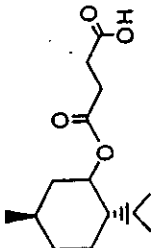
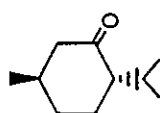
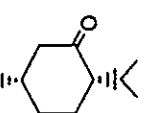
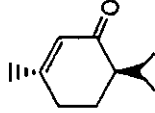
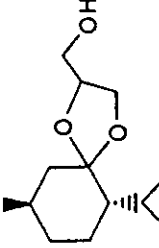
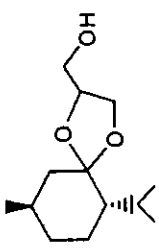


Table 9 (continued)

| Substance                              | No. | CAS structure and no.                                                                             | Step A3 <sup>b</sup><br>Does intake exceed the threshold for human intake? | Step A4<br>Is the substance or are its metabolites endogenous? | Step A5<br>Adequate NOEL for substance or related substance?                                                                                                                           | Conclusion based on current intake |
|----------------------------------------|-----|---------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|----------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|
| mono-Menthyl succinate                 | 447 | 77341-67-4<br> | No<br>Europe: ND<br>USA: 22                                                | NR                                                             | NR                                                                                                                                                                                     | No safety concern                  |
| <b>Structural class II</b><br>Menthone | 429 | 89-80-5<br>   | Yes<br>Europe: 1000<br>USA: 2500                                           | No                                                             | Yes<br>The NOEL of 400mg/kg of body weight per day reported in a 28-day toxicity study in rats is about 10000 times the daily per capita intake of menthone in both Europe and the USA | No safety concern                  |
| (±)-Isomenthone                        | 430 | 491-07-6<br> | No<br>Europe: 200<br>USA: 0.1                                              | NR                                                             | NR                                                                                                                                                                                     | No safety concern                  |

|                                 |     |             |                                                                                      |                              |    |    |                   |
|---------------------------------|-----|-------------|--------------------------------------------------------------------------------------|------------------------------|----|----|-------------------|
| Piperitone                      | 435 | 6091-50-5   |   | No<br>Europe: 51<br>USA: 10  | NR | NR |                   |
| (-)-Menthone 1,2-glycerol ketal | 445 | 563187-91-7 |   | No<br>Europe: ND<br>USA: 190 | NR | NR |                   |
| (±)-Menthone 1,2-glycerol ketal | 446 | 63187-91-7  |  | No<br>Europe: ND<br>USA: 190 | NR | NR | No safety concern |

CAS: Chemical Abstract 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.

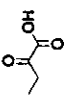
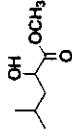
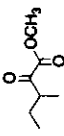
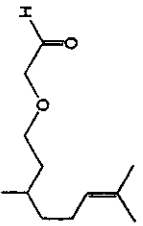
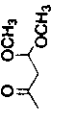
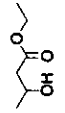
<sup>a</sup> Step 2: All of the substances in this group are metabolized to innocuous products.

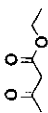
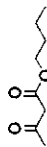
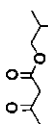
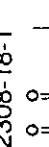
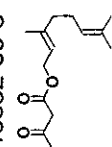
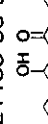
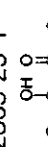
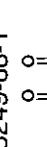
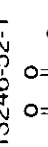
<sup>b</sup> The thresholds for human intake for structural classes I and II are 1800 µg per day and 540 µg per day, respectively. All intake values are expressed in µg per day.

<sup>c</sup> An ADI of 0-4 mg/kg of body weight was established for this substance at the present meeting.

Table 3

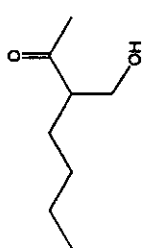
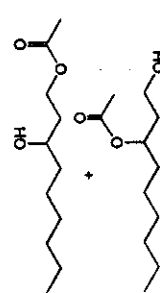
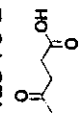
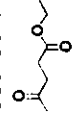
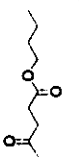
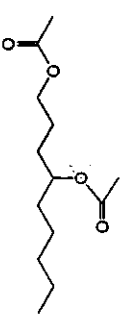
**Summary of the results of the safety evaluation of 47 aliphatic primary alcohols, aldehydes, carboxylic acids, acetals and esters containing additional oxygenated functional groups<sup>a</sup>**

| Substance <sup>b</sup>                                                   | No. | CAS no. and structure                                                                              | Step A3 <sup>c</sup><br>Does intake exceed the threshold for human intake? | Step A4<br>Is the substance or are its metabolites endogenous? | Step A5<br>Adequate NOEL for substance or related substance? | Conclusion<br>based on current intake |
|--------------------------------------------------------------------------|-----|----------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|----------------------------------------------------------------|--------------------------------------------------------------|---------------------------------------|
| 2-Oxobutyric acid<br>(2-oxobutanoic acid)                                | 589 | 600-18-0<br>    | No<br>Europe: 0.03<br>USA: 2                                               | NR                                                             | NR                                                           | No safety concern                     |
| Methyl 2-hydroxy-4-methyl-pentanoate (methyl 2-hydroxy-4-methylvalerate) | 590 | 40348-72-9<br>  | No<br>Europe: ND<br>USA: 0.8                                               | NR                                                             | NR                                                           |                                       |
| Methyl 2-oxo-3-methyl-pentanoate (methyl 3-methyl-2-oxo-pentanoate)      | 591 | 3682-42-6<br>   | No<br>Europe: ND<br>USA: 19                                                | NR                                                             | NR                                                           |                                       |
| Citronelloxyacetaldehyde<br>([(3,7-dimethyl-6-octenyl)oxy]-acetaldehyde) | 592 | 7492-67-3<br> | No<br>Europe: 34<br>USA: 0.1                                               | NR                                                             | NR                                                           |                                       |
| 3-Oxobutanol dimethyl acetal (4,4-dimethoxy-2-butanone)                  | 593 | 5436-21-5<br> | No<br>Europe: 0.01<br>USA: 0.1                                             | NR                                                             | NR                                                           |                                       |
| Ethyl 3-hydroxybutyrate                                                  | 594 | 5405-41-4<br> | No<br>Europe: 12<br>USA: 29                                                | NR                                                             | NR                                                           |                                       |

|                                                                    |     |            |                                                                                       | Yes <sup>d</sup> | Yes<br>Europe: 1900<br>USA: 3900 | NR |
|--------------------------------------------------------------------|-----|------------|---------------------------------------------------------------------------------------|------------------|----------------------------------|----|
| Ethyl acetoacetate                                                 | 595 | 141-97-9   |    | NR               | No<br>Europe: 98<br>USA: 6       | NR |
| Butyl acetoacetate                                                 | 596 | 591-60-6   |    | NR               | No<br>Europe: ND<br>USA: 4       | NR |
| Isobutyl acetoacetate                                              | 597 | 7779-75-1  |    | NR               | No<br>Europe: ND<br>USA: 11      | NR |
| Isoamyl acetoacetate<br>(isopentyl acetoacetate)                   | 598 | 2308-18-1  |    | NR               | No<br>Europe: ND<br>USA: 0.04    | NR |
| Geranyl acetoacetate<br>(3,7-dimethyl-2,6-octadienyl acetoacetate) | 599 | 10032-00-5 |    | NR               | No<br>Europe: 1<br>USA: 1        | NR |
| Methyl 3-hydroxyhexanoate                                          | 600 | 21188-58-9 |    | NR               | No<br>Europe: 93<br>USA: 0.1     | NR |
| Ethyl 3-hydroxyhexanoate                                           | 601 | 2305-25-1  |  | NR               | No<br>Europe: 0.04<br>USA: 1     | NR |
| Ethyl 3-oxohexanoate                                               | 602 | 3249-68-1  |  | NR               | No<br>Europe: ND<br>USA: 0.02    | NR |
| Ethyl 2,4-dioxohexanoate                                           | 603 | 13246-52-1 |  | NR               |                                  | NR |

No safety concern

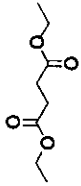
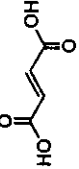
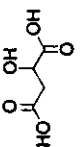
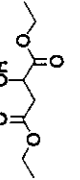
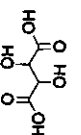
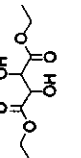
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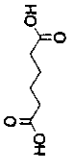


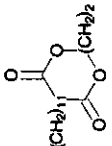
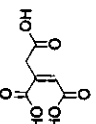
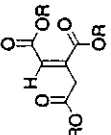
| Substance <sup>b</sup>                                             | No. | CAS no. and structure                                                                               | Step A3 <sup>c</sup><br>Does intake exceed the threshold for human intake? | Step A4<br>Is the substance or are its metabolites endogenous? | Step A5<br>Adequate NOEL for substance or related substance? | Conclusion based on current intake |
|--------------------------------------------------------------------|-----|-----------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|----------------------------------------------------------------|--------------------------------------------------------------|------------------------------------|
| 3-(Hydroxymethyl)-2-heptanone                                      | 604 | 65405-68-7<br>   | No<br>Europe: 38<br>USA: 8                                                 | NR                                                             | NR                                                           | No safety concern                  |
| 1,3-Nonanediol acetate (mixed esters) (1,3-nonanediol monoacetate) | 605 | 1322-17-4<br>    | No<br>Europe: 15<br>USA: 8                                                 | NR                                                             | NR                                                           |                                    |
| Levulinic acid (4-oxopentanoic acid)                               | 606 | 123-76-2<br>     | No<br>Europe: 1600<br>USA: 1200                                            | NR                                                             | NR                                                           |                                    |
| Ethyl levulinatate (ethyl 4-oxopentanoate)                         | 607 | 539-88-8<br>    | No<br>Europe: 740<br>USA: 84                                               | NR                                                             | NR                                                           |                                    |
| Butyl levulinatate (butyl 4-oxopentanoate)                         | 608 | 2052-15-5<br>  | No<br>Europe: ND<br>USA: 3                                                 | NR                                                             | NR                                                           |                                    |
| 1,4-Nonanediol diacetate                                           | 609 | 67715-81-5<br> | No<br>Europe: 0.06<br>USA: 0.4                                             | NR                                                             | NR                                                           |                                    |

|                                                                           |     |            |  |                                |    |    |
|---------------------------------------------------------------------------|-----|------------|--|--------------------------------|----|----|
| Hydroxycitronellol (3,7-dimethyloctane-1,7-diol)                          | 610 | 107-74-4   |  | No<br>Europe: 11<br>USA: 6     | NR | NR |
| Hydroxycitronellal (7-hydroxy-3,7-dimethyloctanal)                        | 611 | 107-75-5   |  | No<br>Europe: 28<br>USA: 30    | NR | NR |
| Hydroxycitronellal dimethyl acetal (8,8-dimethoxy-2,6-dimethyl-2-octanol) | 612 | 141-92-4   |  | No<br>Europe: 0.04<br>USA: 0.8 | NR | NR |
| Hydroxycitronellal diethyl acetal (8,8-diehoxy-2,6-dimethyloctan-2-ol)    | 613 | 7779-94-4  |  | No<br>Europe: 0.01<br>USA: 2   | NR | NR |
| Diethyl malonate (diethyl propanedioate)                                  | 614 | 105-53-3   |  | No<br>Europe: 760<br>USA: 370  | NR | NR |
| Butyl ethyl malonate (butyl ethyl propanedioate)                          | 615 | 17373-84-1 |  | No<br>Europe: ND<br>USA: 0.1   | NR | NR |
| Dimethyl succinate (dimethyl butanedioate)                                | 616 | 106-65-0   |  | No<br>Europe: 78<br>USA: 120   | NR | NR |

No safety concern

Table 3 (continued)

| Substance <sup>b</sup>                                                                                                  | No. | CAS no. and structure                                                                             | Step A3 <sup>c</sup><br>Does intake exceed the threshold for human intake? | Step A4<br>Is the substance or are its metabolites endogenous? | Step A5<br>Adequate NOEL for substance or related substance?                                                                    | Conclusion based on current intake |
|-------------------------------------------------------------------------------------------------------------------------|-----|---------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|----------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|------------------------------------|
| Diethyl succinate (diethyl butanedioate)                                                                                | 617 | 123-25-1<br>   | No<br>Europe: 150<br>USA: 180                                              | NR                                                             | NR                                                                                                                              | No safety concern                  |
| Fumaric acid* (2E)-2-butenedioic acid)                                                                                  | 618 | 110-17-8<br>   | Yes<br>Europe: 920<br>USA: 220000                                          | Yes <sup>d</sup>                                               | NR                                                                                                                              |                                    |
| (-)-Malic acid ((2S)-hydroxybutanedioic acid)                                                                           | 619 | 97-67-6<br>    | Yes<br>Europe: 16000<br>USA: 58000                                         | Yes <sup>e</sup>                                               | NR                                                                                                                              |                                    |
| Diethyl malate (diethyl hydroxybutanedioate)                                                                            | 620 | 7554-12-3<br> | No<br>Europe: 5<br>USA: 34                                                 | NR                                                             | NR                                                                                                                              |                                    |
| Mixture of (+), (-), (+/-)- and meso-tartaric acid (mixture of (+), (-), (+/-)- and meso-2,3-dihydroxybutanedioic acid) | 621 | 87-69-4<br>  | Yes<br>Europe: 4400<br>USA: 14000                                          | No                                                             | Yes; the NOEL of 1200mg/kg of body weight per day reported in a 2-year study in rats is >1000 times the daily per capita intake |                                    |
| Diethyl tartrate (diethyl 2,3-dihydroxybutanedioate)                                                                    | 622 | 87-91-2<br>  | No<br>Europe: 17<br>USA: 0.02                                              | NR                                                             | NR                                                                                                                              |                                    |

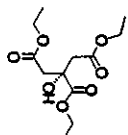
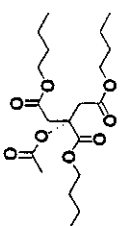
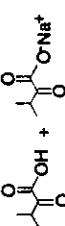
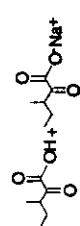
|                                                                       |     |           |                                                                                       |                                 |    |                                                                                                                                                                                             |
|-----------------------------------------------------------------------|-----|-----------|---------------------------------------------------------------------------------------|---------------------------------|----|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Adipic acid (hexanedioic acid)                                        | 623 | 124-04-9  |    | Yes<br>Europe: 12<br>USA: 18000 | No | Yes; the NOEL of 6200 mg/kg of body weight per day reported for the structurally related substance, dibutyl sebacate, in a 2-year study in rats is >10000 times the daily per capita intake |
| Diethyl sebacate (diethyl decanedioate)                               | 624 | 110-40-7  |    | No<br>Europe: 135<br>USA: 76    | NR | NR                                                                                                                                                                                          |
| Dibutyl sebacate (dibutyl decanedioate)                               | 625 | 109-43-3  |    | No<br>Europe: ND<br>USA: 0.08   | NR | NR                                                                                                                                                                                          |
| Ethylene brassylate (1,4-dioxacycloheptadecane-5,17-dione)            | 626 | 105-95-3  |    | No<br>Europe: 4<br>USA: 0.8     | NR | NR                                                                                                                                                                                          |
| Aconitic acid (1-propene-1,2,3-tricarboxylic acid)                    | 627 | 499-12-7  |   | No<br>Europe: 0.01<br>USA: 0.02 | NR | NR                                                                                                                                                                                          |
| Ethyl aconitate (mixed esters) (ethyl 1-propene-1,2,3-tricarboxylate) | 628 | 1321-30-8 |  | No<br>Europe: ND<br>USA: 4      | NR | NR                                                                                                                                                                                          |

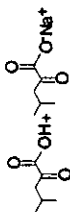


No safety concern

R = C<sub>2</sub>H<sub>5</sub>



Table 3 (continued)

| Substance <sup>b</sup>                                                         | No. | CAS no. and structure                                                                                             | Step A3 <sup>c</sup><br>Does intake exceed the threshold for human intake? | Step A4<br>Is the substance or are its metabolites endogenous? | Step A5<br>Adequate NOEL for substance or related substance? | Conclusion based on current intake |
|--------------------------------------------------------------------------------|-----|-------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|----------------------------------------------------------------|--------------------------------------------------------------|------------------------------------|
| Triethyl citrate <sup>a</sup> (triethyl 2-hydroxy-1,2,3-propanetricarboxylate) | 629 | 77-93-0<br>                    | Yes<br>Europe: 3400<br>USA: 2400                                           | Yes <sup>d</sup>                                               | NR                                                           |                                    |
| Tributyl acetylacrylate (tributyl 2-(acetyloxy)-1,2,3-propanetricarboxylate)   | 630 | 77-90-7<br>                    | No<br>Europe: ND<br>USA: 0.4                                               | NR                                                             | NR                                                           |                                    |
| 3-Methyl-2-oxobutanoic acid and its sodium salt                                | 631 | 759-05-7 and 3715-29-5<br>   | No<br>Europe: 0.01<br>USA: 0.2                                             | NR                                                             | NR                                                           | No safety concern                  |
| 3-Methyl-2-oxopentanoic acid and its sodium salt                               | 632 | 1460-34-0 and 66872-74-0<br> | No<br>Europe: ND<br>USA: 0.2                                               | NR                                                             | NR                                                           |                                    |

|                                                  |     |                        |                                                                                     |                              |    |    |                   |
|--------------------------------------------------|-----|------------------------|-------------------------------------------------------------------------------------|------------------------------|----|----|-------------------|
| 4-Methyl-2-oxopentanoic acid and its sodium salt | 633 | 816-66-0 and 4502-00-5 |  | No<br>Europe: ND<br>USA: 0.2 | NR | NR | No safety concern |
| 2-Oxopentanedioic acid                           | 634 | 328-50-7               |  | No<br>Europe: ND<br>USA: 0.2 | NR | NR | No safety concern |
| 3-Hydroxy-2-oxopropionic acid                    | 635 | 1113-60-6              |  | No<br>Europe: ND<br>USA: 0.2 | NR | NR | No safety concern |

CAS: Chemical Abstracts Service; ND: no data available; NR: not required for evaluation because an adequate NOEL for the substance or a related substance was identified at step A3 or A4 of the Procedure.

<sup>a</sup> Step 1: All of the substances in this group are in structural class 1.

<sup>b</sup> Step 2: All of the substances in this group are metabolized to innocuous products.

<sup>c</sup> The substance names are given as they appear in the specifications monograph (FAO Food and Nutrition Paper, No. 52, Add. 7, 1999). In cases where substances were evaluated under their trivial name, the systematic name is given in parentheses.

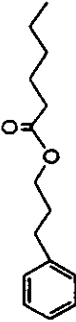


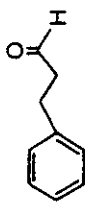

<sup>d</sup> The threshold for human intake of class 1 is 1800 µg per day. All intake values are expressed in µg per day.

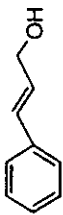

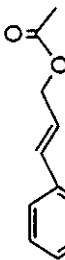
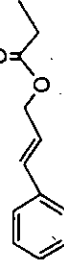



<sup>e</sup> Ethyl acetoacetate is expected to be hydrolysed to acetoacetic acid, which is endogenous in humans.

<sup>f</sup> The ADI for this substance was maintained.

<sup>1</sup> Fumaric acid, (-)-malic acid and triethyl citrate are components of the tricarboxylic acid cycle.

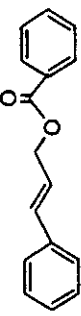

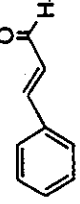
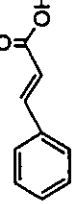
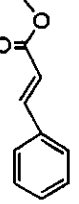
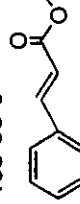
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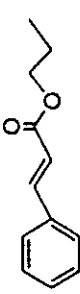
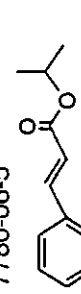
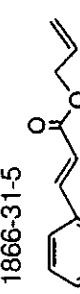
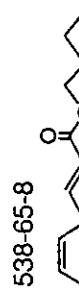
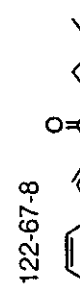
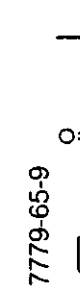
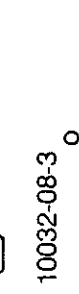
| Flavouring agent <sup>a</sup>                     | No. | CAS no. and structure                                                                             | Step A3 <sup>c</sup><br>Does intake exceed the threshold for human intake? | Step A4<br>Is the substance or are its metabolites endogenous? | Step A5<br>Adequate NOEL for substance or related substance? | Comments   | Conclusion based on current intake |
|---------------------------------------------------|-----|---------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|----------------------------------------------------------------|--------------------------------------------------------------|------------|------------------------------------|
| 3-Phenylpropyl hexanoate                          | 642 | 6281-40-9<br>  | No<br>Europe: ND<br>USA: 0.4                                               | NR                                                             | NR                                                           | See note 2 | No safety concern                  |
| Methyl 3-phenylpropionate                         | 643 | 103-25-3<br>   | No<br>Europe: ND<br>USA: 3                                                 | NR                                                             | NR                                                           | See note 2 |                                    |
| Ethyl 3-phenylpropionate                          | 644 | 2021-28-5<br> | No<br>Europe: 1<br>USA: 0.07                                               | NR                                                             | NR                                                           | See note 2 |                                    |
| 3-Phenylpropionaldehyde<br>(benzenepropanal)      | 645 | 104-53-0<br> | No<br>Europe: 19<br>USA: 19                                                | NR                                                             | NR                                                           | See note 1 |                                    |
| 3-Phenylpropionic acid<br>(benzenepropanoic acid) | 646 | 501-52-0<br> | No<br>Europe: 23<br>USA: 0.5                                               | NR                                                             | NR                                                           | See note 3 |                                    |

|                      |     |                                                                                                   | Yes                              | No | Yes <sup>d</sup> | See note 4 |
|----------------------|-----|---------------------------------------------------------------------------------------------------|----------------------------------|----|------------------|------------|
| Cinnamyl alcohol     | 647 | 104-54-1<br>   | Yes<br>Europe: 1800<br>USA: 1900 | NR | NR               | See note 4 |
| Cinnamyl formate     | 649 | 104-65-4<br>   | No<br>Europe: 2<br>USA: 17       | NR | NR               | See note 5 |
| Cinnamyl acetate     | 650 | 103-54-8<br>   | No<br>Europe: 210<br>USA: 300    | NR | NR               | See note 5 |
| Cinnamyl propionate  | 651 | 103-56-0<br>   | No<br>Europe: 4<br>USA: 25       | NR | NR               | See note 5 |
| Cinnamyl butyrate    | 652 | 103-61-7<br>  | No<br>Europe: 3<br>USA: 2        | NR | NR               | See note 5 |
| Cinnamyl isobutyrate | 653 | 103-59-3<br> | No<br>Europe: 13<br>USA: 22      | NR | NR               | See note 5 |
| Cinnamyl isovalerate | 654 | 140-27-2<br> | No<br>Europe: 5<br>USA: 8        | NR | NR               | See note 5 |

No safety concern

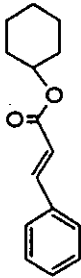
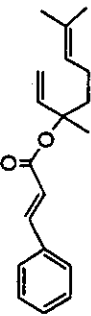
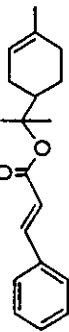
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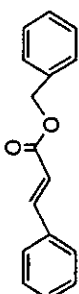
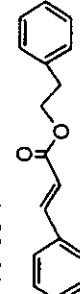
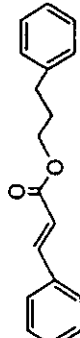
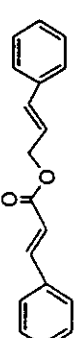

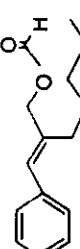
| Flavouring agent <sup>b</sup>             | No. | CAS no. and structure                                                                             | Step A3 <sup>c</sup><br>Does intake<br>exceed the<br>threshold for<br>human intake? | Step A4<br>Is the<br>substance<br>or are its<br>metabolites<br>endogenous? | Step A5<br>Adequate<br>NOEL for<br>substance<br>or related<br>substance? | Comments   | Conclusion<br>based on<br>current<br>intake |
|-------------------------------------------|-----|---------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|----------------------------------------------------------------------------|--------------------------------------------------------------------------|------------|---------------------------------------------|
| Cinnamyl benzoate                         | 760 | 5320-75-2<br>  | No<br>Europe: ND<br>USA: 1                                                          | NR                                                                         | NR                                                                       | See note 6 | No safety<br>concern                        |
| Cinnamyl phenylacetate                    | 655 | 7492-65-1<br>  | No<br>Europe: 0.003<br>USA: 1                                                       | NR                                                                         | NR                                                                       | See note 7 |                                             |
| Cinnamaldehyde<br>(3-phenyl-2-propenal)   | 656 | 104-55-2<br>   | Yes<br>Europe: 2500<br>USA: 59 000                                                  | No                                                                         | Yes <sup>a</sup>                                                         | See note 4 |                                             |
| Cinnamic acid (3-phenyl-2-propenoic acid) | 657 | 621-82-9<br> | No<br>Europe: 32<br>USA: 44                                                         | NR                                                                         | NR                                                                       | See note 8 |                                             |
| Methyl cinnamate                          | 658 | 103-26-4<br> | Yes<br>Europe: 2800<br>USA: 830                                                     | No                                                                         | Yes <sup>d</sup>                                                         | See note 9 |                                             |
| Ethyl cinnamate                           | 659 | 103-36-6<br> | No<br>Europe: 100<br>USA: 70                                                        | NR                                                                         | NR                                                                       | See note 9 |                                             |

|                                                       |     |            |                                                                                       |                               |    |    |            |
|-------------------------------------------------------|-----|------------|---------------------------------------------------------------------------------------|-------------------------------|----|----|------------|
| Propyl cinnamate                                      | 660 | 7778-83-8  |    | No<br>Europe: 0.4<br>USA: 4   | NR | NR | See note 9 |
| Isopropyl cinnamate                                   | 661 | 7780-06-5  |    | No<br>Europe: 19<br>USA: 3    | NR | NR | See note 9 |
| Allyl cinnamate<br>(3-propenyl 3-phenyl-2-propenoate) | 19  | 1866-31-5  |    | No<br>Europe: 5<br>USA: 0.3   | NR | NR | See note 9 |
| Butyl cinnamate                                       | 663 | 538-65-8   |    | No<br>Europe: 0.4<br>USA: 0.2 | NR | NR | See note 9 |
| Isobutyl cinnamate                                    | 664 | 122-67-8   |    | No<br>Europe: 1<br>USA: 3     | NR | NR | See note 9 |
| Isoamyl cinnamate<br>(isopentyl cinnamate)            | 665 | 7779-65-9  |  | No<br>Europe: 8<br>USA: 6     | NR | NR | See note 9 |
| Heptyl cinnamate                                      | 666 | 10032-08-3 |  | No<br>Europe: 2<br>USA: 52    | NR | NR | See note 9 |

No safety concern

Table 1 (continued)

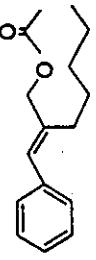

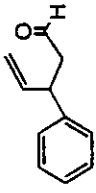
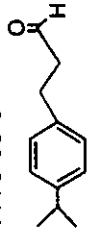
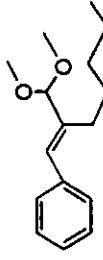
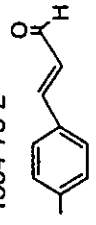
| Flavouring agent <sup>b</sup>                                                               | No. | CAS no. and structure                                                                               | Step A3 <sup>c</sup><br>Does intake exceed the threshold for human intake? | Step A4<br>Is the substance or are its metabolites endogenous? | Step A5<br>Adequate NOEL for substance or related substance? | Comments                                                                                                                                                             | Conclusion based on current intake |
|---------------------------------------------------------------------------------------------|-----|-----------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|----------------------------------------------------------------|--------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|
| Cyclohexyl cinnamate                                                                        | 667 | 7779-17-1<br>    | No<br>Europe: 0.4<br>USA: 0.04                                             | NR                                                             | NR                                                           | Cyclohexyl cinnamate is hydrolysed to cinnamic acid (see note 8) and cyclohexanol. Cyclohexanol is mainly conjugated with glucuronic acid and excreted               | No safety concern                  |
| Linallyl cinnamate                                                                          | 668 | 78-37-5<br>      | No<br>Europe: 7<br>USA: 3                                                  | NR                                                             | NR                                                           | Linallyl cinnamate is hydrolysed to cinnamic acid (see note 8) and linalool. Linalool undergoes ω- and ω-1-oxidation to yield polar metabolites which are excreted   |                                    |
| Terpinyl cinnamate<br>( <i>(Z)</i> -1-methyl-1-(4-methyl-3-cyclohexen-1-yl)ethyl cinnamate) | 669 | 10024-56-3<br> | No<br>Europe: 0.01<br>USA: 0.5                                             | NR                                                             | NR                                                           | Terpinyl cinnamate is hydrolysed to cinnamic acid (see note 8) and terpineol. Terpineol undergoes ω- and ω-1-oxidation to yield polar metabolites which are excreted |                                    |

|                                                                       |     |            |                                                                                       |                               |    |    |                                                                                                                                                                                         |
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| Benzyl cinnamate                                                      | 670 | 103-41-3   |    | No<br>Europe: 44<br>USA: 69   | NR | NR | Benzyl cinnamate is hydrolysed to cinnamic acid (see note 8) and benzyl alcohol. Benzyl alcohol is oxidized to benzoic acid and excreted as hippuric acid                               |
| Phenethyl cinnamate                                                   | 671 | 103-53-7   |    | No<br>Europe: 6<br>USA: 50    | NR | NR | Phenethyl cinnamate is hydrolysed to cinnamic acid (see note 8) and phenethyl alcohol. Phenethyl alcohol is oxidized to phenylacetic acid and excreted as the glucuronic acid conjugate |
| 3-Phenylpropyl cinnamate                                              | 672 | 122-68-9   |    | No<br>Europe: 0.6<br>USA: 37  | NR | NR | See notes 1 and 8                                                                                                                                                                       |
| Cinnamyl cinnamate                                                    | 673 | 122-69-0   |  | No<br>Europe: 2<br>USA: 36    | NR | NR | See notes 4 and 8                                                                                                                                                                       |
| 5-Phenylpentanol<br>(benzenepentan-1-ol)                              | 675 | 10521-91-2 |  | No<br>Europe: ND<br>USA: 0.1  | NR | NR | See note 1                                                                                                                                                                              |
| $\alpha$ -Amylcinnamyl formate<br>(2-(phenylmethylene)heptyl formate) | 676 | 7493-79-0  |  | No<br>Europe: 1.4<br>USA: 0.5 | NR | NR | See note 10                                                                                                                                                                             |

No safety concern



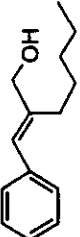
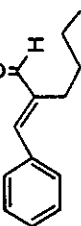
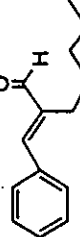
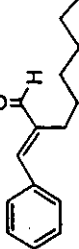
Table 1 (continued)

| Flavouring agent <sup>a</sup>                                                                     | No. | CAS no. and structure                                                                              | Step A3 <sup>c</sup><br>Does intake<br>exceed the<br>threshold for<br>human intake? | Step A4<br>Is the<br>substance<br>or are its<br>metabolites<br>endogenous? | Step A5<br>Adequate<br>NOEL for<br>substance<br>or related<br>substance? | Comments    | Conclusion<br>based on<br>current<br>intake |
|---------------------------------------------------------------------------------------------------|-----|----------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|----------------------------------------------------------------------------|--------------------------------------------------------------------------|-------------|---------------------------------------------|
| $\alpha$ -Amylcinnamyl acetate<br>(2-(phenylmethylene)heptyl<br>acetate)                          | 677 | 7493-78-9<br>   | No<br>Europe: 3<br>USA: 260                                                         | NR                                                                         | NR                                                                       | See note 10 | No safety<br>concern                        |
| $\alpha$ -Amylcinnamyl isovalerate<br>(2-(phenylmethylene)heptyl<br>isovalerate)                  | 678 | 7493-80-3<br>   | No<br>Europe: 0.01<br>USA: 0.5                                                      | NR                                                                         | NR                                                                       | See note 10 |                                             |
| 3-Phenyl-4-pentenal<br>(3-phenylpent-4-enal)                                                      | 679 | 939-21-9<br>    | No<br>Europe: 1<br>USA: 2                                                           | NR                                                                         | NR                                                                       | See note 11 |                                             |
| 3-( <i>p</i> -Isopropylphenyl)<br>propionaldehyde<br>(3-( <i>p</i> -cumenyl)propion-<br>aldehyde) | 680 | 7775-00-0<br>  | No<br>Europe: ND<br>USA: 0.1                                                        | NR                                                                         | NR                                                                       | See note 1  |                                             |
| $\alpha$ -Amylcinnamaldehyde<br>dimethyl acetal<br>((2-(dimethoxymethyl)-1-<br>heptyl)benzene)    | 681 | 91-87-2<br>   | No<br>Europe: 0.01<br>USA: 0.007                                                    | NR                                                                         | NR                                                                       | See note 10 |                                             |
| <i>p</i> -Methylcinnamaldehyde<br>(3-(4-methylphenyl)-2-<br>propenal)                             | 682 | 1504-75-2<br> | No<br>Europe: 0.01<br>USA: 0.9                                                      | NR                                                                         | NR                                                                       | See note 4  |                                             |

|                                                                                              |     |            |                                                                                       |                                  |    |                  |                                                                                                                                                                                                                                                       |
|----------------------------------------------------------------------------------------------|-----|------------|---------------------------------------------------------------------------------------|----------------------------------|----|------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| $\alpha$ -Methylcinnamaldehyde                                                               | 683 | 101-39-3   |    | No<br>Europe: 3<br>USA: 390      | NR | NR               | See note 4                                                                                                                                                                                                                                            |
| <i>p</i> -Methoxycinnamaldehyde                                                              | 687 | 1963-36-6  |    | No<br>Europe: 0.04<br>USA: 0.01  | NR | NR               | See note 4                                                                                                                                                                                                                                            |
| <i>o</i> -Methoxycinnamaldehyde                                                              | 688 | 1504-74-1  |    | No<br>Europe: 0.6<br>USA: 71     | NR | NR               | <i>o</i> -Methoxycinnamaldehyde is oxidized to the corresponding acid, conjugated with glycine, and excreted. Alternatively, the acid may undergo $\beta$ -oxidation to yield the $\beta$ -hydroxy-carboxylic acid derivative, which is also excreted |
| <i>p</i> -Methoxy- $\alpha$ -methylcinnamaldehyde (4'-methoxy-2-methylcinnamaldehyde)        | 689 | 65405-67-6 |   | No<br>Europe: 0.3<br>USA: 0.05   | NR | NR               | See note 4                                                                                                                                                                                                                                            |
| <b>Structural class II</b><br>Cinnamaldehyde ethylene glycol acetal (2-styryl-1,3-dioxolane) | 648 | 5660-60-6  |  | Yes<br>Europe: 690<br>USA: 0.007 | No | Yes <sup>a</sup> | Hydrolysed to the corresponding alcohol and aldehyde                                                                                                                                                                                                  |

No safety concern

Table 1 (continued)

| Flavouring agent <sup>b</sup>                                       | No. | CAS no. and structure                                                                             | Step A3 <sup>c</sup><br>Does intake exceed the threshold for human intake? | Step A4<br>Is the substance or are its metabolites endogenous? | Step A5<br>Adequate NOEL for substance or related substance? | Comments                                                                                                                                        | Conclusion based on current intake |
|---------------------------------------------------------------------|-----|---------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|----------------------------------------------------------------|--------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|
| $\alpha$ -Amylcinnamyl alcohol<br>(2-pentyl-3-phenylprop-2-en-1-ol) | 674 | 101-85-9<br>   | No<br>Europe: 4<br>USA: 1                                                  | NR                                                             | NR                                                           | $\alpha$ -Amylcinnamyl alcohol is oxidized to the corresponding aldehyde, which is further oxidized to $\alpha$ -amylcinnamic acid and excreted | No safety concern                  |
| $\alpha$ -Butylcinnamaldehyde                                       | 684 | 7492-44-6<br>  | No<br>Europe: 0.01<br>USA: 0.07                                            | NR                                                             | NR                                                           | See note 11                                                                                                                                     |                                    |
| $\alpha$ -Amylcinnamaldehyde<br>( $\alpha$ -pentylcinnamaldehyde)   | 685 | 122-40-7<br>  | No<br>Europe: 25<br>USA: 23                                                | NR                                                             | NR                                                           | See note 11                                                                                                                                     |                                    |
| $\alpha$ -Hexylcinnamaldehyde                                       | 686 | 101-86-0<br> | No<br>Europe: 87<br>USA: 11                                                | NR                                                             | NR                                                           | See note 11                                                                                                                                     |                                    |

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.
- b The names of the flavouring agents are given as they appear in the specifications monograph (FAO Food and Nutrition Paper, No. 52, Add. 8, 2000). In cases where flavouring agents were evaluated under their trivial name, the systematic name is given in parentheses.
- c The thresholds for human intake for structural classes I and II are 1800 µg per day and 540 µg per day, respectively. All intake values are expressed in µg per day.
- d The NOEL of 54 mg/kg of body weight per day in a 4-month toxicity study in rats is >1000 times the estimated intake of cinnamyl alcohol when used as a flavouring agent.
- e The NOEL of 620 mg/kg of body weight per day in a 13-week toxicity study in rats is >600 times the estimated intake of cinnamaldehyde when used as a flavouring agent.
- f The NOELs of 54 mg/kg of body weight per day for related substance No. 647 and 80 mg/kg of body weight per day for related substance No. 659 are >1000 times the estimated intake of methyl cinnamate when used as a flavouring agent.
- g The NOEL of 620 mg/kg of body weight per day for related substance No. 656 is >10000 times the estimated intake of cinnamaldehyde ethylene glycol acetal when used as a flavouring agent.

Notes to Table 1

1. Oxidized to yield the corresponding acid, which undergoes further β-oxidation of the side-chains and cleavage to yield the benzoic acid derivative. It then conjugates with glycine and/or glucuronic acid, and is excreted in the urine.
2. Hydrolysed to the corresponding acid and alcohol. The acid is completely oxidized and the alcohol, 3-phenyl-1-propanol, is further metabolized and excreted (see note 1).
3. Undergoes β-oxidation of the side-chains and cleavage to yield the corresponding benzoic acid derivative. It then conjugates with glycine and/or glucuronic acid and is excreted in the urine.
4. Oxidized to cinnamic acid (or its corresponding derivative), which is further oxidized to benzoic acid (or its corresponding derivative). The latter substance is excreted as hippuric acid (or its corresponding derivative).
5. Hydrolysed to cinnamyl alcohol and the corresponding carboxylic acid. Cinnamyl alcohol is oxidized and excreted (see note 4); the carboxylic acid is either completely oxidized or conjugated and excreted primarily in the urine.
6. Hydrolysed to cinnamyl alcohol and benzoic acid. Cinnamyl alcohol is oxidized to cinnamic acid, which is further oxidized to benzoic acid (see note 4).
7. Hydrolysed to cinnamyl alcohol and phenylacetic acid. Cinnamyl alcohol is oxidized to benzoic acid (see note 4). Phenylacetic acid is excreted as the glucuronic acid conjugate.
8. Undergoes β-oxidation and is excreted as hippuric acid.
9. Rapidly hydrolysed to cinnamic acid (see note 8) and the corresponding alcohol. The corresponding alcohol is completely oxidized.
10. Hydrolysed to α-amylocinnamyl alcohol (No. 674) and the corresponding acid, which is excreted. α-Amylocinnamyl alcohol is oxidized to α-amylocinnamaldehyde, which is further oxidized to α-amylocinnamic acid and excreted.
11. Oxidized to the corresponding acid and excreted.