

Table 4 (continued)

Substance	No.	Step A3 ^b Does intake exceed the threshold for human intake?	Step A4 Endogenous or metabolized to endogenous substances?	Conclusion based on current levels of intake
3-Hexenyl 3-methylbutanoate	0202	No Europe: 9.4 USA: 30	NR	No safety concern
2-Methylpropyl 3-methylbutyrate	0203	No Europe: 78 USA: 130	NR	
2-Methylbutyl 3-methylbutanoate	0204	No Europe: 0.86 USA: 0.95	NR	
Methyl 2-methylbutyrate	0205	No Europe: 390 USA: 69	NR	
Ethyl 2-methylbutyrate ^c	0206	Yes Europe: 2200 USA: 560	Yes	
<i>n</i> -Butyl 2-methylbutyrate	0207	No Europe: 26 USA: 0.02	NR	
Hexyl 2-methylbutanoate	0208	No Europe: 4.9 USA: 8.6	NR	
Octyl 2-methylbutyrate	0209	No Europe: 0.01 USA: 0.10	NR	
Isopropyl 2-methylbutyrate	0210	No Europe: 4.9 USA: 0.10	NR	
3-Hexenyl 2-methylbutanoate	0211	No Europe: 5 USA: 8.8	NR	
2-Methylbutyl 2-methylbutyrate	0212	No Europe: 3.6 USA: 0.04	NR	
Methyl 2-methylpentanoate	0213	No Europe: 0.17 USA: 0.02	NR	
Ethyl 2-methylpentanoate	0214	No Europe: 7.6 USA: 320	NR	
Ethyl 3-methylpentanoate	0215	No Europe: 0.31 USA: 5.90	NR	
Methyl 4-methylvalerate	0216	No Europe: 0.03 USA: 0.10	NR	

NR: not required for evaluation because consumption of the substance was determined to be of no safety concern at step A3 of the procedure.

^a Step 1: All of the esters in this group are in structural class I.

Step 2: All of the esters in this group are metabolized to innocuous products.

^b The threshold for human intake for class I is 1800 µg per day. All intake values are expressed in µg per day.

^c The components ethanol and 2-methylbutyric acid are endogenous. The acid is an intermediate in the metabolism of the amino acid.

Table 5

Summary of the results of safety evaluations of 67 esters of aliphatic acyclic primary alcohols with aliphatic linear saturated carboxylic acids^a

Substance	No.	Step A3 ^b Does intake exceed the threshold for human intake?	Step A4 Endogenous or metabolized to endogenous substances?	Conclusion based on current levels of intake
Propyl formate	0117	No Europe: 5.0 USA: 0.38	NA	No safety concern
Butyl formate	0118	No Europe: 21 USA: 0.17	NA	
<i>n</i> -Amyl formate	0119	No Europe: 29 USA: 110	NA	
Hexyl formate	0120	No Europe: 8.7 USA: 8.0	NA	
Heptyl formate	0121	No Europe: 0.00 USA: 0.10	NA	
Octyl formate	0122	No Europe: 0.14 USA: 0.95	NA	
<i>cis</i> -3-Hexenyl formate	0123	No Europe: 43 USA: 1.7	NA	
Isobutyl formate	0124	No Europe: 4.7 USA: 1.5	NA	
Methyl acetate	0125	No Europe: 460 USA: 110	NA	
Propyl acetate	0126	No Europe: 180 USA: 440	NA	
Butyl acetate	0127	No Europe: 1200 USA: 170	NA	
Hexyl acetate	0128	Yes Europe: 3200 USA: 160	Yes ^c	
Heptyl acetate	0129	No Europe: 56 USA: 2.3	NA	
Octyl acetate	0130	No Europe: 83 USA: 9.5	NA	
Nonyl acetate	0131	No Europe: 6.6 USA: 2.5	NA	
Decyl acetate	0132	No Europe: 7.3 USA: 21	NA	

Table 5 (continued)

Substance	No.	Step A3 ^p Does intake exceed the threshold for human intake?	Step A4 Endogenous or metabolized to endogenous substances?	Conclusion based on current levels of intake
Lauryl acetate	0133	No Europe: 9.3 USA: 0.57	NA	No safety concern
<i>cis</i> -3-Hexenyl acetate	0134	No Europe: 640 USA: 57	NA	
<i>trans</i> -3-Heptenyl acetate	0135	No Europe: 0.24 USA: 0.76	NA	
10-Undecen-1-yl acetate	0136	No Europe: 0.83 USA: 0.10	NA	
Isobutyl acetate	0137	No Europe: 1200 USA: 1300	NA	
2-Methylbutyl acetate	0138	No Europe: 130 USA: 360	NA	
2-Ethylbutyl acetate	0140	No Europe: 4.0 USA: 0.17	NA	
Methyl propionate	0141	No Europe: 9.3 USA: 30	NA	
Propyl propionate	0142	No Europe: 9.6 USA: 44	NA	
Butyl propionate	0143	No Europe: 10 USA: 1.1	NA	
Hexyl propionate	0144	No Europe: 5.7 USA: 3.0	NA	
Octyl propionate	0145	No Europe: 0.00 USA: 0.02	NA	
Decyl propionate	0146	No Europe: 0.00 USA: 0.95	NA	
<i>cis</i> -3-Hexenyl propionate and <i>trans</i> -2-hexenyl propionate	0147	No Europe: 0.00 USA: 430	NA	
Isobutyl propionate	0148	No Europe: 12 USA: 6.5	NA	No safety concern
Methyl butyrate	0149	No Europe: 220 USA: 44	NA	

Table 5 (continued)

Substance	No.	Step A3 ^b Does intake exceed the threshold for human intake?	Step A4 Endogenous or metabolized to endogenous substances?	Conclusion based on current levels of intake
Propyl butyrate	0150	No Europe: 75 USA: 38	NA	No safety concern
Butyl butyrate	0151	No Europe: 390 USA: 63	NA	
<i>n</i> -Amyl butyrate	0152	No Europe: 450 USA: 200	NA	
Hexyl butyrate	0153	No Europe: 110 USA: 27	NA	
Heptyl butyrate	0154	No Europe: 6.0 USA: 3.8	NA	
Octyl butyrate	0155	No Europe: 16 USA: 0.38	NA	
Decyl butyrate	0156	No Europe: 0.00 USA: 0.08	NA	
<i>cis</i> -3-Hexenyl butyrate	0157	No Europe: 160 USA: 4.8	NA	
Isobutyl butyrate	0158	No Europe: 47 USA: 7.4	NA	
Methyl valerate	0159	No Europe: 30 USA: 11	NA	
Butyl valerate	0160	No Europe: 3.7 USA: 0.10	NA	
Propyl hexanoate	0161	No Europe: 14 USA: 0.17	NA	
Butyl hexanoate	0162	No Europe: 15 USA: 1.9	NA	
<i>n</i> -Amyl hexanoate	0163	No Europe: 8.7 USA: 8.8	NA	
Hexyl hexanoate	0164	No Europe: 150 USA: 13	NA	
<i>cis</i> -3-Hexenyl hexanoate	0165	No Europe: 42 USA: 1.3	NA	

Table 5 (continued)

Substance	No.	Step A3 ^b Does intake exceed the threshold for human intake?	Step A4 Endogenous or metabolized to endogenous substances?	Conclusion based on current levels of intake
Isobutyl hexanoate	0166	No Europe: 6.1 USA: 1.7	NA	No safety concern
Methyl heptanoate	0167	No Europe: 5.7 USA: 0.10	NA	
Propyl heptanoate	0168	No Europe: 0.14 USA: 0.38	NA	
Butyl heptanoate	0169	No Europe: 0.00 USA: 4.4	NA	
<i>n</i> -Amyl heptanoate	0170	No Europe: 0.61 USA: 0.02	NA	
Octyl heptanoate	0171	No Europe: 0.21 USA: 0.38	NA	
Isobutyl heptanoate	0172	No Europe: 0.01 USA: 1.9	NA	
Methyl octanoate	0173	No Europe: 9.7 USA: 0.17	NA	
<i>n</i> -Amyl octanoate	0174	No Europe: 3.4 USA: 1.9	NA	
Hexyl octanoate	0175	No Europe: 1.3 USA: 0.95	NA	
Heptyl octanoate	0176	No Europe: 0.71 USA: 0.95	NA	
Octyl octanoate	0177	No Europe: 0.03 USA: 2.3	NA	
Nonyl octanoate	0178	No Europe: 0.14 USA: 0.95	NA	
Methyl nonanoate	0179	No Europe: 0.86 USA: 2.3	NA	
Methyl laurate	0180	No Europe: 5.1 USA: 0.76	NA	
Butyl laurate	0181	No Europe: 0.00 USA: 0.10	NA	

Table 5 (continued)

Substance	No.	Step A3 ^b Does intake exceed the threshold for human intake?	Step A4 Endogenous or metabolized to endogenous substances?	Conclusion based on current levels of intake
Isoamyl laurate	0182	No Europe: 0.14 USA: 0.57	NA	No safety concern
Methyl myristate	0183	No Europe: 62 USA: 46	NA	
Butyl stearate	0184	No Europe: 5.1 USA: 5.5	NA	

^a Step 1: All of the esters in this group are in structural class I except 2-ethylbutyl acetate, which is in structural class II.

Step 2: Evaluation of *cis*-3- and *trans*-2-hexenyl propionate was postponed. All of the other substances in this group are metabolized to innocuous products.

^b The thresholds for human intake for classes I and II are 1800 µg per day and 540 µg per day, respectively. All intake values are expressed in µg per day.

^c Hexanoic acid, the metabolite of the component hexyl alcohol, and acetic acid are endogenous in humans.

^d Evaluation postponed, pending consideration of other α,β -unsaturated carbonyl compounds.

acids, which then undergo β -oxidation in the fatty acid and other well-known metabolic pathways.

Application of the Procedure

Step 1. In applying the Procedure for the Safety Evaluation of Flavouring Agents (Fig. 1) to the above-mentioned esters of aliphatic acyclic primary alcohols with aliphatic linear saturated carboxylic acids, the Committee assigned all but one of the 67 esters to structural class I. 2-Ethylbutyl acetate contains a sterically hindered functional group and was therefore assigned to structural class II.

Step 2. At this step the evaluation of *cis*-3- and *trans*-2-hexenyl propionate was postponed, pending consideration of other α,β -unsaturated carbonyl compounds.

The available data indicate that the remaining esters in this group would be hydrolysed in humans to their component alcohols and carboxylic acids. The aliphatic acyclic primary alcohols are oxidized to their corresponding carboxylic acids, which are either conjugated and excreted in the urine, or undergo β -oxidation and cleavage. The aliphatic linear saturated carboxylic acids are endogenous in humans. At the current levels of per capita intake these esters would not be expected to saturate the metabolic pathways. Therefore, the remaining 66 esters of aliphatic acyclic primary alcohols with aliphatic linear

Table 6
Summary of the results of safety evaluations of 26 esters derived from branched-chain terpenoid alcohols and aliphatic acyclic carboxylic acids^a

Substance	No.	Step A3 ^b Does intake exceed the threshold for human intake?	Conclusion based on current levels of intake
Citronellyl formate	0053	No Europe: 103 USA: 2.5	No safety concern
Geranyl formate	0054	No Europe: 330 USA: 48	
Neryl formate	0055	No Europe: 0.01 USA: 0.04	
Rhodinyll formate	0056	No Europe: ND USA: 0.10	
Citronellyl acetate	0057	No Europe: 217 USA: 36	
Geranyl acetate ^c	0058	No Europe: 580 USA: 205	
Neryl acetate	0059	No Europe: 180 USA: 63	
Rhodinyll acetate	0060	No Europe: 1.1 USA: 0.8	
Citronellyl propionate	0061	No Europe: 41 USA: 1.5	
Geranyl propionate	0062	No Europe: 81 USA: 11	
Neryl propionate	0063	No Europe: 4.3 USA: 1.1	
Rhodinyll propionate	0064	No Europe: ND USA: 0.02	
Citronellyl butyrate	0065	No Europe: 32 USA: 5	
Geranyl butyrate	0066	No Europe: 60 USA: 25	
Neryl butyrate	0067	No Europe: 0.4 USA: 0.02	
Rhodinyll butyrate	0068	No Europe: ND USA: 1.0	

Table 6 (continued)

Substance	No.	Step A3 ^b Does intake exceed the threshold for human intake?	Conclusion based on current levels of intake
Citronellyl valerate	0069	No Europe: 0.7 USA: 4.0	No safety concern
Geranyl hexanoate	0070	No Europe: 0.07 USA: 0.5	
Citronellyl isobutyrate	0071	No Europe: 13 USA: 1.3	
Geranyl isobutyrate	0072	No Europe: 124 USA: 3.0	
Neryl isobutyrate	0073	No Europe: 2.0 USA: 0.4	
Rhodinylyl isobutyrate	0074	No Europe: 0.03 USA: 0.04	
Geranyl isovalerate	0075	No Europe: 43 USA: 1.7	
Neryl isovalerate	0076	No Europe: 0.03 USA: 0.04	
Rhodinylyl isovalerate	0077	No Europe: 0.01 USA: 0.02	
Geranyl 2-ethylbutanoate	0078	No Europe: 0.6 USA: 0	

ND, no data reported.

^a Step 1: All of the esters in this group are in structural class I.

Step 2: All of the esters in this group are metabolized to innocuous products.

^b The threshold for human intake for class I is 1800 µg per day. All intake values are expressed in µg per day.

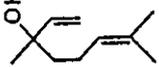
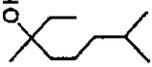
^c The ADI for this substance was maintained.

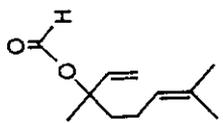
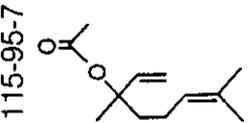
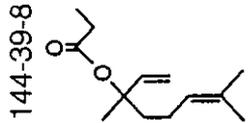
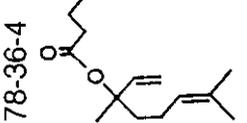
peel oils and 50 g/kg in spices. In the USA terpenoid esters are consumed predominantly as components of traditional foods and the total annual volume of consumption of the most common terpenoid esters as natural components of food is estimated to be approximately 300 tonnes (Stofberg & Grundschober, personal communication, 1987).

Information on absorption, metabolism and elimination

The terpenoid esters are hydrolysed to their corresponding terpenoid alcohols (geraniol, citronellol, nerol and rhodinol) and aliphatic carboxylic acids (formic, acetic, propionic, butyric, valeric, hexanoic,

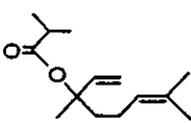
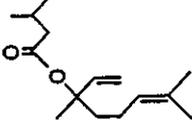
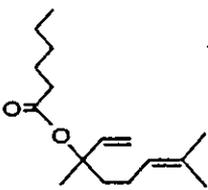
Table 5
Summary of the results of safety evaluations of 23 aliphatic acyclic and alicyclic terpenoid tertiary alcohols and structurally related substances^a

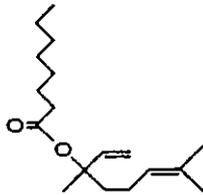
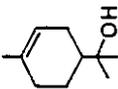
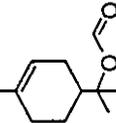
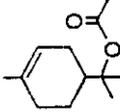
Substance	No.	CAS no. and structure	Step A3/B3 ^b Does intake exceed the threshold for human intake?	Step A4 Is the substance or are its metabolites endogenous?	Step B4/A5 Adequate NOEL for substance or related substance?	Comments	Conclusion based on current intake
Structural class I Linalool ^c	356	78-70-6 	Yes Europe: 2600 USA: 1100	No	Yes The NOEL of 50mg/kg of body weight per day reported in a 90-day study in rats is > 1000 times the daily per capita intake of linalool in Europe and the USA	Oxidation of the allylic methyl group may occur after repeated exposure. See also note 1	No safety concern
Tetrahydrolinalool	357	78-69-3 	No Europe: 55 USA: 0.1	NR	NR	See note 1	

Linalyl formate	358	115-99-1		No Europe: 8 USA: 13	NR	NR	See note 2
Linalyl acetate ^e	359	115-95-7		Yes Europe: 2100 USA: 180	No	Yes The NOEL of 24 mg/kg of body weight per day reported in a 90-day study in rats is >500 times the daily per capita intake of linalyl acetate in Europe and the USA	See note 2
Linalyl propionate	360	144-39-8		No Europe: 16 USA: 2	NR	NR	See note 2
Linalyl butyrate	361	78-36-4		No Europe: 10 USA: 4	NR	NR	See note 2

No safety concern

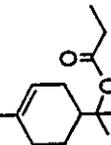
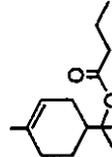
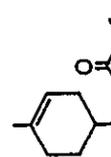
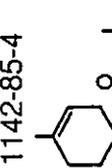
Table 5 (continued)

Substance	No.	CAS no. and structure	Step A3/B3 ^b Does intake exceed the threshold for human intake?	Step A4 Is the substance or are its metabolites endogenous?	Step B4/A5 Adequate NOEL for substance or related substance?	Comments	Conclusion based on current intake
Linalyl isobutyrate	362	78-35-3 	No Europe: 36 USA: 1	NR	NR	See note 2	
Linalyl isovalerate	363	1118-27-0 	No Europe: 5 USA: 6	NR	NR	See note 2	No safety concern
Linalyl hexanoate	364	7779-23-9 	No Europe: 1 USA: 0.4	NR	NR	See note 2	

Linalyl octanoate	365	10024-64-3		No Europe: 0.1 USA: 1	NR	NR	See note 2
α -Terpineol	366	98-55-5		Yes Europe: 3000 USA: 1100	No	Yes The NOEL of 500 mg/kg of body weight per day reported in a 20-week study in rats is > 10000 times the daily per capita intake of α -terpineol in Europe and the USA	See note 3
Terpinyl formate	367	2153-26-6		No Europe: 0.1 USA: 2	NR	NR	See note 4
Terpinyl acetate	368	8007-35-0		No Europe: 260 USA: 390	NR	NR	See note 4

No safety concern

Table 5 (continued)

Substance	No.	CAS no. and structure	Step A3/B3 ^p Does intake exceed the threshold for human intake?	Step A4 Is the substance or are its metabolites endogenous?	Step B4/A5 Adequate NOEL for substance or related substance?	Comments	Conclusion based on current intake
Terpinyl propionate	369	80-27-3 	No Europe: 0.03 USA: 1	NR	NR	See note 4	
Terpinyl butyrate	370	80-26-2 	No Europe: 6 USA: 6	NR	NR	See note 4	
Terpinyl isobutyrate	371	7774-65-4 	No Europe: 0.7 USA: 0.02	NR	NR	See note 4	No safety concern
Terpinyl isovalerate	372	1142-85-4 	No Europe: 0.1 USA: 1	NR	NR	See note 4	

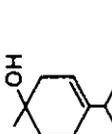
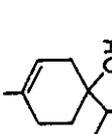
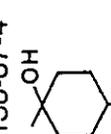
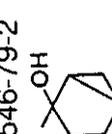
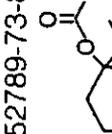
<i>p</i> -Menth-3-en-1-ol	373		586-82-3	No Europe: 41 USA: 0.4	NR	NR	See note 3
4-Carvomenthenol	439		562-74-3	No Europe: 170 USA: 51	NR	NR	See note 3
<i>p</i> -Menth-8-en-1-ol	374		138-87-4	No Europe: 2 USA: 21	NR	NR	See note 3
4-Thujanol	441		546-79-2	No Europe: 1 USA: 0.04	NR	NR	See note 1
Methyl 1-acetoxycyclohexylketone	442		52789-73-8	— Europe: ND USA: 4	NA	No	— Not evaluated ^d

Table 5 (continued)

Substance	No.	CAS no. and structure	Step A3/B3 ^b Does intake exceed the threshold for human intake?	Step A4 Is the substance or are its metabolites endogenous?	Step B4/A5 Adequate NOEL for substance or related substance?	Comments	Conclusion based on current intake
Structural class II 2-Ethyl-1,3,3-trimethyl-2-norbornanol	440	18368-91-7 	No Europe: 1 USA: 0.02	NR	NR	See note 1	No safety concern

CAS: Chemical Abstracts Service; ND: no intake data reported; NR: not required for evaluation because consumption of the substance was determined to be of no safety concern at step A3 of the Procedure.

^a Step 2: All of the substances in this group are expected to be metabolized to innocuous products, except methyl 1-acetoxycyclohexylketone.

^b The thresholds for human intake for classes I and II are 1800 µg per day and 540 µg per day, respectively. All intake values are expressed in µg per day.

^c The group ADI of 0-0.5 mg/kg of body weight per day established at the twenty-third meeting (Annex 1, reference 50) for citral, geranyl acetate, citronellol, linalool and linalyl acetate expressed as citral, was maintained.

^d This substance was not evaluated because a NOEL for this or a related substance was not available and the per capita intake exceeds 1.5 µg per day (step B5).

Notes to Table 5

1. Metabolized primarily by conjugation with glucuronic acid and excreted in the urine.
2. Hydrolysed to linalool and the corresponding carboxylic acid. Linalool is metabolized primarily by conjugation with glucuronic acid and excreted in the urine. Oxidation of the allylic methyl group may occur after repeated exposure.
3. Metabolized primarily by conjugation with glucuronic acid and excreted in the urine. Oxidation of the allylic methyl group followed by hydrogenation to yield the corresponding saturated acid may occur after repeated exposure.
4. Hydrolysed to α-terpineol and the corresponding carboxylic acid. Metabolized primarily by conjugation with glucuronic acid and excreted in the urine. Oxidation of the allylic methyl group followed by hydrogenation to yield the corresponding saturated acid may occur after repeated exposure.

Table 7

Summary of the results of the safety evaluations of 21 ionones and structurally related substances^a

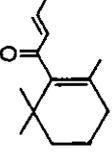
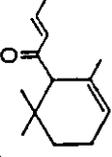
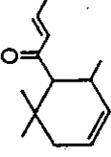
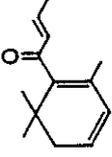
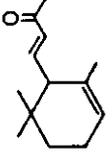
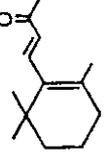
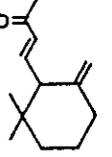
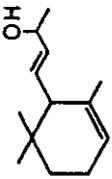
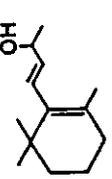
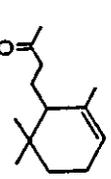
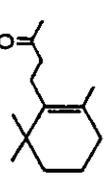
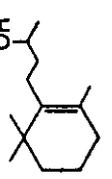
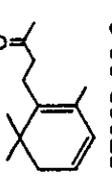
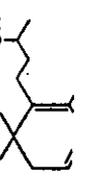
Substance	No.	CAS no. and structure	Step 2 Metabolized to innocuous products?	Step A3/B3 ^b Does intake exceed the threshold for human intake?	Step B4 Adequate NOEL for substance or related substance?	Conclusion based on current intake
β -Damascone	384	23726-92-3 	No	No Europe: 43 USA: 10	Yes	
α -Damascone	385	43052-87-5 	No	No Europe: 8 USA: 0.4	Yes	
δ -Damascone	386	57378-68-4 	No	No Europe: 0.06 USA: 0.6	Yes	
Damascenone	387	23696-85-7 	No	No Europe: 86 USA: 5	Yes	No safety concern
α -Ionone ^c	388	127-41-3 	Yes	No Europe: 310 USA: 150	NA	
β -Ionone ^c	389	14901-07-6 	Yes	No Europe: 150 USA: 100	NA	
γ -Ionone	390	79-76-5 	No	No Europe: 0.01 USA: 15	Yes	

Table 7 (continued)

Substance	No.	CAS no. and structure	Step 2 Metabolized to innocuous products?	Step A3/B3 ^a Does intake exceed the threshold for human intake?	Step B4 Adequate NOEL for substance or related substance?	Conclusion based on current intake
α -Ionol	391	25312-34-9 	Yes	No Europe: 0.7 USA: 0.06	NA	
β -Ionol	392	22029-76-1 	Yes	No Europe: 0.9 USA: 0.1	NA	
Dihydro- α -ionone	393	31499-72-6 	Yes	No Europe: 0.7 USA: 0.02	NA	
Dihydro- β -ionone	394	17283-81-7 	Yes	No Europe: 1 USA: 0.04	NA	No safety concern
Dihydro- β -ionol	395	3293-47-8 	Yes	No Europe: 0.3 USA: 0.02	NA	
Dehydrodihydroionone	396	20483-36-7 	No	No Europe: 0.1 USA: 0.08	Yes	
Dehydrodihydroionol	397	57069-86-0 	No	No Europe: 8 USA: 0.01	Yes	

Methyl- α -ionone	398	127-42-4		Yes	No Europe: 100 USA: 7	NA	No safety concern
Methyl- β -ionone	399	127-43-5		Yes	No Europe: 6 USA: 0.2	NA	
Methyl- δ -ionone	400	7748-98-7		Yes	No Europe: 0.4 USA: 1	NA	
Allyl- α -ionone	401	79-78-7		Yes	No Europe: 35 USA: 25	NA	
1,4-Dimethyl-4-acetyl-1-cyclohexene	402	43219-68-7		—	— Europe: — USA: —	—	Not evaluated ^d
α -Irone	403	79-69-6		Yes	No Europe: 9 USA: 3	NA	No safety concern
α -iso-Methylionone	404	127-51-5		Yes	No Europe: 6 USA: 1	NA	

CAS: Chemical Abstracts Service; NA: not applicable.

^a Step 1: All of the substances in this group are in structural class I.

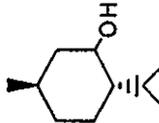
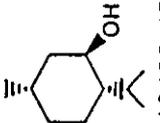
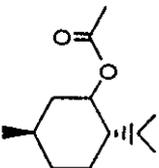
^b The threshold for human intake for class I is 1800 μg per day. All intake values are expressed in μg per day.

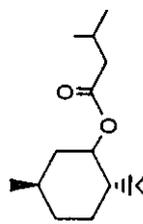
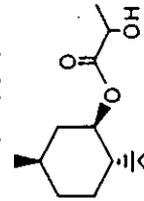
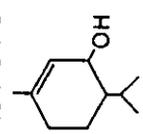
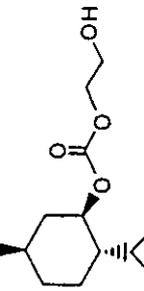
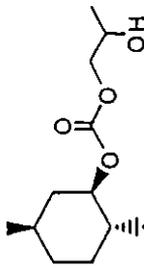
^c The group ADI of 0-0.1 mg/kg of body weight established at the twenty-eighth meeting of the Committee (Annex 1, reference 66) for α -ionone and β -ionone was maintained.

^d 1,4-Dimethyl-4-acetyl-1-cyclohexene was not considered to have sufficient structural similarities to the ionones to be included in this group. Accordingly, the safety evaluation of this compound was not considered at the present meeting.

Table 9

Summary of the results of safety evaluations of menthol and 13 structurally related substances^a

Substance	No.	CAS structure and no.	Step A3 ^b Does intake exceed the threshold for human intake?	Step A4 Is the substance or are its metabolites endogenous?	Step A5 Adequate NOEL for substance or related substance?	Conclusion based on current intake
Structural class I						
Menthol ^c	427	89-78-1 	Yes Europe: 18000 USA: 10000	No	Yes The NOEL of 380 mg/kg of body weight per day reported in a 2-year toxicity/carcinogenicity study in rats is > 1000 times the daily per capita intake of menthol in both Europe and the USA	No safety concern
(+)-neo-Menthol	428	2216-52-6 	No Europe: 3 USA: 27	NR	NR	No safety concern
Menthyl acetate	431	16409-45-3 	No Europe: 420 USA: 560	NR	NR	No safety concern

Menthyl isovalerate	432	16409-46-4		No Europe: 9 USA: 27	NR	NR
(-)-Menthyl lactate	433	59259-38-0		No Europe: 26 USA: 0.1	NR	NR
p-Menth-1-en-3-ol	434	491-04-3		No Europe: 0.02 USA: 0.02	NR	NR
(-)-Menthol ethylene glycol carbonate	443	156324-78-6		No Europe: ND USA: 760	NR	NR
Mixture of (-)-menthol 1- and 2-propylene glycol carbonate	444	156329-82-2		No Europe: ND USA: 380	NR	NR

No safety concern