MAXIMUM USAGE LEVELS

Food	Permitted Percent	Function
Baked goods and baking mixes, § 121.1(l)(1)	0.15	Flavoring agent, § 121.1(m)(11); stabilizer and thickener, § 121.1(m)(26).
Beverages and beverage bases, nonalcoholic, § 121.1(l)(3).	0.25	Flavoring agent, § 121.1(m)(11); stabilizer and thickener, § 121.1(m)(26).
Cheeses, § 121.1(l)(5)	0.75	Stabilizer and thickener, § 121.1(m)(26).
Gelatins, puddings, and fillings, § 121.1(l)(22)	0.40	Stabilizer and thickener, § 121.1(m)(26).
All other food categories	0.50	Flavoring agent, § 121.1(m)(11); stabilizer and thickener, § 121.1(m)(26).

(d) The label and labeling of the additive and any intermediate mix of the additive for use in finished food shall bear, in addition to the other labeling required by the act:

(1) The name of the additive;

(2) A statement of the concentration of the additive in any intermediate mix; and

(3) Adequate information to assure that the final food product complies with the limitations prescribed in paragraph (c) of this section.

The Commissioner hereby gives notice that he is unaware of any prior sanction for the use of this ingredient in food under conditions different from those proposed above. Any person who intends to assert or rely on such a sanction shall submit proof of its existence in response to this proposal. The regulation proposed above will constitute a determination that excluded uses would result in adulteration of the food in violation of section 402 of the act, and the failure of any person to come forward with proof of such an applicable prior sanction in response to this proposal constitutes a waiver of the right to assert or rely on such sanction at any later time. This notice also constitutes a proposal to establish a regulation under Subpart E incorporating the same provisions, in the event that such a regulation is determined to be appropriate as a result of submission of proof of such an applicable prior sanction in response to this proposal.

Interested persons may, on or before October 24, 1973, file with the Hearing Clerk, Food and Drug Administration, Rm. 6-88, 5600 Fishers Lane, Rockville, MD 20852, written comments (preferably in quintuplicate) regarding this proposal. Comments may be accompanied by a memorandum or brief in support thereof. Received comments may be seen in the above office during working hours, Monday through Friday.

Dated: July 19, 1973.

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

[FR Doc.73-15215 Filed 7-25-73;8:45 am]

[21 CFR Part 121]

FOOD CATEGORIES AND FOOD INGREDIENT FUNCTIONS

Proposed Designation

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 this study progresses, the Commissioner of Food and Drugs will publish in the FEDERAL REGISTER, appropriate proposals 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 under review. The Commissioner is proposing regulations in this issue of the FEDERAL REGISTER with respect to the first ingredients subject to this review.

In regulations published since 1958 under the Food Additives Amendment, it has frequently been appropriate to designate broad food categories in which an ingredient may properly be used, and to state the functional purpose for which the ingredient may be used. To date, no standardized definitions of the food categories or functional descriptions have been adopted.

In conducting the industry survey of production and use of GRAS and prior-sanctioned food substances, under contract with the Food and Drug Administration, for use in the review of the safety of these ingredients, the National Academy of Sciences developed standardized food categories. Food categories of a similar type were also used by the United States Department of Agriculture and the Market Research Corporation of America (MRCA), in their respective surveys, to determine the sizes of servings used by consumers and the frequency of consumption of specific foods.

The Commissioner has concluded that the food categories adopted by the National Academy of Sciences (NAS) represent a valid and useful method of dividing food products into general classes of related products. Where tolerances or limitations are established for the use of direct human food ingredients, and there is significant variation with respect to appropriate tolerances or limitations for one or more specific food categories, this method of classification will permit designation of the foods to be covered without requiring a detailed list of each of the individual products included. In many instances, tolerances or limitations may be imposed uniformly for all foods. It may also be necessary to impose, with relatively few exceptions, tolerances or limitations for specific food categories at levels higher or lower than the general rule. It is the Commissioner's intent to utilize the broadest possible approach, in the interests of simplification, wherever justified by the available safety data and information.

It is appropriate that the same food classification system developed by the NAS for its production and consumption survey should also be utilized by the Food and Drug Administration in imposing tolerances and limitations for use of specific ingredients. NAS Survey data was accumulated using these food categories, and they are consequently of great assistance in determining whatever tolerances and limitations are justified. The same classification system, already cross-indexed to the MRCA and USDA consumption data, also provides an immediate reference to consumption patterns on which those tolerances and limitations are in part based.

The proposal set out below contains a general description of each food category, without attempting to list in detail all the products within it. Wherever any question arises with respect to the proper classification of a specific food product which might reasonably fall within two or more categories, proper classification will be determined by referring to the more detailed and specific classification lists established by the MRCA and cross-indexed to NAS food categories, as contained in the final NAS report to the Food and Drug Administration. The Final Report of the NAS is now available from the National Technical Information Service (NTIS), in accordance with the notice on this matter published in this issue of the FEDERAL REGISTER. Accordingly, the Commissioner is incorporating this specific classification list, by reference, into this proposed regulation, for purposes of resolving close questions with respect to proper classification.

The NAS also found it necessary to establish a similar classification system with respect to the technical functions performed by the various specific ingredients directly added to human food. These functional effects are contained in the final NAS report to the Food and Drug Administration and are the subject of production, use, and consumption data on the technical functions of numerous food ingredients, added to the various NAS food categories. Thus, these tables describe the specific technical purposes for which GRAS and prior-sanctioned ingredients are added to NAS food categories, and they consequently serve as an excellent reference to consumption patterns on which ingredient tolerances and limitations are in part based. Accordingly, the Commissioner is proposing to standardize the technical functional descriptions submitted by the NAS, so that regulations permitting the use of ingredients in food will accurately describe their purpose. A standardized system of classification will also assist consumers in understanding the functions performed by these ingredients in the foods they consume.

Therefore, pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (secs. 201(s), 409, 701(a), 52 Stat. 1055, 72 Stat. 1784-1788 as amended; 21 U.S.C. 321(s), 348, 371(a)) and under authority delegated to him (21 CFR 2.-120), the Commissioner proposes to amend Part 121 by adding to § 121.1 the following two new paragraphs:

§ 121.1 Definitions and interpretations.

* * * * *

(l) The following general food categories are established to group specific related foods together for the purpose of establishing tolerances or limitations for the use of direct human food ingredients. Individual food products will be classified within these categories according to the detailed classification lists contained in Exhibit 33B of the report of the National Academy of Sciendes on "A Comprehensive Survey of Industry on the use of Food Chemicals Generally Recognized as Safe" (September 1972).[1]

(1) Baked goods and baking mixes (includes ready-to-eat or ready-to-bake products and all dry flour, meal, and multipurpose mixes).

(2) Beverages, alcoholic (includes malt beverages, wines, and distilled liquors).

(3) Beverages and beverage bases, non-alcoholic (includes dry and liquid imitation concentrates and ready-to-drink products, except for coffee or tea).

(4) Breakfast cereals (includes cold and hot breakfast cereals).

(5) Cheeses (includes standardized, non-standardized, snack, and other miscellaneous cheeses).

(6) Chewing gum (includes all flavored gums).

(7) Coffee and tea (includes regular and instant products).

(8) Condiments and relishes (includes plain seasoning sauces and spreads, olives, pickles, and relishes).

(9) Confections and frostings (includes candy and flavored frostings and frosting sugars).

(10) Dairy product analogs (includes non-dairy derived products such as toppings, toppings, mixes, and coffee whiteners.

(11) Egg products (includes liquid, frozen, or dried eggs, and egg products).

(12) Fats and oils (includes salad dressings, margarines, butter, and cooking oils).

(13) Fish products (includes all prepared or frozen products containing fish, shellfish, and other aquatic animals, except fresh fish).

(14) Fresh eggs (includes only whole fresh eggs).

(15) Fresh fish (includes only fresh and home-frozen fish, shellfish, and other aquatic animals).

(16) Fresh fruits and fruit juices (includes only raw fruits and fruit juices and fruit blends).

(17) Fresh meats (includes only fresh and home-frozen beef, pork, lamb, and game animals).

(18) Fresh poultry (includes only fresh and home-frozen poultry).

(19) Fresh vegetables and potatoes (includes only fresh, home-canned, and home-frozen vegetables and potatoes).

(20) Frozen dairy desserts and mixes (includes ice cream, ice milk, sherbets, and frozen novelties).

(21) Fruit and water ices (includes all frozen fruit and water ices).

(22) Gelatins, puddings, and fillings (includes flavored gelatins, puddings, custards, parfaits, and pie fillings).

(23) Grain products and pastas (includes macaroni, noodle, and rice dishes, without meat or vegetables).

(24) Gravies and Sauces (includes flavored meat souces, gravies, and marinades).

(25) Hard candy and cough drops (includes all hard sucker type candies).

(26) Herbs, seeds, spices, seasonings, blends, extracts, and flavorings (includes all natural spices and blends and artificial flavors).

(27) Jams and jellies, homemade (includes fruit butters and preserves).

(28) Jams, jellies, and sweet spreads (includes fruit butters and preserves).

(29) Meat products (includes all prepared and frozen products containing beef, pork, or lamb).

(30) Milk, whole and skim (includes only whole and skim milks).

(31) Milk products (includes dried and fluid milk products such as concentrated, evaporated, and flavored milk, and cream products).

(32) Nuts and nut products (includes whole or shelled nuts, coconut, and nut spreads).

(33) Poultry products (includes all prepared and frozen products containing poultry).

(34) Processed fruits and juices (includes canned or frozen fruits and fruit juices, concentrates, dilutions, ades, and drink substitutes).

(35) Processed vegetables and juices (includes canned or frozen vegetables, vegetable juices, and blends).

(36) Reconstituted vegetable proteins (includes only meat substitute products and dishes).

(37) Snack foods (includes chips, pretzels, and other novelty snacks).

(38) Soft candy (includes all soft and nougat candies).

(39) Soups, homemade (includes all homemade soups).

(40) Soups and soup mixes (includes all meat and vegetable soups).

(41) Sugar, white, granulated (includes only white granulated sugar).

(42) Sugar substitutes (includes all forms of sugar substitutes).

(43) Sweet sauces, toppings, and syrups (includes all fruit, berry, or other flavored products).

(m) The following terms describe the physical or technical functional effects for which direct human food ingredients may be added to foods. They are adopted from the National Academy of Sciences national survey of food industries, reported to the Food and Drug Administration under the contract title, "A Comprehensive Survey of Industry on the Use of Food Chemicals Generally Recognized as Safe" (September 1972).

(1) "Anticaking agents and free-flow agents": substances added to finely powdered or crystalline food products to prevent caking, lumping, or agglomeration.

(2) "Antioxidants": substances used to retard deterioration, rancidity, or discoloration due to oxidation.

(3) "Colors and coloring adjuncts" (including color stabilizers, color fixatives, color-retention agents, etc.): substances used to impart, preserve, or enhance the color or shading of a food.

(4) "Curing and pickling agents": substances imparting a unique flavor and/or color to a foodstuff, usually producing an increase in shelf life stability.

(5) "Dough conditioners" (including yeast foods): substances used to modify the gluten and enhance the property of making an elastic and stable dough.

(6) "Drying agents": substances with moisture-absorbing ability, used to maintain an atmosphere of low moisture.

(7) "Emulsifiers and emulsifier salts": substances which modify surface tension in the component phase of an emulsion to establish a uniform dispersion or emulsion.

(8) "Enzymes": enzymes used to improve food processing.

(9) "Firming agents": substances added to precipitate residual pectin, thus strengthening the supporting tissue and preventing its collapse during processing.

(10) "Flavor enhancers": substances added to supplement, enhance, or modify the original taste and/or aroma of a food without imparting a characteristic taste or aroma of its own.

(11) "Flavoring agents and adjuvants": substances added to impart or help impart a taste or aroma.

(12) "Flour-treating agents" (including bleaching and maturing agents): substances added to milled flour to improve its color and baking qualities.

(13) "Formulation aids" (including carriers, binders, fillers, plasticizers, film-formers, and tableting aids, etc): substances used to promote or produce a physical state or texture in food.

(14) "Fumigants": volatile substances used for controlling insects or pests.

(15) "Humectants" (including moisture-retention agents and anti-dusting agents): hygroscopic substances incorporated in food to promote retention of moisture.

(16) "Leavening agents": substances used to produce carbon dioxide in baked goods to impart a light texture.

(17) "Lubricants and release agents": substances added to food contact surfaces to prevent confections and baked goods from sticking to their containers.

(18) "Non-nutritive sweetners": substances used as a substitute for sugar when intake of sugar or its bulk is undesirable.

(19) "Nutrient supplements": food components, or their synthetic substitutes, which are necessary for the body's nutritional and metabolic processes.

(20) "pH control agents" (including buffers, acids, alkalies, and neutralizing agents): substances added to change or maintain active acidity or basicity.

(21) "Preservatives" (including antimicrobial agents, fungistats, and mold and rope inhibitors, etc.): substances added to prevent growth of contaminating microorganisms and subsequent spoilage.

(22) "Processing aids" (including clarifying agents, clouding agents, cata-

[1] Copies may be obtained from: National Technical Information Service (NTIS) 5285 Port Royal Road Springfield, VA 22151

lysts, flocculents, and filter aids, etc.): substances used as manufacturing aids to enhance the appeal or utility of a food or food component.

(23) "Propellants, aerating agents, and gasses": chemically inert gasses used to supply force to expel a product or used to reduce the amount of oxygen in contact with the food in packaging processes.

(24) "Sequestrants": substances which combine with polyvalent metal ions to form a soluble metal complex, to improve the quality and stability of products.

(25) "Solvents and vehicles": substances used to extract or dissolve another substance.

(26) "Stabilizers and thickeners" (including suspending and bodying agents, setting agents, jelling agents, and bulking agents, etc.): substances used to produce viscous solutions or dispersions, to impart body, improve consistency, or stabilize emulsification.

(27) "Surface—active agents" (other than emulsifiers, but including solubilizing agents, dispersants, detergents, wetting agents, rehydration enhancers, whipping agents, foaming agents, and defoaming agents, etc.): substances used to modify surface properties of food components for a variety of effects.

(28) "Surface—finishing agents" (including glazes, polishes, waxes, and protective coatings): substances used to increase palatability, preserve gloss, and inhibit discoloration of foods.

(29) "Sweeteners": substances used to sweeten the taste of food.

(30) "Synergists": substances used to act or react with another food ingredient to produce a total effect different or greater than the sum of the individual effects.

(31) "Texturizers": substances which affect the appearance or feel of the composition of a food.

Interested persons may, on or before October 24, 1973, file with the Hearing Clerk, Food and Drug Administration, Room 6-88, 5600 Fishers Lane, Rockville, MD 20852, written comments (preferably in quintuplicate) regarding this proposal. Comments may be accompanied by a memorandum or brief in support thereof. Received comments may be seen in the above office during working hours, Monday through Friday.

Dated: July 19, 1973.

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

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[21 CFR Part 121]

MANNITOL AND SORBITOL

Affirmation of GRAS Status of Direct Human Food Ingredients

The Food and Drug Administration is conducting a comprehensive study of direct human food ingredients classified as generally recognized as safe (GRAS) or subject to a prior sanction. Pursuant to this review, the safety of mannitol and sorbitol has been evaluated. In accordance with the provisions of § 121.40, the Commissioner of Food and Drugs proposes to affirm the GRAS status of these two ingredients.

Mannitol (1,2,3,4,5,6-hexanehexol) and its sterioisomer sorbitol are both solid hexahydric alcohols prepared commercially by catalytic reduction of glucose. Both occur naturally in small amounts in a variety of foods. Mannitol is found in olives, beets, celery and in the exudate of certain trees. Sorbitol is a normal constituent of such fruits as cherries, plums, pears, apples, and many berries.

Mannitol and sorbitol were listed in § 121.101(d)(2) as GRAS for use in special dietary foods at a maximum of 5 percent and 7 percent respectively in the FEDERAL REGISTER of January 31, 1961 (26 FR 939). Subsequently, food additive regulations were published for mannitol under § 121.1115 in the FEDERAL REGISTER of August 9, 1961 (28 FR 1540) and for sorbitol under § 121.1053 in the FEDERAL REGISTER of February 19, 1963 (26 FR 7127) to provide for other uses of these substances, with levels for use being restricted only to the amount reasonably required to accomplish the intended effect.

Mannitol and Sorbitol have been the subject of a search of the published scientific literature from 1920 to the present. The parameters used in the search were chosen 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 sponse, (8) reproductive effects, (9) histology, (10) embryology, (11) behavioral effects, (12) detection methodology and (13) processing. A total of 968 abstracts on mannitol were reviewed and 11 particularly pertinent reports from the literature survey have been summarized in a Scientific Literature Review. A total of 870 abstracts on sorbitol were reviewed and 26 particularly pertinent reports from the literature survey have been summarized in a Scientific Literature Review.

A representative cross-section of food manufacturers was surveyed to determine the specific foods in which these substances were used and at what levels. Available surveys of consumer consumption were obtained and combined with the production information to obtain an estimate of the consumer exposure to mannitol and sorbitol. The total mannitol used in food in 1970 is reported to be about 90 times that used in 1960. The total sorbitol used in food in 1970 is reported to be about seven times that used in food in 1960.

The Scientific Literature Review shows, among other studies, the following information is summarized in the report of the Select Committee on GRAS Substances:

Mannitol is absorbed from the gastrointestinal tract of animals and man, and does not accumulate in the organism; it is partially metabolized and partly excreted in the urine. There is evidence that the intestinal flora may convert mannitol to more readily utilized substances and this transformation may influence the reported amount of mannitol absorbed and metabolized by the liver. A wide variety of microorganisms and fungi convert mannitol to sugars and other carbohydrate fragments.

The absorption of mannitol in a 50 cm segment of the proximal small intestine, in children varying in age from 8 months to 4 years, has been reported. The mannitol was perfused in an isotonic solution in concentrations varying from 50 to 150 millimoles per liter. From 9 to 18 percent of the mannitol was found to be absorbed.

A more extensive study in 16 human adult volunteers, ranging in age from 20 to 66, revealed that, in the oral dosage range of 40 to 100 g, 88 percent of the ingested mannitol was absorbed. Of the absorbed mannitol, about a third was excreted intact in the urine and the remainder was oxidized to carbon dioxide. Excretion was virtually complete by four days, with about 91 percent excreted within the first day.

In experiments where 25 g of mannitol were fed to normal men, little evidence was found that the substance was utilized, as measured by blood sugar levels or respiratory quotients. The threshold laxative dose was found to be between 10 and 20 g of mannitol as compared with 50 g of sorbitol.

There are no reported long-term animal feeding studies (extending for more than half of the life span of the species) on mannitol. Relevant short-term animal studies and studies on man are summarized below.

The oral LD_{50} for the mouse is reported to be 22 g per kg, and for the rat to be 17.3 g per kg. The minimum lethal dose for the rat is reported to be greater than 13 g per kg.

In rats and monkeys fed mannitol (5 percent of the rat diet, and 3 g daily to monkeys) no significant chronic toxicity was observed over a period of 3 months. A study on one man, fed 10 g daily for a month, revealed no evidence of toxicity; but the same authors have shown that the ingestion of 10 to 20 g of crystalline mannitol as part of the diet results in a laxative effect. The latter observation has been confirmed.

Preliminary teratologic tests in mice, rats, and hamsters have been negative. Oral doses up to 1.6 g per kg of body weight of mannitol to pregnant mice and rats for 10 consecutive days, or up to 1.2 g per kg of body weight to pregnant hamsters for 5 consecutive days, produced no clearly discernible effects or nidation or on maternal or fetal survival. The frequency of abnormalities in either soft or skeletal tissues of the test animals was comparable to that occurring spontaneously in the sham-treated controls.

The Select Committee is unaware of any reports on mannitol indicating evidence of its carcinogenicity, mutagenicity, or effects on reproduction.

When injected intravenously, mannitol is filtered by the glomeruli of the kidneys and not appreciably reabsorbed by the tubules. For this reason, mannitol has been employed extensively as a substance to measure glomerular filtration rate in man. It has also been used medically as an intravenous diuretic, to lower intracranial pressure, and to decrease intraocular pressure in glaucoma. This wide usage of mannitol has not resulted in untoward toxic effects. However, a single allergic reaction to mannitol was observed when the substance was administered intravenously for the treatment of glaucoma. In the experience of these investigators, over 1500 patients had received similar medication without a serious allergic reaction. It appears from this report that allergic reactions to mannitol are possible, but that it does not constitute a dietary hazard for this reason.

The Joint FAO/WHO Expert Committee on Food Additives classified mannitol, in amounts of 50-150 mg per kg of body weight daily, as "conditionally acceptable". This term means that the substance may be employed within the specified limits with an