4)	Concluded at step B4 to be of no safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach

Table 2: Summary of Safety Evaluation of the JECFA substances in the present group

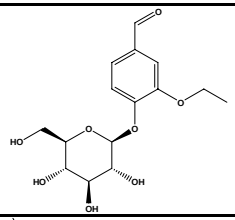
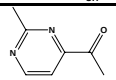
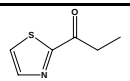
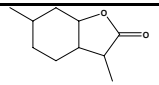
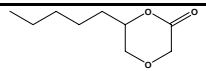
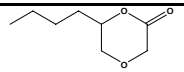
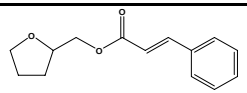
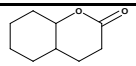
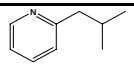
FL-no JECFA-no	EU Register name	Structural formula	EU MSDI 1) US MSDI (µg/*capita*/day)	Class 2) Evaluation procedure path 3)	Outcome on the named compound [4) or 5)]	EFSA conclusion on the named compound (Procedure steps, intake estimates, NOAEL, genotoxicity)	EFSA conclusion on the material of commerce
16.075 892	Ethyl vanillin beta-D-glucopyranoside		28 30	Class II A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	CASrn to be included in the Register: 122397-96-0. No safety concern at the estimated level of intake based on the MSDI approach.
14.070 1565	4-Acetyl-2-methylpyrimidine		0.011 0.01	Class II B3: Intake below threshold, B4: Adequate NOAEL exists	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
15.027 1042	2-Propionylthiazole		0.056 0.2	Class II B3: Intake below threshold, B4: Adequate NOAEL exists	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
10.050 1161	Hexahydro-3,6-dimethyl-2(3H)-benzofuranone		8.0 12	Class III A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	CASrn in Register does not specify stereoisomers. Composition of stereoisomeric mixture to be specified.
13.027 1485	2-Pentyl-5 or 6-keto-1,4-dioxane		0.12 0.2	Class III A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
13.028 1484	2-Butyl-5 or 6-keto-1,4-dioxane		0.43 0.5	Class III A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
13.060 1447	Tetrahydrofurfuryl cinnamate		0.012 0.01	Class III A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	Composition of stereoisomeric mixture to be specified.
13.161 1166	Octahydrocoumarin		1.3 0.07	Class III A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
14.058 1311	2-Isobutylpyridine		0.0061 0.9	Class III A3: Intake below threshold	4)	Concluded at step B4 to be of no safety concern at the estimated level of intake based on the MSDI	No safety concern at the estimated level of intake based on the MSDI approach.

Table 2: Summary of Safety Evaluation of the JECFA substances in the present group

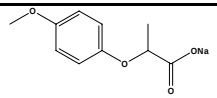
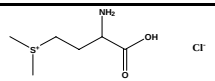
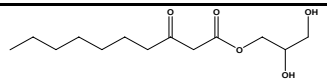
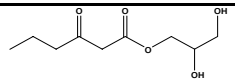
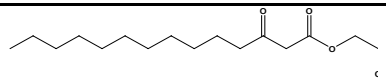
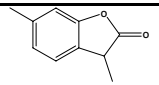
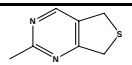
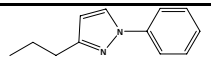
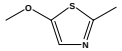
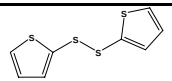
FL-no JECFA-no	EU Register name	Structural formula	EU MSDI 1) US MSDI (µg/*capita*/day)	Class 2) Evaluation procedure path 3)	Outcome on the named compound [4) or 5)]	EFSA conclusion on the named compound (Procedure steps, intake estimates, NOAEL, genotoxicity)	EFSA conclusion on the material of commerce
						approach	
16.041 1029	Sodium 2-(4-methoxyphenoxy)propionate		0.012 6	Class III A3: Intake below threshold	4)	No safety concern at the estimated level of intake based on the MSDI approach	Racemate. No safety concern at the estimated level of intake based on the MSDI approach.
17.015 1427	S-Methylmethioninesulphonium chloride		350 75	Class III A3: Intake below threshold	4)	Concluded at step B4 to be of no safety concern at the estimated level of intake based on the MSDI approach	Register name to be changed to L-Methylmethioninesulphonium chloride. No safety concern at the estimated level of intake based on the MSDI approach.
09.552 914	3-Oxodecanoic acid glyceride		52 270	Class III A3: Intake above threshold, A4: Endogenous	4)	No safety concern at the estimated level of intake based in the MSDI approach. EFSA concluded at step A3: No	Racemate (EFFA, 2010a). No safety concern at the estimated level of intake based on the MSDI approach.
09.555 910	3-Oxohexanoic acid glyceride		0.061 270	Class III A3: Intake above threshold, A4: Endogenous	4)	No safety concern at the estimated level of intake based in the MSDI approach. EFSA concluded at step A3: No	Racemate (EFFA, 2010a). No safety concern at the estimated level of intake based on the MSDI approach.
09.557 916	3-Oxotetradecanoic acid glyceride		0.012 270	Class III A3: Intake above threshold, A4: Endogenous	4)	No safety concern at the estimated level of intake based in the MSDI approach. EFSA concluded at step A3: No	Racemate (EFFA, 2010a). No safety concern at the estimated level of intake based on the MSDI approach.
10.072 1167	Dimethyl-3,6-benzo-2(3H)-furanone		0.84 2	Class III B3: Intake below threshold, B4: Adequate NOAEL exists	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
14.014 1566	5,7-Dihydro-2-methylthieno(3,4-d)pyrimidine		0.012 0.4	Class III B3: Intake below threshold, B4: Adequate NOAEL exists	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
14.029 1568	1-Phenyl-(3 or 5)-propylpyrazole	 1-Phenyl-3-propylpyrazole shown	0.17 0.2	Class III B3: Intake below threshold, B4: Adequate NOAEL exists	4)	No safety concern at the estimated level of intake based on the MSDI approach	CASrn in the Register corresponds to an incompletely defined structure.

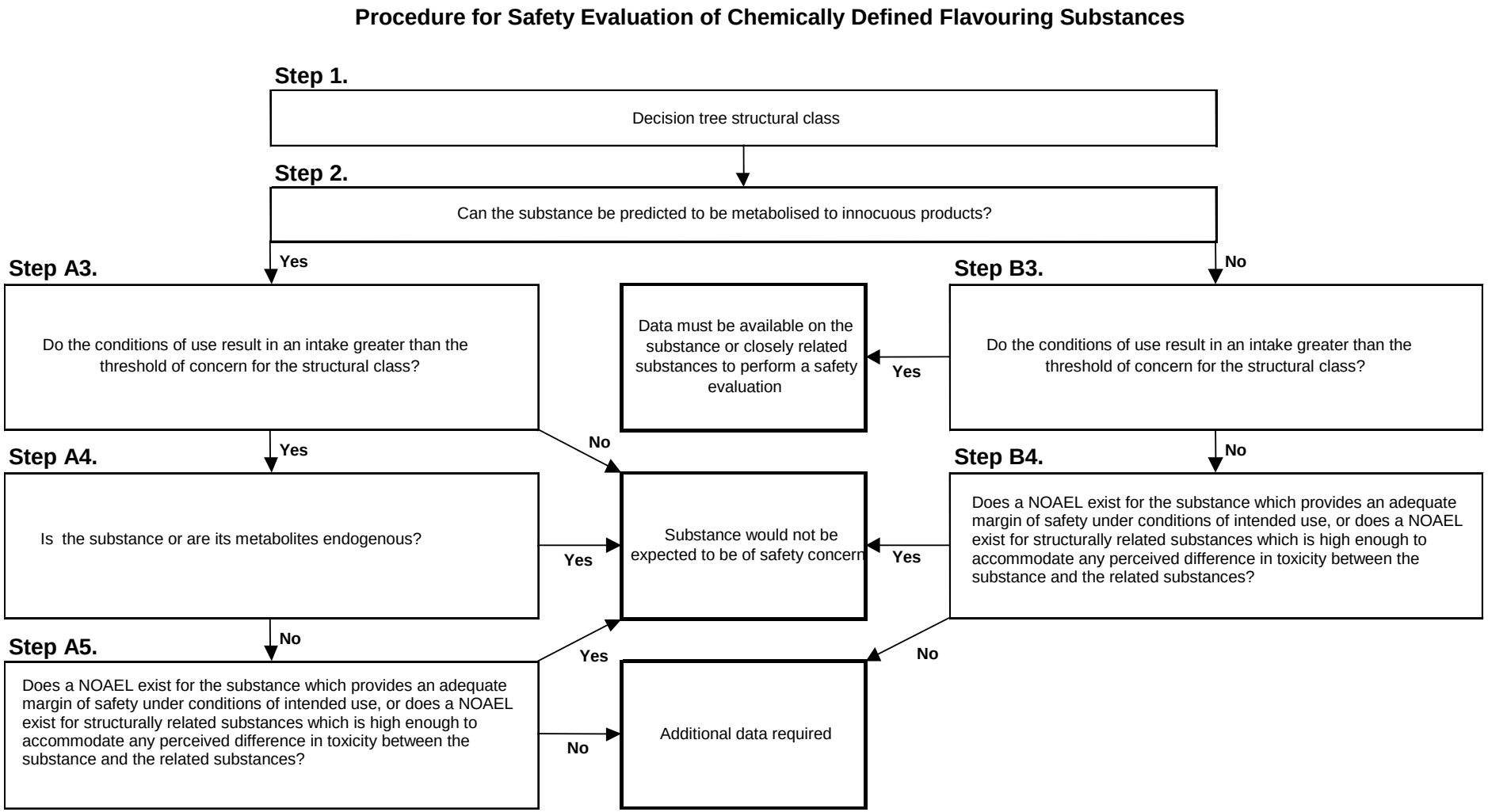
Table 2: Summary of Safety Evaluation of the JECFA substances in the present group

FL-no JECFA-no	EU Register name	Structural formula	EU MSDI 1) US MSDI (µg/*capita*/day)	Class 2) Evaluation procedure path 3)	Outcome on the named compound [4) or 5)]	EFSA conclusion on the named compound (Procedure steps, intake estimates, NOAEL, genotoxicity)	EFSA conclusion on the material of commerce
							No safety concern at the estimated level of intake based on the MSDI approach. CASrn in Register corresponds to an incompletely defined structure.
15.002 1057	2-Methyl-5-methoxythiazole		0.012 0.01	Class III B3: Intake below threshold, B4: Adequate NOAEL exists	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.
15.008 1053	2-Thienyl disulfide		0.061 0.07	Class III B3: Intake below threshold, B4: Adequate NOAEL exists	4)	No safety concern at the estimated level of intake based on the MSDI approach	No safety concern at the estimated level of intake based on the MSDI approach.

1) EU MSDI: Amount added to food as flavour in (kg / year) x 10E9 / (0.1 x population in Europe (= 375 x 10E6) x 0.6 x 365) = µg/capita/day.
2) Thresholds of concern: Class I = 1800, Class II = 540, Class III = 90 µg/person/day.
3) Procedure path A substances can be predicted to be metabolised to innocuous products. Procedure path B substances cannot.
4) No safety concern based on intake calculated by the MSDI approach of the named compound.
5) Data must be available on the substance or closely related substances to perform a safety evaluation.

ND: not determined.

ANNEX I


Procedure for Safety Evaluation of Chemically Defined Flavouring Substances
Step 1.
Decision tree structural class
Step 2.
Can the substance be predicted to be metabolised to innocuous products?
Yes
No
Step A3.
Do the conditions of use result in an intake greater than the threshold of concern for the structural class?
Data must be available on the substance or closely related substances to perform a safety evaluation
Yes
Step B3.
Do the conditions of use result in an intake greater than the threshold of concern for the structural class?
Yes
No
Step A4.
Is the substance or are its metabolites endogenous?
Yes
Substance would not be expected to be of safety concern
Yes
Step B4.
Does a NOAEL exist for the substance which provides an adequate margin of safety under conditions of intended use, or does a NOAEL exist for structurally related substances which is high enough to accommodate any perceived difference in toxicity between the substance and the related substances?
No
No
Step A5.
Does a NOAEL exist for the substance which provides an adequate margin of safety under conditions of intended use, or does a NOAEL exist for structurally related substances which is high enough to accommodate any perceived difference in toxicity between the substance and the related substances?
Yes
No
Additional data required

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ABBREVIATIONS

ADI	Accetable Daily Intake
BW	Body weight
CAS	Chemical Abstract Service
CEF	Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids
CoE	Council of Europe
EFSA	The European Food Safety Authority
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
FGE	Flavouring Group Evaluation
FLAVIS (FL)	Flavour Information System (database)
ID	Identity
IR	Infrared spectroscopy
JECFA	The Joint FAO/WHO Expert Committee on Food Additives
MSDI	Maximised Survey-derived Daily Intake
mTAMDI	Modified Theoretical Added Maximum Daily Intake
No	Number
NOAEL	No observed adverse effect level
NTP	National Toxicology Program
SCF	Scientific Committee on Food
WHO	World Health Organisation