the European Union during the previous year. Manufacturers were requested to exclude use of flavouring agents in pharmaceutical, tobacco or cosmetic products. In the USA, a series of surveys was conducted between 1970 and 1987 by the National Research Council of the National Academy of Sciences (under contract to the Food and Drug Administration) in which information was obtained from ingredient manufacturers and food processors on the amount of each substance destined for addition to the food supply and on the usual and maximum levels at which each substance was added to a number of broad food categories.

In using the data from these surveys to estimate intakes of flavouring agents, the Committee assumed that only 60% of the total amount used is reported and that the total amount used in food is consumed by only 10% of the population.

$$\text{Intake } (\mu g/\text{person per day}) = \frac{\text{Annual volume of production (kg)} \times 10^9\ (\mu g/kg)}{\text{Population of consumers} \times 0.6 \times 365 \text{ days}}$$

The population of consumers was assumed to be 32×10^6 in Europe and 24×10^6 in the USA.

In applying the Procedure, the Committee compared the estimated intakes with the thresholds for human intake for the respective structural classes. These are 1800 µg per day per person for class I, 540 µg per day per person for class II and 90 µg per day per person for class III.

4.1 Simple aliphatic and aromatic sulfides and thiols

The Committee evaluated a group of 137 flavouring agents that includes aliphatic and aromatic sulfides and thiols, with and without an additional oxygenated functional group (Table 1), using the Procedure for the Safety Evaluation of Flavouring Agents (see Fig. 1). The Committee had not previously evaluated any member of the group.

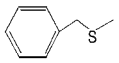
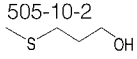
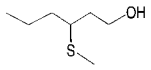
4.1.1 *Intake data*

The total annual volume of production of the 137 simple aliphatic and aromatic sulfides and thiols in this group destined for use as flavouring agents is approximately 6 tonnes in Europe and 5.3 tonnes in the USA. Methyl sulfide (no. 452) accounts for 51% of the total annual volume of production in Europe and 52% of the total annual volume of production in the USA. The estimated daily intake of methyl sulfide by consumers of this substance is 10 µg/kg of body weight in Europe and 9 µg/kg of body weight in the USA. The estimated daily intakes of the remaining substances in this group are much lower, the next highest values being 2 µg/kg of body weight

Table 1
Summary of the results of safety evaluations of 137 aliphatic and aromatic sulfides and thiols[a]

Substance[b]	No.	CAS no. and structure	*Step B3*[c] Does intake exceed the threshold for human intake?	*Step B4* Adequate NOEL for substance or structurally related substance?	*Step B5* Intake >1.5 µg/day?	Conclusion based on current intake
Subgroup i — simple sulfides (thioethers)						
Structural class I						
Methyl sulfide	452	75-18-3	No Europe: 590 USA: 527	Yes, a NOEL of 250 mg/kg of body weight per day was reported in a 14-week study in rats treated by gavage at multiple doses	NR	No safety concern
Methyl ethyl sulfide (ethyl methyl sulfide)	453	624-89-5 	No Europe: ND USA: 2	Yes, related substance no. 452	NR	
Diethyl sulfide	454	352-93-2	No Europe: ND USA: 13	Yes, related substance no. 452	NR	
Butyl sulfide	455	544-40-1 	No Europe: 4 USA: 0.1	Yes, related substance no. 452	NR	
(1-Buten-1-yl)methyl sulfide	457	32951-19-2	No Europe: ND USA: 0.1	Yes, related substance no. 452	NR	
bis(Methylthio)methane	533	1618-26-4 	No Europe: ND USA: 94	Yes, related substance no. 452	NR	
Structural class II						
Allyl sulfide	458	592-88-1	No Europe: ND USA: 0.4	No, related substance no. 521, subgroup iv, is not predicted to be a metabolite of allyl sulfide	No	No safety concern

Table 1 (*continued*)

Substance[b]	No.	CAS no. and structure	*Step B3*[c] Does intake exceed the threshold for human intake?	*Step B4* Adequate NOEL for substance or structurally related substance?	*Step B5* Intake >1.5 µg/day?	Conclusion based on current intake
Subgroup i — continued						
Structural class II (continued)						
Methyl phenyl sulfide	459	100-68-5 	No Europe: ND USA: 0.4	No	No	No safety concern
Benzyl methyl sulfide	460	766-92-7 	No Europe: 0.2 USA: 0.02	No	No	
Subgroup ii — acyclic sulfides with oxidized side-chains						
Structural class I						
3-(Methylthio)propanol	461	505-10-2 	No Europe: 4 USA: 1	Yes, related substance no. 505; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	No safety concern
4-(Methylthio)butanol	462	20582-85-8 	No Europe: 0.02 USA: 0.1	Yes, related substance no. 461; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	
3-(Methylthio)-1-hexanol	463	51755-66-9 	No Europe: 5 USA: 0.1	Yes, related substance no. 461; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	

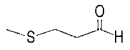
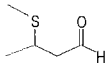
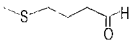
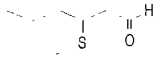
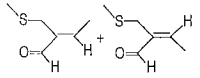
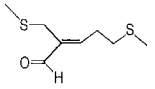
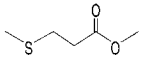
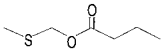
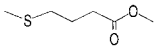
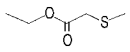
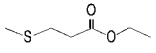
2-(Methylthio)acetaldehyde ((methylthio)acetaldehyde)	465	23328-62-3 	No Europe: ND USA: 1	Yes, related substance no. 461; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	No safety concern
3-(Methylthio)propionaldehyde	466	3268-49-3 	No Europe: 45 USA: 25	Yes, related substance no. 461; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	
3-(Methylthio)butanal	467	16630-52-7 	No Europe: 0.1 USA: 0.1	Yes, related substance no. 461; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	
4-(Methylthio)butanal	468	42919-64-2 	No Europe: ND USA: 0.02	Yes, related substance no. 461; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	
3-(Methylthio)hexanal	469	38433-74-8 	No Europe: ND USA: 1	Yes, related substance no. 461; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	
2-[(Methylthio)methyl]-2-butenal	470	40878-72-6 	No Europe: 0.04 USA: 0.1	No	No	
2,8-Dithianon-4-ene-4-carboxaldehyde (5-(methylthio)-2[(methylthio)methyl]-2-pentenal)	471	59902-01-1 	No Europe: 0.01 USA: 0.1	No	No	

Table 1 (*continued*)

Substance[b]	No.	CAS no. and structure	*Step B3*[c] Does intake exceed the threshold for human intake?	*Step B4* Adequate NOEL for substance or structurally related substance?	*Step B5* Intake >1.5 µg/day?	Conclusion based on current intake
Subgroup ii — continued						
Structural class I (continued)						
Methyl 3-(methylthio)propionate	472	13532-18-8 	No Europe: 146 USA: 9	Yes, related substance no. 461; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain; the simple side-chain acid and ester would be predicted to be of low toxicity	NR	No safety concern
(Methylthio)methyl butyrate	473	74758-93-3 	No Europe: ND USA: 0.1	Yes, related substance no. 461; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	
Methyl 4-(methylthio)butyrate	474	53053-51-3 	No Europe: 0.1 USA: 0.1	Yes, related substance no. 461; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	
Ethyl 2-(methylthio)acetate (ethyl(methylthio)acetate)	475	4455-13-4 	No Europe: ND USA: 0.1	Yes, related substance no. 461; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	
Ethyl 3-(methylthio)propionate	476	13327-56-5 	No Europe: 37 USA: 2	Yes, related substance no. 461; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	

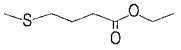
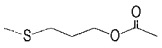
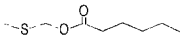
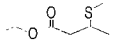
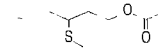
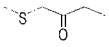
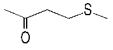
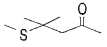
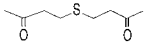
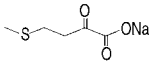
Ethyl 4-(methylthio)butyrate	477	22014-48-8 	No Europe: ND USA: 2	Yes, related substance no. 461; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	No safety concern
3-(Methylthio)propyl acetate	478	16630-55-0 	No Europe: ND USA: 11	Yes, related substance no. 461; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	
(Methylthio)methyl hexanoate	479	74758-91-1 	No Europe: ND USA: 0.1	Yes, related substance no. 461; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	
Ethyl 3-(methylthio)butyrate	480	Pending 	No Europe: ND USA: 0.1	Yes, related substance no. 461; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	
3-(Methylthio)hexyl acetate (3-(methylthio)-1-hexanol acetate)	481	51755-85-2 	No Europe: 0.1 USA: 9	Yes, related substance no. 461; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	
1-(Methylthio)-2-propanone	495	14109-72-9 	No Europe: ND USA: 0.2	Yes, related substance no. 461; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	
1-(Methylthio)-2-butanone	496	13678-58-5 	No Europe: 0.01 USA: 0.02	Yes, related substance no. 461; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	

Table 1 (*continued*)

Substance[b]	No.	CAS no. and structure	*Step B3*[c] Does intake exceed the threshold for human intake?	*Step B4* Adequate NOEL for substance or structurally related substance?	*Step B5* Intake >1.5 µg/day?	Conclusion based on current intake
Subgroup ii — continued						
Structural class I (continued)						
4-(Methylthio)-2-butanone	497	34047-39-7 	No Europe: 0.02 USA: 0.4	Yes, related substance no. 461; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	No safety concern
4-(Methylthio)-4-methyl-2-pentanone (4-methyl-4-(methylthio)-2-pentanone)	500	23550-40-5 	No Europe: 0.04 USA: 0.1	Yes, related substance no. 461; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	
Di(butan-3-one-1-yl) sulfide (4,4′-thiobis-2-butanone)	502	40790-04-3 	No Europe: ND USA: 0.02	Yes, related substance no. 461; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	
Structural class II						
o-(Methylthio)phenol	503	1073-29-6 	No Europe: 1 USA: 1	Yes, related substance nos 461 and 505; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	No safety concern
Structural class III						
Sodium 4-(methylthio)-2-oxobutanoate	501	— 	No Europe: ND USA: 0.2	Yes, related substance no. 461; data for substance no. 452, subgroup i, are relevant to compounds with a simple oxidized side-chain	NR	No safety concern

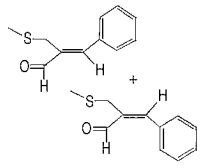
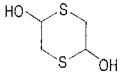
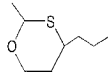
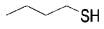
2-(Methylthiomethyl)-3-phenylpropenal (2-[(methylthio) methyl]-3-phenyl-2-propenal)	505	65887-08-3 	No Europe: ND USA: 2	Yes, a NOEL of 1.4 mg/kg of body weight per day was reported in a 90-day study in rats treated at only that dose	NR	No safety concern
Subgroup iii — cyclic sulfides ***Structural class I***						
2,5-Dimethyl-2,5-dihydroxy-1,4-dithiane (2,5-dimethyl-1,4-dithiane-2,5-diol)	562	55704-78-4 	No Europe: 0.2 USA: 0.2	Yes, a NOEL of 3.1 mg/kg of body weight per day was reported in a 90-day study in rats treated at only that dose	NR	No safety concern
2,5-Dihydroxy-1,4-dithiane (1,4-dithiane-2,5-diol)	550	40018-26-6 	No Europe: ND USA: 0.1	Yes, related substance no. 562	NR	
Structural class II						
2-Methyl-4-propyl-1,3-oxathiane	464	67715-80-4 	No Europe: 2 USA: 1	Yes, a NOEL of 0.44 mg/kg of body weight per day was reported in a 90-day study in rats treated at only that dose	NR	No safety concern
4,5-Dihydro-3(2*H*)-thiophenone (dihydro-3(2*H*)-thiophenone)	498	1003-04-9 	No Europe: 1 USA: 2	Yes, a NOEL of 9.2 mg/kg of body weight per day was reported in a 90-day study in rats treated at only that dose	NR	
2-Methyltetrahydrothiophen-3-one (dihydro-2-methyl-3(2*H*)-thiophenone)	499	13679-85-1 	No Europe: 19 USA: 0.1	Yes, related substance no. 498	NR	
1,4-Dithiane	456	505-29-3 	No Europe: ND USA: 0.1	Yes, related substance nos 464, 534 and 543	NR	

Table 1 (*continued*)

Substance[b]	No.	CAS no. and structure	*Step B3*[c] Does intake exceed the threshold for human intake?	*Step B4* Adequate NOEL for substance or structurally related substance?	*Step B5* Intake >1.5 µg/day?	Conclusion based on current intake
Subgroup iii — continued						
Structural class II (continued)						
2-Methyl-1,3-dithiolane	534	5616-51-3 	No Europe: 0.1 USA: 4	Yes, a NOEL of 7 mg/kg of body weight per day was reported in a 90-day study in rats treated at only that dose	NR	No safety concern
2,2,4,4,6,6-Hexamethyl-1,3,5-trithiane	543	828-26-2 	No Europe: 2 USA: 0.4	Yes, a NOEL of 0.21 mg/kg of body weight per day was reported in a 90-day study in rats treated at only that dose	NR	
Subgroup iv — simple thiols						
Structural class I						
Methyl mercaptan (methanethiol)	508	74-93-1 	No Europe: 83 USA: 0.2	Yes, related substance no. 516	NR	No safety concern
1-Propanethiol	509	107-03-9 	No Europe: 3 USA: 7	Yes, related substance no. 516	NR	
2-Propanethiol	510	75-33-2 	No Europe: ND USA: 0.004	Yes, related substance no. 516	NR	
1-Butanethiol	511	109-79-5 	No Europe: 0.5 USA: 0.04	Yes, related substance no. 516	NR	
2-Methyl-1-propanethiol	512	513-44-0 	No Europe: ND USA: 1.3	Yes, related substance no. 516	NR	

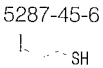
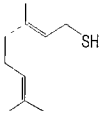
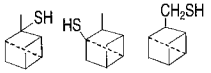
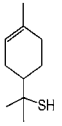
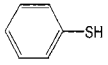
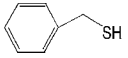
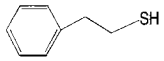
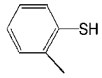
3-Methyl-1-butanethiol	513	541-31-1 	No Europe: ND USA: 0.01	Yes, related substance no. 516	NR	No safety concern
Pentane-2-thiol	514	2084-19-7 	No Europe: 2 USA: 2	Yes, related substance no. 516	NR	
2-Methyl-1-butanethiol	515	1878-18-8 	No Europe: 0.5 USA: 0.02	Yes, related substance no. 516	NR	
3-Methyl-2-butanethiol	517	2084-18-6 	No Europe: 0.02 USA: 0.02	Yes, related substance no. 516	NR	
1-Hexanethiol	518	111-31-9 	No Europe: ND USA: 0.01	Yes, related substance no. 516	NR	
2-Ethylhexane-1-thiol	519	7341-17-5 	No Europe: ND USA: 0.01	Yes, related substance no. 516	NR	
Prenylthiol (3-methyl-2-butene-1-thiol)	522	5287-45-6 	No Europe: ND USA: 0.2	Yes, related substance no. 516; related substance no. 587, subgroup ix, which is predicted to be metabolized to allyl disulfide and allyl mercaptan	NR	
Thiogeraniol (3,7-dimethyl-2(*E*), 6-octadiene-1-thiol)	524	39067-80-6 	No Europe: 2 USA: 0.02	Yes, related substance no. 516; related substance no. 587, subgroup ix, which is predicted to be metabolized to allyl disulfide and allyl mercaptan	NR	
Structural class II						
Cyclopentanethiol	516	1679-07-8 	No Europe: ND USA: 1	Yes, a NOEL of 0.56 mg/kg of body weight per day was reported in a 90-day study in rats treated at only that dose	NR	No safety concern

Table 1 (*continued*)

Substance[b]	No.	CAS no. and structure	*Step B3*[c] Does intake exceed the threshold for human intake?	*Step B4* Adequate NOEL for substance or structurally related substance?	*Step B5* Intake >1.5 µg/day?	Conclusion based on current intake
Subgroup iv — continued ***Structural class II (continued)***						
Mixture of 2-,3- and 10-mercaptopinane (mixture of 2,6,6-trimethyl-bicyclo(3.1.1) heptane-2-,3- and 10-thiols)	520	23832-18-0 	No Europe: 0.1 USA: 10	Yes, related substance nos 516, 528, 530 and 531; a NOEL of 0.06 mg/kg of body weight per day was reported in a 90-day study in rats treated at only that dose	NR	No safety concern
Allyl mercaptan (2-propene-1-thiol)	521	870-23-5 	No Europe: 0.2 USA: 2	Yes, related substance no. 516; related substance no. 587, subgroup ix, which is predicted to be metabolized to allyl disulfide and allyl mercaptan	NR	
1-*p*-Menthene-8-thiol (α,α-4-trimethyl-3-cyclohexene-1-methanethiol)	523	71159-90-5 	No Europe: 1 USA: 1	Yes, related substance no. 516; related substance no. 587, subgroup ix, which is predicted to be metabolized to allyl disulfide and allyl mercaptan	NR	
Benzenethiol	525	108-98-5 	No Europe: 1 USA: 30	Yes, related substance nos 528, 530 and 531	NR	
Benzyl mercaptan (benzene-methanethiol)	526	100-53-8 	No Europe: 2 USA: 0.4	Yes, related substance nos 528, 530 and 531	NR	
Phenylethyl mercaptan (2-phenyl-ethanethiol)	527	4410-99-5 	No Europe: ND USA: 0.2	Yes, related substance nos 528, 530 and 531	NR	
o-Toluenethiol	528	137-06-4 	No Europe: 27 USA: 0.2	Yes, a NOEL of 0.52 mg/kg of body weight per day was reported in a 90-day study in rats treated at only that dose	NR	

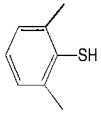
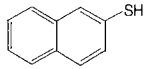
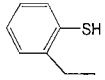
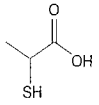
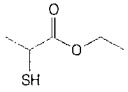
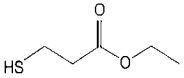
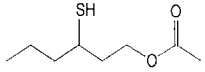
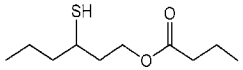
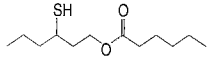
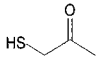
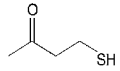
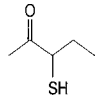
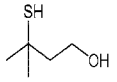
2,6-Dimethylthiophenol (2,6-dimethylbenzenethiol)	530	118-72-9 	No Europe: 2 USA: 0.02	Yes, a NOEL of 0.43 mg/kg of body weight per day was reported in a 90-day study in rats treated at only that dose	NR	No safety concern
2-Naphthalenethiol	531	91-60-1 	No Europe: ND USA: 0.1	Yes, a NOEL of 3.4 mg/kg of body weight per day was reported in a 90-day study in rats treated at only that dose	NR	
Structural class III						
2-Ethylthiophenol (2-ethylbenzenethiol)	529	4500-58-7 	No Europe: 0.0002 USA: 0.1	Yes, related substance nos 528, 530 and 531	NR	No safety concern
Subgroup v — thiols with oxidized side-chains						
Structural class I						
2-Mercaptopropionic acid	551	79-42-5 	No Europe: 3 USA: 84	Yes, related substance nos 546, 547 and 560	NR	No safety concern
Ethyl 2-mercaptopropionate	552	19788-49-9 	No Europe: 0.5 USA: 0.4	Yes, related substance nos 546, 547 and 560	NR	
Ethyl 3-mercaptopropionate	553	5466-06-8 	No Europe: 0.1 USA: 43	Yes, related substance nos 546, 547 and 560	NR	
3-Mercaptohexyl acetate	554	136954-20-6 	No Europe: ND USA: 0.2	Yes, related substance nos 546, 547 and 560	NR	

Table 1 (*continued*)

Substance[b]	No.	CAS no. and structure	*Step B3*[c] Does intake exceed the threshold for human intake?	*Step B4* Adequate NOEL for substance or structurally related substance?	*Step B5* Intake >1.5 µg/day?	Conclusion based on current intake
Subgroup v — continued						
Structural class I (continued)						
3-Mercaptohexyl butyrate	555	136954-21-7 	No Europe: ND USA: 0.2	Yes, related substance nos 546, 547 and 560	NR	No safety concern
3-Mercaptohexyl hexanoate	556	136954-22-8 	No Europe: ND USA: 0.2	Yes, related substance nos 546, 547 and 560	NR	
1-Mercapto-2-propanone	557	24653-75-6 	No Europe: ND USA: 0.09	Yes, related substance nos 546, 547 and 560	NR	
3-Mercapto-2-butanone	558	40789-98-8 	No Europe: 5 USA: 0.04	Yes, related substance nos 546, 547 and 560	NR	
2-Keto-4-butanethiol (4-mercapto-2-butanone)	559	34619-12-0 	No Europe: ND USA: 0.1	Yes, related substance nos 546, 547 and 560	NR	
3-Mercapto-2-pentanone	560	67633-97-0 	No Europe: ND USA: 0.1	Yes, a NOEL of 1.9 mg/kg of body weight per day was reported in a 90-day study in rats treated at only that dose	NR	
3-Mercapto-3-methyl-1-butanol	544	34300-94-2 	No Europe: ND USA: 2	Yes, related substance nos 546, 547 and 560	NR	

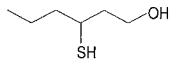
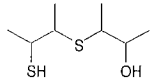
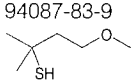
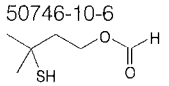
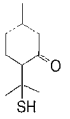
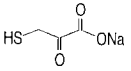
3-Mercaptohexanol	545	51755-83-0 	No Europe: ND USA: 1	Yes, related substance nos 546, 547 and 560	NR	
2-Mercapto-3-butanol ((*R*,*S*)-3-mercaptobutan-2-ol)	546	37887-04-0 	No Europe: 6 USA: 0.1	Yes, a NOEL of 1.9 mg/kg of body weight per day was reported in a 90-day study in rats treated at only that dose	NR	
α-Methyl-β-hydroxypropyl α-methyl-β-mercaptopropyl sulfide (3-[(2-mercapto-1-methylpropyl)thio]-2-butanol)	547	54957-02-7 	No Europe: ND USA: 1	Yes, a NOEL of 2.8 mg/kg of body weight per day was reported in a 90-day study in rats treated at only that dose	NR	No safety concern
4-Methoxy-2-methyl-2-butanethiol	548	94087-83-9 	No Europe: ND USA: 0.8	Yes, related substance nos 546, 547 and 560	NR	
3-Mercapto-3-methylbutyl formate	549	50746-10-6 	No Europe: ND USA: 0.1	Yes, related substance nos 546, 547 and 560	NR	
Structural class II						
p-Mentha-8-thiol-3-one (2-(1-mercapto-1-methylethyl)-5-methylcyclohexanone)	561	38462-22-5 	No Europe: 16 USA: 2	Yes, related substance nos 546, 547 and 560	NR	No safety concern
Structural class III						
Sodium 3-mercapto-oxopropionate (sodium 3-mercaptopyruvate)	563	10255-67-1 	No Europe: ND USA: 0.2	Yes, related substance nos 546, 547 and 560; see related substance no. 452, subgroup i, for the sulfur moiety; the oxopropionate moiety would be predicted to be of low toxicity	NR	No safety concern

Table 1 (*continued*)

Substance[b]	No.	CAS no. and structure	*Step B3*[c] Does intake exceed the threshold for human intake?	*Step B4* Adequate NOEL for substance or structurally related substance?	*Step B5* Intake >1.5 µg/day?	Conclusion based on current intake
Subgroup vi — dithiols						
Structural class I						
1,2-Ethanedithiol	532	540-63-6	No Europe: 0.002 USA: 0.9	Yes, related substance nos 539 and 541	NR	No safety concern
1,3-Propanedithiol	535	109-80-8	No Europe: 1 USA: 0.9	Yes, related substance nos 539 and 541	NR	
1,2-Propanedithiol	536	814-67-5	No Europe: ND USA: 0.9	Yes, related substance nos 539 and 541	NR	
1,2-Butanedithiol	537	16128-68-0	No Europe: ND USA: 0.2	Yes, related substance nos 539 and 541	NR	
1,3-Butanedithiol (butane-1,3-dithiol)	538	24330-52-7 	No Europe: ND USA: 0.9	Yes, related substance nos 539 and 541	NR	
2,3-Butanedithiol	539	4532-64-3	No Europe: 0.1 USA: 0.2	Yes, a NOEL of 0.7 mg/kg of body weight per day was reported in a 90-day study in rats treated at only that dose	NR	
1,6-Hexanedithiol (hexane-1,6-dithiol)	540	1191-43-1 	No Europe: 2.5 USA: 0.1	Yes, related substance nos 539 and 541	NR	

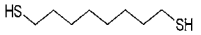
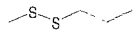
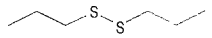
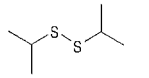
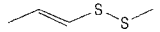
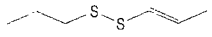
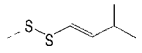
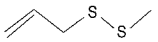
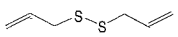
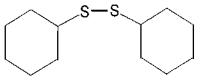
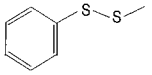
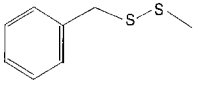
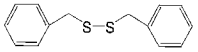
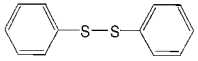
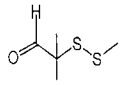
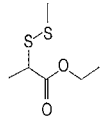
1,8-Octanedithiol (octane-1,8-dithiol)	541	1191-62-4 	No Europe: 3 USA: 0.9	Yes, a NOEL of 0.7 mg/kg of body weight per day was reported in a 90-day study in rats treated at only that dose	NR	No safety concern
1,9-Nonanedithiol	542	3489-28-9 	No Europe: 0.002 USA: 0.9	Yes, related substance nos 539 and 541	NR	
Subgroup vii — simple disulfides ***Structural class I***						
Dimethyl disulfide	564	624-92-0 	No Europe: 11 USA: 2	Yes, related substance no. 566	NR	
Methyl propyl disulfide	565	2179-60-4 	No Europe: 6 USA: 0.02	Yes, related substance no. 566	NR	
Propyl disulfide	566	629-19-6 	No Europe: 5 USA: 0.1	Yes, a NOEL of 7.3 mg/kg of body weight per day was reported in a 90-day study in rats treated at multiple doses	NR	
Diisopropyl disulfide	567	4253-89-8 	No Europe: ND USA: 8	Yes, related substance nos 566 and 575	NR	No safety concern
Methyl 1-propenyl disulfide	569	5905-47-5 	No Europe: ND USA: 1	Yes, related substance no. 566	NR	
1-Propenyl propyl disulfide	570	5905-46-4 	No Europe: ND USA: 8	Yes, related substance no. 566	NR	
Methyl 3-methyl-1-butenyl disulfide	571	Pending 	No Europe: ND USA: 0.1	Yes, related substance no. 566	NR	

Table 1 (*continued*)

Substance[b]	No.	CAS no. and structure	*Step B3*[c] Does intake exceed the threshold for human intake?	*Step B4* Adequate NOEL for substance or structurally related substance?	*Step B5* Intake >1.5 µg/day?	Conclusion based on current intake
Subgroup vii — continued						
Structural class II						
Allyl methyl disulfide	568	2179-58-0 	No Europe: 0.002 USA: 0.02	Yes, related substance no. 587, subgroup ix, which is predicted to be metabolized to allyl mercaptan	NR	
Allyl disulfide	572	2179-57-9 	No Europe: 92 USA: 8	Yes, related substance no. 587, subgroup ix, which is predicted to be metabolized to allyl mercaptan	NR	
Dicyclohexyl disulfide	575	2550-40-5 	No Europe: 0.02 USA: 0.2	Yes, a NOEL of 0.23 mg/kg of body weight per day was reported in a 90-day study in rats treated at only that dose	NR	
Methyl phenyl disulfide	576	14173-25-2 	No Europe: ND USA: 0.2	Yes, related substance no. 531, subgroup iv, which is predicted to be rapidly reduced to thiophenol	NR	No safety concern
Benzyl methyl disulfide	577	699-10-5 	No Europe: 0.02 USA: 0.1	Yes, a NOEL of 1.2 mg/kg of body weight per day was reported in a 90-day study in rats treated at only that dose	NR	
Benzyl disulfide	579	150-60-7 	No Europe: 0.01 USA: 0.1	Yes, related substance no. 577	NR	
Structural class III						
Phenyl disulfide	578	882-33-7 	No Europe: ND USA: 0.04	Yes, related substance no. 531, subgroup iv, which is predicted to be rapidly reduced to thiophenol	NR	No safety concern

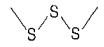
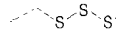
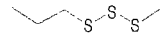
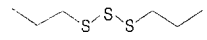
Subgroup viii — disulfides with oxidized side-chains

Structural class I

2-Methyl-2-(methyldithio)propanal	580	67952-60-7 	No Europe: ND USA: 2	Yes, related substance nos 566, 575 and 577, subgroup vii, and no. 560, subgroup v; see related substance no. 516, subgroup iv, for the thiol products of reduction	NR	No safety concern
Ethyl 2-(methyldithio)propionate	581	23747-43-5 	No Europe: ND USA: 0.1	Yes, related substance nos 566, 575 and 577, subgroup vii, and no. 560, subgroup v; see related substance no. 516, subgroup iv, for the thiol products of reduction	NR	

Subgroup ix — trisulfides and polysulfides

Structural class I

Dimethyl trisulfide	582	3658-80-8 	No Europe: 2 USA: 0.02	Yes, related substance no. 585	NR	No safety concern
Ethyl methyl trisulfide	583	31499-71-5 	No Europe: ND USA: 1	Yes, related substance no. 585	NR	
Methyl propyl trisulfide	584	17619-36-2 	No Europe: 0.3 USA: 0.1	Yes, related substance no. 585	NR	
Dipropyl trisulfide	585	6028-61-1 	No Europe: 11 USA: 1	Yes, a NOEL of 4.8 mg/kg of body weight per day was reported in a 90-day study in rats treated at only that dose	NR	

Structural class II

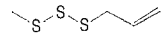
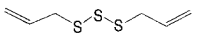
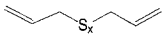
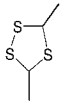
Allyl methyl trisulfide	586	34135-85-8 	No Europe: ND USA: 0.9	Yes, related substance no. 587	NR	No safety concern

Table 1 (*continued*)

Substance[b]	No.	CAS no. and structure	*Step B3*[c] Does intake exceed the threshold for human intake?	*Step B4* Adequate NOEL for substance or structurally related substance?	*Step B5* Intake >1.5 µg/day?	Conclusion based on current intake
Subgroup ix — continued						
Structural class II (continued)						
Diallyl trisulfide	587	2050-87-5 	No Europe: 6 USA: 0.02	Yes, a NOEL of 4.6 mg/kg of body weight per day was reported in a 90-day study in rats treated at only that dose	NR	No safety concern
Diallyl polysulfide	588	72869-75-1  x=2,3,4 or 5	No Europe: 2 USA: 0.02	Yes, related substance no. 587	NR	
Subgroup x — heterocyclic disulfides						
Structural class II						
3,5-Dimethyl-1,2,4-trithiolane	573	23654-92-4 	No Europe: 0.04 USA: 0.1	Yes, a NOEL of 1.9 mg/kg of body weight per day was reported in a 90-day study in rats treated at only that dose	NR	No safety concern
3-Methyl-1,2,4-trithiane	574	43040-01-3 	No Europe: 0.1 USA: 43	Yes, related substance no. 573; a NOEL of 0.3 mg/kg of body weight per day was reported in a 90-day study in rats treated at only that dose	NR	
Subgroup xi — thioesters						
Structural class I						
Methyl thioacetate	482	1534-08-3 	No Europe: ND USA: 0.002	Yes, related substance nos 483 and 484	NR	No safety concern