W. A. K.

JUN 7 [illegible]

MANUFACTURING CHEMISTS ASSOCIATION

1825 CONNECTICUT AVENUE, N.W. WASHINGTON, D.C. 20009 (202) 483-6126

May 31, 1974

TO: Food Additive Contacts in MCA Member Companies
Food, Drug, and Cosmetic Chemicals Committee

SUBJECT: GRAS Review

Gentlemen:

It was decided at the May 15, 1974 meeting of the MCA Food, Drug, and Cosmetic Chemicals Committee that MCA member companies sould be informed of the total process of the GRAS Review, and be requested to advise as to deficiencies or omissions encountered to date in conncetion with the review, with the objective of identifying problems affecting a significant number of member companies for possible MCA action.

First, by way of background, President Nixon in his Consumer Message of 1969, directed the Food and Drug Administration to re-evaluate all items on the Generally Recognized As Safe (GRAS) list for safety.

Then, as one phase in this review, FDA contracted with the National Academy of Sciences to conduct a survey of such substances. This survey (which went to manufacturers, processors, and distributors) covered poundage, types of specifications, processing and storage effects, safety information, and usage.

FDA also contracted for Scientific Literature Reviews, and for testing (teratology screening).

For the "wrapping up" phase of the review, FDA contracted with the Federation of American Societies for Experimental Biology (FASEB) to conduct the initial evaluation of the NAS production and consumption data, the Scientific Literature Reviews, and the additional toxicological test data, and to provide a report on the safety of each individual ingredient.

After evaluation by FDA of a FASEB report, the procedure calls for FDA to publish in the Federal Register an appropriate proposal to (1) affirm GRAS status, (2) publish a prior sanction, (3) establish an interim food additive regulation, (4) establish a permanent food additive regulation, or (5) eliminate food use of the ingredient.

The status of 439 non-flavor substances in the review, as reported in the April 1 issue of Food Chemical News, indicates that the Scientific Literature Reviews (monographs) are 70% complete, but that the FASEB Select Committee reports are only 6% complete. It was reported that this lag is due to the need for hearing and peer review, and that FASEB has completed a preliminary review of 202 ingredients.

With reference to the first paragraph of this letter, there are indications that the adequacy of some of the completed Scientific Literature are open to question, although this could be due partly at least to failure to take advantage of the opportunities to provide unpublished safety data and make other inputs. The Federal Register of July 26, 1973 (pages 20051-20054) and that of April 17, 1974 (page 13798) gave notices of these opportunities.

It will be appreciated if you will advise concerning any "deficiencies or omissions" you may have encountered to date in connection with any phase of the GRAS Review, for referral to the involved subcommittee of the MCA Food, Drug, and Cosmetic Chemicals Committee.

Sincerely yours,

M. M. Hoover, Secretary
Food, Drug, and Cosmetic
Chemicals Committee

MMH:sh
Distribution "A"

P.S. Notices from the July 26, 1973 and April 17, 1974 issues of the Federal Register concerning opportunities for input and availability of information are attached for your information.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

GRAS OR PRIOR-SANCTIONED DIRECT HUMAN FOOD INGREDIENTS

Notice of Opportunity To Submit Unpublished Safety Data

The Food and Drug Administration is conducting a study of the direct human food ingredients classified as generally recognized as safe (GRAS) or subject to a prior sanction. As part of this study, information on each ingredient (or group of ingredients) is being summarized in a series of Scientific Literature Reviews by organizations under contract with the Food and Drug Administration. The organizations preparing the Scientific Literature Reviews are responsible for including a summary of the world literature on safety published since January 1, 1920.

In order to assure that all pertinent safety information is obtained for inclusion in each Scientific Literature Review, this notice solicits from any source unpublished data and information that may be appropriate in determining the safety of the substances. The organizations preparing the Scientific Literature Reviews, and the Reviews now in active preparation or planned for preparation, are as follows:

1. Food and Drug Research Laboratories, Inc.,
   60 Evergreen Place,
   East Orange, NJ 07018.
2. Franklin Institute Research Laboratories,
   The Benjamin Franklin Parkway,
   Philadelphia, PA 19103.
3. Informatics, Inc.,
   6000 Executive Boulevard,
   Rockville, MD 20852.
4. Tractor Jitco, Inc.,
   1300 East Gude Dr.,
   Rockville, MD 20851.

Ingredients	Organizations	Estimated date of completion
Aluminum compounds.	Tracor Jitco, Inc.	June 29, 1973
Silicates	do	July 27, 1973
Magnesium salts	do	July 20, 1973
Manganese salts	do	Aug. 3, 1973
Starter distillate	do	Oct. 19, 1973
Acetic acid & derivatives.	do	Aug. 10, 1973
Formic acid & derivatives.	do	Aug. 31, 1973
Methyl & ethyl acrylate.	do	Oct. 19, 1973
Hydrosulfites	do	July 20, 1973
Salts of fatty acids	do	July 27, 1973
Sodium and potassium hydroxides.	do	Oct. 5, 1973
Vitamin D	do	Sept. 7, 1973
Corn silk	do	Oct. 5, 1973
Sulfamic acid	do	July 13, 1973
Tall oil	do	July 27, 1973
Fish oil, hydrogenated.	do	Aug. 24, 1973
Soy bean oil, hydrogenated.	do	Do.
Glutamic acid and derivatives.	do	June 29, 1973
Cholic acid & derivatives.	Informatics, Inc.	June 22, 1973
Calcium sequestrants	do	Do.
Choline salts	do	Do.
Algae	do	Do.
Iodine salts used in foods.	do	Do.
Pulps	do	Do.
Aconitic acid	do	Do.
Corn sugar-syrup	do	July 2, 1973
Sorbase	do	Do.
Tannic acid	do	July 9, 1973
Inositol	do	July 18, 1973
Gelatin	do	July 25, 1973
Tallow	do	Aug. 15, 1973
Succinic acid	do	Do.
Beeswax and japan wax.	Franklin Research Institute.	June 29, 1973
Carnauba wax	do	Do.
Sodium thiosulfate	do	July 30, 1973
Citrates	Food and Drug Research Labs, Inc.	June 29, 1973
Calcium oxide & calcium hydroxide.	do	Do.
Sorbates	do	Do.
Butylated hydroxyanisole.	do	Do.
Malic acid	do	Do.
Ascorbates	do	July 7, 1973
Propionates	do	July 20, 1973
Gluconate radical	do	Aug. 3, 1973
Dextrins	do	Aug. 10, 1973
Pantothenates	do	Do.
Soy protein isolated	do	Aug. 18, 1973
Rennet	do	Do.
Copper salts used in foods.	do	Aug. 24, 1973
Hydrochloric acid	do	Do.
Tartaric acid & tartrates.	do	Aug. 31, 1973
Lard & lard oil	do	Do.
Bentonite & clay	do	Sept. 7, 1973
Papain	do	Sept. 14, 1973
Gases used in foods	do	Do.
Starches	do	Sept. 21, 1973
Hydrogen peroxide	do	Do.
Carbon dioxide	do	Sept. 28, 1973
Lactic acid & derivatives.	do	Do.
Vitamin A	do	Do.

In addition, the Flavor and Extract Manufacturer's Association, 1001 Connecticut Avenue, NW., Wash., DC 20036, is preparing a Scientific Literature Review on the following 276 aliphatic alcohols, acids, aldehydes, and esters, used as flavor ingredients. The Reviews are scheduled for completion by December 15, 1973.

ALIPHATIC ALCOHOLS

LINEAR SATURATED

Amyl alcohol
Butyl alcohol
1-Decanol
Ethyl alcohol
Heptyl alcohol
1-Hexadecanol
Hexyl alcohol
Lauryl alcohol
Nonyl alcohol
1-Octanol
Propyl alcohol
Undecyl alcohol

LINEAR UNSATURATED

2-Hexen-1-ol
3-Hexen-1-ol
2,6-Nonadien-1-ol
trans-2-Nonen-1-ol

BRANCHED SATURATED

iso-Amyl alcohol
iso-Butyl alcohol
3,7-Dimethyl-1-octanol
2-Ethyl-1-hexanol
3,5,5-Trimethyl-1-hexanol

BRANCHED UNSATURATED

Geranol
Citronellol
Nerol
Rhodinol
Farnesol

ALIPHATIC ACIDS

LINEAR SATURATED

Acetic acid
Butyric acid
Decanoic acid
Formic acid
Hexanoic acid
Lauric acid
Myristic acid
Nonanoic acid
Octanoic acid
Palmitic acid
Propionic acid
Stearic acid
Valeric acid
Undecanoic acid
Heptanoic acid

LINEAR UNSATURATED

Oleic acid
4-Pentenoic acid
trans-2-Hexenoic acid
3-Hexenoic acid
10-Undecenoic acid
9, 12-Octadecadienoic acid (48%) and
9, 12, 15-Octadecatrienoic acid (52%)

BRANCHED SATURATED

iso-Butyric acid
2-Ethylbutyric acid
2-Methylbutyric acid
2-Methylhexanoic acid
2-Methylheptanoic acid
2-Methylvaleric acid
iso-Valeric acid

BRANCHED UNSATURATED

3,7-Dimethyl-6-octenoic acid
3-Methylcrotonic acid
2-Methyl-2-pentenoic acid
2,3-Dionethyl-2-pentenoic acid

ALIPHATIC ALDEHYDES

LINEAR SATURATED

Acetaldehyde
Butyraldehyde
Decanal
Heptanal
Hexanal
Lauric aldehyde
Myristaldehyde
Nonanal
Octanal
Propionaldehyde
Undecanal
Valeraldehyde

LINEAR UNSATURATED

cis-3-Hexenal
10-Undecenal
9-Undecenal
4-Heptenal
4-Decenal

CONJUGATED

2-Decenal
2-Dodecenal
2-Heptenal
2,4-Nonadienal
2-Hexenal
2-Tridecenal
2-*trans*, 4-*trans*-Decadienal
2,4-Heptadienal
2-Nonenal
2-Octenal
2,4-Pentadienal
2-Pentenal
Nona-2-*trans*, 6-*cis*-Dienal

BRANCHED SATURATED

iso-Butyraldehyde
2,6-Dimethyl octanal
2-Methylbutyraldehyde
3-Methylbutyraldehyde
2-Ethylbutyraldehyde
2-Methyloctanal
2-Methylundecanal

BRANCHED UNSATURATED

Citronellal
2,6-Dimethyl-5-heptenal

CONJUGATED

Citral
2,6-Dimethyl-10-methylene-2,6,11-dodecatrienal
2-Ethyl-2-heptenal
2-Methyl-2-pentenal

ALIPHATIC ESTERS

(with linear saturated acid portion and alcohol portion as indicated)

LINEAR SATURATED

Amyl butyrate
Amyl heptanoate
Amyl octanoate
Butyl butyrate
Butyl heptanoate
Butyl laurate
Butyl stearate
Decyl acetate
Decyl propionate
Ethyl butyrate
Amyl formate
Amyl hexanoate
Butyl acetate
Butyl formate
Butyl hexanoate
Butyl propionate
Butyl valerate
Decyl butyrate
Ethyl acetate
Ethyl decanoate
Ethyl formate
Ethyl hexanoate
Ethyl myristate
Ethyl octadecanoate
Ethyl palmitate
Ethyl undecanoate
Heptyl acetate
Heptyl formate
Hexyl acetate
Hexyl formate
Hexyl octanoate
Lauryl acetate
Methyl butyrate
Methyl hexanoate
Methyl myristate
Methyl octanoate
Methyl valerate
Nonyl octanoate
Octyl butyrate
Octyl heptanoate
Octyl propionate
Propyl butyrate
Propyl heptanoate
Propyl propionate
Ethyl heptanoate
Ethyl laurate
Ethyl nonanoate
Ethyl octanoate
Ethyl propionate
Ethyl valerate
Heptyl butyrate
Heptyl octanoate
Hexyl butyrate
Hexyl hexanoate
Hexyl propionate
Methyl acetate
Methyl heptanoate
Methyl laurate
Methyl nonanoate
Methyl propionate
Nonyl acetate
Octyl acetate
Octyl formate
Octyl octanoate
Propyl acetate
Propyl formate
Propyl hexanoate

LINEAR UNSATURATED

Allyl butyrate
Allyl hexanoate
Allyl octanoate
2-Hexen-1-yl acetate
cis-3-Hexen-1-yl acetate
Allyl heptanoate
Allyl nonanoate
Allyl propionate
10-Undecen-1-yl acetate
3-Hexenyl formate

BRANCH SATURATED

iso-Amyl acetate
iso-Amyl formate
iso-Amyl laurate
iso-Amyl octanoate
iso-Butyl acetate
iso-Butyl formate
iso-Butyl hexanoate
2-Ethyl butyl acetate
iso-Amyl butyrate
iso-Amyl hexanoate
iso-Amyl nonanoate
iso-Amyl propionate
iso-Butyl butyrate
iso-Butyl heptanoate
iso-Butyl propionate

BRANCH UNSATURATED

Citronellyl acetate
Citronellyl formate
Citronellyl valerate
Geranyl butyrate
Geranyl hexanoate
Citronellyl butyrate
Citronellyl propionate
Geranyl acetate
Geranyl formate
Geranyl propionate

ALIPHATIC ESTERS

(with linear unsaturated acid portion and alcohol portion as indicated)

LINEAR SATURATED

Butyl 2-decenoate
Ethyl acrylate
Ethyl 2-nonynoate
Ethyl sorbate
Methyl 2-hexenoate
Methyl 2-nonynoate
Methyl 9-undecenoate
Ethyl *trans*-2, *cis*-4-Decadienoate
Ethyl *cis*-4-octenoate
Methyl 3-hexenoate
Butyl 10-undecenoate
Ethyl crotonate
Ethyl oleate
Ethyl 10-undecenoate
Methyl 2-nonenoate
Methyl 2-octynoate
Methyl 2-undecynoate
Ethyl 3-hexenoate
n-Hexyl 2-butenoate
Methyl *cis*-4-ctenoate

LINEAR UNSATURATED

Allyl sorbate
2-Methylallyl butyrate
Neryl butyrate
Neryl propionate
Rhodinyl butyrate
Rhodinyl propionate
Allyl 10-undecenoate
Neryl acetate
Neryl formate
Rhodinyl acetate
Rhodinyl formate

ALIPHATIC ESTERS

(with branched saturated acid portion and alcohol portion as indicated)

LINEAR SATURATED

Butyl *iso*-Butyrate
Butyl *iso*-Valerate
Ethyl *iso*-Butyrate
Ethyl *iso*-Valerate
Hexyl *iso*-Valerate
Methyl 2-Methylbutyrate
Methyl *iso*-Valerate
Octyl *iso*-Butyrate
Propyl *iso*-Butyrate
Hexyl *iso*-Butyrate
Ethyl 2-Methylbutyrate
Heptyl *iso*-Butyrate
Methyl *iso*-Butyrate
Methyl 4-methylvalerate
Nonyl *iso*-Valerate
Octyl *iso*-Valerate
Propyl *iso*-Valerate

LINEAR UNSATURATED

Allyl 2-ethylbutyrate
3-Hexenyl *iso*-Valerate
Allyl *iso*-Valerate
3-Hexenyl-2-methylbutyrate

BRANCH SATURATED

Hexyl-2-methylbutyrate
iso-Amyl *iso*-Valerate
3,7-Dimethyllocta-2,6-dienyl 2-ethylbutanoate
2-Methylbutyl-*iso*-Valerate
2-Methylpropyl 3-Methylbutyrate
iso-Amyl-*iso*-Butyrate
iso-Amyl-2-methylbutyrate
2-Methylbutyl 2-methylbutyrate

BRANCH UNSATURATED

Citronellyl *iso*-Butyrate
Geranyl *iso*-Valerate
Neryl *iso*-Valerate
Rhodinyl *iso*-Valerate
Geranyl *iso*-Butyrate
Neryl *iso*-Butyrate
Rhodinyl *iso*-Butyrate

ALIPHATIC ESTERS

(with branched unsaturated acid portion and alcohol portion as indicated)

LINEAR SATURATED

Ethyl tiglate
Methyl 3,7-dimethyl-6-octenoate

LINEAR UNSATURATED

Allyl tiglate

BRANCH SATURATED

iso-Butyl angelate

The above list of 276 flavor ingredients represents the initiation of Scientific Literature Reviews of 1,550 natural and synthetic flavor substances. An announcement will be made in the FEDERAL REGISTER when other flavor compounds are selected for Review, so that appropriate unpublished information and data may be submitted. All flavor ingredients listed in §§ 121.101(e) and (g), 121.1163 and 121.1164, or otherwise submitted or known to FDA, are intended for eventual inclusion in a Scientific Literature Review.

Other GRAS and prior sanctioned food ingredients intended for an immediate or planned Scientific Literature Review are listed below under their appropriate categories.

IMMEDIATE SCIENTIFIC LITERATURE REVIEW

Adipic acid
Casein and caseinates
Hypophosphites
Pectin and pectinates
Gum guaiac
Ascorbic acid
Carotenes
Iron, reduced
Niacin and niacinamide
Pyridoxine and pyridoxine hydrochloride
Riboflavin and riboflavin-5-phosphate
Caffeine
Glycerophosphates
Dextrans

Vegetable oils
Sucrose
Biotin
Citric acid
Lecithins
Para-hydroxylbenzylisothiayanate
Thiamine
Urea
Vitamin B_{12}
Sodium and potassium chlorides

PLANNED SCIENTIFIC LITERATURE REVIEW

Amines (filming)
Benzoyl peroxide
Borax
Brandy
Calcium stearate
Carbon
Char smoke flavor
Collagen (avitene)
Cyclohexylamine
Enzymes (proteolytic)
Ferrocyanide salts
Glucono delta lactone
Glycerol lactopalmitate
Hesperidin complex
Lignin
Malt syrup
Milk powder (whole, enzyme modified)
Amino tri (methylene phosphoric acid) sodium salt
Bergamot oil
Bouillon (vegetable, smoked)
Butter fat, enzyme modified w/added butyric acid
Candelilla wax
Carboxymethyl hydroxyethyl cellulose
Chlorophyll
Corn mint oil (mentha arvenis oil)
Enzymes (bacterial)
Ferrous citrate
Furcelleran
Gluten (corn)
Gums (vegetable)
Iron citrate
Liver fractions
Methylpolysilicone
Mono and diglycerides (sodium sulfoacetate derivatives)
< Morpholine
<Nickel
< Octadecylamines
Otticia
Peptone (pepsin-modified soy bean protein; brewers peptone)
Piperazine dihydrochloride
Potassium gluconate
Rutin
Silver-silver dragees
Sodium fluoride
Sodium metasilicate
Soya fatty acid amine (ethoxylated)
Starch (food, modified)
Vitamin B complex and syrup
Yeasts
Pepsin
Potassium bromate
Potassium phosphates
Sausage casings (HCl and cellulose fibers)
Sodium chlorite
Sodium hypochlorite
Sodium zinc metasilicate
Stearyl alcohol
Wax (shellac)
Zein powder

To be considered for inclusion in a Scientific Literature Review, two copies of all relevant safety data, and information shall be submitted to the organization preparing the Review before the listed completion date, and the original and two copies of all such information shall simultaneously be sent to GRAS Review Branch (BF-335), Bureau of Foods, Food and Drug Administration, 200 "C" Street SW., Wash., DC 20204. Immediately upon receipt of any such submission, one copy will be placed on display at the Office of the Hearing Clerk, Food and Drug Administration, Rm. 6-88, 5600 Fishers Lane, Rockville, MD 20852, where it may be reviewed during working hours, Monday through Friday.

If the contractor has not been named, the original and four copies of any such data and information shall be submitted to the GRAS Review Branch (address above), which will distribute two copies to the contractor for the Scientific Literature Review when he is selected. A copy of all such submissions will also immediately be placed on display at the office of the Hearing Clerk, at the above address.

If the estimated date of completion of the Review has passed, copies of any such safety data and information shall be submitted to the Select Committee on GRAS Substances and the GRAS Review Branch as provided by the notice published elsewhere in this issue of the FEDERAL REGISTER, and a copy of any such submission will immediately be placed on display at the office of the Hearing Clerk pursuant to that notice.

Dated: July 19, 1973.

A. M. SCHMIDT,
Commissioner of Food and Drugs.

[FR Doc.73-15220 Filed 7-25-73;8:45 am]

SAFETY OF GRAS AND PRIOR-SANCTIONED DIRECT HUMAN FOOD INGREDIENTS

Notice of Opportunity To Present Data Information and Views

The Food and Drug Administration is conducting a study of the safety of direct human food ingredients classified as generally recognized as safe (GRAS) or subject to a prior sanction. As part of this study, information on each such ingredient (or group of ingredients), gathered from literature searches and other sources, is being summarized in a series of written Scientific Literature Reviews by organizations under contract with the Food and Drug Administration. The organizations preparing the Scientific Literature Reviews are responsible for including a summary of the world literature on safety published since January 1, 1920. Opportunity is provided, elsewhere in this issue of the FEDERAL REGISTER, for any interested person to submit unpublished safety data and information on these food ingredients for inclusion in Scientific Literature Reviews now under preparation.

Several Scientific Literature Reviews have now been completed and submitted to the Food and Drug Administration. A list of those completed Reviews appears elsewhere in this issue of the FEDERAL REGISTER, (38 FR), and notice is given of their public availability.

The Food and Drug Administration briefly examines each Scientific Literature Review before accepting it. This brief examination covers only the general quality of the work, to make certain that the major scientific information is included in a balanced and complete presentation. The examination is not intended to determine that all pertinent scientific information is included. Notice is therefore hereby given that any interested person who, after study of a Scientific Literature Review, believes that additional pertinent published or unpublished data or information should be included in considering the safety of the ingredient(s) covered in the Scientific Literature Review, may submit ten copies of such written data, information, or views to:

Select Committee on GRAS Substances,
Federation of American Societies for Experimental Biology,
9650 Rockville Pike,
Bethesda, MD 20014

The original of this material and two additional copies shall simultaneously be sent to:

Bureau of Foods,
Food and Drug Administration,
GRAS Review Branch (BF-335),
200 "C" Street, S.W.,
Washington, DC. 20204.

Immediately upon receipt, one copy of any such submission will be placed on display at the office of the Hearing Clerk, Food and Drug Administration, Room 6-88, 5600 Fishers Lane, Rockville, MD 20852, where it may be reviewed during working hours, Monday through Friday.

The Select Committee on GRAS Substances is utilizing the services of special consultants with particular expertise in considering specific issues that arise in the evaluation of these substances. The Select Committee also recognizes that the presentation of oral views with respect to the safety of these substances may be helpful in its work. Therefore, an opportunity will be provided for any interested person to present oral views on the safety of these substances to the Select Committee at a hearing, as part of the evaluation process. Notices providing an opportunity to participate in a hearing, for the presentation of such oral views to the Select Committee, will be published in the FEDERAL REGISTER at the appropriate time.

Following completion of its evaluation, the Select Committee will prepare a report to the Commissioner of Food and Drugs containing its evaluation and recommendations, with respect to the safety of the particular ingredient(s) covered by a Scientific Literature Review. Upon acceptance of the report by the Food and Drug Administration, it will be made available to the public in accordance with the notice on this matter published elsewhere in this issue of the FEDERAL REGISTER. After evaluating this report, the Commissioner will publish in the FEDERAL REGISTER, an appropriate proposal to (1) affirm GRAS status, (2) publish a prior sanction, (3) establish an interim food additive regulation, (4) establish a permanent food additive regulation, or (5) eliminate food use of the ingredient. These proposals will be issued pursuant to the procedural provisions contained in §§ 121.40, 121.41 published in the FED-

ERAL REGISTER of December 2, 1972 (37 FR 25705), and § 121.2000 published in the FEDERAL REGISTER of May 15, 1973 (38 FR 12737). The Commissioner is proposing elsewhere in this issue of the FEDERAL REGISTER, to establish new §§ 121.104 *Substances added directly to human food affirmed as generally recognized as safe (GRAS)*, 121.105 *Substances in food contact surfaces affirmed as generally recognized as safe (GRAS)*, and 121.106 *Substances prohibited from use in food*. Thus, each food ingredient will be proposed for inclusion in one of these three new sections, in Subpart D (direct human food additives), in Subpart E (prior sanctions), in Subpart F (indirect human food additives), or in Subpart H (interim human food additives).

Following publication of any such proposal, all interested persons will have an opportunity to submit written comments on the proposal. Where good cause is shown, the Commissioner may order a public hearing at which an oral presentation of data, information, and views may be made. The final regulation will be final agency action from which appeal lies to the courts.

The Commissioner urges the cooperation of all segments of the public in this important work.

Dated: July 19, 1973.

A. M. SCHMIDT,
Commissioner of Food and Drugs.

[FR Doc.73-15221 Filed 7-25-73;8:45 am]

STATUS OF REVIEW OF GRAS AND PRIOR-SANCTIONED DIRECT HUMAN FOOD INGREDIENTS

Notice of Availability of Information

Food ingredients that are generally recognized as safe (GRAS), or that were sanctioned through action by the Food and Drug Administration or the United States Department of Agriculture prior to enactment of the Food Additives Amendment of 1958, may be utilized in food without first obtaining approval through a food additive regulation. After enactment of the law, the Food and Drug Administration published a partial list of GRAS and prior-sanctioned ingredients in § 121.101. This list was developed without a thorough scientific review of each ingredient.

In his Consumer Message of October 30, 1969, President Nixon directed the Secretary of Health, Education, and Welfare to initiate a full review of all GRAS ingredients. To implement this mandate, the Food and Drug Administration contracted with the Food Protection Committee of the National Academy of Sciences to survey the entire food industry to determine the national production of all GRAS ingredients and the amount of each such ingredient used in any particular food. The National Academy of Sciences report to the Food and Drug Administration incorporated the results of independent surveys conducted by the United States Department of Agriculture as part of its 1965 Household Food Consumption surveys to determine the sizes of food servings used by consumers, and by the Market Research Corporation of America, to determine how frequently representative consumers eat individual servings of foods in specific food categories. The results of the NAS Survey, describing incorporation of USDA and MRCA data, is now available. The complete Survey report also contains various tabular computer printouts describing the use of GRAS food ingredients in NAS food categories and the total exposure of GRAS food ingredients in human foods.

The Food and Drug Administration also contracted with the Franklin Institute Research Laboratories, The Benjamin Franklin Parkway, Philadelphia, PA 19103, to conduct a search of the world literature since January 1, 1920 on the following 72 GRAS food ingredients that were determined to be a matter of high priority:

Ammoniated glycyrrhizin
Sodium nitrite
Sodium nitrate
Potassium nitrate
Potassium nitrite
Saccharin (acid)
Sodium saccharin
Calcium saccharin
Ammonium saccharin
Potassium bisulfite
Potassium metabisulfite
Sodium bisulfite
Sodium metabisulfite
Sulfur dioxide
Oil of mustard

Oil of garlic
Oil of nutmeg
Oil of rue
Oil of clove
Caramel
Benzoic acid
Sodium benzoate
Methyl paraben
Propyl paraben
Propyl gallate
Carrageenan
Sodium alginate
Gun tragacanth
Gum arabic (acacia)
Carob bean gum
Ghatti gum
Sterculia gum
Guar gum
Furcelleran
Sodium carrageenan
Sorbitol
Mannitol
Butylated hydroxyanisole
Butylated hydroxytoluene
Hydrogen peroxide
Diacety tartaric acid esters of mono- and diglycerides of edible fats and oils, or edible fat-forming acids
Stannous chloride
Diacetyl
Monosodium glutamate
Monopotassium glutamate
Glutamic acid
Glutamic acid hydrochloride
Monoammonium glutamate
Zinc sulfate
Zinc gluconate
Sodium thiosulfate
Dilauryl thiodipropionate
Thiodipropionic acid
Calcium propionate
Bentonite
Carnauba wax
Sodium aluminosilicate
Tricalcium silicate
Vitamin A
Vitamin A acetate
Vitamin A palmitate
Vitamin D_2
Vitamin D_3
Zinc chloride
Zinc oxide
Zinc stearate
Aluminum calcium silicate
Calcium silicate
Magnesium silicate
Sodium calcium aluminosilicate, hydrated

This literature search is being expanded to include all of the GRAS substances for direct human food use included in § 121.101(d) and a number of substances possessing such GRAS status by virtue of a communication from the Food and Drug Administration. A complete list of these substances, and their scheduled coverage by Scientific Literature Reviews, is included in a notice published elsewhere in this issue of the FEDERAL REGISTER.

Each scientific literature search is designed to discover any articles that considered (1) chemical toxicity, (2) occupational hazards, (3) metabolism, (4) reaction products, (5) degradation products, (6) reported carcinogenicity, teratogenicity, or mutagenicity, (7) dose response, (8) reproductive effects, (9) histology, (10) embryology, (11) behavioral effects, (12) detection methodology, and (13) processing. The results of this search are then incorporated in a Scientific Literature Review on each ingredient (or group of chemically similar ingredients).

Additional toxicological screening tests were conducted on 42 selected GRAS ingredients for mutagenisis and teratology. Teratological screening was conducted on all 42 ingredients in four mammalian species: Rat, mouse, hamster, and rabbit. Chick embryo tests were also conducted on 41 of those ingredients. The mutogenic test conducted on 40 of the ingredients, used the host mediated assay, the dominant lethal, and the cytogenic assay procedures. These studies were designed primarily to evaluate these relatively new toxicological screening tests, and an assessment of their value is not yet possible.

The Food and Drug Administration then contracted with the Federation of American Societies for Experimental Biology (FASEB) to conduct the initial evaluation of the Scientific Literature Reviews, the NAS production and consumption data, and the additional toxicological test data, and to provide a report on the safety of each individual ingredient. The Life Sciences Research Office of FASEB in turn appointed a Select Committee on GRAS Substances (SCOGS) which has been working since June 1972 to conduct this evaluation. Notices appear elsewhere in this issue of the FEDERAL REGISTER requesting nominations for additional qualified scientists to serve on this Select Committee, providing an opportunity to submit unpublished safety data and information on GRAS or prior-sanctioned direct human food ingredients to the organizations preparing the Scientific Literature Reviews, and providing an opportunity to present data, information, and views on the safety of these ingredients directly to the Select Committee for their consideration in the evaluation process.

To implement the review of GRAS and prior-sanctioned direct human food ingredients, the Commissioner of Food and Drugs has published in the FEDERAL REGISTER several regulations and notices. In announcing the review of GRAS food ingredients in the FEDERAL REGISTER of December 8, 1970 (35 FR 18632), the Commissioner proposed new criteria for determining GRAS status. These criteria were promulgated in final form in the FEDERAL REGISTER of June 25, 1971 (36 FR 12084).

A notice published in the FEDERAL REGISTER of October 23, 1971 (36 FR 20546) urged that all interested persons obtain and complete the survey questionnaire being used by the National Academy of Sciences to obtain broad representative information on the production and use of direct human food ingredients that have been listed in § 121.101 as GRAS or that were subject to a prior sanction. In additional to published GRAS substances and known prior-sanctioned substances, the NAS questionnaire also requested information on direct human food ingredients used on the basis of a conclusion that they are GRAS, but which are not published in § 121.101. Neither the Food and Drug Administration study nor the NAS survey includes indirect human food ingredients or animal food ingredients.

A procedure governing affirmation of GRAS status and determination of food additive status was promulgated in the FEDERAL REGISTER for December 2, 1972 (37 FR 25705). The same FEDERAL REGISTER notice promulgated a new Subpart H to govern the promulgation of interim food additive regulations. Subpart E was amended in the FEDERAL REGISTER for May 15, 1973 (38 FR 12737) to provide for publication of all prior sanctions for food ingredients, and to permit the addition of limitations where justified by new toxicological information.

The list of direct human food ingredients published as GRAS in § 121.101 includes 533 ingredients, 261 of which are flavors. The 272 non-flavor published GRAS ingredients will be covered in 120 Scientific Literature Reviews, all of which are completed, in progress, or planned for contract, as indicated elsewhere in this issue of the FEDERAL REGISTER.

The Food and Drug Administration has contracted with the Flavor and Extract Manufacturers Association to prepare similar Scientific Literature Reviews with respect to 276 flavor substances, listed elsewhere in this issue of the FEDERAL REGISTER. Scientific Literature Reviews will then be prepared on all remaining flavor substances, including those published as GRAS in § 121.101, those published in such food additive regulations as §§ 121.1163 and 121.1164, and those used on the conclusion that they are GRAS although they are not published in § 121.101.

The next priority matter will involve additional substances subject to food additive regulations and prior sanctions. A schedule and priorities for these have not yet been determined.

Upon receiving a Report from the FASEB Select Committee evaluating the safety of an ingredient, the Commissioner, after conducting his own evaluation, will publish in the FEDERAL REGISTER an appropriate proposal to affirm GRAS status, to publish a prior sanction, to establish an interim food additive regulation, to establish a permanent food additive regulation, or to eliminate food use of the ingredient. These proposals will be published pursuant to the procedural provisions contained in §§ 121.40, 121.41, and 121.2000. The Commissioner is proposing to establish new § 121.104 *Substances added directly to human food affirmed as generally recognized as safe (GRAS)*, § 121.105 *Substances in food-contact surfaces affirmed as generally recognized as safe (GRAS)*, and § 121.106 *Substances prohibited from use in food*, elsewhere in this issue of the FEDERAL REGISTER. Thus, each of these food ingredients will be proposed for inclusion in one of these three new sections, in Subpart D (direct human food additives), in Subpart E (prior sanctions), in Subpart F (indirect human food additives), or in Subpart H (interim human food additives).

Following publication of any such proposal, all interested persons will have an opportunity to submit written comments on the proposal. Where good cause

is shown, the Commissioner may order a public hearing at which an oral presentation of data, information, and views may be made. The final regulation will be final agency action from which appeal lies to the courts.

Section 121.101 is not limited to direct human food ingredients. Many of the substances listed in § 121.101 have been regarded as GRAS for indirect food ingredient use, in or on food-contact surfaces, and for use in pet food and animal feed. Accordingly, when an ingredient listed in § 121.101 is affirmed as GRAS for direct human food use, it will be retained in § 121.101, with the explanation that it has been affirmed as GRAS, and cross-referenced to the applicable paragraph in new § 121.104. When an ingredient is transferred to an interim food additive regulation, permanent food additive regulation, or prohibited status, for direct human use, a decision will be made as to whether the ingredient may remain as GRAS for uses other than direct human food use, or should be restricted or eliminated from such uses, and § 121.101 and other applicable regulations will be amended accordingly.

In the event that additional toxicological testing is required before the ingredient may be affirmed as GRAS or approved by a permanent food additive regulation, an interim food additive regulation will be proposed (unless there is a reasonable likelihood that a health hazard exists). Pursuant to § 121.4000, use of the ingredient must cease unless an interested person satisfies the Commissioner, in writing within 60 days following the effective date of the interim food additive regulation, that studies adequate and appropriate to resolve the questions raised about the ingredient have been undertaken. The Food and Drug Administration may itself undertake such studies, but this will occur only in very rare instances, if at all. As a general rule, the Food and Drug Administration intends to institute little or no testing for the purpose of providing data necessary to justify continued marketing of food ingredients, because of its conclusion that this is properly the function of private industry.

Many of the substances published as GRAS in § 121.101, or used on a determination that they are GRAS without publication in § 121.101, were approved by the United States Department of Agriculture for use in meat or poultry, or were approved by the Food and Drug Administration for use in various foods pursuant to correspondence, food standards, regulations, informal announcements, or in other ways, prior to 1958. Thus, many of these ingredients are subject to specific prior sanctions in addition to GRAS status. No comprehensive list of such prior sanctions exists. To the extent that one of these substances is affirmed as GRAS for all prior-sanctioned uses, the fact that it may also be subject to a prior sanction is largely of historical interest and has no regulatory significance. To the extent that one of these substances is not affirmed as GRAS for all prior-sanctioned uses, any restrictions or limitations imposed upon its use could in any event also be imposed on the prior-sanctioned uses under the adulteration provisions of the Act as provided in § 121.2000, published in the FEDERAL REGISTER of May 15, 1973 (38 FR 12738).

Accordingly, the Commissioner has concluded that regulations based upon the review of GRAS and prior-sanctioned direct human food ingredients will initially be proposed on the assumption that no prior sanction exists. Because prior-sanctioned status constitutes an exemption from section 409 of the Act, it should be construed narrowly, and the burden of coming forward with evidence of the sanction properly rests upon the person who asserts it. In the event that any person responds to a proposed regulation with proof of a valid prior sanction, a final regulation will be issued under Subpart E Substances for which prior sanctions have been granted, as well under any other applicable sections of the regulations. In this way, all possible uses of the ingredient will be fully covered. Any regulation promulgated pursuant to this review will constitute a determination that excluded uses would result in adulteration of the food in violation of section 402 of the act, and failure to submit proof of an applicable prior sanction in response to any proposed regulation will also constitute a waiver of the right to assert such sanction at any later point in time. Any proposed regulation will also be construed as a proposal under Subpart E, in the event that a prior sanction is asserted in comments submitted on it. This procedure is necessary because of the unavailability of any comprehensive list of prior sanctions.

In the past, it has been customary practice for the Food and Drug Administration to issue advisory opinions that a substance is GRAS, or is subject to a prior sanction, or is not a food additive because it is used in or on food-contact surfaces and there is no detectable migration. The Commissioner has concluded that all such past correspondence is publicly available, except that trade secrets will be retained as confidential, and that all future opinions relating to GRAS or prior-sanctioned status will be issued in the form of FEDERAL REGISTER notices proposing appropriate new regulations. Opinions solely with respect to no-migration status of food-contact ingredients will continue to be handled by letter rather than by regulation because of their limited applicability, and all such correspondence will be publicly available, except that trade secrets will be retained as confidential.

The Commissioner recognizes that the data and information obtained in the process of conducting this review of direct human food ingredients is of broad interest to the public. Accordingly, this information is available for public disclosure in the following ways.

1. The report of the National Academy of Sciences on "A Comprehensive Survey of Industry on the Use of Food Chemicals Generally Recognized As Safe" (September 1972) may be purchased from the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, VA 22151. This report is now available.

2. A series of computer print-outs of the combined data from the NAS, USDA, and MRCA Surveys may be purchased from NTIS. These print-outs are now available and are explained in the NAS report.

3. The reports of the 1965 USDA Survey on "Food Consumption of Households in the United States" may be purchased separately from Superintendent of Documents, U.S. Government Printing Office, Wash., D.C. 20402, order number HFCS 1965–66, Report No. 1. These documents are now available.

4. Each Scientific Literature Review may be purchased from NTIS as it becomes available. The following Scientific Literature Reviews are now available:

Review title	Ordering No.	Printed copy price
Gum Arabic (Acacia)	PB-221-201	$4.65
Butylated Hydroxytoluene	PB-221-202	4.50
Carob Bean Gum	PB-221-203	3.00
Gum Tragacanth	PB-221-204	3.00
Sterculia	PB-221-205	3.00
Carrageenan	PB-221-206	4.50
Propyl Gallate	PB-221-207	3.75
Benzoates	PB-221-208	5.45
Parabens	PB-221-209	3.75
Sorbitol	PB-221-210	4.65
Mannitol	PB-221-211	4.65
Oil of Rue	PB-221-212	3.00
Gum Ghatti	PB-221-213	3.00
Zinc Salts	PB-221-214	5.45
Oil of Mustard	PB-221-215	4.50
Guar Gum	PB-221-216	3.75
Sulfiting Agents	PB-221-217	6.00
Caramel	PB-221-218	3.75
Oil of Garlic	PB-221-219	3.75
Nitrates-Nitrites	PB-221-220	9.00
Oil of Clove	PB-221-221	3.75
Oil of Nutmeg	PB-221-222	3.00
Dill	PB-221-223	3.00
Phosphates	PB-221-224	6.0
Agar-Agar	PB-221-225	3.7
Alginates	PB-221-226	4.50
Glycerine and Glycerides	PB-221-227	6.75
Cellulose	PB-221-228	4.85
Caprylic Acid	PB-221-229	4.50
Glycyrrhiza	PB-221-230	3.75
Carbonates	PB-221-231	5.15
Stannous Chloride	PB-221-232	4.50
Propylene Glycol and Derivatives	PB-221-233	4.50
Sulfates	PB-221-234	4.85
Ammonium Ion	PB-221-235	5.15
Iron and Iron Salts Used in Foods	PB-221-236	5.45
Tocopherols	PB-221-237	6.75

Each Scientific Literature Review may be purchased in microfiche form for $.95 with the same ordering numbers listed above.

5. Copies of each Scientific Literature Review will be placed in the Library of Congress as they become available, under the title, "Scientific Literature Reviews on GRAS Food Ingredients," L.C. Card No. 73-600105.

6. Each report to the Commissioner from the FASEB Select Committee may be purchased from NTIS as it becomes available. The following reports are now available:

Carob Bean (Locust Bean) Gum
Parabens
Sorbitol
Mannitol

7. A copy of each of the reports of the following toxicological screening tests may be purchased from NTIS:

Ingredient	Teratology	Mutagenesis
Ammoniated Glycyrrhizin	X	
Amaranth (Red No. 2)	X	X
Sodium Saccharin	X	
Calcium Saccharin	X	
Saccharin (Insoluble)	X	X
Ammonium Saccharin	X	
Sodium Nitrate	X	X
Potassium Nitrate	X	
Sodium Nitrite	X	X
Potassium Nitrite	X	
Glycine	XY	
Sodium Bisulfite	XY	
Sodium Meta-bisulfite	XY	X
Butylated Hydroxyanisole	XY	
Butylated Hydroxytoluene	XY	X
Mannitol	XY	
Sorbitol	XY	X
Sodium Thiosulfate	XY	
Stannous Chloride	XY	
Calcium Propionate	X	
Sodium Benzoate	X	
Propyl Gallate	XY	
Methyl Paraben	XY	
Dilauryldithiodipropionic Acid	XY	
Calcium Silicated (Hydrated)	XY	
Sodium Carrageenan	X	
Calcium Carrageenan	X	X
Carob Bean (Locust Bean) Gum	X	X
Gum Arabic (Acacia)	X	X
Gum Tragacanth	X	
Gum Ghatti	X	X
Guar Gum	XY	X
Sterculia (Karaya) Gum	XY	X
Propylene Glycol Alginate	XY	X
Talc	XY	
Caffeine	XY	
Oil of Nutmeg	XY	
Sodium Tripolyphosphate	XY	
Zinc Sulfate	XY	
Lactose	XY	
Adipic Acid	XY	
Furcelleran	XY	

No final chick embryo test reports have been received, to date.
X—Tested in Rats, Mice, Hamsters and Rabbits.
XY—Tested in Rats, Mice and Hamsters.

8. A single copy of all of the above data and information is available for review in the Office of the Hearing Clerk, Food and Drug Administration, Rm. 6–88, 5600 Fishers Lane, Rockville, MD 20852, during working hours, Monday through Friday. Additional information relating to these matters will also be placed on display at this office as they become available.

Dated: July 19, 1973.

A. M. SCHMIDT,
Commissioner of Food and Drugs.

[FR Doc.73–15206 Filed 7–25–73;8:45 am]

GRAS OR PRIOR-SANCTIONED DIRECT HUMAN FOOD INGREDIENTS

Notice of Availability of Information

In notices published in the FEDERAL REGISTER of July 26, 1973, the Commissioner of Food and Drugs announced the current status of the review of food ingredients classified as generally recognized as safe (GRAS) and the availability of data and information compiled during this review (38 FR 20054); solicited public participation in the review by requesting nominations for the Select Committee on GRAS Substances (38 FR 20054); provided public opportunity to present unpublished safety data to organizations under contract to the Food and Drug Administration for preparing Scientific Literature Reviews on GRAS substances (38 FR 20051); and provided public opportunity to present data, information, and views on GRAS substances directly to the Select Committee on GRAS Substances (38 FR 20053).

Elsewhere in this issue of the FEDERAL REGISTER, opportunity is provided for interested persons to submit unpublished safety data to organizations under contract to FDA to prepare additional Scientific Literature Reviews.

This notice announces the public availability of new data and information obtained by the Food and Drug Administration in conducting its safety review of GRAS substances. In addition to the announcement of new materials now available, purchasing information on available reports and screening tests not previously announced is included.

The Commissioner recognizes that data and information on GRAS food ingredients are of broad interest to the public. Accordingly, this information is available for public disclosure in the following ways:

1. Copies of each Scientific Literature Review have been placed in the Library of Congress under the title, "Scientific Literature Reviews on GRAS Food Ingredients," L.C. Card No. 73-600105.

2. The following Scientific Literature Reviews, Reports of the Select Committee on GRAS Substances to the Commissioner of Food and Drugs, and reports of toxicological screening tests are now available for purchase from the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, VA 22151. In addition to the NTIS ordering information given below, each document may be purchased in microfiche form with the same ordering number. Microfiche document prices are $1.45 each (for those designated—/AS) and $0.95 each for all others.

Scientific literature reviews

Review title	Ordering No.	Printed copy price
Butylated Hydroxyanisole (BHA).	PB-223-863/AS	$3.50
Aluminum Compounds	PB-223-862/AS	4.50
Sorbic Acid and Derivatives	PB-223-864/AS	3.75
Citrates	PB-223-850/AS	4.25
Calcium Oxide and Hydroxide.	PB-223-851/AS	2.75
Malic Acid	PB-223-865/AS	3.75
Ascorbates	PB-223-866/AS	3.75
Cholic Acid and Derivatives	PB-223-844/AS	4.25
Calcium Sequestrants	PB-223-843/AS	4.50
Tallow and Stearic Acid	PB-223-850/AS	3.75
Beeswax and Japan Wax	PB-223-854/AS	3.00
Choline Salts	PB-223-845/AS	3.00
Algae	PB-223-846/AS	3.00
Iodine and Iodine Salts	PB-223-849/AS	3.75
Corn Sugar	PB-223-853/AS	8.00
Carnauba Wax	PB-223-855/AS	2.75
Pulps	PB-223-848/AS	2.75
Aconitic Acid	PB-223-847/AS	2.75
Sorbose	PB-223-852/AS	2.75
Tannic Acid	PB-223-858/AS	3.75
Sodium Thiosulfate	PB-223-856/AS	3.50
Succinic Acid	PB-223-860/AS	3.00
Inositol	PB-223-861/AS	3.50
Gelatin	PB-223-857/AS	4.25

Reports of the Select Committee to the Commissioner

Report title	Ordering No.	Printed copy price
Carob Bean (Locust Bean) Gum.	PB-221-952	$3.00
Parabens (Methyl and Propyl).	PB-221-950	3.00
Sorbitol	PB-221-951	3.00
Mannitol	PB-221-953	3.00

Teratology screening tests

Ingredient [1]	Ordering No.	Printed copy price [2]
Ammoniated glycyrrhizin (X)	PB-221-793	$3.75
Amaranth (Red No. 2) (X)	PB-221-771	4.50
Sodium saccharin (X)	PB-221-772	4.50
Calcium saccharin (X)	PB-221-773	4.50
Saccharin (insoluble) (X)	PB-221-791	4.50
Ammonium saccharin (X)	PB-221-792	4.50
Sodium nitrate (X)	PB-221-775	4.50
Potassium nitrate (X)	PB-221-774	4.50
Sodium nitrite (X)	PB-221-794	4.50
Potassium nitrite (X)	PB-221-796	4.50
Glycine (XY)	PB-221-809	3.75
Sodium bisulfite (XY)	PB-221-788	3.75
Sodium metabisulfite (XY)	PB-221-795	3.75
Butylated hydroxyanisole (XY).	PB-221-783	3.75
Butylated hydroxytoluene (XY).	PB-221-782	3.75
Mannitol (XY)	PB-221-781	3.75
Sorbitol (XY)	PB-221-806	3.75
Sodium thiosulfate (XY)	PB-221-779	3.75
Stannous chloride (XY)	PB-221-780	3.75
Calcium propionate (X)	PB-221-778	4.50
Sodium benzoate (X)	PB-221-777	4.50
Propyl gallate (XY)	PB-221-790	3.75
Methyl paraben (XY)	PB-221-785	3.75
Dilaurylthiodipropionic acid (XY).	PB-221-776	3.75
Calcium silicate (hydrated) (XY).	PB-221-801	3.75
Sodium carrageenan (X)	PB-221-812	4.50
Calcium carrageenan (X)	PB-221-787	4.50
Carob bean (locust bean) gum (X).	PB-221-784	4.50
Gum arabic (acacia) (X)	PB-221-796	4.50
Gum tragacanth (X)	PB-221-797	4.50
Gum ghatti (X)	PB-221-799	4.50
Guar gum (XY)	PB-221-800	3.75
Sterculia (karaya) gum (XY)	PB-221-789	3.75
Propylene glycol alginate (XY).	PB-221-786	3.75
Talc (XY)	PB-221-804	3.75
Caffeine (XY)	PB-221-803	3.75
Oil of nutmeg (XY)	PB-221-807	3.75
Sodium tripolyphosphate (XY).	PB-221-808	3.75
Zinc sulfate (XY)	PB-221-805	3.75
Lactose (XY)	PB-221-811	3.75
Adipic acid (XY)	PB-221-802	3.75

Teratology screening tests—Continued

Ingredient [1]	Ordering No.	Printed copy price [2]
Furcelleran (XY)	PB-221-810	3.75
Silica aerogel (syloid) (X)	PB-223-808/AS	3.50
DL-Alpha tocopherol acetate (X).	PB-223-809/AS	3.50
Sodium silicoaluminate (X)	PB-223-810/AS	3.50
Oil of clove (X)	PB-223-811/AS	3.50
Oil of mustard (X)	PB-223-812/AS	3.50
Manganese sulfate (monohydrate) (X).	PB-223-813/AS	3.50
Citric acid (X)	PB-223-814/AS	3.50
Menthol (natural Brazilian) (X).	PB-223-815/AS	3.50
Propyl gallate (Y)	PB-223-816/AS	2.75
Methyl paraben (Y)	PB-223-817/AS	2.75
Sterculia (karaya) gum (Y)	PB-223-818/AS	2.75
Guar gum (Y)	PB-223-819/AS	2.75
Agar-agar (X)	PB-223-820/AS	3.50
Tartaric acid (X)	PB-223-821/AS	3.50
Propylene glycol (X)	PB-223-822/AS	3.50
Methocel (methylcellulose) (X)	PB-223-823/AS	3.50
Dilaurylthiodipropionic acid (Y).	PB-223-824/AS	2.75
Lactose (Y)	PB-223-825/AS	2.75
Sodium tripolyphosphate (Y).	PB-223-826/AS	2.75
Caffeine (Y)	PB-223-827/AS	2.75
Talc (Y)	PB-223-828/AS	2.75
Calcium silicate (hydrated) (Y).	PB-223-829/AS	2.75
Gluconodeltalactone (X)	PB-223-830/AS	3.50
Sodium acid pyrophosphate (X).	PB-223-831/AS	3.50
Sodium aluminum sulfate (XY).	PB-223-832/AS	3.00
Starter distillate (XY)	PB-223-833/AS	3.00
MUTAGENIC SCREENING TESTS		
Amaranth (Red No. 2) (X)	PB-221-814	$5.45
Saccharin (insoluble) (X)	PB-221-824	4.85
Sodium nitrate (X)	PB-221-817	5.45
Sodium nitrite (X)	PB-221-818	5.45
Sodium metabisulfite (X)	PB-221-825	5.45
Butylated hydroxytoluene (X).	PB-221-827	5.45
Sorbitol (X)	PB-221-816	5.45
Calcium carrageenan (X)	PB-221-820	4.85
Carob bean (locust bean) gum (X).	PB-221-819	4.85
Gum arabic (acacia) (X)	PB-221-821	5.45
Gum ghatti (X)	PB-221-822	4.85
Guar gum (X)	PB-221-815	5.45
Sterculia (karaya) gum (X)	PB-221-823	4.85
Propylene glycol alginate (X)	PB-221-826	5.45

[1] (X), (Y), or (XY) listed next to an ingredient indicates the following: X = Report of rats, mice, hamsters, and rabbits; Y = Report of rabbits only; and XY = Report of rats, mice, and hamsters.

[2] The first 42 teratology reports listed above (PB-221-771 through PB-221-812) are available from NTIS for $119 (PB-221-770 SET).

3. The report of the National Academy of Sciences to the Food and Drug Administration, "A Comprehensive Survey of Industry on the Use of Food Chemicals Generally Recognized as Safe," was reported available in the FEDERAL REGISTER of July 26, 1973 (38 FR 20054), without ordering instructions. This report is available for purchase from NTIS for $9.00 with the order number PB-221-949 and may also be purchased with all 28 accompanying use and consumption tables for $154.00 (PB-221-920 SET). The tables may be purchased separately or in microfiche form by requesting this specific information from NTIS.

4. A single copy of all of the data and information given above is available for review in the office of the Hearing Clerk, Food and Drug Administration, Rm. 6-86, 5600 Fishers Lane, Rockville, MD 20852, during working hours, Monday through Friday. Additional information relating to the review of GRAS substances will also be placed on display at this office as it becomes available.

Dated: April 9, 1974.

SAM D. FINE,
Associate Commissioner for Compliance.

[FR Doc.74-8662 Filed 4-16-74;8:45 am]

SCIENTIFIC LITERATURE REVIEWS ON GRAS OR PRIOR-SANCTIONED DIRECT HUMAN FOOD INGREDIENTS

Notice of Opportunity To Submit Unpublished Safety Data

In the FEDERAL REGISTER of July 26, 1973 (38 FR 20051), the Commissioner of Food and Drugs published a notice soliciting public submission of unpublished data and information that may be significant in determining the safety of generally recognized as safe (GRAS) or prior-sanctioned food ingredients. The notice included a list of the Scientific Literature Reviews then being prepared by organizations under contract to the Food and Drug Administration. Many of these Scientific Literature Reviews have been completed, and notice of their availability is published elsewhere in this issue of the FEDERAL REGISTER.

This notice gives information on assignments of new contracts for the preparation of Scientific Literature Reviews on ingredients (or groups of ingredients) previously listed as planned for immediate public review, and it also solicits public submission of unpublished safety data and information on these ingredients. The organizations assigned each Review are as follows:

1. Informatics, Inc., 6000 Executive Boulevard, Rockville, MD 20852.
2. Tracor Jitco, Inc., 1300 East Gude Dr., Rockville, MD 20851.

Ingredients	Organizations	Estimated date of completion
Biotin	Informatics, Inc.	Aug. 5, 1974
Niacin and niacinamide.	do	Do.
Pyridoxines	do	Do.
Thiamin	do	Do.
Riboflavins	do	Do.
Carotenes	do	July 1, 1974
Caffeine	do	Do.
Dextrans	do	Do.
Sodium and potassium chlorides.	Tracor Jitco, Inc.	Do.
Casein and caseinates	do	Do.
Citric acid	do	Aug. 5, 1974
Lecithins	do	Do.
Urea	do	Do.
Vitamin B_{12}	do	Do.
Ascorbic acid	do	Do.
Nickel	do	July 1, 1974

To be considered for inclusion in a Scientific Literature Review, two copies of all data or information should be submitted to the organization preparing the Review before the listed completion date, and the original and two copies of all such information simultaneously sent to the GRAS Review Branch (BF-335), Bureau of Foods, Food and Drug Administration, 200 "C" St., SW., Washington, DC 20204. Immediately upon receipt of any such submission, one copy will be placed on display at the office of the Hearing Clerk, Food and Drug Administration, Rm. 6-86, 5600 Fishers Lane, Rockville, MD 20852, where it may be reviewed during working hours, Monday through Friday.

Dated: April 9, 1974.

SAM D. FINE,
Associate Commissioner for Compliance.

[FR Doc.74-8661 Filed 4-16-74;8:45 am]