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RECENT PROGRESS in the Consideration of Flavoring Ingredients Under the Food Additives Amendment

5. GRAS Substances

BERNARD L. OSER and RICHARD L. HALL

 \square RESEARCH in the field of food flavors has been greatly stimulated by the application of modern analytical techniques, particularly gas chromatography and mass spectroscopy, which have permitted the identification of the chemical components of many natural flavors (1–5). As a consequence, improved artificial flavoring agents have been and are being developed which faithfully reproduce the nuances of natural flavors and intensify their characteristic properties.

THE EXPERT PANEL

It has been the policy of the Flavor and Extract Manufacturers Association (FEMA) to urge member companies to submit to an independent panel of qualified scientists, flavoring substances intended for commercial application, whether or not they are analogs of natural substances, for appraisal of safety under conditions of proposed use. Results of this expert panel's GRAS (generally recognized as safe) evaluations have been published in *Food Technology* (6-9).

The basis for selection of the original panel of toxicologists, pharmacologists, and biochemists, has been previously described (7). It should be emphasized that the members of the panel were affiliated with academic institutions and organizations having no connection with the flavoring industry, either directly or indirectly. The panel that evaluated the items reported herein consisted of: Dr. Anthony M. Ambrose, Medical College of Virginia; Dr. Frank R. Blood, Vanderbilt University; Dr. David W. Fassett, Eastman Kodak Company; Dr. Horace W. Gerarde, Fairleigh Dickinson University; Dr. Maurice H. Seevers, University of Michigan; Dr. Howard C. Spencer, Dow Chemical Co.; Dr. Frank M. Strong, University of Wisconsin; Dr. Lauren A. Woods, Medical College of Virginia.

WHY PUBLISH GRAS LISTS?

Data concerning the usage levels of flavoring substances, and all available scientific information relevant to safety evaluation have been the basis for the development over a period of several years of lists of GRAS flavoring substances. The policy of FEMA to publish the GRAS lists has resulted in their receiving wide recognition. The Federal Food And Drug Administration has adopted (with very few deletions) the first such list of substances in the form of two Food Additive Regulations (10).

It has been the view of the U.S. Food and Drug Administration, with which there can be no disagreement, that only by publication can the scientific community have 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 present the additions to the list of GRAS substances made in 1970-71.

CRITERIA FOR JUDGEMENTS

The criteria employed by the Expert Panel in arriving at judgements of GRAS status have been discussed in previous publications of GRAS lists (6–9) and in a review on the safety of flavoring substances by Hall and Oser (11). 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

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level as a naturally occurring constituent of foods, intended use levels, and any pertinent metabolic or toxicologic data. From the accumulated experience in the evaluation of large numbers of chemically related substances has evolved certain general principles which have established the rationale and facilitated the process of safety evaluation by the Expert Panel.

TOXICOLOGICAL INSIGNIFICANCE

A nationwide survey of the flavor and food industries conducted in 1960 revealed that of the 1121 substances on the FEMA GRAS list, 859 were estimated to be used in total amounts not exceeding 1000 lb annually. Moreover, the average maximum use levels in food were below 10 ppm in 399 of these substances. These criteria of total annual usage and minimal levels in foods, together with a safe history of common use in food, have been regarded by the FEMA panel as a basis for "toxicological insignificance," in the absence of any specific evidence or reasonable suspicion (based, for example, on chemical structure) to the contrary.

In this connection, reference may be made to the recent guidelines for evaluating toxicological insignificance published by the Food Protection Committee of the National Academy of Sciences-National Research Council (12), from which the following quotation is relevant.

For many substances that are functionally effective in food at dietary concentrations above 0.1 ppm, but still much below any reasonable judgment as to their maximum safe level, as previously defined, there is need to arrive at estimates of toxicologically insignificant levels. For these substances, it is justifiable to employ accumulated scientific experience and to recognize their structural analogy to other chemicals whose metabolism or toxicity is known. Reasoning by analogy may be used to arrive at conclusions of toxicological insignificance. If a substance meets all the following criteria, it may be presumed to be toxicologically insignificant at a level of 1.0 ppm or less in the human diet:

1. The substance in question is of known structure and purity;

2. It is structurally simple;

3. The structure suggests that the substance will be readily handled through known metabolic pathways; and 4. It is a member of a closely related group of substances, that, without known exception, are or can be presumed to be low in toxicity.

TOTAL PER CAPITA INTAKE OF FLAVORING SUBSTANCES

It is interesting to note in this connection that if a flavoring agent were used at a level of 10 ppm in every major category of flavored foods, the total per capita intake of that substance (based on USDA Food Consumption data for all urbanizations) would be 2.336 mg per day. This would be equivalent to 1.3 ppm of the total diet or 0.0334 mg per kg body weight for a 70 kg adult. On the highly exaggerated assumption of the daily ingestion of average portions of all classes of flavored foods and the presence of 10 ppm of flavoring substance in each of them, the total daily intake would reach 11.5 mg or only 0.164 mg per kg body weight (Table 1).

Nearly a decade has passed since the original survey

Table 1—TOTAL DAILY PER CAPITA INTAKE OF FLAVORING SUBSTANCES based on the exaggerated assumption of the daily ingestion of average portions of all classes of flavored foods and the presence of 10 ppm in each of them

		Flavored Food Consumptions								
Class of Flavored Food	per Household¤ (lb/wk)	per Capitaª (g/day)	Flavor Component at 10 ppm (mg/day)	"Average Portion" (g/day)	Flavor Component at 10 ppm (mg/day)					
Soft drinks	5.09	100.3	1.00	540	5.40					
Frozen milk desserts:										
ice cream, ice milk, sherbet	1.36	26.8	0.268	90	0.90					
Candy, toppings	0.52	10.2	0.102	40	0.40					
Baked goods*	1			340	3.40					
prepared mixes	0.48	9.5	0.095							
"other" bakery products	3.28	64.6	0.646							
Jelly, jam, fruit, gelatin				120	1.20					
puddings, ices	0.45	8.9	0.089							
popsicles, icings	0.31	6.1	0.061							
Condiments	0.38	7.5	0.075	20	0.20					
Total intake, mg per day			2.336		11.50					
Total intake, ppm diet*			1.30		6.40					
Total intake, mg per kg body weight (70 kg)			0.0334		0.164					

Includes cakes, pies, crackers, muffins, biscuits, cookies, coffee cake, doughnuts

* Household food consumption levels based on 1965-66 survey, U.S. Dept. of Agriculture (all urbanizations)

^c Household food consumption tests $\frac{1}{2}$ = g per capita per day

3.29 persons X 7 days * 1800 g food per day (estimate based on USDA Food Consumption statistics)

^{...} text / continued on p. 42 ...

SURVEY OF FLAVORING INGREDIENT USAGE LEVELS

Flavor and Extract Manufacturers Association average maximum use levels (in ppm) on which the expert panel based its judgements that the substances are generally recognized as safe.

FEMA No. and Substan ce	Bayaragas	Ice Cream, Ices, Etc.	Candy	Baked	Gelatins & Puddings	Chewing Gum	Meat, Meat Sauces, Soups	Milk, Dairy Product	Condi- ments, Pickles	Other Category Uses
	Develages	ices, Etc.	Calldy	Goods	& ruduings	Gum	Soups	1100000	I ICAICS	
3,250 2-Acetyl-3-ethyl pyrazine 2-Acetyl-3-ethyl-1,4-diazine (see 3,250)	10.	10.	10.	10.	10.	_	10.	10.		Cereals 10.
3.251 2-Acetylpyridine	_	_	3.0	5.0	_	_	3.0	3.0		Cereals 3.0
3.252 β-Alanine	10.		_	10.	_	_	10.	10.	10.	Cereals 10.
3.253 Allyl methyl trisulfide	_	_	_	2.0	_		2.0	_	2.0	
Allyl trisulfide (see 3,265) Aminoacetic acid (see 3,287) Aminoethanoic acid (see 3,287) Aminoglutaric acid (see 3,285) a-Aminoisocaproic acid (see 3,297) 2-Amino-3-methylpentanoic acid (see 3,295)										
2-Amino-4-methylpentanoic acid (see 3,297) 2-Amino-3-mercaptopropanoic acid (see 3,263) α-Amino-β-mercaptopropionic acid (see 3,263)										
2-Amino-4- (methylthio)-butanoic acid (see 3,30 a-Amino- γ - (methylthio)-butyric acid (see 3,30 a-Amino- β -methylvaleric acid (see 3,295) 2-Aminopropanoic acid (see 3,252) β -Aminopropionic acid see 3,252) a-Angelica lactone (see 3,293)										
3,254 Arabinogalactan			85%	-	-	-	-		-	Preserves
3,255 L-Arabinose	450.		450.	450.	_			_	450.	& Spreads 450.
3,256 Benzothiazole	0.5	-	0.5	0.5		_	0.5	0.5	_	
3,257 Bis(2-furfuryl) disulfide	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	
3.258 Bis(2-furfuryl) sulfide	5.0	5.0	5.0	5.0	5.0	5.0	5.0		5.0	
3,259 Bis(2-methyl-3-furyl) disulfide	-		-	0.1		-	0.1	-	0.1	a 1
3.260 Bis (2-methyl-3-furyl) tetrasulfide 3.261	-		-	0.1	-	-	0.1	0.1	0.1	Cereals 0.1
2-sec-Butylcyclohexanone γ-Butyrolactone (see 3,291) Cinnamic acid. tetrahydrofurfuryl ester (see 3,320)	25.	25.	150.	100.	-	1000.	_	-	_	
Cyclohexapyrazine (see 3,321) 3,262 Cyclopentanethiol				0.1			0.1	0.1	0.1	Cereals 0.1
Cyclopentyl mercaptan (see 3,262) 3,263	-		-	0.1	-	-	0.1	0.1	0.1	
L-Cysteine 3,264	100.	-	-	100.	-		100.	100.	100.	Cereals 100.
4-Decenal 3.265		0.5	-	1.0	_	-	0.5	0.5	-	
Diallyl trisulfide Difurfuryl disulfide (see 3,257) Difurfuryl sulfide (see 3,258)	-	_	-	1.0	_	-	1.0	-	1.0	
3.266 4,5-Dihydro-3(2H) thiophenone 3.267	1.0	1.0	1.0	_	1.0	1.0	1.0	1.0	1.0	Cereals 1.0
2,4-Dimethyl-5-acetylthiazole 3.268	_	10. /	10.	6.0	-	-	10.			D (1 D - 1
3,4-Dimethyl-1,2-cyclopentadione 3,269	-	0.3	4.0		-	1.9		_	_	Protein Foods 3.5
3,5-Dimethyl-1,2-cyclopentadione	2.4	6 .0	5 .0		-			-	-	
3.270 spiro[2,4-Dithia-1-methyl-8-oxabicyclo[3.3.0] octane-3.3'-(1'-oxa-2'-methyl) cyclopentane and spiro[2,4-dithia-6-methyl-7-oxabi- cyclo[3.3.0]octane-3.3'-(1'-oxa-2-methyl) cyclopentane] 2.3 Dimethyl 1.4 dispine (see 2.271)] 0.045	0.25	0.1	_	_		0.07	_	_	Protein Foods 0.4 Mayonnaise 2.4
2,3-Dimethyl-1,4-diazine (see 3,271) 2,5-Dimethyl-1,4-diazine (see 3,272)										
2,6-Dimethyl-1,4-diazine (see 3,273)										
3,271 2,3-Dimethylpyrazine	10.	10.	10.	10.	10.	_	10.	-	-	

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$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Condi- ments, Pickles	Other
2.6 Dimethylpyrazine 10. 10		Cereals 10.
4.5 Dimethylthizable - 10. 10. 10. 6.0 - 20. - 3.275 Dimethylthizable - - - 1.0 - - 1.0 - 3.276 Dimethylthizable - - - 1.0 - - 1.0 - 3.275 Dimethylthizable 0.0 - - 0.0	_	Cereals 10.
Dimetely transfide $ 1.0$ $ 1.0$ $ 1.0$ $ 1.0$ $ 1.0$ $ 1.0$ $ 1.0$ $ 1.0$ $ 1.0$ $ 1.0$ $ -$	20.	
Dipropy Infaultifie $ 1.0$ $ 1.0$ $ 0.0$ $ 0.0$ $ 0.0$ $ 0.0$ $ 0.0$ $ 0.0$ $ 0.0$ $ 0.0$ $ 0.0$ $ 0.0$ $ 0.0$ $ 0.0$ $ -$	1.0	
Diadum succinate 60. - - 60. - - 60. 60. 3.273 Diable bile (see 3.283) Exp() 1.4 diatrice (see 3.283) 3.273 S.275 S.275	1.0	Cereals
3.228 15. 20. 120. - - 10. 3.279 Ethyl 2. merceptopropionate 0.1 0.1 1.2 1.5 - - - - 3.280 S.Ma d 6) -methorypyrazine (B5%) plus 2. Methyl - (3.5 and 6) -methorypyrazine (1375) 5.0 5.0 5.0 5.0 5.0 5.0 5.0 -	-	60.
Ethyl 2-mercaptopropionale 0.1 0.1 1.2 1.5 $ -$	-	Hard Candy 120. Syrups 60. Jellies
2 Ethyl. (1.3, 5 and 6) -methorypyrazine (135%) 5.0 1.0	_	30. Mint Oils 10. Jellied Produ 0.2 Other
3.24 2.23 2.23 3.24 3.24 3.24 3.24 3.251 3.243 3.243 3.243 3.243 3.243 3.243 3.244 $741uryl subfields (see 3.253)$ 3.244 $741uryl subfields (see 3.254)$ 3.243 7244 $741uryl subfields (see 3.254)$ 3.253 3.244 $741uryl subfields (see 3.254)$ 3.254 7244 $741uryl subfields (see 3.254)$ 3.257 $19xceryl tripropanoate 20. 3.257 19yceroll (see 3.267) 3.258 Heptanol 100 100 3.289 Heptanol 100 3.291 Heptanol 100 3.291 Heptanol 100$	_	0.01 Cereals 5.0
ihyl thioacetate 1.0 <td>_</td> <td>Cereals 10.</td>	_	Cereals 10.
3.23^{1} Furfuryl sulfide (see 3,258) 3.234 Y.Furfuryl pyrole 2.0 2.26	1.0	Cereals 1.0
X-Furfurylpyrrole 2.0 <td>→</td> <td></td>	→	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	-	Cereals 2.0
Clyceryl tripropanoate 20. - 50. - - - - 3.287 Slycene 150. - 150. - 150. -	400.	Cereals 400.
Silycone 150. - 150. - - 150. - Silycocoll (see 3,287) 3.288 Heptanol 0.5 0.5 1.0 15.0 5.0 10. - - 3.289 1.0 1.0 - - 1.0 1.0 - - 3.289 1.0 1.0 - - 1.0 1.0 - - - 3.290 20.		Desserts 20. Preserves,
3.288 0.5 0.5 1.0 15.0 5.0 10. - - 3.289	150.	Spreads 150.
Heptenal (cis and trans) 1.0 $ 1.0$ $ 1.0$ 1.0 $ 1.0$ 1.0 3.290 Hexanone $20.$ $ 20.$ $20.$ <td>_</td> <td>Dips, Spread 12. Salad Dressia 80.</td>	_	Dips, Spread 12. Salad Dressia 80.
Hexanone 20. $-$ 20. 20. $-$ 20. $-$ 20. $-$ 20. $ -$		Cereals 1.0
Hydroxybutanoic acid lactone 10. 10. 10. 20. 10. 10. 3.292 (Hydroxymethyl) -2-octanone 0.3 0.3 5.0 10. 10. 10. 10. 10. 10. 10. 10. <td< td=""><td></td><td>Cereals 20.</td></td<>		Cereals 20.
-(Hydroxymethyl) -2-octanone 0.3 0.3 5.0 10.	_	Cereals 20.
Hydroxy-3-pentenoic acid lactone	10.	Casala
Hydroxyundecanoic acid lactone 2.0 5.0 5.0 25. 1.0 10. 3.295 50. 50. 50. 50. 3.296 sopropenylpyrazine 10. 10. 10. 50. 50. -lsopropenylpyrazine 10. 10. 10. 10. 10. -lsopropenyl-1,4-diazine (see 3,296) arch gum (see 3,254) 3.297	-	Cereals 2.0 Cereals
3.296 sopropenylpyrazine 10. 10		5.0 Cereals
-lsopropenyl-1,4-diazine (see 3,296) arch gum (see 3,254) 3.297 -Leucine 50 50 50. 50. 3.298	50.	50. Cereals
-Leucine 50 50 50. 50.		10.
	50.	Cereals 50.
		Cereals 0.2
3.299 -Mercaptomethylpyrazine	10.	

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FEMA No. and Substance	Beverages	Ice Cream, Ices, Etc.	Candy		Gelatins & Puddings	Chewing Gum	Meat Sauces, Soups	Milk, Dairy Product	Condi- ments, Pickles	Othe Category
3.,300	- 0.0		<u>.</u>	0.0	_					Cereal
3-Mercapto-2-pentanone	0.2		0.2 -	0.2			0.2	0.2	_	0.2
2-Mercaptopropionic acid, ethyl ester (see 3,3 Methanethicl n-butyrate (see 3,310)	[19]									
Methanethiol n-butyrate (see 3,310) 3.301										Cereal
D,L-Methionine	50.			50.			50.	50.	50.	50.
3.302										Cereal
Methoxypyrazine	10.	10.	10.	10.	10.	—	10.	10.		10.
2-Methoxy-1,4-diazine (see 3,302)										
Methyl allyl trisulfide (see 3,253)										
Methyl n-amyl carbinol (see 3,288)										~ ·
3.303 2-Methyl-1-butanethiol	0.8		0.8	0.8			0.8	.0.8	_	Cereal 0.8
3.304										Cereal
3-Methyl-2-butanethiol	1.2	-	1.2	1.2	-	—	1.2	1.2	-	1.2
3.305	0.0				• •					
1-Methyl-2,3-cyclohexadione	0.6	-	9. 0	6.0	0.2	-			-	
2-Methyl-1,4-diazine (see 3,309)										Dentsie 7
3.306 5H-5-Methyl-6,7-dihydrocyclopenta[b]pyraziu	ne 0.045	0.25	1.0	_	·	0.15				Protein F 0.5
5-Methyl-2(3H)-furanone (see 3,293)						10				0.0
.3.307										Protein F
3-(5-Methyl-2-furyl) butanal	0.1	0.4	1.2			2.5	_	-	-	0.1
3- (5-Methyl-2-furyl)butyraldehyde (see 3,307)									
2-Methyl-3-furyl disulfide (see 3,259)										
2-Methyl-3-furyl tetrasulfide (see 3,260) Methyl n-heptyl carbinol (see 3,315)										
3-Methylmercaptopropyl isothiocyanate										
(see 3,312)										
Methyl n-propyl carbinol (see 3,316) 2-(1-Methylpropyl)-cyclohexanone (see 3,261)									
3,308	•									
Methyl propyl trisulfide			-	2.0	_	—	2.0		2.0	<u> </u>
3.309 2-Methylpyrazine	10.	10.	10.	10.	10.		10.	10.		Cer e al 10.
Methyl 2-pyridyl ketone (see 3,251)	10.	10.		10.	10.		10.	10.	_	
3.310			~ -							Protein F
Methyl thiobutyrate 3.311	0.000	5 0.05	0.5	7.0	0.06	-	_			5.0
Methyl thiofuroate	3.0	3.0	3.0	5.0			3.0		3.0	
3.312					4.0					Frozen 1
3-Methylthiopropyl isothiocyanate Methyl trisulfide (see 3,275)	-	-		—	4.0			_	-	4.0
2-(1-Methylvinyl)pyrazine (see 3,296)										
3.313 4 Methyl 5 vipulthiosole		0.0								
4-Methyl-5-vinylthiazole 3.314		2.0	2.0	8.0	8.0	-	6.0	-		Cereal
2-Naphthalenthiol		—		0.5	-		0.5			0.5
2-Naphthyl mercaptan (see 3,314) 3.315										Dips, Spre
2-Nonanol	_			15.					80.	12.
Pectin sugar (see 3,255)				-						~ ·
3.316 2-Pentanol	2.0	_		2.0	2.0	_	2.0	_	2.0	Cereal 2.0
3,317	2.0	-	-	2.0	2.0	_	2.0	_	2.0	Cereal
2-Pentyl furan	3.0		3.0	3.0		_	3.0	3.0	_	3.0
3.318 3-Phenyl-4-pentenal	1.0		1.0	1.0	_	_	1.0	1.0	_	Cereal - 1.0
3.319			1.5							Cereal
L-Proline	50.			50.	—	-	50.	50.	50.	50.
Propionic acid, triglyceride (see 3,286) Propyl methyl trisulfide (see 3,308)										
Propyl trisulfide (see 3,276)										
Pyrazinemethanethiol (see 3,299)										
2-Pyrrolidinecarboxylic acid (see.3,319) Sodium succinate (see 3.277)										
Succinic acid, disodium salt (see 3,277)										
3,320		~ ~								
Tetrahydrofurfuryl cinnamate .3.321	20.	20.		20.			-	_		Cereal
5,6,7,8-Tetrahydroquinoxaline	5.0		5.0	5.0	2.0	_	2.0	1.0	2.0	2.0
3-Tetrahydrothiophenone (see 3,266)			1		-		-			
3,3'-Tetrathio-bis(2-methylfuran) (see 3,260) 3,322										Cereal
3,322 Thiamine hydrochloride	50.		_	50.		-	50.	50.	50.	50.
3,323										Cereal
2-Thienyl disulfide Thioscetic soid, ethyl ester (see 3 282)		-		0.15			0.15	-	0.15	0.15
Thioacetic acid, ethyl ester (see 3,282) Thiobutyric acid, methyl ester (see 3,310)										
Thiofuroic acid, methyl ester (see 3,311)										
2-Thionaphthol (see 3,314)										
3-Thiophenone (see 3,266) 3,324										
3,5,5-Trimethyl-1-hexanol		_		30.	_				3 0 .	
3,325			2.0				60		6.0	
2,4,5-Trimethylthiazole Tripropionin (see 3,286)	_	2.0	2.0				6.0	-	6.0	
△-Undecalactone (see 3,294)										
B-Vinylhydrocinnamaldehyde (see 3,318)										

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GRAS Substances . . .

of usage of flavoring substances by the food industry was conducted by the Flavor and Extract Manufacturers Association. The accumulated data from this survey were considered in relation to certain arbitrary daily consumption levels of the various categories of flavored food in arriving at the FEMA lists of GRAS flavoring substances published in 1960 and 1965.

GRAS LIST REVIEWS & POSSIBLE REVISIONS

Recognizing that the patterns of use of flavoring substances may change in both kind and degree. the FEMA undertook to repeat and extend the survey. It is currently underway (1972), concomitantly with the survey of GRAS food substances by the National Academy of Sciences-National Research Council under contract with the Food and Drug Administration.

Data from both of these surveys will be computerized and analyzed for the purpose of reviewing and possibly revising the status of substances listed therein. In this connection it should be recognized that the FEMA survey will cover all adjuncts and flavoring ingredients used in foods, including those originally published in the FEMA GRAS list which were subsequently incorporated by the Food and Drug Administration into Food Additive Regulations for natural and synthetic flavoring substances (10).

REFERENCES

- (1) Hornstein, I. and Teranishi, R. 1967. The chemistry of flavor. Chem. and Eng. News. 45: 92. (2) Ziegler, V.E. 1970. Constituents of citrus oils. Deutsch. Lebensm.
- Rundschau 66: 290.
- (3) Macleod, A.J. 1970. Flavor volatiles from some cooked vegetables. J. Food Sci. 35: 734.
- (4) Johnson, A.E., Nursten, H.E., and Williams, A.A. 1971. Fruit aromas. A survey of component identification. Part 2. Chem. and Indy. 556-565. Downey, W.J. and Eiserle, R.J. 1971. Critical Reviews in Food
- (5) Technology. A Review of the Literature Concerned with Flavor Research as it Applies to the Problem of the Flavor Industry. Julv 159.
- (6) Hall, R.L. 1960. Recent progress in the consideration of flavoring ingredients under the Food Additives Amendment. Food Technol.
- (7) Hall, R.L. and Oser, B.L. 1961. Recent progress in the consideration of flavoring ingredients under the Food Additives Amendment. 2. Food Technol. 15: 1. Hall, R.L. and Oser, B.L. 1965.
- (8) Hall, R.L. and Oser, B.L. Recent progress in the consid-(a) Hall, R.L. and Oser, B.L. 1900. Hold the Food Additives Amendment.
 (9) Hall, R.L. and Oser, B.L. 1970. Recent progress in the consider-
- ation of flavoring ingredients under the Food Additives Amendment.
 4. GRAS substances. Food Technol. 24: 25.
 (10) Code of Federal Regulations Title 21. Part 121. Sections 1163 and
- (11) Hall, R.L. and Oser, B.L. 1968. The safety of flavoring sub-stances. Residue Reviews 24: 1.
- (12) Evaluating the Safety of Food Chemicals. 1970. Appendix: Guide lines for estimating toxicologically insignificant levels of chemicals in food. National Academy of Sciences. Washington, D.C.

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