

Recent Progress in the Consideration of Flavoring Ingredients Under the Food Additives Amendment

9. GRAS Substances

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□ IN KEEPING with previously outlined policies of the Flavor and Extract Manufacturers' Association, this paper reports the latest results of evaluations of the GRAS (Generally Recognized as Safe) status of a number of substances.

These evaluations were made by an independent panel of qualified scientists chosen as described before (Hall and Oser, 1961) and consisting of: Dr. Anthony M. Ambrose, Medical College of Virginia; Dr. David W. Fassett; Dr. Maurice H. SeEVERS, University of Michigan; Dr. Howard C. Spencer; Dr. Frank Strong, University of Wisconsin; and Dr. Lauren A. Woods, Virginia Commonwealth University.

The F.E.M.A. maintains the policy of urging member companies to submit to this expert panel flavoring substances intended for commercial application, whether or not they are analogs of naturally occurring substances, for appraisal of safety under conditions of proposed use. The F.E.M.A. adopted the program of publishing the GRAS lists consistent with the recommendation of the U.S. Food and Drug Administration, in order to provide the scientific community with the opportunity to comment on, or take issue with, the opinion of other specialists in the field of food safety evaluation. The purpose of the present report is to extend the lists of GRAS substances published since 1965 (Hall, 1960; Hall and Oser, 1961, 1965, 1970; Oser and Hall, 1972; Oser and Ford, 1973a, 1973b, 1974).

The Expert Panel periodically reviews the criteria employed to arrive at judgments of GRAS status. In essence, these requirements include evidence for the identity and purity of the substance, its chemical and

pharmacological relation to structurally analogous substances, its presence and level as a naturally occurring constituent of foods, intended use levels, and any pertinent biochemical, metabolic or toxicologic data. From the accumulated experience in the evaluation of a large number of chemical substances there have evolved general principles governing the rationale and process of safety evaluation by the Expert Panel, and recommendations for priorities where further toxicological data are suggested.

The following minor corrections to the GRAS 7 publication (Oser and Ford, 1973b) should be made: No. 3398, GLYCERYL TRIBENZOATE, use level in beverages should read 85 ppm instead of 190 ppm; No. 3419, PROPYLENE GLYCOL DIBENZOATE, use level in beverages should read 190 ppm instead of 85 ppm.

REFERENCES

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GRAS FLAVORING INGREDIENTS AND USAGE LEVELS

Flavor and Extract Manufacturers' Association average maximum levels (in ppm) on which the Expert Panel based its judgments that the substances are generally recognized as safe for their intended uses.

Substance	Bever- ages (non-al- coholic)	Frozen desserts (Ice Cream, Confec- tionary Ices, etc.)	Baked Goods	Puddings, Gelatins, Jams	Chewing Gum	Meat, Meat Sauces, Soups	Milk, Dairy Products	Condi- ments, Pickles	Other Category Use
Ambrox (see 3471)									
3445 DL-(3-AMINO-3-CARBOXYPROPYL) DIMETHYLSULFONIUM CHLORIDE									Fish-1000.
1-Benzazone (see 3470)									
Benzo[6]pyridine (see 3470)									
Chinoleine (see 3470)									
o-Cumamol (see 3461)									

	Bever- ages (non-al- coholic)	Frozen desserts (Ice Cream, Ices, etc.)	Confec- tionery	Baked Goods	Puddings, Gelatins, Jams	Chewing Gum	Meat, Meat Sauces, Soups	Milk, Dairy Products	Condl- ments, Pickles	Other Category Use
1,2-Cyclohexanedione (see 3458)										
Cyclohexyl disulfide (see 3448)										
3446 DEHYDRODIHYDROIONOL	0.01	0.02	2.0	2.0	0.3	10.	—	0.5	—	
3447 DEHYDRODIHYDROIONONE	0.2	0.4	4.0	4.0	0.6	10.	—	1.0	—	
3448 DICYCLOHEXYL DISULFIDE	0.05	—	0.05	0.05	0.05	—	0.05	—	—	
3449 1,4-DIMETHYL-4-ACETYL-1- CYCLOHEXENE	—	2.0	2.0	3.0	2.0	—	—	2.0	—	
1,4-Dimethylcyclohex-3-enyl methyl ketone (see 3449)										
3450 2,5-DIMETHYL-2,5-DIHYDROXY-1,4- DITHIANE	—	—	—	7.5	—	—	2.0	—	—	Soups-1.0
3451 2,5-DIMETHYL-3-FURANTHIOL	—	—	—	0.25	—	—	0.25	—	0.25	
3,7-Dimethyl-2,6-octadien-1-thiol (see 3472)										
3452 DODECYL ISOBUTYRATE	0.5	2.0	2.0	3.0	2.0	—	—	—	—	
Dodecyl 2-methylpropanoate (see 3452)										
3453 3-ETHYL-2-HYDROXY-4-METHYL- CYCLOPENT-2-EN-1-ONE	0.2	0.4	4.0	4.0	0.6	5.0	—	1.0	—	
3454 5-ETHYL-2-HYDROXY-3-METHYL- CYCLOPENT-2-EN-1-ONE	2.0	3.0	2.0	2.0	2.0	—	—	1.0	—	
3455 N-ETHYL-2-ISOPROPYL-5-METHYL- CYCLOHEXANE CARBOXAMIDE	10.	10.	10.	—	10.	1200.	—	—	—	Beverages, alcoholic-10.
N-Ethyl-p-menthane-3-carboxamide (see 3455)										
5-Ethyl-3-methylcyclohexene (see 3454)										
3-Ethyl-4-methylcyclohexene (see 3454)										
3456 ETHYL 2-METHYL-3-PENTENOATE	0.5	0.5	2.0	1.0	0.5	5.0	—	0.5	—	
Ethyl 2-phenyl-3-furoate (see 3468)										
3457 HEXYL PHENYLACETATE	2.0	3.0	3.0	—	2.0	—	—	—	—	
<i>β</i> -Homocyclocitral (see 3474)										
3458 2-HYDROXY-2-CYCLOHEXEN-1-ONE	—	3.0	7.0	—	7.0	—	5.0	—	7.0	
1-Hydroxy-2-isopropylbenzene (see 3461)										
3459 2-HYDROXY-3,5,5-TRIMETHYL-2- CYCLOHEXENONE	1.0	3.0	3.0	—	—	—	—	—	—	
Isocaproic acid (see 3463)										
Isohexanoic acid (see 3463)										
3460 <i>d,l</i> -ISOMENTHONE	—	—	60.	—	—	600.	—	—	—	
3461 2-ISOPROPYLPHENOL	—	—	—	—	—	—	3.0	—	2.0	Seasoning-2.0

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	Beverages (non-alcoholic)	Frozen desserts (Ice Cream, Confectionery Ices, etc.)	Baked Goods	Puddings, Gelatin, Jams	Chewing Gum	Meat, Meat Sauces, Soups	Milk, Dairy Products	Condiments, Pickles	Other Category Use
o-Isopropylphenol (see 3461)									
Leucoline (see 3470)									
3462 MALTYL ISOBUTYRATE	50.	100.	200.	300.	120.	—	—	—	Preserves & spreads—100; beverages, alcoholic—100
cis-para-Menthan-3-one (see 3460)									
cis-1-Methyl-4-isopropyl-3-cyclohexanone (see 3460)									
DL-Methylmethionine sulfonium chloride (see 3445)									
3463 4-METHYLPENTANOIC ACID	10.	10.	2.0	40.	—	10.	20.	40.	40. Seasoning—20.
3464 2-METHYL-3-PENTENOIC ACID	10.	10.	10.	10.	10.	10.	—	—	Cereals—10.
2-Methyl-4-pyrone-3-yl 2-methylpropanoate (see 3462)									
4-Methylvaleric acid (see 3463)									
MMS (see 3445)									
3465 cis-6-NONEN-1-OL	0.1	0.2	0.2	0.3	0.2	—	—	—	—
3466 2-trans-6-trans-OCTADIENAL	—	—	—	—	—	—	2.0	2.0	— Cereals—0.5
3467 cis-3-OCTEN-1-OL	1.0	3.0	3.0	5.0	3.0	—	—	—	—
Phenylacetic acid, hexyl ester (see 3457)									
3468 2-PHENYL-3-CARBETHOXY FURAN	2.5	2.5	2.5	—	2.5	2.5	—	2.5	—
Phenylethyl ketone (see 3469)									
1-Phenyl-1-propanone (see 3469)									
Propionylbenzene (see 3469)									
3469 PROPIOPHENONE	0.2	1.0	1.0	1.0	1.0	—	—	—	—
3470 QUINOLINE	1.0	2.5	3.0	3.0	2.5	—	2.5	—	—
α ,2,6,6-Tetramethyl-1,3-cyclohexadien-1-propanol (see 3446)									
3471 1,5,5,9-TETRAMETHYL-13-OXATRICYCLO[8.3.0.0 ^{1,2}] TRIDECAENE	0.01	0.01	0.01	0.01	0.01	—	—	—	—
3472 THIOGERANIOL	0.002	0.01	0.02	0.03	—	—	—	—	0.01 Preserves & spreads—0.02
4-(2,6,6-Trimethylcyclohexadien-1-yl)-2-butanone (see 3447)									
3,5,5-Trimethyl-1,2-cyclohexanedione (see 3459)									
3473 2,2,6-TRIMETHYLCYCLOHEXANONE	1.0	3.0	3.0	—	—	—	—	—	—
3474 2,6,6-TRIMETHYL-1-CYCLOHEXEN-1-ACETALDEHYDE	0.1	0.2	2.0	2.0	0.3	10.	—	0.5	—
5-Trithiane,2,2,4,4,6,6-hexamethyl (see 3475)									
3475 TRITHIOACETONE	0.12	0.04	0.50	—	0.075	—	—	0.08	—
3476 Vitamin U (see 3445)									