AUTHENTICATED
U.S. GOVERNMENT
INFORMATION
GPO

§ 182.8217 Calcium phosphate.

(a) *Product.* Calcium phosphate (mono-, di-, and tribasic).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing practice.

§ 182.8223 Calcium pyrophosphate.

(a) *Product.* Calcium pyrophosphate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing practice.

§ 182.8250 Choline bitartrate.

(a) *Product.* Choline bitartrate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing practice.

§ 182.8252 Choline chloride.

(a) *Product.* Choline chloride.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing practice.

§ 182.8778 Sodium phosphate.

(a) *Product.* Sodium phosphate (mono-, di-, and tribasic).

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing practice.

§ 182.8890 Tocopherols.

(a) *Product.* Tocopherols.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing practice.

§ 182.8892 α-Tocopherol acetate.

(a) *Product.* α-Tocopherol acetate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing practice.

§ 182.8985 Zinc chloride.

(a) *Product.* Zinc chloride.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing practice.

§ 182.8988 Zinc gluconate.

(a) *Product.* Zinc gluconate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing practice.

§ 182.8991 Zinc oxide.

(a) *Product.* Zinc oxide.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing practice.

§ 182.8994 Zinc stearate.

(a) *Product.* Zinc stearate prepared from stearic acid free from chickedema factor.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing practice.

§ 182.8997 Zinc sulfate.

(a) *Product.* Zinc sulfate.

(b) *Conditions of use.* This substance is generally recognized as safe when used in accordance with good manufacturing practice.

PART 184—DIRECT FOOD SUBSTANCES AFFIRMED AS GENERALLY RECOGNIZED AS SAFE

Subpart A—General Provisions

Sec.
184.1 Substances added directly to human food affirmed as generally recognized as safe (GRAS).

Subpart B—Listing of Specific Substances Affirmed as GRAS

184.1005 Acetic acid.
184.1007 Aconitic acid.
184.1009 Adipic acid.
184.1011 Alginic acid.
184.1012 α-Amylase enzyme preparation from Bacillus stearothermophilus.
184.1021 Benzoic acid.
184.1024 Bromelain.
184.1025 Caprylic acid.
184.1027 Mixed carbohydrase and protease enzyme product.
184.1033 Citric acid.
184.1034 Catalase (bovine liver).
184.1061 Lactic acid.
184.1063 Enzyme-modified lecithin.
184.1065 Linoleic acid.
184.1069 Malic acid.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 1 of 100

184.1077 Potassium acid tartrate.
184.1081 Propionic acid.
184.1090 Stearic acid.
184.1091 Succinic acid.
184.1095 Sulfuric acid.
184.1097 Tannic acid.
184.1099 Tartaric acid.
184.1101 Diacetyl tartaric acid esters of mono- and diglycerides.
184.1115 Agar-agar.
184.1120 Brown algae.
184.1121 Red algae.
184.1133 Ammonium alginate.
184.1135 Ammonium bicarbonate.
184.1137 Ammonium carbonate.
184.1138 Ammonium chloride.
184.1139 Ammonium hydroxide.
184.1140 Ammonium citrate, dibasic.
184.1141a Ammonium phosphate, monobasic.
184.1141b Ammonium phosphate, dibasic.
184.1143 Ammonium sulfate.
184.1148 Bacterially-derived carbohydrase enzyme preparation.
184.1150 Bacterially-derived protease enzyme preparation.
184.1155 Bentonite.
184.1157 Benzoyl peroxide.
184.1165 n–Butane and iso–butane.
184.1185 Calcium acetate.
184.1187 Calcium alginate.
184.1191 Calcium carbonate.
184.1193 Calcium chloride.
184.1195 Calcium citrate.
184.1199 Calcium gluconate.
184.1201 Calcium glycerophosphate.
184.1205 Calcium hydroxide.
184.1206 Calcium iodate.
184.1207 Calcium lactate.
184.1210 Calcium oxide.
184.1212 Calcium pantothenate.
184.1221 Calcium propionate.
184.1229 Calcium stearate.
184.1230 Calcium sulfate.
184.1240 Carbon dioxide.
184.1245 Beta-carotene.
184.1250 Cellulase enzyme preparation derived from Trichoderma longibrachiatum.
184.1257 Clove and its derivatives.
184.1259 Cocoa butter substitute.
184.1260 Copper gluconate.
184.1261 Copper sulfate.
184.1262 Corn silk and corn silk extract.
184.1265 Cuprous iodide.
184.1271 L-Cysteine.
184.1272 L-Cysteine monohydrochloride.
184.1277 Dextrin.
184.1278 Diacetyl.
184.1282 Dill and its derivatives.
184.1287 Enzyme-modified fats.
184.1293 Ethyl alcohol.
184.1295 Ethyl formate.
184.1296 Ferric ammonium citrate.
184.1297 Ferric chloride.
184.1298 Ferric citrate.
184.1301 Ferric phosphate.
184.1304 Ferric pyrophosphate.
184.1307 Ferric sulfate.
184.1307a Ferrous ascorbate.
184.1307b Ferrous carbonate.
184.1307c Ferrous citrate.
184.1307d Ferrous fumarate.
184.1308 Ferrous gluconate.
184.1311 Ferrous lactate.
184.1315 Ferrous sulfate.
184.1316 Ficin.
184.1317 Garlic and its derivatives.
184.1318 Glucono delta-lactone.
184.1321 Corn gluten.
184.1322 Wheat gluten.
184.1323 Glyceryl monooleate.
184.1324 Glyceryl monostearate.
184.1328 Glyceryl behenate.
184.1329 Glyceryl palmitostearate.
184.1330 Acacia (gum arabic).
184.1333 Gum ghatti.
184.1339 Guar gum.
184.1343 Locust (carob) bean gum.
184.1349 Karaya gum (sterculia gum).
184.1351 Gum tragacanth.
184.1355 Helium.
184.1366 Hydrogen peroxide.
184.1370 Inositol.
184.1372 Insoluble glucose isomerase enzyme preparations.
184.1375 Iron, elemental.
184.1386 Isopropyl citrate.
184.1387 Lactase enzyme preparation from Candida pseudotropicalis.
184.1388 Lactase enzyme preparation from Kluyveromyces lactis.
184.1400 Lecithin.
184.1408 Licorice and licorice derivatives.
184.1409 Ground limestone.
184.1415 Animal lipase.
184.1420 Lipase enzyme preparation derived from Rhizopus niveus.
184.1425 Magnesium carbonate.
184.1426 Magnesium chloride.
184.1428 Magnesium hydroxide.
184.1431 Magnesium oxide.
184.1434 Magnesium phosphate.
184.1440 Magnesium stearate.
184.1443 Magnesium sulfate.
184.1443a Malt.
184.1444 Maltodextrin.
184.1445 Malt syrup (malt extract).
184.1446 Manganese chloride.
184.1449 Manganese citrate.
184.1452 Manganese gluconate.
184.1461 Manganese sulfate.
184.1472 Menhaden oil.
184.1490 Methylparaben.
184.1498 Microparticulated protein product.
184.1505 Mono- and diglycerides.
184.1521 Monosodium phosphate derivatives of mono- and diglycerides.
184.1530 Niacin.
184.1535 Niacinamide.
184.1537 Nickel.
184.1538 Nisin preparation.
184.1540 Nitrogen.
184.1545 Nitrous oxide.
184.1553 Peptones.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 2 of 100

184.1555 Rapeseed oil.
184.1560 Ox bile extract.
184.1563 Ozone.
184.1583 Pancreatin.
184.1585 Papain.
184.1588 Pectins.
184.1595 Pepsin.
184.1610 Potassium alginate.
184.1613 Potassium bicarbonate.
184.1619 Potassium carbonate.
184.1622 Potassium chloride.
184.1625 Potassium citrate.
184.1631 Potassium hydroxide.
184.1634 Potassium iodide.
184.1635 Potassium iodate.
184.1639 Potassium lactate.
184.1643 Potassium sulfate.
184.1655 Propane.
184.1660 Propyl gallate.
184.1666 Propylene glycol.
184.1670 Propylparaben.
184.1676 Pyridoxine hydrochloride.
184.1685 Rennet (animal-derived) and chymosin preparation (fermentation-derived).
184.1695 Riboflavin.
184.1697 Riboflavin-5′-phosphate (sodium).
184.1698 Rue.
184.1699 Oil of rue.
184.1702 Sheanut oil.
184.1721 Sodium acetate.
184.1724 Sodium alginate.
184.1733 Sodium benzoate.
184.1736 Sodium bicarbonate.
184.1742 Sodium carbonate.
184.1751 Sodium citrate.
184.1754 Sodium diacetate.
184.1763 Sodium hydroxide.
184.1764 Sodium hypophosphite.
184.1768 Sodium lactate.
184.1769a Sodium metasilicate.
184.1784 Sodium propionate.
184.1792 Sodium sesquicarbonate.
184.1801 Sodium tartrate.
184.1804 Sodium potassium tartrate.
184.1807 Sodium thiosulfate.
184.1835 Sorbitol.
184.1845 Stannous chloride (anhydrous and dihydrated).
184.1848 Starter distillate.
184.1851 Stearyl citrate
184.1854 Sucrose.
184.1857 Corn sugar.
184.1859 Invert sugar.
184.1865 Corn syrup.
184.1866 High fructose corn syrup.
184.1875 Thiamine hydrochloride.
184.1878 Thiamine mononitrate.
184.1890 α-Tocopherols.
184.1901 Triacetin.
184.1903 Tributyrin.
184.1911 Triethyl citrate.
184.1914 Trypsin.
184.1923 Urea.
184.1924 Urease enzyme preparation from Lactobacillus fermentum.
184.1930 Vitamin A.
184.1945 Vitamin B_{12}.
184.1950 Vitamin D.
184.1973 Beeswax (yellow and white).
184.1976 Candelilla wax.
184.1978 Carnauba wax.
184.1979 Whey.
184.1979a Reduced lactose whey.
184.1979b Reduced minerals whey.
184.1979c Whey protein concentrate.
184.1983 Bakers yeast extract.
184.1984 Zein.
184.1985 Aminopeptidase enzyme preparation derived from lactococcus lactis.

AUTHORITY: 21 U.S.C. 321, 342, 348, 371.

SOURCE: 42 FR 14653, Mar 15, 1977, unless otherwise noted.

Subpart A—General Provisions

§ 184.1 Substances added directly to human food affirmed as generally recognized as safe (GRAS).

(a) The direct human food ingredients listed in this part have been reviewed by the Food and Drug Administration and determined to be generally recognized as safe (GRAS) for the purposes and under the conditions prescribed. The regulations in this part shall sufficiently describe each ingredient to identify the characteristics of the ingredient that has been affirmed as GRAS and to differentiate it from other possible versions of the ingredient that have not been affirmed as GRAS. Ingredients affirmed as GRAS in this part are also GRAS as indirect human food ingredients, subject to any limitations prescribed in parts 174, 175, 176, 177, 178 or § 179.45 of this chapter or in part 186 of this chapter. The purity specifications in this part do not apply when the ingredient is used in indirect applications. However, when used in indirect applications, the ingredient must be of a purity suitable for its intended use in accordance with § 170.30(h)(1) of this chapter.

(b) Any ingredient affirmed as GRAS in this part shall be used in accordance with current good manufacturing practice. For the purpose of this part, current good manufacturing practice includes the requirements that a direct human food ingredient be of appropriate food grade; that it be prepared and handled as a food ingredient; and that the quantity of the ingredient added to food does not exceed the

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 3 of 100

amount reasonably required to accomplish the intended physical, nutritional, or other technical effect in food.

(1) If the ingredient is affirmed as GRAS with no limitations on its conditions of use other than current good manufacturing practice, it shall be regarded as GRAS if its conditions of use are consistent with the requirements of paragraph (b), (c), and (d) of this section. When the Food and Drug Administration (FDA) determines that it is appropriate, the agency will describe one or more current good manufacturing practice conditions of use in the regulation that affirms the GRAS status of the ingredient. For example, when the safety of an ingredient has been evaluated on the basis of limited conditions of use, the agency will describe in the regulation that affirms the GRAS status of the ingredient, one or more of these limited conditions of use, which may include the category of food(s), the technical effect(s) or functional use(s) of the ingredient, and the level(s) of use. If the ingredient is used under conditions that are significantly different from those described in the regulation, that use of the ingredient may not be GRAS. In such a case, a manufacturer may not rely on the regulation as authorizing that use but shall independently establish that that use is GRAS or shall use the ingredient in accordance with a food additive regulation. Persons seeking FDA approval of an independent determination that a use of an ingredient is GRAS may submit a GRAS petition in accordance with § 170.35 of this chapter.

(2) If the ingredient is affirmed as GRAS with specific limitation(s), it shall be used in food only within such limitation(s), including the category of food(s), the functional use(s) of the ingredient, and the level(s) of use. Any use of such an ingredient not in full compliance with each such established limitation shall require a food additive regulation.

(3) If the ingredient is affirmed as GRAS for a specific use, without a general evaluation of use of the ingredient, other uses may also be GRAS.

(c) The listing of a food ingredient in this part does not authorize the use of such substance in a manner that may lead to deception of the consumer or to any other violation of the Federal Food, Drug, and Cosmetic Act (the Act).

(d) The listing of more than one ingredient to produce the same technological effect does not authorize use of a combination of two or more ingredients to accomplish the same technological effect in any one food at a combined level greater than the highest level permitted for one of the ingredients.

(e) If the Commissioner of Food and Drugs is aware of any prior sanction for use of an ingredient under conditions different from those proposed to be affirmed as GRAS, he will concurrently propose a separate regulation covering such use of the ingredient under part 181 of this chapter. If the Commissioner is unaware of any such applicable prior sanction, the proposed regulation will so state and will require any person who intends to assert or rely on such sanction to submit proof of its existence. Any regulation promulgated pursuant to this section constitutes 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 the proposal will constitute a waiver of the right to assert or rely on such sanction at any later time. The notice will also constitute a proposal to establish a regulation under part 181 of this chapter, 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 the proposal.

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

(1) The name of the ingredient, except where exempted from such labeling in part 101 of this chapter.

(2) A statement of concentration of the ingredient in any intermediate mix; or other information to permit a food processor independently to determine that use of the ingredients will be in accordance with any limitations and

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 4 of 100

good manufacturing practice gudelines prescribed.

(3) Adequate directions for use to provide a final food product that complies with any limitations prescribed for the ingredient(s).

[42 FR 14653, Mar. 15, 1977, as amended at 42 FR 55205, Oct. 14, 1977; 48 FR 48457, 48459, Oct. 19, 1983; 62 FR 15110, Mar. 31, 1997]

Subpart B—Listing of Specific Substances Affirmed as GRAS

§ 184.1005 Acetic acid.

(a) Acetic acid ($C_2H_4O_2$, CAS Reg. No. 64–19–7) is known as ethanoic acid. It occurs naturally in plant and animal tissues. It is produced by fermentation of carbohydrates or by organic synthesis. The principal synthetic methods currently employed are oxidation of acetaldehyde derived from ethylene, liquid phase oxidation of butane, and reaction of carbon monoxide with methanol derived from natural gas.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 8, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as a curing and pickling agent as defined in § 170.3(o)(5) of this chapter; flavor enhancer as defined in § 170.3(o)(11) of this chapter; flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter; pH control agent as defined in § 170.3(o)(23) of this chapter; as a solvent and vehicle as defined in § 170.3(o)(27) of this chapter; and as a boiler water additive complying with § 173.310 of this chapter.

(d) The ingredient is used in food at levels not to exceed current good manufacturing practice in accordance with § 184.1(b)(1). Current good manufacturing practice results in a maximum level as served, of 0.25 percent for baked goods as defined in § 170.3(n)(1) of this chapter; 0.8 percent for cheeses as defined in § 170.3(n)(5) of this chapter and dairy product analogs as defined in § 170.3(n)(10) of this chapter; 0.5 percent for chewing gum as defined in § 170.3(n)(6) of this chapter; 9.0 percent for condiments and relishes as defined in § 170.3(n)(8) of this chapter; 0.5 percent for fats and oils as defined in § 170.3(n)(12) of this chapter; 3.0 percent for gravies and sauces as defined in § 170.3(n)(24) of this chapter; 0.6 percent for meat products as defined in § 170.3(n)(29) of this chapter; and 0.15 percent or less for all other food categories. The ingredient may also be used in boiler water additives at levels not to exceed current good manufacturing practice.

(e) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[47 FR 27814, June 25, 1982]

§ 184.1007 Aconitic acid.

(a) Aconitic acid (1,2,3-propenetricarboxylic acid ($C_6H_6O_6$), CAS Reg. No. 000499–12–7) occurs in the leaves and tubers of *Aconitum napellus* L. and other *Ranunculaceae*. Transaconitic acid can be isolated during sugarcane processing, by precipitation as the calcium salt from cane sugar or molasses. It may be synthesized by sulfuric acid dehydration of citric acid, but not by the methanesulfonic acid method.

(b) The ingredient meets the following specifications:

(1) *Assay*. Not less than 98.0 percent of $C_3H_3(COOH)_3$, using the ''Food Chemicals Codex,'' 4th ed. (1996), pp. 102–103, test for citric acid, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51, and a molecular weight of 174.11. Copies of the material incorporated by reference are available from the National Academy Press, Box 285, 2101 Constitution Ave. NW., Washington, DC 20055 (Internet address ''http://www.nap.edu''), or may be examined at the Center for Food Safety and Applied Nutrition's Library, Food and Drug Administration, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(2) *Melting point*. Not less than 195 °C and the determination results in decomposition of aconitic acid.

(3) *Heavy metals* (*as Pb*). Not more than 10 parts per million.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 5 of 100

(4) *Arsenic* (*as As*). Not more than 3 parts per million.

(5) *Oxalate.* Passes test.

(6) *Readily carbonizable substances.* Passes the test for citric acid of the ''Food Chemicals Codex,'' 4th ed. (1996), pp. 102–103, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. The availability of this incorporation by reference is given in paragraph (b)(1) of this section.

(7) *Residue on ignition.* Not more than 0.1 percent as determined by the ''Food Chemicals Codex,'' 4th ed. (1996), pp. 102–103, test for citric acid, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. The availability of this incorporation by reference is given in paragraph (b)(1) of this section.

(c) The ingredient is used as a flavoring substance and adjuvant as defined in § 170.3(o)(12) of this chapter.

(d) The ingredient is used in food, in accordance with § 184.1(b)(1), at levels not to exceed good manufacturing practice. Current good manufacturing practice results in a maximum level, as served, of 0.003 percent for baked goods as defined in § 170.3(n)(1) of this chapter, 0.002 percent for alcoholic beverages as defined in § 170.3(n)(2) of this chapter, 0.0015 percent for frozen dairy products as defined in § 170.3(n)(20) of this chapter, 0.0035 percent for soft candy as defined in § 170.3(n)(38) of this chapter, and 0.0005 percent or less for all other food categories.

(e) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[43 FR 47724, Oct. 17, 1978, as amended at 49 FR 5610, Feb. 14, 1984; 64 FR 1759, Jan. 12, 1999]

§ 184.1009 Adipic acid.

(a) Adipic acid ($C_6H_{10}O_4$, CAS Reg. No. 00124–04–9) is also known as 1,4-butanedicarboxylic acid or hexanedioic acid. It is prepared by nitric acid oxidation of cyclohexanol or cyclohexanone or a mixture of the two.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 11, which is incorporated by reference (copies are available from the National Academy Press, 2101 Constitution Ave., NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408), and the following additional specifications:

(1) The adipic acid is converted to its corresponding amide. The amide is purified by recrystallization from water or aqueous ethanol. The melting range of the amide is 219° to 220 °C.

(2) The adipic acid is converted to its corresponding *bis-p-p*-bromophenacyl ester. The ester is purified by recrystallization from ethanol. The melting range of the ester is 153° to 154 °C.

(c) The ingredient is used as a flavoring agent as defined in § 170.3(o)(12) of this chapter; leavening agent as defined in § 170.3(o)(17) of this chapter; and pH control agent as defined in § 170.3(o)(23) of this chapter.

(d) The ingredient is used in foods at levels not to exceed current good manufacturing practice in accordance with § 184.1(b)(1). Current good manufacturing practice results in maximum levels, as served, of 0.05 percent for baked goods as defined in § 170.3(n)(1) of this chapter; 0.005 percent for nonalcoholic beverages as defined in § 170.3(n)(3) of this chapter; 5.0 percent for condiments and relishes as defined in § 170.3(n)(8) of this chapter; 0.45 percent for dairy product analogs as defined in § 170.3(n)(10) of this chapter; 0.3 percent for fats and oil as defined in § 170.3(n)(12) of this chapter; 0.0004 percent for frozen dairy desserts as defined in § 170.3(n)(20) of this chapter; 0.55 percent for gelatin and puddings as defined in § 170.3(n)(22) of this chapter; 0.1 percent for gravies as defined in § 170.3(n)(24) of this chapter; 0.3 percent for meat products as defined in § 170.3(n)(29) of this chapter; 1.3 percent for snack foods as defined in § 170.3(n)(37) of this chapter; and 0.02

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 6 of 100

percent or less for all other food categories.

(e) Prior sanctions for adipic acid different from the uses established in this section do not exist or have been waived.

[47 FR 27810, June 25, 1982]

§ 184.1011 Alginic acid.

(a) Alginic acid is a colloidal, hydrophilic polysaccharide obtained from certain brown algae by alkaline extraction.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 13, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(2), the ingredient is used in food only within the following specific limitations:

Category of food	Maximum level of use in food (as served)	Functional use
Soup and soup mixes, § 170.3(n) (40) of this chapter.	Not to exceed current good manufacturing practice.	Emulsifier, emulsifier salt, § 170.3(o)(8) of this chapter; formulation aid, § 170.3(o)(14) of this chapter; stabilizer, thickener, § 170.3(o)(28) of this chapter.

(d) Prior sanctions for this ingredient different from the use established in this section do not exist or have been waived.

[47 FR 47375, Oct. 26, 1982]

§ 184.1012 α-Amylase enzyme preparation from Bacillus stearothermophilus.

(a) α-Amylase enzyme preparation is obtained from the culture filtrate that results from a pure culture fermentation of a nonpathogenic and nontoxicogenic strain of *Bacillus stearothermophilus*. Its characterizing enzyme activity is α-amylase (1,4 α-D glucan glucanohydrolase (E.C. 3.2.1.1)).

(b) The ingredient meets the general and additional requirements for enzyme preparations in the ''Food Chemicals Codex,'' 3d ed. (1981), pp. 107–110, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of Premarket Approval (HFS–200), Center for Food Safety and Applied Nutrition, Food and Drug Administration, 1110 Vermont Ave. NW., suite 1200, Washington, DC, or the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practices. The affirmation of this ingredient as GRAS as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an enzyme, as defined in § 170.3(o)(9) of this chapter, in the hydrolysis of edible starch to produce maltodextrins and nutritive carbohydrate sweeteners.

(2) The ingredient is used at levels not to exceed current good manufacturing practices.

[60 FR 55789, Nov. 3, 1995]

§ 184.1021 Benzoic acid.

(a) Benzoic acid is the chemical benzenecarboxylic acid ($C_7H_6O_2$), occurring in nature in free and combined forms. Among the foods in which benzoic acid occurs naturally are cranberries, prunes, plums, cinnamon, ripe cloves, and most berries. Benzoic acid is manufactured by treating molten phthalic anhydride with steam in the presence of a zinc oxide catalyst, by the hydrolysis of benzotrichloride, or by the oxidation of toluene with nitric acid or sodium bichromate or with air in the presence of a transition metal salt catalyst.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), p. 35, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 7 of 100

(c) The ingredient is used as an antimicrobial agent as defined in § 170.3(o)(2) of this chapter, and as a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter.

(d) The ingredient is used in food at levels not to exceed good manufacturing practice. Current usage results in a maximum level of 0.1 percent in food. (The Food and Drug Administration has not determined whether significantly different conditions of use would be GRAS).

(e) Prior sanctions for this ingredient different from those uses established in this section, or different from that set forth in part 181 of this chapter, do not exist or have been waived.

[42 FR 14653, Mar. 15, 1977, as amended at 49 FR 5610, Feb. 14, 1984]

§ 184.1024 Bromelain.

(a) Bromelain (CAS Reg. No. 9001–00–7) is an enzyme preparation derived from the pineapples *Ananas comosus* and *A. bracteatus* L. It is a white to light tan amorphous powder. Its characterizing enzyme activity is that of a peptide hydrolase (EC 3.4.22.32).

(b) The ingredient meets the general requirements and additional requirements for enzyme preparations in the Food Chemicals Codex, 3d ed. (1981), p. 110, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC, or may be examined at the Office of Premarket Approval (HFS–200), Food and Drug Administration, 200 C St. SW., Washington, DC, and the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as GRAS as a direct food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an enzyme as defined in § 170.3(o)(9) of this chapter to hydrolyze proteins or polypeptides.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

[60 FR 32910, June 26, 1995]

§ 184.1025 Caprylic acid.

(a) Caprylic acid [$CH_3(CH_2)_6COOH$, CAS Reg. No. 124–07–2] is the chemical name for octanoic acid. It is considered to be a short or medium chain fatty acid. It occurs normally in various foods and is commercially prepared by oxidation of *n*-octanol or by fermentation and fractional distillation of the volatile fatty acids present in coconut oil.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), p. 207, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter.

(d) The ingredient is used in foods in accordance with § 184.1(b)(1), at levels not to exceed good manufacturing practice. Current good manufacturing practices result in maximum levels, as served, of: 0.013 percent for baked goods as defined in § 170.3(n)(1) of this chapter; 0.04 percent for cheeses as defined in § 170.3(n)(5) of this chapter; 0.005 percent for fats and oils as defined in § 170.3(n)(12) of this chapter, for frozen dairy desserts as defined in § 170.3(n)(20) of this chapter, for gelatins and puddings as defined in § 170.3(n)(22) of this chapter, for meat products as defined in § 170.3(n)(29) of this chapter, and for soft candy as defined in § 170.3(n)(38) of this chapter; 0.016 percent for snack foods as defined in § 170.3(n)(37) of this chapter; and 0.001 percent or less for all other food categories.

(e) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[43 FR 19843, May 9, 1978, as amended at 49 FR 5611, Feb. 14, 1984]

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 8 of 100

§ 184.1027 Mixed carbohydrase and protease enzyme product.

(a) Mixed carbohydrase and protease enzyme product is an enzyme preparation that includes carbohydrase and protease activity. It is obtained from the culture filtrate resulting from a pure culture fermentation of a nonpathogenic strain of *B. licheniformis*.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 107, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an enzyme, as defined in § 170.3(o)(9) of this chapter, to hydrolyze proteins or carbohydrates.

(2) The ingredient is used in the following foods at levels not to exceed current good manufacturing practice: alcoholic beverages, as defined in § 170.3(n)(2) of this chapter, candy, nutritive sweeteners, and protein hydrolyzates.

[48 FR 240, Jan. 4, 1983]

§ 184.1033 Citric acid.

(a) Citric acid ($C_6H_8O_7$, CAS Reg. No. 77–92–9) is the compound 2-hydroxy-1,2,3-propanetricarboxylic acid. It is a naturally occurring constituent of plant and animal tissues. It occurs as colorless crystals or a white powder and may be anhydrous or contain one mole of water per mole of citric acid. Citric acid may be produced by recovery from sources such as lemon or pineapple juice; by mycological fermentation using *Candida spp.*, described in §§ 173.160 and 173.165 of this chapter; and by the solvent extraction process described in § 173.280 of this chapter for the recovery of citric acid from *Aspergillus niger* fermentation liquor.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d ed. (1981), pp. 86–87, and its third supplement (March 1992), pp. 107–108, which are incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, and the Center for Food Safety and Applied Nutrition (HFS–200), 200 C St. SW., Washington, DC 20204, or may be examined at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitations other than current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[59 FR 63895, Dec. 12, 1994]

§ 184.1034 Catalase (bovine liver).

(a) Catalase (bovine liver) (CAS Reg. No. 9001–05–2) is an enzyme preparation obtained from extracts of bovine liver. It is a partially purified liquid or powder. Its characterizing enzyme activity is catalase (EC 1.11.1.6).

(b) The ingredient meets the general requirements and additional requirements for enzyme preparations in the Food Chemicals Codex, 3d ed. (1981), p. 110, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave., NW., Washington, DC 20418, or may be examined at the Office of Premarket Approval (HFS–200), Food and Drug Administration, 200 C St., SW., Washington, DC, and the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as GRAS as a direct food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an enzyme as defined in § 170.3(o)(9) of this

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 9 of 100

chapter to decompose hydrogen peroxide.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

[60 FR 32910, June 26, 1995]

§ 184.1061 Lactic acid.

(a) Lactic acid ($C_3H_6O_3$, CAS Reg. Nos.: DL mixture, 598–82–3; L-isomer, 79–33–4; D-isomer, 10326–41–7), the chemical 2-hydroxypropanoic acid, occurs naturally in several foods. It is produced commercially either by fermentation of carbohydrates such as glucose, sucrose, or lactose, or by a procedure involving formation of lactonitrile from acetaldehyde and hydrogen cyanide and subsequent hydrolysis to lactic acid.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 159, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Avenue, NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an antimicrobial agent as defined in § 170.3(o)(2) of this chapter; a curing and pickling agent as defined in § 170.3(o)(5) of this chapter; a flavor enhancer as defined in § 170.3(o)(11) of this chapter; a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter; a pH control agent as defined in § 170.3(o)(23) of this chapter; and a solvent and vehicle as defined in § 170.3(o)(27) of this chapter.

(2) The ingredient is used in food, except in infant foods and infant formulas, at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[49 FR 35367, Sept. 7, 1984]

§ 184.1063 Enzyme-modified lecithin.

(a) Enzyme-modified lecithin is prepared by treating lecithin with either phospholipase A_2 (EC 3.1.1.4) or pancreatin.

(b) The ingredient meets the specifications in paragraphs (b)(1) through (b)(8) of this section. Unless otherwise noted, compliance with the specifications listed below is determined according to the methods set forth for lecithin in the Food Chemicals Codex, 4th ed. (1996), pp. 220–221, which are incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington DC 20418, or may be examined at the Center for Food Safety and Applied Nutrition's Library, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(1) Acetone-insoluble matter (phosphatides), not less than 50.0 percent.

(2) Acid value, not more than 40.

(3) Lead, not more than 1.0 part per million, as determined by atomic absorption spectroscopy.

(4) Heavy metals (as Pb), not more than 20 parts per million.

(5) Hexane-insoluble matter, not more than 0.3 percent.

(6) Peroxide value, not more than 20.

(7) Water, not more than 4.0 percent.

(8) Lysolecithin, 50 to 80 mole percent of total phosphatides as determined by ''Determination of Lysolecithin Content of Enzyme-Modified Lecithin: Method I,'' dated 1985, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the Division of Petition Control, Center for Food Safety and Applied Nutrition (HFS–215), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, or may be examined at the Center for Food Safety and Applied Nutrition's Library, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 10 of 100

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an emulsifier as defined in § 170.3(o)(8) of this chapter.

(2) The ingredient is used at levels not to exceed current good manufacturing practice.

[61 FR 45889, Aug. 30, 1996]

§ 184.1065 Linoleic acid.

(a) Linoleic acid ((Z, Z)–9, 12-octadecadienoic acid ($C_{17}H_{31}COOH$) (CAS Reg. No. 60–33–3)), a straight chain unsaturated fatty acid with a molecular weight of 280.5, is a colorless oil at room temperature. Linoleic acid may be prepared from edible fats and oils by various methods including hydrolysis and saponification, the Twitchell method, low pressure splitting with catalyst, continuous high pressure counter current splitting, and medium pressure autoclave splitting with catalyst.

(b) FDA is developing food-grade specifications for linoleic acid in cooperation with the National Academy of Sciences. In the interim, this ingredient must be of a purity suitable for its intended use. The ingredient must also meet the specifications in § 172.860(b) of this chapter.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter and as a nutrient supplement as defined in § 170.3(o)(20) of this chapter.

(2) The ingredient is used in foods at levels not to exceed current good manufacturing practice. The ingredient may be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) or with regulations promulgated under section 412(a)(2) of the act.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[49 FR 48534, Dec. 13, 1984]

§ 184.1069 Malic acid.

(a) Malic acid ($C_4H_6O_5$, CAS Reg. No. of L-form 97–67–6, CAS Reg. No. of DL-form 617–48–1) is the common name for 1-hydroxy-1, 2-ethanedicarboxylic acid. L (+) malic acid, referred to as L-malic acid, occurs naturally in various foods. Racemic DL-malic acid does not occur naturally. It is made commercially by hydration of fumaric acid or maleic acid.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), pp. 183–184, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredients are used as a flavor enhancer as defined in § 170.3(o)(11) of this chapter, flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter, and pH control agent as defined in § 170.3(o)(23) of this chapter.

(d) The ingredients are used in food, except baby food, at levels not to exceed good manufacturing practice in accordance with § 184.1(b)(1). Current good manufacturing practice results in a maximum level, as served, of 3.4 percent for nonalcoholic beverages as defined in § 170.3(n)(3) of this chapter; 3.0 percent for chewing gum as defined in § 170.3(n)(6) of this chapter; 0.8 percent for gelatins, puddings, and fillings as defined in § 170.3(n)(22) of this chapter; 6.9 percent for hard candy as defined in § 170.3(n)(25) of this chapter; 2.6 percent for jams and jellies as defined in § 170.3(n)(28) of this chapter; 3.5 percent for processed fruits and fruit juices as defined in § 170.3(n)(35) of this chapter; 3.0 percent for soft candy as defined in § 170.3(n)(38) of this chapter; and 0.7 percent for all other food categories.

(e) Prior sanctions for malic acid different from the uses established in this

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 11 of 100

section do not exist or have been waived.

[44 FR 20656, Apr. 6, 1979, as amended at 49 FR 5611, Feb. 14, 1984]

§ 184.1077 Potassium acid tartrate.

(a) Potassium acid tartrate ($C_4H_5KO_6$, CAS Reg. No. 868–14–4) is the potassium acid salt of L−(+)−tartaric acid and is also called potassium bitartrate or cream of tartar. It occurs as colorless or slightly opaque crystals or as a white, crystalline powder. It has a pleasant, acid taste. It is obtained as a byproduct of wine manufacture.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), P. 238, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an anticaking agent as defined in § 170.3(o)(1) of this chapter; an antimicrobial agent as defined in § 170.3(o)(2) of this chapter; a formulation aid as defined in § 170.3(o)(14) of this chapter; a humectant as defined in § 170.3(o)(16) of this chapter; a leavening agent as defined in § 170.3(o)(17) of this chapter; A pH control agent as defined in § 170.3(o)(23) of this chapter; a processing aid as defined in § 170.3(o)(24) of this chapter; a stabilizer and thickener as defined in § 170.3(o)(28) of this chapter; and a surface-active agent as defined in § 170.3(o)(29) of this chapter.

(2) The ingredient is used in the following foods at levels not to exceed current good manufacturing practice: baked goods as defined in § 170.3(n)(1) of this chapter; confections and frostings as defined in § 170.3(n)(9) of this chapter; gelatins and puddings as defined in § 170.3(n)(22) of this chapter; hard candy as defined in § 170.3(n)(25) of this chapter; jams and jellies as defined in § 170.3(n)(28) of this chapter; and soft candy as defined in § 170.3(n)(38) of this chapter.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 52446, Nov. 18, 1983]

§ 184.1081 Propionic acid.

(a) Propionic acid ($C_3H_6O_2$, CAS Reg. No. 79–09–4) is an oily liquid having a slightly pungent, rancid odor. It is manufactured by chemical synthesis or by bacterial fermentation.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 254, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an antimicrobial agent as defined in § 170.3(o)(2) of this chapter and a flavoring agent as defined in § 170.3(o)(12) of this chapter.

(2) The ingredient is used in foods at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[49 FR 13141, Apr. 3, 1984]

§ 184.1090 Stearic acid.

(a) Stearic acid ($C_{16}H_{36}O_2$, CAS Reg. No. 57–11–4) is a white to yellowish white solid. It occurs naturally as a glyceride in tallow and other animal or vegetable fats and oils and is a principal constituent of most commercially

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 12 of 100

hydrogenated fats. It is produced commercially from hydrolyzed tallow derived from edible sources or from hydrolyzed, completely hydrogenated vegetable oil derived from edible sources.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 313, which is incorporated by reference, and the requirements of § 172.860(b)(2) of this chapter. Copies of the Food Chemicals Codex are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter.

(2) The ingredient is used in foods at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 52445, Nov. 18, 1983, as amended at 50 FR 49536, Dec. 3, 1985]

§ 184.1091 Succinic acid.

(a) Succinic acid ($C_4H_6O_4$, CAS Reg. No. 110–15–6), also referred to as amber acid and ethylenesuccinic acid, is the chemical 1,4-butanedioic acid. It is commercially prepared by hydrogenation of maleic or fumaric acid. It can also be produced by aqueous alkali or acid hydrolysis of succinonitrile.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), pp. 314–315, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as a flavor enhancer as defined in § 170.3(o)(11) of this chapter and pH control agent as defined in § 170.3(o)(23) of this chapter.

(d) The ingredient is used in food at levels not to exceed good manufacturing practice in accordance with § 184.1(b)(1). Current good manufacturing practice results in a maximum level, as served, of 0.084 percent in condiments and relishes as defined in § 170.3(n)(8) of this chapter and 0.0061 percent in meat products as defined in § 170.3(n)(29) of this chapter.

(e) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[44 FR 20657, Apr. 6, 1979, as amended at 49 FR 5611, Feb. 14, 1984]

§ 184.1095 Sulfuric acid.

(a) Sulfuric acid (H_2SO_4, CAS Reg. No. 7664–93–9), also known as oil of vitriol, is a clear, colorless, oily liquid. It is prepared by reacting sulfur dioxide (SO_2) with oxygen and mixing the resultant sulfur trioxide (SO_3) with water, or by reacting nitric oxide (NO) with sulfur dioxide and water.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), pp. 317–318, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as a pH control agent as defined in § 170.3(o)(23) of this chapter and processing aid as defined in § 170.3(o)(24) of this chapter.

(d) The ingredient is used in food at levels not to exceed good manufacturing practice in accordance with § 184.1(b)(1). Current good manufacturing practice results in a maximum level, as served, of 0.014 percent for alcoholic beverages as defined in § 170.3(n)(2) of this chapter and 0.0003 percent for cheeses as defined in § 170.3(n)(5) of this chapter.

(e) Prior sanctions for this ingredient different from the uses established in

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 13 of 100

this section do not exist or have been waived.

[45 FR 6085, Jan. 25, 1980, as amended at 49 FR 5611, Feb. 14, 1984]

§ 184.1097 Tannic acid.

(a) Tannic acid (CAS Reg. No. 1401–55–4), or hydrolyzable gallotannin, is a complex polyphenolic organic structure that yields gallic acid and either glucose or quinic acid as hydrolysis products. It is a yellowish-white to light brown substance in the form of an amorphous, bulky powder, glistening scales, or spongy masses. It is also ordorless, or has a faint characteristic odor, and has an astringent taste. Tannic acid is obtained by solvent extraction of nutgalls or excrescences that form on the young twigs of *Quercus infectoria Oliver* and related species of *Quercus*. Tannic acid is also obtained by solvent extraction of the seed pods of Tara (*Caesalpinia spinosa*) or the nutgalls of various sumac species, including *Rhus semialata, R. coriaria, R. galabra,* and *R. typhia*.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 319, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c)(1) In accordance with § 184.1(b)(2), the ingredient is used in food only within the following specific limitations:

Category of food	Maximum level of use in food (as served) (percent)	Functional use
Baked goods and baking mixes, § 170.3(n)(1) of this chapter.	0.01	Flavoring agent and adjuvant, § 170.3(o)(12) of this chapter.
Alcoholic beverages, § 170.3(n)(2) of this chapter	0.015	Flavor enhancer, § 170.3(o)(11) of this chapter; flavoring agent and adjuvant, § 170.3(o)(12) of this chapter; processing aid, § 170.3(o)(24) of this chapter.
Nonalcoholic beverages and beverage bases, § 170.3(n)(3) of this chapter and for gelatins, puddings, and fillings, § 170.3(n)(22) of this chapter.	0.005	Flavoring agent and adjuvant, § 170.3(o)(12) of this chapter; pH control agent, § 170.3(o)(23) of this chpater.
Frozen dairy desserts and mixes, § 170.3(n)(20) of this chapter and for soft candy, § 170.3(n)(38) of this chapter.	0.04	Flavoring agent and adjuvant, § 170.3(o)(12) of this chapter.
Hard candy and cough drops, §170.3(n)(25) of this chapter.	0.013	Do.
Meat products, § 170.3(n)(29) of this chapter	0.001	Do.

(2) Tannic acid may be used in rendered animal fat in accordance with 9 CFR 318.7.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[50 FR 21043, May 22, 1985]

§ 184.1099 Tartaric acid.

(a) Food grade tartaric acid ($C_4H_6O_6$, CAS Reg. No. 87–69–4) has the L configuration. The L form of tartaric acid is dextrorotatory in solution and is also known as L−(+)−tartaric acid. Tartaric acid occurs as colorless or translucent crystals or as a white, crystalline powder. It is odorless and has an acid taste. It is obtained as a byproduct of wine manufacture.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), P. 320, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 14 of 100

the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a firming agent as defined in § 170.3(o)(10) of this chapter; a flavor enhancer as defined in § 170.3(o)(11) of this chapter; a flavoring agent as defined in § 170.3(o)(12) of this chapter; a humectant as defined in § 170.3(o)(16) of this chapter; and a pH control agent as defined in § 170.3(o)(23) of this chapter.

(2) The ingredient is used in foods at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 52447, Nov. 18, 1983, as amended at 50 FR 49536, Dec. 3, 1985]

§ 184.1101 Diacetyl tartaric acid esters of mono- and diglycerides.

(a) Diacetyl tartaric acid esters of mono- and diglycerides, also know as DATEM, are composed of mixed esters of glycerin in which one or more of the hydroxyl groups of glycerin has been esterified by diacetyl tartaric acid and by fatty acids. The ingredient is prepared by the reaction of diacetyl tartaric anhydride with mono- and diglycerides that are derived from edible sources.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d. Ed. (1981), pp. 98–99, which is incorporated by reference in accordance with 5 U.S.C. 552(a). Copies are available from the National Academy Press, 2101 Constitution Avenue NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20005.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used in food as an emulsifier and emulsifier salt as defined in § 170.3(o)(8) of this chapter and a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter.

(2) The ingredient is used in the following foods at levels not to exceed current good manufacturing practice: baked goods and baking mixes as defined in § 170.3(n)(l) of this chapter; nonalcoholic beverages as defined in § 170.3(n)(3) of this chapter; confections and frostings as defined in § 170.3(n)(9) of this chapter; dairy product analogs as defined in § 170.3(n)(10) of this chapter; and fats and oils as defined in § 170.3(n)(12) of this chapter.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

(e) *Labeling:* The acronym ''DATEM'' may be used on food labeling as the alternate common or usual name for the ingredient diacetyl tartaric acid esters of mono- and diglycerides.

[54 FR 7403, Feb. 21, 1989, as amended at 54 FR 13168, Mar. 31, 1989; 54 FR 18382, Apr. 28, 1989; 60 FR 15872, Mar. 28, 1995]

§ 184.1115 Agar-agar.

(a) Agar-agar (CAS Reg. No. PM 9002–18–0) is a dried, hydrophyllic, colloidal polysaccharide extracted from one of a number of related species of red algae (class *Rhodophyceae*).

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), p. 11, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used in food in accordance with § 184.1(b)(2) under the following conditions:

MAXIMUM USAGE LEVELS PERMITTED

Foods (as served)	Percent	Functions
Baked goods and baking mixes, § 170.3(n)(1) of this chapter.	0.8	Drying agent, § 170.3(o)(7) of this chapter; flavoring agent, § 170.3(o)(12) of this chapter; stabilizer, thickener, § 170.3(o)(28) of this chapter.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 15 of 100

MAXIMUM USAGE LEVELS PERMITTED—Continued

Foods (as served)	Percent	Functions
Confections and frostings, § 170.3(n)(9) of this chapter.	2.0	Flavoring agent, § 170.3(o)(12) of this chapter; stabilizer, thickener, § 170.3(o)(28) of this chapter; surface finisher, § 170.3(o)(30) of this chapter.
Soft candy, § 170.3(n)(38) of this chapter	1.2	Stabilizer and thickener, § 170.3(o)(28) of this chapter.
All other food categories	.25	Flavoring agent, § 170.3(o)(12) of this chapter; formulation aid, § 170.3(o)(14) of this chapter; humectant, § 170.3(o)(16) of this chapter; stabilizer, thickener, § 170.3(o)(28) of this chapter.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[44 FR 19391, Apr. 3, 1979, as amended at 49 FR 5611, Feb. 14, 1984]

§ 184.1120 Brown algae.

(a) Brown algae are seaweeds of the species *Analipus japonicus, Eisenia bicyclis, Hizikia fusiforme, Kjellmaniella gyrata, Laminaria angustata, Laminaria claustonia, Laminaria digitata, Laminaria japonica, Laminaria longicruris, Laminaria longissima, Laminaria ochotensis, Laminaria saccharina, Macrocystis pyrifera, Petalonia fascia, Scytosiphon lomentaria* and *Undaria pinnatifida*. They are harvested principally in coastal waters of the northern Atlantic and Pacific oceans. The material is dried and ground or chopped for use in food.

(b) The ingredient meets the specifications for kelp in the Food Chemicals Codex, 3d Ed. (1981), p. 157, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(2), the ingredient is used in food only within the following specific limitations:

Category of food	Maximum level of use in food (as served)	Functional use
Spices, seasonings, and flavorings, § 170.3(n) (26) of this chapter.	Not to exceed current good manufacturing practice.	Flavor enhancer, § 170.3(o)(11) of this chapter; flavor adjuvant, § 170.3(o)(12) of this chapter.

(d) Prior sanctions for this ingredient different from the use established in this section do not exist or have been waived.

[47 FR 47376, Oct. 26, 1982]

§ 184.1121 Red algae.

(a) Red algae are seaweeds of the species *Gloiopeltis furcata, Porphyra crispata, Porphyra deutata, Porphyra perforata, Porphyra suborbiculata, Porphyra tenera* and *Rhodymenia palmata*. *Porphyra* and *Rhodymenia* are harvested principally along the coasts of Japan, Korea, China, Taiwan, and the East and West coasts of the United States. *Gloiopeltis* is harvested principally in southern Pacific coastal waters. The material is dried and ground or chopped for use in food.

(b) The ingredient meets the specifications for kelp in the Food Chemicals Codex, 3d Ed. (1981), p. 157, which is incorporated by reference, except that the loss on drying is not more than 20 percent and the maximum allowable level for iodine is 0.05 percent. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(2), the ingredient is used in food only within the following specific limitations:

Category of food	Maximum level of use in food (as served)	Functional use
Spices, seasonings, and flavorings, § 170.3(n) (26) of this chapter.	Not to exceed current good manufacturing practice.	Flavor enhancer, § 170.3(o)(11) of this chapter; flavor adjuvant, § 170.3(o)(12) of this chapter.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 16 of 100

(d) Prior sanctions for this ingredient different from the use established in this section do not exist or have been waived.

[47 FR 47376, Oct. 26, 1982]

§ 184.1133 Ammonium alginate.

(a) Ammonium alginate (CAS Reg. No. 9005–34–9) is the ammonium salt of alginic acid, a natural polyuronide constituent of certain brown algae. Ammonium alginate is prepared by the neutralization of purified alginic acid with appropriate pH control agents.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 18, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(2), the ingredient is used in food only within the following specific limitations:

Category of food	Maximum level of use in food (as served) (percent)	Functional use
Confections, frostings, § 170.3(n)(9) of this chapter.	0.4	Stabilizer, thickener, § 170.3(o)(28) of this chapter.
Fats and oils, § 170.3(n)(12) of this chapter.	0.5	Do.
Gelatins, puddings, § 170.3(n)(22) of this chapter.	0.5	Do.
Gravies and sauces, § 170.3(n)(24) of this chapter.	0.4	Do.
Jams and jellies, § 170.3(n)(28) of this chapter.	0.4	Do.
Sweet sauces, § 170.3(n)(43) of this chapter.	0.5	Do.
All other food categories.	0.1	Humectant, § 170.3(o)(16) of this chapter; stabilizer, thickener, § 170.3(o)(28) of this chapter.

(d) Prior sanctions for ammonium alginate different from the uses established in this section do not exist or have been waived.

[47 FR 29950, July 9, 1982]

§ 184.1135 Ammonium bicarbonate.

(a) Ammonium bicarbonate (NH_4HCO_3, CAS Reg. No. 1066–33–7) is prepared by reacting gaseous carbon dioxide with aqueous ammonia. Crystals of ammonium bicarbonate are precipitated from solution and subsequently washed and dried.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 19, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a dough strengthener as defined in § 170.3(o)(6) of this chapter; a leavening agent as defined in § 170.3(o)(17) of this chapter; a pH control agent as defined in § 170.3(o)(23) of this chapter; and a texturizer as defined in § 170.3(o)(32) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 52439, Nov. 18, 1983]

§ 184.1137 Ammonium carbonate.

(a) Ammonium carbonate ($(NH_4)_2CO_3$, CAS Reg. No. 8000–73–5) is a mixture of ammonium bicarbonate (NH_4HCO_3) and ammonium carbamate (NH_2COONH_4). It is prepared by the sublimation of a mixture of ammonium sulfate and calcium carbonate and occurs as a white powder or a hard, white or translucent mass.

(b) The ingredient meets the specifications of the Food Chemicals Codex,

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 17 of 100

3d Ed. (1981), p. 19, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a leavening agent as defined in § 170.3(o)(17) of this chapter and a pH control agent as defined in § 170.3(o)(23) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 52439, Nov. 18, 1983]

§ 184.1138 Ammonium chloride.

(a) Ammonium chloride (NH_4Cl, CAS Reg. No. 12125–02–9) is produced by the reaction of sodium chloride and an ammonium salt in solution. The less soluble sodium salt separates out at elevated temperatures, and ammonium chloride is recovered from the filtrate on cooling. Alternatively, hydrogen chloride formed by the burning of hydrogen in chlorine is dissolved in water and then reacted with gaseous ammonia. Ammonium chloride is crystallized from the solution.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 20, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave, NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a dough strengthener as defined in § 170.3(o)(6) of this chapter; a flavor enhancer as defined in § 170.3(o)(11) of this chapter; a leavening agent as defined in § 170.3(o)(17) of this chapter; and a processing aid as defined in § 107.3(o)(24) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 52439, Nov. 18, 1983]

§ 184.1139 Ammonium hydroxide.

(a) Ammonium hydroxide (NH_4 OH, CAS Reg. No. 1336–21–6) is produced by passing ammonia gas into water.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 20, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a leavening agent as defined in § 170.3(o)(17) of this chapter; a pH control agent as defined in § 170.3(o)(23) of this chapter; a surface-finishing agent as defined in § 170.3(o)(30) of this chapter; and as a boiler water additive complying with § 173.310 of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice. The ingredient may also be used as a boiler water additive at levels not to exceed current good manufacturing practice.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 18 of 100

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 52440, Nov. 18, 1983, as amended at 59 FR 14551, Mar. 29, 1994]

§ 184.1140 Ammonium citrate, dibasic.

(a) Ammonium citrate, dibasic ($(NH_4)_2HC_6H_5O_7$, CAS Reg. No. 3012–65–5) is the diammonium salt of citric acid. It is prepared by partially neutralizing citric acid with ammonia.

(b) The Food and Drug Administration, in cooperation with the National Academy of Sciences, is developing food-grade specifications for ammonium citrate, dibasic. In the interim, this ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a flavor enhancer as defined in § 170.3(o)(11) of this chapter and as a pH control agent as defined in § 170.3(o)(23) of this chapter.

(2) The ingredient is used in nonalcoholic beverages as defined in § 170.3(n)(3) of this chapter and in cheeses as defined in § 170.3(n)(5) of this chapter at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section, or different from those set forth in part 181 of this chapter, do not exist or have been waived.

[59 FR 63896, Dec. 12, 1994]

§ 184.1141a Ammonium phosphate, monobasic.

(a) Ammonium phosphate, monobasic ($NH_4H_2PO_4$, CAS Reg. No. 7722–76–1) is manufactured by reacting ammonia with phosphoric acid at a pH below 5.8.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 21, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a dough strengthener as defined in § 170.3(o)(6) of this chapter and a pH control agent as defined in § 170.3(o)(23) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 52440, Nov. 18, 1983]

§ 184.1141b Ammonium phosphate, dibasic.

(a) Ammonium phosphate, dibasic ($(NH_4)_2HPO_4$, CAS Reg. No. 7783–28–0) is manufactured by reacting ammonia with phosphoric acid at a pH above 5.8.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 21, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a dough strengthener as defined in § 170.3(o)(6) of this chapter; a firming agent as defined in § 170.3(o)(10) of this chapter; a leavening agent as defined in

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 19 of 100

§ 170.3(o)(17) of this chapter; a pH control agent as defined in § 170.3(o)(23) of this chapter; and a processing aid as defined in § 170.3(o)(24) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 52440, Nov. 18, 1983]

§ 184.1143 Ammonium sulfate.

(a) Ammonium sulfate ($(NH_4)_2SO_4$, CAS Reg. No. 7783–20–2) occurs naturally and consists of colorless or white, odorless crystals or granules. It is prepared by the neutralization of sulfuric acid with ammonium hydroxide.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), pp. 22–23, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as a dough strengthener as defined in § 170.3(o)(6) of this chapter, firming agent as defined in § 170.3(o)(10) of this chapter, and processing aid as defined in § 170.3(o)(24) of this chapter.

(d) The ingredient is used in food at levels not to exceed good manufacturing practice in accordance with § 184.1(b)(1). Current good manufacturing practice results in a maximum level, as served, of 0.15 percent for baked goods as defined in § 170.3(n)(1) of this chapter and 0.1 percent for gelatins and puddings as defined in § 170.1(n)(22) of this chapter.

(e) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[45 FR 6086, Jan. 25, 1980; 45 FR 16469, Mar. 14, 1980, as amended at 49 FR 5611, Feb. 14, 1984]

§ 184.1148 Bacterially-derived carbohydrase enzyme preparation.

(a) Bacterially-derived carbohydrase enzyme preparation is obtained from the culture filtrate resulting from a pure culture fermentation of a nonpathogenic and nontoxigenic strain of *Bacillus subtilis* or *B. amyloliquefaciens*. The preparation is characterized by the presence of the enzymes α-amylase (EC 3.2.1.1) and β-glucanase (EC 3.2.1.6), which catalyze the hydrolysis of *O*-glycosyl bonds in carbohydrates.

(b) The ingredient meets the general requirements and additional requirements in the monograph on enzyme preparations in the Food Chemicals Codex, 4th ed. (1996), pp. 128–135, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Center for Food Safety and Applied Nutrition's Library, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol Street, NW., Suite 700, Washington, DC. In addition, antibiotic activity is absent in the enzyme preparation when determined by an appropriate validated method such as the method ''Determination of antibiotic activity'' in the Compendium of Food Additive Specifications, vol. 2, Joint FAO/WHO Expert Committee on Food Additives (JECFA), Food and Agriculture Organization of the United Nations, Rome, 1992. Copies are available from Bernan Associates, 4611–F Assembly Dr., Lanham, MD 20706, or from The United Nations Bookshop, General Assembly Bldg., rm. 32, New York, NY 10017, or by inquiries sent to ''http://www.fao.org''. Copies may be examined at the Center for Food Safety and Applied Nutrition's Library, 200 C St. SW., rm. 3321, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as GRAS as a direct food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an enzyme as defined in § 170.3(o)(9) of this chapter to hydrolyze polysaccharides (e.g., starch).

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 20 of 100

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

[64 FR 19894, Apr. 23, 1999]

§ 184.1150 Bacterially-derived protease enzyme preparation.

(a) Bacterially-derived protease enzyme preparation is obtained from the culture filtrate resulting from a pure culture fermentation of a nonpathogenic and nontoxigenic strain of *Bacillus subtilis* or *B. amyloliquefaciens.* The preparation is characterized by the presence of the enzymes subtilisin (EC 3.4.21.62) and neutral proteinase (EC 3.4.24.28), which catalyze the hydrolysis of peptide bonds in proteins.

(b) The ingredient meets the general requirements and additional requirements in the monograph on enzyme preparations in the Food Chemicals Codex, 4th ed. (1996), pp. 128–135, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Center for Food Safety and Applied Nutrition's Library, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol Street, NW., Suite 700 Washington, DC. In addition, antibiotic activity is absent in the enzyme preparation when determined by an appropriate validated method such as the method ''Determination of antibiotic activity'' in the Compendium of Food Additive Specifications, vol. 2, Joint FAO/WHO Expert Committee on Food Additives (JECFA), Food and Agriculture Organization of the United Nations, Rome, 1992. Copies are available from Bernan Associates, 4611–F Assembly Dr., Lanham, MD 20706, or from The United Nations Bookshop, General Assembly Bldg., rm. 32, New York, NY 10017, or by inquiries sent to ''http://www.fao.org''. Copies may be examined at the Center for Food Safety and Applied Nutrition's Library, 200 C St. SW., rm. 3321, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as GRAS as a direct food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an enzyme as defined in § 170.3(o)(9) of this chapter to hydrolyze proteins or polypeptides.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

[64 FR 19895, Apr. 23, 1999]

§ 184.1155 Bentonite.

(a) Bentonite ($Al_2O_34SiO_2nH_2O$, CAS Reg. No. 1302–0978–099) is principally a colloidal hydrated aluminum silicate. Bentonite contains varying quantities of iron, alkalies, and alkaline earths in the commercial products. Depending on the cations present, natural deposits of bentonite range in color from white to gray, yellow, green, or blue. Bentonite's fine particles provide large total surface area and, hence, pronounced adsorptive capability.

(b) FDA is developing food-grade specifications for bentonite in cooperation with the National Academy of Sciences. In the interim, the ingredient must be of a suitable purity for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a processing aid as defined in § 170.3(o)(24) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice. Current good manufacturing practice results in no significant residue in foods.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[47 FR 43367, Oct. 1, 1982]

§ 184.1157 Benzoyl peroxide.

(a) Benzoyl peroxide ($(C_6H_5CO)_2O_2$, CAS Reg. No. 94–36–0) is a colorless,

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 21 of 100

rhombic crystalline solid. It is prepared by reaction of benzoyl chloride, sodium hydroxide, and hydrogen peroxide.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 35, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a bleaching agent in food.

(2) The ingredient is used in the following foods at levels not to exceed current good manufacturing practice: flour; milk used for production of Asiago fresh and Asiago soft cheese (§ 133.102), Asiago medium cheese (§ 133.103), Asiago old cheese (§ 133.104), Blue cheese (§ 133.106), Caciocavallo siciliano chesse (§ 133.111), Gorgonzola cheese (§ 133.141), Parmesan and reggiano cheese (§ 133.165), Provolone cheese (§ 133.181), Romano cheese (§ 133.183), and Swiss and emmentaler cheese (§ 133.195) in part 133 of this chapter; and annatto-colored whey, such that the final bleached product conforms to the descriptions and specifications for whey, concentrated whey, or dried whey in § 184.1979(a) (1), (2), or (3), respectively.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[51 FR 27173, July 30, 1986]

§ 184.1165 n-Butane and iso-butane.

(a) *n*-Butane and iso-butane (empirical formula C_4H_{10}, CAS Reg. Nos. 106–97–8 and 75–28–5, respectively) are colorless, odorless, flammable gases at normal temperatures and pressures. They are easily liquefied under pressure at room temperature and are stored and shipped in the liquid state. The butanes are obtained from natural gas by fractionation following absorption in oil, adsorption to surface-active agents, or refrigeration.

(b) The Food and Drug Administration is developing food-grade specifications for *n*-butane and iso-butane in cooperation with the National Academy of Sciences. In the interim, the ingredients must be of a purity suitable for their intended use.

(c) In accordance with § 184.1(b)(1), these ingredients are used in food with no limitations other than current good manufacturing practice. The affirmation of these ingredients as generally recognized as safe (GRAS) as direct human food ingredients is based upon the following current good manufacturing practice conditions of use:

(1) The ingredients are used as propellants, aerating agents, and gases as defined in § 170.3(o)(25) of this chapter.

(2) The ingredients are used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for these ingredients different from the uses established in this section do not exist or have been waived.

[48 FR 57270, Dec. 29, 1983]

§ 184.1185 Calcium acetate.

(a) Calcium acetate ($Ca(C_2H_3O_2)_2$, CAS Reg. No. 62–54–4), also known as acetate of lime or vinegar salts, is the calcium salt of acetic acid. It may be produced by the calcium hydroxide neutralization of acetic acid.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 44, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as a firming agent as defined in § 170.3(o)(10) of this chapter; pH control agent as defined in § 170.3(o)(23) of this chapter; processing aid as defined in § 170.3(o)(24) of this chapter; sequestrant as defined in § 170.3(o)(26) of this chapter; stabilizer and thickener as defined in § 170.3(o)(28) of this chapter; and

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 22 of 100

texturizer as defined in § 170.3(o)(32) of this chapter.

(d) The ingredient is used in food at levels not to exceed current good manufacturing practices in accordance with § 184.1(b)(1). Current good manufacturing practices result in a maximum level, as served, of 0.2 percent for baked goods as defined in § 170.3(n)(1) of this chapter; 0.02 percent for cheese as defined in § 170.3(n)(5) of this chapter; 0.2 percent for gelatins, puddings, and fillings as defined in § 170.3(n)(22) of this chapter; 0.15 percent for sweet sauces, toppings, and syrups as defined in § 170.3(n)(43) of this chapter; and 0.0001 percent for all other food categories.

(e) Prior sanctions for this ingredient different from the uses established in this section or in part 181 of this chapter do not exist or have been waived.

[47 FR 27807, June 25, 1982]

§ 184.1187 Calcium alginate.

(a) Calcium alginate (CAS Reg. No. 9005–35–0) is the calcium salt of alginic acid, a natural polyuronide constituent of certain brown algae. Calcium alginate is prepared by the neutralization of purified alginic acid with appropriate pH control agents, or from sodium alginate by metathesis with appropriate calcium salts.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 45, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(2), the ingredient is used in food only within the following specific limitations:

Category of food	Maximum level of use in food (as served) (percent)	Functional use
Baked goods, § 170.3(n)(1) of this chapter.	0.002	Stabilizer, thickener, § 170.3(o)(28) of this chapter.
Alcoholic beverages, § 170.3(n)(2) of this chapter.	0.4	Do.
Confections and frostings, § 170.3(n)(9) of this chapter.	0.4	Do.
Egg products, § 170.3(n)(11) of this chapter.	0.6	Do.
Fats and oils, § 170.3(n)(12) of this chapter.	0.5	Do.
Gelatins, puddings, § 170.3(n)(22) of this chapter.	0.25	Do.
Gravies and sauces, § 170.3(n)(24) of this chapter.	0.4	Do.
Jams and jellies, § 170.3(n)(28) of this chapter.	0.5	Do.
Sweet sauces, § 170.3(n)(43) of this chapter.	0.5	Do.
All other food categories.	0.3	Do.

(d) Prior sanctions for calcium alginate different from the uses established in this section do not exist or have been waived.

[47 FR 29951, July 9, 1982]

§ 184.1191 Calcium carbonate.

(a) Calcium carbonate ($CaCO_3$, CAS Reg. No. 471–34–1) is prepared by three common methods of manufacture:

(1) As a byproduct in the ''Lime soda process'';

(2) By precipitation of calcium carbonate from calcium hydroxide in the ''Carbonation process''; or

(3) By precipitation of calcium carbonate from calcium chloride in the ''Calcium chloride process''.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 46, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 23 of 100

this section, or different from that set forth in part 181 of this chapter, do not exist or have been waived.

[48 FR 52441, Nov. 18, 1983]

§ 184.1193 Calcium chloride.

(a) Calcium chloride ($CaCl_2 \cdot 2H_2O$, CAS Reg. No. 10035–04–8) or anhydrous calcium chloride ($CaCl_2$, CAS Reg. No. 10043–52–4) may be commercially obtained as a byproduct in the ammonia-soda (Solvay) process and as a joint product from natural salt brines, or it may be prepared by substitution reactions with other calcium and chloride salts.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 47, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as an anticaking agent as defined in § 170.3(o)(1) of this chapter; antimicrobial agent as defined in § 170.3(o)(2) of this chapter; curing or pickling agent as defined in § 170.3(o)(5) of this chapter; firming agent as defined in § 170.3(o)(10) of this chapter; flavor enhancer as defined in § 170.3(o)(11) of this chapter; humectant as defined in § 170.3(o)(16) of this chapter; nutrient supplement as defined in § 170.3(o)(20) of this chapter; pH control agent as defined in § 170.3(o)(23) of this chapter; processing aid as defined in § 170.3(o)(24) of this chapter; stabilizer and thickener as defined in § 170.3(o)(28) of this chapter; surface-active agent as defined in § 170.3(o)(29) of this chapter; synergist as defined in § 170.3(o)(31) of this chapter; and texturizer as defined in § 170.3(o)(32) of this chapter.

(d) The ingredient is used in foods at levels not to exceed current good manufacturing practices in accordance with § 184.1(b)(1). Current good manufacturing practices result in a maximum level, as served, of 0.3 percent for baked goods as defined in § 170.3(n)(1) of this chapter and for dairy product analogs as defined in § 170.3(n)(10) of this chapter; 0.22 percent for nonalcoholic beverages and beverage bases as defined in § 170.3(n)(3) of this chapter; 0.2 percent for cheese as defined in § 170.3(n)(5) of this chapter and for processed fruit and fruit juices as defined in § 170.3(n)(35) of this chapter; 0.32 percent for coffee and tea as defined in § 170.3(n)(7) of this chapter; 0.4 percent for condiments and relishes as defined in § 170.3(n)(8) of this chapter; 0.2 percent for gravies and sauces as defined in § 170.3(n)(24) of this chapter; 0.1 percent for commercial jams and jellies as defined in § 170.3(n)(28) of this chapter; 0.25 percent for meat products as defined in § 170.3(n)(29) of this chapter; 2.0 percent for plant protein products as defined in § 170.3(n)(33) of this chapter; 0.4 percent for processed vegetables and vegetable juices as defined in § 170.3(n)(36) of this chapter; and 0.05 percent for all other food categories.

(e) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[47 FR 27808, June 25, 1982, as amended at 61 FR 14247, Apr. 1, 1996]

§ 184.1195 Calcium citrate.

(a) Calcium citrate ($Ca_3(C_6H_5O_7)_2 \cdot 4H_2O$, CAS Reg. No. 813–0994–095) is the calcium salt of citric acid. It is prepared by neutralizing citric acid with calcium hydroxide or calcium carbonate. It occurs as a fine white, odorless powder and usually contains four moles of water per mole of calcium citrate.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d ed. (1981), pp. 49 and 50, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, and the Center for Food Safety and Applied Nutrition (HFS–200), 200 C St. SW., Washington, DC 20204, or may be examined at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. Calcium citrate may also be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 24 of 100

(the act) or with regulations promulgated under section 412(a)(2) of the act.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[59 FR 63896, Dec. 12, 1994]

§ 184.1199 Calcium gluconate.

(a) Calcium gluconate ($[CH_2OH(CHOH)_4COO]_2Ca$, CAS Reg. No. 299–28–5) is the calcium salt of gluconic acid which may be produced by neutralization of gluconic acid with lime or calcium carbonate.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 51, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as a firming agent as defined in § 170.3(o)(10) of this chapter; formulation aid as defined in § 170.3(o)(14) of this chapter; sequestrant as defined in § 170.3(o)(26) of this chapter; stabilizer or thickener as defined in § 170.3(o)(28) of this chapter; and texturizer as defined in § 170.3(o)(32) of this chapter.

(d) The ingredient is used in foods at levels not to exceed current good manufacturing practices in accordance with § 184.1(b)(1). Current good manufacturing practices result in a maximum level, as served, of 1.75 percent for baked goods as defined in § 170.3(n)(1) of this chapter; 0.4 percent for dairy product analogs as defined in § 170.3(n)(10) of this chapter; 4.5 percent for gelatins and puddings as defined in § 170.3(n)(22) of this chapter; and 0.01 percent for sugar substitutes as defined in § 170.3(n)(42) of this chapter.

(e) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[47 FR 27808, June 25, 1982]

§ 184.1201 Calcium glycerophosphate.

(a) Calcium glycerophosphate ($C_3H_7CaO_6P$, CAS Reg. No. 27214–00–2) is a fine, white, odorless, almost tasteless, slightly hygroscopic powder. It is prepared by neutralizing glycerophosphoric acid with calcium hydroxide or calcium carbonate. The commercial product is a mixture of calcium β-, and *D*-, and *L*-α-glycerophosphate.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), pp. 51–52, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a nutrient supplement as defined in § 170.3(o)(20) of this chapter.

(2) The ingredient is used in gelatins, puddings, and fillings as defined in § 170.3(n)(22) of this chapter.

(d) Prior sanctions for this ingredient different from the uses established in this section or different from that as set forth in part 181 of this chapter, do not exist or have been waived.

[57 FR 10813, Mar. 31, 1992]

§ 184.1205 Calcium hydroxide.

(a) Calcium hydroxide ($Ca(OH)_2$, CAS Reg. No. 1305–62–0) is also known as slaked lime or calcium hydrate. It is produced by the hydration of lime.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 52, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 25 of 100

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[49 FR 26714, June 29, 1984]

§ 184.1206 Calcium iodate.

(a) Calcium iodate [$Ca(IO_3)_2 \cdot H_2O$, CAS Reg. No. 7789–80–2], also referred to as lautarite, does not occur naturally but can be prepared by passing chlorine into a hot solution of lime ($CaCO_3$) in which iodine has been dissolved.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), p. 53, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as a dough strengthener as defined in § 170.3(o)(6) of this chapter.

(d) The ingredient is used in the manufacture of bread in accordance with § 184.1(b)(2) of this chapter in an amount not to exceed 0.0075 percent based on the weight of the flour.

(e) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[43 FR 11699, Mar. 21, 1978, as amended at 49 FR 5611, Feb. 14, 1984]

§ 184.1207 Calcium lactate.

(a) Calcium lactate ($C_6H_{10}CaO_6.xH_2O$, where x is any integer up to 5, CAS Reg. No. 814–80–2) is prepared commercially by the neutralization of lactic acid with calcium carbonate or calcium hydroxide.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 53, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Avenue NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a firming agent as defined in § 170.3(o)(10) of this chapter; a flavor enhancer as defined in § 170.3(o)(11) of this chapter; a flavoring agent or adjuvant as defined in § 170.3(o)(12) of this chapter; a leavening agent as defined in § 170.3(o)(17) of this chapter; a nutrient supplement as defined in § 170.3(o)(20) of this chapter; and a stabilizer and thickener as defined in § 170.3(o)(28) of this chapter.

(2) The ingredient is used in food, except in infant foods and infant formulas, at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[49 FR 35367, Sept. 7, 1984]

§ 184.1210 Calcium oxide.

(a) Calcium oxide (CaO, CAS Reg. No. 1305–78–8) is also known as lime, quick lime, burnt lime, or calx. It is produced from calcium carbonate, limestone, or oyster shells by calcination at temperatures of 1,700–2,450 °F.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 55, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[49 FR 26714, June 29, 1984]

§ 184.1212 Calcium pantothenate.

(a) Calcium pantothenate ($(C_9H_{16}NO_5)_2Ca$, CAS Reg. No. of the *D-*

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 26 of 100

isomer, 137–08–6) is a salt of pantothenic acid, one of the vitamins of the B complex. Only the *D*-isomer of pantothenic acid has vitamin activity, although both the *D*-isomer and the *DL*-racemic mixture of calcium pantothenate are used in food. Commercial calcium pantothenate is prepared synthetically from isobutyraldehyde and formaldehyde via 1,1-dimethyl-2-hydroxy-propionaldehyde and pantolactone.

(b) Calcium pantothenate meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 56, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a nutrient supplement as defined in § 170.3(o)(20) of this chapter.

(2) The ingredient is used in foods at levels not to exceed current good manufacturing practice. Calcium pantothenate may be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) or with regulations promulgated under section 412(a)(2) of the Act.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 51908, Nov. 15, 1983]

§ 184.1221 Calcium propionate.

(a) Calcium propionate ($C_6H_{10}CaO_4$, CAS Reg. No. 4075–81–4) is the calcium salt of propionic acid. It occurs as white crystals or a crystalline solid, possessing not more than a faint odor of propionic acid. It is prepared by neutralizing propionic acid with calcium hydroxide.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 60, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an antimicrobial agent as defined in § 170.3(o)(2) of this chapter.

(2) The ingredient is used in the following foods at levels not to exceed current good manufacturing practice: baked goods as defined in § 170.3(n)(1) of this chapter; cheeses as defined in § 170.3(n)(5) of this chapter; confections and frostings as defined in § 170.3(n)(9) of this chapter; gelatins, puddings, and fillings as defined in § 170.3(n)(22) of this chapter; and jams and jellies as defined in § 170.3(n)(28) of this chapter.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[49 FR 13141, Apr. 3, 1984]

§ 184.1229 Calcium stearate.

(a) Calcium stearate ($Ca(C_{17}H_{35}COO)_2$, CAS Reg. No. 1529–23–0) is the calcium salt of stearic acid derived from edible sources. It is prepared as a white precipitate by mixing calcium chloride and sodium stearate in aqueous solution.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 64, which is incorporated by reference, and the requirements of § 172.860(b)(2) of this chapter. Copies of the Food Chemicals Codex are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 27 of 100

limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter; a lubricant and release agent as defined in § 170.3(o)(18) of this chapter; and a stabilizer and thickener as defined in § 170.3(o)(28) of this chapter.

(2) The ingredient is used in foods at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 52445, Nov. 18, 1983]

§ 184.1230 Calcium sulfate.

(a) Calcium sulfate ($CaSO_4$, CAS Reg. No. 7778–18–9 or $CaSO_4 \cdot 2H_2O$, CAS Reg. No. 10101–41–4), also known as plaster of Paris, anhydrite, and gypsum, occurs naturally and exists as a fine, white to slightly yellow-white odorless powder. The anhydrous form is prepared by complete dehydration of gypsum, below 300 °C, in an electric oven.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), p. 66, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as an anticaking agent as defined in § 170.3(o)(1) of this chapter, color and coloring adjunct as defined in § 170.3(o)(4) of this chapter, dough strengthener as defined in § 170.3(o)(6) of this chapter, drying agent as defined in § 170.3(o)(7) of this chapter, firming agent as defined in § 170.3(o)(10) of this chapter, flour treating agent as defined in § 170.3(o)(13) of this chapter, formulation aid as defined in § 170.3(o)(14) of this chapter, leavening agent as defined in § 170.3(o)(17) of this chapter, nutrient supplement as defined in § 170.3(o)(20) of this chapter, pH control agent as defined in § 170.3(o)(23) of this chapter, processing aid as defined in § 170.3(o)(24) of this chapter, stabilizer and thickener as defined in § 170.3(o)(28) of this chapter, synergist as defined in § 170.3(o)(31) of this chapter, and texturizer as defined in § 170.3(o)(32) of this chapter.

(d) The ingredient is used in food at levels not to exceed good manufacturing practice in accordance with § 184.1(b)(1). Current good manufacturing practice results in a maximum level, as served, of 1.3 percent for baked goods as defined in § 170.3(n)(1) of this chapter, 3.0 percent for confections and frostings as defined in § 170.3(n)(9) of this chapter, 0.5 percent for frozen dairy desserts and mixes as defined in § 170.3(n)(20) of this chapter, 0.4 percent for gelatins and puddings as defined in § 170.3(n)(22) of this chapter, 0.5 percent for grain products and pastas as defined in § 170.3(n)(23) of this chapter, 0.35 percent for processed vegetables as defined in § 170.3(n)(36) of this chapter, and 0.07 percent or less for all other food categories.

(e) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[45 FR 6086, Jan. 25, 1980; 45 FR 26319, Apr. 18, 1980, as amended at 49 FR 5611, Feb. 14, 1984]

§ 184.1240 Carbon dioxide.

(a) Carbon dioxide (empirical formula CO_2, CAS Reg. No. 124–38–9) occurs as a colorless, odorless, noncombustible gas at normal temperatures and pressures. The solid form, dry ice, sublimes under atmospheric pressure at a temperature of −78.5 °C. Carbon dioxide is prepared as a byproduct of the manufacture of lime during the ''burning'' of limestone, from the combustion of carbonaceous material, from fermentation processes, and from gases found in certain natural springs and wells.

(b) The Food and Drug Administration is developing food-grade specifications for carbon dioxide in cooperation with the National Academy of Sciences. In the interim, the ingredient must be of purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitations other than current good

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 28 of 100

manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a leavening agent as defined in § 170.3(o)(17) of this chapter; a processing aid as defined in § 170.3(o)(24) of this chapter; and a propellant, aerating agent, and gas as defined in § 170.3(o)(25) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 57270, Dec. 29, 1983]

§ 184.1245 Beta-carotene.

(a) *Beta*-carotene (CAS Reg. No. 7235–40–7) has the molecular formula $C_{40}H_{56}$. It is synthesized by saponification of vitamin A acetate. The resulting alcohol is either reacted to form vitamin A Wittig reagent or oxidized to vitamin A aldehyde. Vitamin A Wittig reagent and vitamin A aldehyde are reacted together to form *beta*-carotene.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 73, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washingtion, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a nutrient supplement as defined in § 170.3(o)(20) of this chapter.

(2) The ingredient is used in the following foods at levels not to exceed current good manufacturing practice: dairy product analogs as defined in § 170.3(n)(10) of this chapter; fats and oils as defined in § 170.3(n)(12) of this chapter; and processed fruits and fruit juices as defined in § 170.3(n)(35) of this chapter. *Beta*-carotene may be used in infant formula as a source of vitamin A in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act or with regulations promulgated under section 412(g) of the act.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[52 FR 25211, July 6, 1987]

§ 184.1250 Cellulase enzyme preparation derived from Trichoderma longibrachiatum.

(a) Cellulase enzyme preparation is derived from a nonpathogenic, nontoxicogenic strain of *Trichoderma longibrachiatum* (formerly *T. reesei*). The enzyme, cellulase, catalyzes the endohydrolysis of 1,4-beta-glycosidic linkages in cellulose. It is obtained from the culture filtrate resulting from a pure culture fermentation process.

(b) The ingredient meets the general and additional requirements for enzyme preparations in the monograph specifications on enzyme preparations in the ''Food Chemicals Codex,'' 4th ed. (1996), pp. 129 to 134, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Box 285, Washington, DC 20055 (Internet ''http://www.nap.edu''), or may be examined at the Center for Food Safety and Applied Nutrition's Library, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used in food as an enzyme as defined in § 170.3(o)(9) of this chapter for the breakdown of cellulose.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 29 of 100

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

[64 FR 28361, May 26, 1999]

§ 184.1257 Clove and its derivatives.

(a) Cloves are the dried unopened flower buds and calyx tubes, harvested before the flowers have opened, of the clove tree *Eugenia caryophyllata* Thunberg, native to tropical Asia. Their derivatives include essential oils (cloves, CAS Reg. No. 8000–34–8; buds; leaves, CAS Reg. No. 8015–97–2; stems, CAS Reg. No. 8015–98–3; and eugenol, CAS Reg. No. 97–53–0), oleoresins, and natural extractives obtained from clove buds, leaves, and stems.

(b) Clove bud oil, clove leaf oil, clove stem oil, and eugenol meet the specifications of the ''Food Chemicals Codex,'' 4th ed. (1996), pp. 104–105, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, Box 285, 2101 Constitution Ave. NW., Washington, DC 20055 (Internet address ''http://www.nap.edu''), or may be examined at the Center for Food Safety and Applied Nutrition's Library, Food and Drug Administration, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC. As determined by analytical methods in the ''Food Chemicals Codex,'' clove oleoresin or other natural extractives (other than clove oils) meet the ''Food Chemicals Codex'' specifications for clove (clove bud) oil and the following modifications:

(1) The assay for phenols, as eugenol, by the ''Food Chemicals Codex'' test, 4th ed. (pp. 104–105), or the volatile oils content by the ''Food Chemicals Codex'' test, 4th ed. (pp. 104–105) should conform to the representation of the vendor;

(2) Optical rotation of the volatile oil between $^{-}2°$ and 0°;

(3) Refractive index of the volatile oil between 1.527 and 1.538 at 20 °C;

(4) Specific gravity of the volatile oil between 1.036 and 1.060; and

(5) Residual solvent free, except those solvents that are GRAS or within tolerance levels as specified in part 173, subpart C, of this chapter.

(c) Clove and its derivatives are used as flavoring agents and adjuvants as defined in § 170.3(0)(12) of this chapter.

(d) The ingredients are used in food at levels not to exceed good manufacturing practice in accordance with § 184.1(b)(1).

(e) Prior sanctions for these ingredients different from the uses established in this section do not exist or have been waived.

[44 FR 3964, Jan 19, 1979, as amended at 47 FR 11852, Mar. 19, 1982; 49 FR 5611, Feb. 14, 1984; 64 FR 1759, Jan. 12, 1999]

§ 184.1259 Cocoa butter substitute.

(a) The common or usual name for the triglyceride 1-palmitoyl-2-oleoyl-3-stearin is ''cocoa butter substitute primarily from palm oil.'' The common or usual name for the triglyceride 1-3-distearoyl-2-olein is ''cocoa butter substitute primarily from high-oleic safflower or sunflower oil.''

(1) The ingredient 1-palmitoyl-2-oleoyl-3-stearin is manufactured by:

(i) Directed esterification of fully saturated 1,3-diglycerides (derived from palm oil) with the anhydride of food-grade oleic acid in the presence of the catalyst trifluoromethane sulfonic acid (§ 173.395 of this chapter), or

(ii) By interesterification of partially saturated 1,2,3-triglycerides (derived from palm oil) with ethyl stearate in the presence of a suitable lipase enzyme preparation that is either generally recognized as safe (GRAS) or has food additive approval for such use.

(2) The ingredient 1-3-distearoyl-2-olein is manufactured by interesterification of partially unsaturated 1,2,3-triglycerides (derived from high-oleic safflower or sunflower oil) with ethyl stearate or stearic acid in the presence of a suitable lipase enzyme preparation that is either GRAS or has food additive approval for such use.

(b) The ingredient meets the following specifications:

(1) Over 90 percent triglycerides, not more than 7 percent diglycerides, not more than 1 percent monoglycerides, and not more than 1 percent free fatty acids.

(2) Total glycerides—98 percent minimum.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 30 of 100

(3) Heavy metals (as lead), not more than 10 milligrams per kilogram, as determined by the Heavy Metals Test of the ''Food Chemicals Codex,'' 4th ed. (1996), pp. 760–761, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, Box 285, 2101 Constitution Ave. NW., Washington, DC 20055 (Internet address ''http://www.nap.edu''), or may be examined at the Center for Food Safety and Applied Nutrition's Library, Food and Drug Administration, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(4) Color—clear, bright, and free from suspended matter.

(5) Odor and taste—free from foreign and rancid odor and taste.

(6) Residual catalyst (''Official Methods of Analysis of the Association of Official Analytical Chemists,'' 13th Ed. (1980), sections 25.049–25.055, which is incorporated by reference), residual fluorine; limit of detection 0.2 part per million F; multiply fluoride result by 2.63 to convert to residual catalyst. Copies of the material incorporated by reference may be obtained from the Association of Official Analytical Chemists, P.O. Box 540, Benjamin Franklin Station, Washington, DC 20044, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408. The ingredient shall be washed three times in batches with 0.5 percent sodium bicarbonate to remove catalyst residuals in accordance with good manufacturing practice.

(7) Residual methanol—5 parts per million maximum.

(8) Residual fatty acid ethyl esters—not more than 20 parts per million as determined by a ''Modification of Japan Institute of Oils and Fats: Analysis Method of Residual Ethyl Esters of Fatty Acids'' issued by the Fuji Oil Co., which is incorporated by reference. Copies are available from the Division of Food and Color Additives, Center for Food Safety and Applied Nutrition (HFS–200), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(9) Hexane—not more than 5 parts per million as determined by the method of Dupuy et al., ''Rapid Quantitative Determination of Residual Hexane in Oils by Direct Gas Chromatography,'' published in the ''Journal of the American Oil Chemists' Society,'' Vol. 52, p. 118–120, 1975, which is incorporated by reference. Copies are available from the Division of Food and Color Additives, Center for Food Safety and Applied Nutrition (HFS–200), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in the following food categories at levels not to exceed current good manufacturing practice: Confections and frostings as defined in § 170.3(n)(9) of this chapter; coatings of soft candy as defined in §170.3(n)(38) of this chapter; and sweet sauces and toppings as defined in §170.3(n)(43) of this chapter; except that the ingredient may not be used in a standardized food unless permitted by the standard of identity.

(d) The ingredient is used in food in accordance with § 184.1(b)(1) at levels not to exceed good manufacturing practice.

[43 FR 54239, Nov. 11, 1978, as amended at 47 FR 11852, Mar. 19, 1982; 49 FR 5611, Feb. 14, 1984; 49 FR 22799, June 1, 1984; 52 FR 47920, Dec. 17, 1987; 52 FR 48905, Dec. 28, 1987; 61 FR 36290, July 10, 1996; 64 FR 1760, Jan. 12, 1999]

§ 184.1260 Copper gluconate.

(a) Copper gluconate (cupric gluconate $(CH_2OH(CHOH)_4COO)_2Cu$, CAS Reg. No. 527–09–3) is a substance that occurs as light blue to bluish-green, odorless crystals, or as a fine, light blue powder. It is prepared by the reaction of gluconic acid solutions with cupric oxide or basic cupric carbonate.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 90, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC. 20418, or available for inspection at the Office of the Federal

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 31 of 100

Register, 800 North Capitol Street, NW., suite 700, Washington, DC. 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a nutrient supplement as defined in § 170.3(o)(20) of this chapter and as a synergist as defined in § 170.3(o)(31) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice. Copper gluconate may be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the Act) or with regulations promulgated under section 412(a)(2) of the Act.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[49 FR 24119, June 12, 1984]

§ 184.1261 Copper sulfate.

(a) Copper sulfate (cupric sulfate, $CuSO_4 \cdot 5H_2O$, CAS Reg. No. 7758–98–7) usually is used in the pentahydrate form. This form occurs as large, deep blue or ultramarine, triclinic crystals; as blue granules, or as a light blue powder. The ingredient is prepared by the reaction of sulfuric acid with cupric oxide or with copper metal.

(b) FDA is developing food-grade specifications for copper sulfate in cooperation with the National Academy of Sciences. In the interim, this ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a nutrient supplement as defined in § 170.3(o)(20) of this chapter and as a processing aid as defined in § 170.3(o)(24) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice. Copper sulfate may be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the Act) or with regulations promulgated under section 412(a)(2) of the Act.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[49 FR 24119, June 12, 1984]

§ 184.1262 Corn silk and corn silk extract.

(a) Corn silk is the fresh styles and stigmas of *Zea mays* L. collected when the corn is in milk. The filaments are extracted with dilute ethanol to produce corn silk extract. The extract may be concentrated at a temperature not exceeding 60 °C.

(b) The Food and Drug Administration, in cooperation with the National Academy of Sciences, is developing food-grade specifications for corn silk and corn silk extract. In the interim, this ingredient must be of a suitable purity for its intended use.

(c) In accordance with § 184.1(b)(2), the ingredients are used in food only within the following specific limitations:

Category of food	Maximum level of use in food (as served)[1]	Functional use
Baked goods and baking mixes, § 170.3(n)(1) of this chapter.	30	Flavoring agent, § 170.3(o)(12) of this chapter.
Nonalcoholic beverages, § 170.3(n)(3) of this chapter.	20	Do.
Frozen dairy desserts, § 170.3(n)(20) of this chapter.	10	Do.
Soft candy, § 170.3(n)(38) of this chapter.	20	Do.
All other food categories.	4	Do.

[1] Parts per million.

(d) Prior sanctions for this ingredient different from the uses established in

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 32 of 100

this section do not exist or have been waived.

[47 FR 29953, July 9, 1982]

§ 184.1265 Cuprous iodide.

(a) Cuprous iodide (copper (I) iodide, CuI, CAS Reg. No. 7681–65–4) is a pure white crystalline powder. It is prepared by the reaction of copper sulfate with potassium iodide under slightly acidic conditions.

(b) FDA is developing food-grade specifications for cuprous iodide in cooperation with the National Academy of Sciences. In the interim, this ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(2), the ingredient is used in food only within the following specific limitations:

Category of food	Maximum treatment level in food	Functional use
Table salt.	0.01 percent	Source of dietary iodine.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[49 FR 24119, June 12, 1984]

§ 184.1271 L-Cysteine.

(a) L-Cysteine is the chemical L-2-amino-3-mercaptopropanoic acid ($C_3H_7O_2NS$).

(b) The ingredient meets the appropriate part of the specification set forth in the ''Food Chemicals Codex,'' 3d Ed. (1981), pp. 92–93, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used to supply up to 0.009 part of total L-cysteine per 100 parts of flour in dough as a dough strengthener as defined in § 170.3(o)(6) of this chapter in yeast-leavened baked goods and baking mixes as defined in § 170.3(n)(1) of this chapter.

(d) This regulation is issued prior to a general evaluation of use of this ingredient in order to affirm as GRAS the specific use named.

[42 FR 14653, Mar. 15, 1977, as amended at 49 FR 5612, Feb. 14, 1984]

§ 184.1272 L-Cysteine monohydrochloride.

(a) L-Cysteine monohydrochloride is the chemical L-2-amino-3-mercaptopropanoic acid monohydrochloride monohydrate ($C_3H_7O_2NS\ HCl\ H_2O$).

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), pp. 92–93, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used to supply up to 0.009 part of total L-cysteine per 100 parts of flour in dough as a dough strengthener as defined in § 170.3(o)(6) of this chapter in yeast-leavened baked goods and baking mixes as defined in § 170.3(n)(1) of this chapter.

(d) This regulation is issued prior to a general evaluation of use of this ingredient in order to affirm as GRAS the specific use named.

[42 FR 14653, Mar. 15, 1977, as amended at 49 FR 5612, Feb. 14, 1984]

§ 184.1277 Dextrin.

(a) Dextrin ($(C_6H_{10}O_5)_n \cdot H_2O$, CAS Reg. No. 9004–53–9) is an incompletely hydrolyzed starch. It is prepared by dry heating corn, waxy maize, waxy milo, potato, arrowroot, wheat, rice, tapioca, or sago starches, or by dry heating the starches after: (1) Treatment with safe and suitable alkalis, acids, or pH control agents and (2) drying the acid or alkali treated starch.

(b) The ingredient meets the specification of the Food Chemicals Codex, 3d Ed. (1981), p. 96, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 33 of 100

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a formulation aid as defined in § 170.3(o)(14) of this chapter; as a processing aid as defined in § 170.3(o)(24) of this chapter; as a stabilizer and thickener as defined in § 170.3(o)(28) of this chapter; and as a surface-finishing agent as defined in § 170.3(o)(30) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 51909, Nov. 15, 1983]

§ 184.1278 Diacetyl.

(a) Diacetyl ($C_4H_6O_2$, CAS Reg. No. 431–03–8) is a clear yellow to yellowish green liquid with a strong pungent odor. It is also known as 2,3-butanedione and is chemically synthesized from methyl ethyl ketone. It is miscible in water, glycerin, alcohol, and ether, and in very dilute water solution, it has a typical buttery odor and flavor.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 368, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 51907, Nov. 15, 1983]

§ 184.1282 Dill and its derivatives.

(a) Dill (American or European) is the herb and seeds from *Anethum graveolens* L., and dill (Indian) is the herb and seeds from *Anethum sowa*, D.C. Its derivatives include essential oils, oleoresins, and natural extractives obtained from these sources of dill.

(b) Dill oils meet the description and specifications of the ''Food Chemicals Codex,'' 4th ed. (1996), pp. 122–123, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, Box 285, 2101 Constitution Ave. NW., Washington, DC 20055 (Internet address ''http://www.nap.edu''), or may be examined at the Center for Food Safety and Applied Nutrition's Library, Food and Drug Administration, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) Dill and its derivatives are used as flavoring agents and adjuvants as defined in § 170.3(o)(12) of this chapter.

(d) The ingredients are used in food at levels not to exceed good manufacturing practice.

(e) [Reserved]

(f) Prior sanctions for these ingredients different from the uses established in this section do not exist or have been waived.

[42 FR 14653, Mar. 15, 1977, as amended at 42 FR 55205, Oct. 14, 1977; 49 FR 5612, Feb. 14, 1984; 64 FR 1760, Jan. 12, 1999]

§ 184.1287 Enzyme-modified fats.

(a) Enzyme-modified refined beef fat, enzyme-modified butterfat, and enzyme-modified steam-rendered chicken fat are prepared from refined beef fat; butterfat or milkfat; and steam-rendered chicken fat, respectively, with enzymes that are generally recognized as safe (GRAS). Enzyme-modified milk powder may be prepared with GRAS

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 34 of 100

enzymes from reconstituted milk powder, whole milk, condensed or concentrated whole milk, evaporated milk, or milk powder. The lipolysis is maintained at a temperature that is optimal for the action of the enzyme until appropriate acid development is attained. The enzymes are then inactivated. The resulting product is concentrated or dried.

(b) FDA is developing food-grade specifications for these enzyme-modified ingredients in cooperation with the National Academy of Sciences. In the interim, the ingredients must be of purity suitable for their intended use.

(c) In accordance with § 184.1(b)(1), the ingredients are used in food with no limitation other than current good manufacturing practice. The affirmation of these ingredients as generally recognized as safe (GRAS) as direct human food ingredients is based upon the following current good manufacturing practice conditions of use:

(1) The ingredients are used as flavoring agents and adjuvants as defined in § 170.3(o)(12) of this chapter.

(2) The ingredients are used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for these ingredients different from the uses established in this section do not exist or have been waived.

[52 FR 25976, July 10, 1987]

§ 184.1293 Ethyl alcohol.

(a) Ethyl alcohol (ethanol) is the chemical C_2H_5OH.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 4th ed. (1996), p. 136, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, Box 285, 2101 Constitution Ave. NW., Washington, DC 20055 (Internet address ''http://www.nap.edu''), or may be examined at the Center for Food Safety and Applied Nutrition's Library, Food and Drug Administration, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) The ingredient is used as an antimicrobial agent as defined in § 170.3(o)(2) of this chapter on pizza crusts prior to final baking at levels not to exceed 2.0 percent by product weight.

(d) This regulation is issued prior to general evaluation of use of this ingredient in order to affirm as GRAS the specific use named.

[42 FR 14653, Mar. 15, 1977, as amended at 49 FR 5612, Feb. 14, 1984; 64 FR 1760, Jan. 12, 1999]

§ 184.1295 Ethyl formate.

(a) Ethyl formate ($C_3H_6O_2$, CAS Reg. No. 109–94–4) is also referred to as ethyl methanoate. It is an ester of formic acid and is prepared by esterification of formic acid with ethyl alcohol or by distillation of ethyl acetate and formic acid in the presence of concentrated sulfuric acid. Ethyl formate occurs naturally in some plant oils, fruits, and juices but does not occur naturally in the animal kingdom.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), p. 376, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter.

(d) The ingredient is used in food at levels not to exceed good manufacturing practice in accordance with § 184.1(b)(1). Current good manufacturing practice results in a maximum level, as served, of 0.05 percent in baked goods as defined in § 170.3(n)(1) of this chapter; 0.04 percent in chewing gum as defined in § 170.3(n)(6), hard candy as defined in § 170.3(n)(25), and soft candy as defined in § 170.3(n)(38) of this chapter; 0.02 percent in frozen dairy desserts as defined in § 170.3(n)(20) of this chapter; 0.03 percent in gelatins, puddings, and fillings as defined in § 170.3(n)(22) of this chapter; and 0.01 percent in all other food categories.

(e) Prior sanctions for ethyl formate different from the uses established in this section do not exist or have been waived.

[45 FR 22915, Apr. 4, 1980, as amended at 49 FR 5612, Feb. 14, 1984]

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 35 of 100

§ 184.1296 Ferric ammonium citrate.

(a) Ferric ammonium citrate (iron (III) ammonium citrate) is prepared by the reaction of ferric hydroxide with citric acid, followed by treatment with ammonium hydroxide, evaporating, and drying. The resulting product occurs in two forms depending on the stoichiometry of the initial reactants.

(1) Ferric ammonium citrate (iron (III) ammonium citrate, CAS Reg. No. 1332–98–5) is a complex salt of undetermined structure composed of 16.5 to 18.5 percent iron, approximately 9 percent ammonia, and 65 percent citric acid and occurs as reddish brown or garnet red scales or granules or as a brownish-yellowish powder.

(2) Ferric ammonium citrate (iron (III) ammonium citrate, CAS Reg. No. 1333–00–2) is a complex salt of undetermined structure composed of 14.5 to 16 percent iron, approximately 7.5 percent ammonia, and 75 percent citric acid and occurs as thin transparent green scales, as granules, as a powder, or as transparent green crystals.

(b) The ingredients meet the specifications of the Food Chemicals Codex, 3d Ed. (1981), pp. 116–117 (Ferric ammonium citrate, brown) and p. 117 (Ferric ammonium citrate, green), which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredients are used in food as nutrient supplements as defined in § 170.3(o)(20) of this chapter, with no limitation other than current good manufacturing practice. The ingredients may also be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 350a(g)) or with regulations promulgated under section 412(a)(2) of the act (21 U.S.C. 350a(a)(2)).

(d) Prior sanctions for these ingredients different from the uses established in this section do not exist or have been waived.

[53 FR 16864, May 12, 1988]

§ 184.1297 Ferric chloride.

(a) Ferric chloride (iron (III) chloride, $FeC1_3$, CAS Reg. No. 7705–08–0) may be prepared from iron and chlorine or from ferric oxide and hydrogen chloride. The pure material occurs as hydroscopic, hexagonal, dark crystals. Ferric chloride hexahydrate (iron (III) chloride hexahydrate, $FeC1_3$, $6H_20$, CAS Reg. No. 10025–77–1) is readily formed when ferric chloride is exposed to moisture.

(b) The Food and Drug Administration is developing food-grade specifications for ferric chloride in cooperation with the National Academy of Sciences. In the interim, this ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1) the ingredient is used in food as a flavoring agent as defined in § 170.3(o)(12) of this chapter, with no limitation other than current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[53 FR 16864, May 12, 1988]

§ 184.1298 Ferric citrate.

(a) Ferric citrate (iron (III) citrate, $C_6H_5FeO_7$, CAS Reg. No. 2338–05–8) is prepared from reaction of citric acid with ferric hydroxide. It is a compound of indefinite ratio of citric acid and iron.

(b) The Food and Drug Administration is developing food-grade specifications for ferric citrate in cooperation with the National Academy of Sciences. In the interim, this ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food as a nutrient supplement as defined in § 170.3(o)(20) of this chapter, with no limitation other than current good manufacturing practice. The ingredient may also be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 350a(g)) or with regulations promulgated under section 412(a)(2) of the act (21 U.S.C. 350a(a)(2)).

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 36 of 100

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[53 FR 16865, May 12, 1988]

§ 184.1301 Ferric phosphate.

(a) Ferric phosphate (ferric orthophosphate, iron (III) phosphate, $FePO_4 \cdot xH_2O$, CAS Reg. No. 10045–86–0) is an odorless, yellowish-white to buff-colored powder and contains from one to four molecules of water of hydration. It is prepared by reaction of sodium phosphate with ferric chloride or ferric citrate.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), pp. 118–120, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food as nutrient supplement as defined in § 170.3(o)(20) of this chapter, with no limitation other than current good manufacturing practice. The ingredient may also be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 350a(g)) or with regulations promulgated under section 412(a)(2) of the act (21 U.S.C. 350a(a)(2)).

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[53 FR 16865, May 12, 1988]

§ 184.1304 Ferric pyrophosphate.

(a) Ferric pyrophosphate (iron (III) pyrophosphate, $Fe_4(P_{207})_3 \cdot xH_2O$, CAS Reg. No. 10058–44–3) is a tan or yellowish white colorless powder. It is prepared by reacting sodium pyrophosphate with ferric citrate.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 120, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food as a nutrient supplement as defined in § 170.3(o)(20) of this chapter, with no limitation other than current good manufacturing practice. The ingredient may also be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 350a(g)) or with regulations promulgated under section 412(a)(2) of the act (21 U.S.C. 350a(a)(2)).

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[53 FR 16865, May 12, 1988; 53 FR 20939, June 7, 1988]

§ 184.1307 Ferric sulfate.

(a) Ferric sulfate (iron (III) sulfate, $Fe_2(SO_4)_3$, CAS Reg. No. 10028–22–5) is a yellow substance that may be prepared by oxidizing iron (II) sulfate or by treating ferric oxide or ferric hydroxide with sulfuric acid.

(b) The Food and Drug Administration is developing food-grade specifications for ferric sulfate in cooperation with the National Academy of Sciences. In the interim, this ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food as a flavoring agent as defined in § 170.3(o)(12) of this chapter, with no limitation other than current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[53 FR 16865, May 12, 1988]

§ 184.1307a Ferrous ascorbate.

(a) Ferrous ascorbate (CAS Reg. No. 14536–17–5) is a reaction product of ferrous hydroxide and ascorbic acid. It is a blue-violet product containing 16 percent iron.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 37 of 100

(b) The Food and Drug Administration is developing food-grade specifications for ferrous ascorbate in cooperation with the National Academy of Sciences. In the interim, this ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food as a nutrient supplement as defined in § 170.3(o)(20) of this chapter, with no limitation other than current good manufacturing practice. The ingredient may also be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 350a(g)) or with regulations promulgated under section 412(a)(2) of the act (21 U.S.C. 350a(a)(2)).

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[53 FR 16865, May 12, 1988]

§ 184.1307b Ferrous carbonate.

(a) Ferrous carbonate (iron (II) carbonate, $FeCO_3$, CAS Reg. No. 563–71–3) is an odorless, white solid prepared by treating solutions of iron (II) salts with alkali carbonate salts.

(b) The Food and Drug Administration is developing food-grade specifications for ferrous carbonate in cooperation with the National Academy of Sciences. In the interim, this ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food as a nutrient supplement as defined in § 170.3(o)(20) of this chapter, with no limitation other than current good manufacturing practice. The ingredient may also be used in infant formula in accordance with section 412(g) of the Federal Foods, Drug, and Cosmetic Act (the act) (21 U.S.C. 350a(g)) or with regulations promulgated under section 412(a)(2) of the act (21 U.S.C. 350a(a)(2)).

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[53 FR 16865, May 12, 1988]

§ 184.1307c Ferrous citrate.

(a) Ferrous citrate (iron (II) citrate, ($C_6H_6FeO_7$), CAS Reg. No. 23383–11–1) is a slightly colored powder or white crystals. It is prepared from the reaction of sodium citrate with ferrous sulfate or by direct action of citric acid on iron filings.

(b) The Food and Drug Administration is developing food-grade specifications for ferrous citrate in cooperation with the National Academy of Sciences. In the interim, this ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1) the ingredient is used in food as a nutrient supplement as defined in § 170.3(o)(20) of this chapter, with no limitation other than current good manufacturing practice. The ingredient may also be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 350a(g)) or with regulations promulgated under section 412(a)(2) of the act (21 U.S.C. 350a(a)(2)).

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[53 FR 16866, May 12, 1988]

§ 184.1307d Ferrous fumarate.

(a) Ferrous fumarate (iron (II) fumarate, ($C_4H_2FeO_4$), CAS Reg. No. 141–01–5) is an odorless, reddish-orange to reddish-brown powder. It may contain soft lumps that produce a yellow streak when crushed. It is prepared by admixing hot solutions of ferrous sulfate and sodium fumarate.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), pp. 120–122, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1) the ingredient is used in food as a nutrient supplement as defined in § 170.3(o)(20) of this chapter, with no limitation other than current good manufacturing practice. The ingredient may also be used

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 38 of 100

in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 350a(g)), or with regulations promulgated under section 412(a)(2) of the act (21 U.S.C. 350a(a)(2)).

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[53 FR 16866, May 12, 1988]

§ 184.1308 Ferrous gluconate.

(a) Ferrous gluconate (iron (II) gluconate dihydrate, $C_{12}H_{22}FeO_{14}\cdot 2H_2O$, CAS Reg. No. 6047-12-7) is a fine yellowish-gray or pale greenish-yellow powder or granules. It is prepared by reacting hot solutions of barium or calcium gluconate with ferrous sulfate or by heating freshly prepared ferrous carbonate with gluconic acid in aqueous solution.

(b) The ingredient meets the specifications of the Food Chemcials Codex, 3d Ed. (1981), pp. 122–123, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Avenue NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food as a nutrient supplement as defined in § 170.3(o)(20) of this chapter, with no limitation other than current good manufacturing practice. The ingredient may also be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 350a(g)) or with regulations promulgated under section 412(a)(2) of the act (21 U.S.C. 350a(a)(2)).

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[53 FR 16866, May 12, 1988; 53 FR 20939, June 7, 1988]

§ 184.1311 Ferrous lactate.

(a) Ferrous lactate (iron (II) lactate, $C_6H_{10}FeO_6$, CAS Reg. No. 5905–52–2) in the trihydrate form is a greenish-white powder or crystalline mass. It is prepared by reacting calcium lactate or sodium lactate with ferrous sulfate, direct reaction of lactic acid with iron filings, reaction of ferrous chloride with sodium lactate, or reaction of ferrous sulfate with ammonium lactate.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 4th ed. (1996), pp. 154 to 155, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Center for Food Safety and Applied Nutrition's library, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food as a nutrient supplement as defined in § 170.3(o)(20) of this chapter and as a color fixative for ripe olives, with no other limitation other than current good manufacturing practice. The ingredient may also be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 350a(g)) or with regulations promulgated under section 412(a)(2) of the act (21 U.S.C. 350a(a)(2)).

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[53 FR 16866, May 12, 1988, as amended at 61 FR 40319, Aug. 2, 1996]

§ 184.1315 Ferrous sulfate.

(a) Ferrous sulfate heptahydrate (iron (II) sulfate heptahydrate, $FeSO_4\cdot 7H_2O$, CAS Reg. No. 7782–63–0) is prepared by the action of sulfuric acid on iron. It occurs as pale, bluish-green crystals or granules. Progressive heating of ferrous sulfate heptahydrate produces ferrous sulfate (dried). Ferrous sulfate (dried) consists primarily of ferrous sulfate monohydrate (CAS Reg. No. 17375–41–6) with varying amounts of ferrous sulfate tetrahydrate (CAS Reg. No. 20908–72–9) and occurs as a grayish-white to buff-colored powder.

(b) The ingredients meet the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 123 (Ferrous sulfate

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 39 of 100

heptahydrate) and p. 124 (ferrous sulfate, dried), which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave., NW., Washington, DC 20418, or available for inspection at the Office of Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredients are used in food as nutrient supplements as defined in § 170.3(o)(20) of this chapter and as a processing aid as defined in § 170.3(o)(24) of this chapter, with no limitation other than current good manufacturing practice. The ingredients may also be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 350a(g)) or with regulations promulgated under section 412(a)(2) of the act (21 U.S.C. 350a(a)(2)).

(d) Prior sanctions for these ingredients different from the uses established in this section do not exist or have been waived.

[53 FR 16866, May 12, 1988]

§ 184.1316 Ficin.

(a) Ficin (CAS Reg. No. 9001–33–6) is an enzyme preparation obtained from the latex of species of the genus *Ficus*, which include a variety of tropical fig trees. It is a white to off-white powder. Its characterizing enzyme activity is that of a peptide hydrolase (EC 3.4.22.3).

(b) The ingredient meets the general requirements and additional requirements for enzyme preparations in the Food Chemicals Codex, 3d ed. (1981), p. 110, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave., NW., Washington, DC 20418, or may be examined at the Office of Premarket Approval (HFS–200), Food and Drug Administration, 200 C St., SW., Washington, DC, and the Office of the Federal Register, 800 North Capitol St., NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as GRAS as a direct food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an enzyme as defined in § 170.3(o)(9) of this chapter to hydrolyze proteins or polypeptides.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

[60 FR 32910, June 26, 1995]

§ 184.1317 Garlic and its derivatives.

(a) Garlic is the fresh or dehydrated bulb or cloves obtained from *Allium sativum*, a genus of the lily family. Its derivatives include essential oils, oleoresins, and natural extractives obtained from garlic.

(b) Garlic oil meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), p. 132, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) Garlic and its derivatives are used as flavoring agents and adjuvants as defined in § 170.3(o)(12) of this chapter.

(d) The ingredients are used in food at levels not to exceed good manufacturing practice.

(e) [Reserved]

(f) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[42 FR 14653, Mar. 15, 1977, as amended at 42 FR 55205, Oct. 14, 1977; 49 FR 5612, Feb. 14, 1984]

§ 184.1318 Glucono delta-lactone.

(a) Glucono delta-lactone ($C_6H_{10}O_6$, CAS Reg. No. 90–80–2), also called *D*-gluconic acid delta-lactone or *D*-glucono-1,5-lactone, is the cyclic 1,5-intramolecular ester of *D*-gluconic acid. It is prepared by direct crystallization from the aqueous solution of gluconic acid. Gluconic acid may be produced by the oxidation of *D*-glucose with bromine water, by the oxidation of *D*-glucose by microorganisms that are nonpathogenic and nontoxicogenic

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 40 of 100

to man or other animals, or by the oxidation of *D*-glucose with enzymes derived from these microorganisms.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 134, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a curing and pickling agent as defined in § 170.3(o)(5) of this chapter, leavening agent as defined in § 170.3(o)(17) of this chapter; pH control agent as defined in § 170.3(o)(23) of this chapter; and sequestrant as defined in § 170.3(o)(26) of this chapter.

(2) The ingredient is used at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[51 FR 33896, Sept. 24, 1986]

§ 184.1321 Corn gluten.

(a) Corn gluten (CAS Reg. No. 66071–96–3), also known as corn gluten meal, is the principal protein component of corn endosperm. It consists mainly of zein and glutelin. Corn gluten is a byproduct of the wet milling of corn for starch. The gluten fraction is washed to remove residual water soluble proteins. Corn gluten is also produced as a byproduct during the conversion of the starch in whole or various fractions of dry milled corn to corn syrups.

(b) FDA is developing food-grade specifications for corn gluten in cooperation with the National Academy of Sciences. In the interim, the ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a nutrient supplement as defined in § 170.3(o)(20) of this chapter and a texturizer as defined in § 170.3(o)(32) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[50 FR 8998, Mar. 6, 1985]

§ 184.1322 Wheat gluten.

(a) Wheat gluten (CAS Reg. No. 8002–80–0) is the principal protein component of wheat and consists mainly of gliadin and glutenin. Wheat gluten is obtained by hydrating wheat flour and mechanically working the sticky mass to separate the wheat gluten from the starch and other flour components. Vital gluten is dried gluten that has retained its elastic properties.

(b) FDA is developing food-grade specifications for wheat gluten in cooperation with the National Academy of Sciences. In the interim, the ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a dough strengthener as defined in § 170.3(o)(6) of this chapter; a formulation aid as defined in § 170.3(o)(14) of this chapter; a nutrient supplement as defined in § 170.3(o)(20) of this chapter; a processing aid as defined in § 170.3(o)(24) of this chapter; a stabilizer and thickener as defined in § 170.3(o)(28) of this chapter; a surface-finishing agent as defined

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 41 of 100

in § 170.3(o)(30) of this chapter; and a texturizing agent as defined in § 170.3(o)(32) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[50 FR 8998, Mar. 6, 1985]

§ 184.1323 Glyceryl monooleate.

(a) Glyceryl monooleate is prepared by esterification of commerical oleic acid that is derived either from edible sources or from tall oil fatty acids meeting the requirements of § 172.862 of this chapter. It contains glyceryl monooleate ($C_{21}H_{40}O_4$, CAS Reg. No. 25496–72–4) and glyceryl esters of fatty acids present in commercial oleic acid.

(b) FDA is developing food-grade specifications for glyceryl monooleate in cooperation with the National Academy of Sciences. In the interim, this ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter and as a solvent and vehicle as defined in § 170.3(o)(27) of this chapter.

(2) The ingredient is used in the following foods at levels not to exceed current good manufacturing practice: baked goods and baking mixes as defined in § 170.3(n)(1) of this chapter; nonalcoholic beverages and beverage bases as defined in § 170.3(n)(3) of this chapter; chewing gum as defined in § 170.3(n)(6) of this chapter; and meat products as defined in § 170.3(n)(29) of this chapter.

(d) Prior sanctions for this ingredient different from the use established in this section do not exist or have been waived.

[54 FR 7403 Feb. 21, 1989]

§ 184.1324 Glyceryl monostearate.

(a) Glyceryl monostearate, also known as monostearin, is a mixture of variable proportions of glyceryl monostearate ($C_{21}H_{42}O_4$, CAS Reg. No. 31566–31–1), glyceryl monopalmitate ($C_{19}H_{38}O_4$, CAS Reg. No. 26657–96–5) and glyceryl esters of fatty acids present in commercial stearic acid. Glyceryl monostearate is prepared by glycerolysis of certain fats or oils that are derived from edible sources or by esterification, with glycerin, of stearic acid that is derived from edible sources.

(b) FDA is developing food-grade specifications for glyceryl monostearate in cooperation with the National Academy of Sciences. In the interim, this ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not not exist or have been waived.

[54 FR 7403 Feb. 21, 1989]

§ 184.1328 Glyceryl behenate.

(a) Glyceryl behenate is a mixture of glyceryl esters of behenic acid made from glycerin and behenic acid (a saturated C_{22} fatty acid). The mixture contains predominately glyceryl dibehenate.

(b) The ingredient meets the following specifications:

(1) 10 to 20 percent monoglyceride, 47 to 59 percent diglyceride, 26 to 38 percent triglyceride, and not more than 2.5 percent free fatty acids.

(2) *Behenic acid.* Between 80 and 90 percent of the total fatty acid content.

(3) *Acid value.* Not more than 4.

(4) *Saponification value.* Between 145 and 165.

(5) *Iodine number.* Not more than 3.

(6) *Heavy metals (as Pb).* Not more than 10 parts per million.

(c) In accordance with § 184.1(b)(1) of this chapter, the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient is generally recognized as safe (GRAS) as a

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 42 of 100

direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a formulation aid, as defined in § 170.3(o)(14) of this chapter.

(2) The ingredient is used in excipient formulations for use in tablets at levels not to exceed good manufacturing practice.

[52 FR 42430, Nov. 5, 1987]

§ 184.1329 Glyceryl palmitostearate.

(a) Glyceryl palmitostearate is a mixture of mono-, di-, and triglyceryl esters of palmitic and stearic acids made from glycerin, palmitic acid, and stearic acid.

(b) The ingredient meets the following specifications:

(1) The substance is a mixture of mono-, di-, and triglycerides of palmitic acid and stearic acid.

(2) Heavy metals (as lead): Not more than 10 parts per million.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a formulation aid, as defined in § 170.3(o)(14) of this chapter.

(2) The ingredient is used in excipient formulations for use in tablets at levels not to exceed good manufacturing practice.

[60 FR 63621, Dec. 12, 1995]

§ 184.1330 Acacia (gum arabic).

(a) Acacia (gum arabic) is the dried gummy exudate from stems and branches of trees of various species of the genus *Acacia,* family Leguminosae.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), p. 7, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used in food under the following conditions:

MAXIMUM USAGE LEVELS PERMITTED

Food (as served)	Percent	Function
Beverages and beverage bases, § 170.3(n)(3) of this chapter.	2.0	Emulsifier and emulsifier salt, § 170.3(o)(8) of this chapter; flavoring agent and adjuvant, § 170.3(o)(12) of this chapter; formulation aid, § 170.3(o)(14) of this chapter; stabilizer and thickener, § 170.3(o)(28) of this chapter.
Chewing gum, § 170.3(n)(6) of this chapter	5.6	Flavoring agent and adjuvant, § 170.3(o)(12) of this chapter; formulation aid, § 170.3(o)(14) of this chapter; humectant, § 170.3(o)(16) of this chapter; surface-finishing agent, § 170.3(o)(30) of this chapter.
Confections and frostings, § 170.3(n)(9) of this chapter.	12.4	Formulation aid, § 170.3(o)(14) of this chapter; stabilizer and thickener, § 170.3(o)(28) of this chapter; surface-finishing agent, § 170.3(o)(30) of this chapter.
Dairy product analogs, § 170.3(n)(10) of this chapter	1.3	Formulation aid, § 170.3(o)(14) of this chapter; stabilizer and thickener, § 170.3(o)(28) of this chapter.
Fats and oils, § 170.3(n)(12) of this chapter	1.5	Formulation aid, § 170.3(o)(14) of this chapter; stabilizer and thickener, § 170.3(o)(28) of this chapter.
Gelatins, puddings, and fillings, § 170.3(n)(22) of this chapter.	2.5	Emulsifier and emulsifier salt, § 170.3(o)(8) of this chapter; formulation aid, § 170.3(o)(14) of this chapter.; stabilizer and thickener, § 170.3(o)(28) of this chapter.
Hard candy and cough drops, § 170.3(n)(25) of this chapter.	46.5	Flavoring agent and adjuvant, § 170.3(o)(12) of this chapter; formulation aid, § 170.3(o)(14) of this chapter.
Nuts and nut products, § 170.3(n)(32) of this chapter	8.3	Formulation aid, § 170.3(o)(14) of this chapter; surface-finishing agent, § 170.3(o)(30) of this chapter.
Quiescently frozen confection products	6.0	Formulation aid, § 170.3(o)(14) of this chapter; stabilizer and thickener, § 170.3(o)(28) of this chapter.
Snack foods, § 170.3(n)(37) of this chapter	4.0	Emulsifier and emulsifier salt, § 170.3(o)(8) of this chapter; formulation aid, § 170.3(o)(14) of this chapter.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 43 of 100

MAXIMUM USAGE LEVELS PERMITTED—Continued

Food (as served)	Percent	Function
Soft candy, § 170.3(n)(38) of this chapter	85.0	Emulsifier and emulsifier salt, § 170.3(o)(8) of this chapter; firming agent, § 170.3(o)(10) of this chapter; flavoring agent and adjuvant, § 170.3(o)(12) of this chapter; formulation aid, § 170.3(o)(14) of this chapter, humectant, § 170.3(o)(16) of this chapter; stabilizer and thickener, § 170.3(o)(28) of this chapter; surface-finishing agent, § 170.3(o)(30) of this chapter.
All other food categories	1.0	Emulsifier and emulsifier salt, § 170.3(o)(8) of this chapter; flavoring agent and adjuvant, § 170.3(o)(12) of this chapter; formulation aid, § 170.3(o)(14) of this chapter; processing aid, § 170.3(o)(24) of this chapter; stabilizer and thickener, § 170.3(o)(28) of this chapter; surface-finishing agent, § 170.3(o)(30) of this chapter; texturizer, § 170.3(o)(32) of this chapter.

(d) [Reserved]

(e) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[42 FR 14653, Mar. 15, 1977, as amended at 42 FR 55205, Oct. 14, 1977; 49 FR 5612, Feb. 14, 1983; 53 FR 5766, Feb. 26, 1988]

§ 184.1333 Gum ghatti.

(a) Gum ghatti (Indian gum) is an exudate from wounds in the bark of *Anogeissus latifolia,* a large tree found in the dry deciduous forests of India and Ceylon.

(b) The ingredient complies with the following specifications:

(1) *Viscosity of a 1-percent solution.* Not less than the minimum or within the range claimed by the vendor.

(2) *Limits of impurities*—(i) *Arsenic* (*as AL*). Not more than 3 parts per million (0.0003 percent);

(ii) *Ash* (*acid-insoluble*). Not more than 1.75 percent;

(iii) *Ash* (*total*). Not more than 6.0 percent;

(iv) *Heavy metals* (*as Pb*). Not more than 40 parts per million (0.004 percent); and

(v) *Lead.* Not more than 10 parts per million (0.001 percent).

(3) *Loss on drying.* Not more than 14 percent dried at 105 °C for 5 hours.

(4) *Identification test.* Add 0.2 ml of diluted lead acetate as outlined in ''Official Methods of Analysis of the Association of Official Analytical Chemists,'' 13th Ed. (1980), section 31.178(b), p. 529, under ''Dilute Basic Lead Acetate Standard Solution,'' which is incorporated by reference (copies are available from the Association of Official Analytical Chemists, P.O. Box 540, Benjamin Franklin Station, Washington, DC 20044, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408), to 5 ml of a cold 1-in-100 aqueous solution of the gum. An immediate, voluminous, opaque precipitate indicates acacia. A small precipitate or clear solution which produces an opaque flocculent precipitate upon the additon of 1 ml of 3 *N* ammonimum hydroxide indicates gum ghatti.

(c) The ingredient is used in food under the following conditions:

Maximum Usage Levels Permitted

Food (as served)	Percent	Function
Beverages and beverage bases, nonalcoholic, § 170.3(n)(3) of this chapter.	0.2	Emulsifier and emulsifier salt, § 170.3(o)(8) of this chapter.
All other food categories	.1	Emulsifier and emulsifier salt, § 170.3(o)(8) of this chapter.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 44 of 100

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[42 FR 14653, Mar. 15, 1977, as amended at 49 FR 5612, Feb. 14, 1984]

§ 184.1339 Guar gum.

(a) Guar gum is the natural substance obtained from the maceration of the seed of the guar plant, *Cyamopsis tetragonoloba* (Linne) Taub., or *Cyamopsis psoraloides* (Lam.) D.C.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), p. 141, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used in food under the following conditions:

MAXIMUM USAGE LEVELS PERMITTED

Food (as served)	Percent	Function
Baked goods and baking mixes, § 170.3(n)(1) of this chapter.	0.35	Emulsifier and emulsifier salts, § 170.3(o)(8) of this chapter; formulation aid, § 170.3(o)(14) of this chapter; stabilizer and thickener; § 170.3(o)(28) of this chapter.
Breakfast cereals, § 170.3(n)(4) of this chapter	1.2	Formulation aid, § 170.3(o)(14) of this chapter; stabilizer and thickener, § 170.3(o)(28) of this chapter.
Cheese, § 170.3(n)(5) of this chapter	.8	Do.
Dairy products analogs, § 170.3(n)(10) of this chapter.	1.0	Firming agent, § 170.3(o)(10) of this chapter; formulation aid, § 170.3(o)(14) of this chapter; stabilizer and thickener, § 170.3(o)(28) of this chapter.
Fats and oils, § 170.3(n)(12) of this chapter	2.0	Do.
Gravies and sauces, § 170.3(n)(24) of this chapter	1.2	Formulation aid, § 170.3(o)(14) of this chapter; stabilizer and thickener, § 170.3(o)(28) of this chapter.
Jams and jellies, commercial, § 170.3(n)(28) of this chapter.	1.0	Do.
Milk products, § 170.3(n)(31) of this chapter	.6	Do.
Processed vegetables and vegetable juices, § 170.3(n)(36) of this chapter.	2.0	Formulation aid, § 170.3(o)(14) of this chapter; stabilizer and thickener, § 170.3(o)(28) of this chapter.
Soups and soup mixes, § 170.3(n)(40) of this chapter.	.8	Do.
Sweet sauces, toppings and syrups, § 170.3(n)(43) of this chapter.	1.0	Do.
All other food categories	.5	Emulsifier and emulsifier salts, § 170.3(o)(8) of this chapter; firming agent, § 170.3(o)(10) of this chapter; formulation aid, § 170.3(o)(14) of this chapter; stabilizer and thickener, § 170.3(o)(28) of this chapter.

(d) [Reserved]

(e) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[42 FR 14653, Mar. 15, 1977, as amended at 42 FR 55205, Oct. 14, 1977; 49 FR 5612, Feb. 14, 1984]

§ 184.1343 Locust (carob) bean gum.

(a) Locust (carob) bean gum is primarily the macerated endosperm of the seed of the locust (carob) bean tree, *Ceratonia siliqua* (Linne), a leguminous evergreen tree, with lesser quantities of seed coat and germ.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), pp. 174–175, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used at levels not to exceed the following maximum levels:

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 45 of 100

MAXIMUM USAGE LEVELS PERMITTED

Food (as served)	Percent	Function
Baked goods and baking mixes, § 170.3(n)(1) of this chapter.	0.15	Stabilizer and thickener, § 170.3(o)(28) of this chapter.
Beverages and beverage bases, nonalcoholic, § 170.3(n)(3) of this chapter.	.25	Do.
Cheeses, § 170.3(n)(5) of this chapter	.8	Do.
Gelatins, puddings, and fillings, § 170.3(n)(22) of this chapter.	.75	Do.
Jams and jellies, commercial, § 170.3(n)(28) of this chapter.	.75	Do.
All other food categories	.5	Do.

(d) [Reserved]

(e) Prior sanctions for this ingredient different from the uses established in this regulation do not exist or have been waived.

[42 FR 14653, Mar. 15, 1977, as amended at 42 FR 55205, Oct. 14, 1977; 49 FR 5612, Feb. 14, 1984]

§ 184.1349 Karaya gum (sterculia gum).

(a) Karaya gum (sterculia gum) is the dried gummy exudate from the trunk of trees of various species of the genus *Sterculia*.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), p. 157, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used in food under the following conditions:

MAXIMUM USAGE LEVELS PERMITTED

Food (as served)	Percent	Function
Frozen dairy desserts and mixes, § 170.3(n)(20) of this chapter.	0.3	Formulation aid, § 170.3(o)(14) of this chapter; stabilizer and thickener, § 170.3(o)(28) of this chapter.
Milk products, § 170.3(n)(31) of this chapter	.02	Stabilizer and thickener, § 170.3(o)(28) of this chapter.
Soft candy, § 170.3(n)(38) of this chapter	.9	Emulsifier and emulsifier salt, § 170.3(o)(8) of this chapter; stabilizer and thickener, § 170.3(o)(28) of this chapter.
All other food categories	.002	Formulation aid, § 170.3(o)(14) of this chapter; stabilizer and thickener, § 170.3(o)(28) of this chapter.

(d) [Reserved]

(e) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[42 FR 14653, Mar. 15, 1977, as amended at 42 FR 55205, Oct. 14, 1977; 49 FR 5612, Feb. 14, 1984]

§ 184.1351 Gum tragacanth.

(a) Gum tragacanth is the exudate from one of several species of *Astragalus gummifier* Labillardiere, a shrub that grows wild in mountainous regions of the Middle East.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), p. 337, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used in food under the following conditions:

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 46 of 100

MAXIMUM USAGE LEVELS PERMITTED

Food (as served)	Percent	Function
Baked goods and baking mixes, § 170.3(n)(1) of this chapter.	0.2	Emulsifier and emulsifier salt, § 170.3(o)(8) of this chapter; formulation aid, § 170.3(o)(14) of this chapter; stabilizer and thickener, § 170.3(o)(28) of this chapter.
Condiments and relishes, § 170.3(n)(8) of this chapter.	.7	Do.
Fats and oils, § 170.3(n)(12) of this chapter	1.3	Do.
Gravies and sauces, § 170.3(n)(24) of this chapter	.8	Do.
Meat products, § 170.3(n)(29) of this chapter	.2	Formulation aid, § 170.3(o)(14) of this chapter; stabilizer and thickener, § 170.3(o)(28) of this chapter.
Processed fruits and fruit juices, § 170.3(n)(35) of this chapter.	.2	Emulsifier and emulsifier salt, § 170.3(o)(8) of this chapter; formulation aid, § 170.3(o)(14) of this chapter; stabilizer and thickener, § 170.3(o)(28) of this chapter.
All other food categories	.1	Do.

(d) [Reserved]

(e) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[42 FR 14653, Mar. 15, 1977, as amended at 42 FR 55205, Oct. 14, 1977; 49 FR 5612, Feb. 14, 1984]

§ 184.1355 Helium.

(a) Helium (empirical formula He, CAS Reg. No. 7440–59–7) is a colorless, odorless, flavorless, nonflammable, inert gas. It is lighter than air and is produced by the liquefaction and purification of natural gas.

(b) The Food and Drug Administration is developing food-grade specifications for helium in cooperation with the National Academy of Sciences. In the interim, the ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitations other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a processing aid as defined in § 170.3(o)(24) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 57270, Dec. 29, 1983]

§ 184.1366 Hydrogen peroxide.

(a) Hydrogen peroxide (H_2O_2, CAS Reg. No. 7722–84–1) is also referred to as hydrogen dioxide. It is made by the electrolytic oxidation of sulfuric acid or a sulfate to persulfuric acid or a persulfuric acid salt with subsequent hydrolysis and distillation of the hydrogen peroxide formed; by decomposition of barium peroxide with sulfuric or phosphoric acid; by hydrogen reduction of 2-ethylanthraquinone, followed by oxidation with air, to regenerate the quinone and produce hydrogen peroxide; or by electrical discharge through a mixture of hydrogen, oxygen, and water vapor.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d ed. (1981), pp. 146–147,[1] which is incorporated by reference.

(c) In accordance with § 184.1(b)(2), the ingredient is used to treat food only within the following specific limitations:

[1] Copies may be obtained from the National Academy of Sciences, 2101 Constitution Ave. NW, Washington, DC 20037, or examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 47 of 100

Food	Maximum treatment level in food (percent)	Functional use
Milk, intended for use during the cheesemaking process as permitted in the appropriate standards of identity for cheese and related cheese products under part 133 of this chapter.	0.05	Antimicrobial agent as defined in § 170.3 (o)(2) of this chapter
Whey, during the preparation of modified whey by electrodialysis methods.	0.04	do.
Dried eggs, dried egg whites, and dried egg yolks as in §§ 160.105, 160.145, and 160.185 of this chapter.	Amount sufficient for the purpose.	Oxidizing and reducing agent as defined in § 170.3 (o)(22) of this chapter
Tripe	do	Bleaching agent.
Beef feet	Amount sufficient for the purpose. (Hydrogen peroxide may be in the form of a compound salt, sodium carbonate peroxide).	Bleaching agent.
Herring	Amount sufficient for the purpose.	do.
Wine	do	Oxidizing and reducing agent as defined in § 170.3 (o)(22) of this chapter.
Starch	0.15	Antimicrobial agent as defined in §170.3 (o)(2) of this chapter, to produce thermophile-free starch; Remove sulfur dioxide from starch slurry following steeping and grinding operations of corn refining.
Instant tea	Amount sufficient for the purpose.	Bleaching agent.
Corn syrup	0.15	Reduce sulfur dioxide levels in the finished corn syrup.
Colored (annatto) cheese whey	0.05	Bleaching agent.
Wine vinegar	Amount sufficient for the purpose.	Remove sulfur dioxide from wine prior to fermentation to produce vinegar.
Emulsifiers containing fatty acid esters	1.25	Bleaching agent.

(d) Residual hydrogen peroxide is removed by appropriate physical and chemical means during the processing of food where it has been used according to paragraph (c) of this section.

(e) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[46 FR 44439, Sept. 4, 1981, as amended at 51 FR 27172, July 30, 1986]

§ 184.1370 Inositol.

(a) Inositol, or myo-inositol ($C_6H_{12}O_6$, CAS Reg. No. 87–89–8), is *cis*-1,2,3,5-*trans*-4,6-cyclohexanehexol. It occurs naturally and is prepared from an aqueous (0.2 percent sulfur dioxide) extract of corn kernels by precipitation and hydrolysis of crude phytate.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 150, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitations other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a nutrient supplement as defined in § 170.3(o)(20) of this chapter.

(2) The ingredient is used in special dietary foods as defined in part 105 of this chapter at levels not to exceed current good manufacturing practice. It may also be used in infant formula in accordance with section 412(g) of the Act, or with regulations promulgated under section 412(a)(2) of the Act.

(d) Prior sanctions for this ingredient different from the uses established by

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 48 of 100

this section do not exist or have been waived.

[47 FR 38278, Aug. 31, 1982]

§ 184.1372 Insoluble glucose isomerase enzyme preparations.

(a) Insoluble glucose isomerase enzyme preparations are used in the production of high fructose corn syrup described in § 184.1866. They are derived from recognized species of precisely classified nonpathogenic and nontoxicogenic microorganisms, including *Streptomyces rubiginosus, Actinoplanes missouriensis, Streptomyces olivaceus, Streptomyces olivochromogenes,* and *Bacillus coagulans,* that have been grown in a pure culture fermentation that produces no antibiotics. They are fixed (rendered insoluble) for batch production with GRAS ingredients or may be fixed for further immobilization with either GRAS ingredients or materials approved under § 173.357 of this chapter.

(b) The ingredient meets the general and additional requirements for enzyme preparations in the Food Chemicals Codex, 3d Ed. (1981), p. 107, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an enzyme, as defined in § 170.3(o)(9) of this chapter, to convert glucose to fructose.

(2) The ingredient is used in high fructose corn syrup, at levels not to exceed current good manufacturing practice.

[48 FR 5720, Feb. 8, 1983, as amended at 61 FR 43450, Aug. 23, 1996]

§ 184.1375 Iron, elemental.

(a) Iron, elemental (CAS Reg. No. 7439–89–6) is metallic iron obtained by any of the following processes: reduced iron, electrolytic iron, and carbonyl iron.

(1) Reduced iron is prepared by reacting ground ferric oxide with hydrogen or carbon monoxide at an elevated temperature. The process results in a grayish-black powder, all of which should pass through a 100-mesh sieve. It is lusterless or has not more than a slight luster. When viewed under a microscope, it appears as an amorphous powder free from particles having a crystalline structure. It is stable in dry air.

(2) Electrolytic iron is prepared by electrodeposition. It is an amorphous, lusterless, grayish-black powder. It is stable in dry air.

(3) Carbonyl iron is prepared by the decomposition of iron pentacarbonyl. It occurs as a dark gray powder. When viewed under a microscope, it appears as spheres built up with concentric shells. It is stable in dry air.

(b) Iron, elemental (carbonyl, electrolytic, or reduced) meets the specifications of the Food Chemicals Codex, 3d Ed. (1981) (iron, carbonyl, p. 151; iron, electrolytic, pp. 151–152; iron, reduced; pp. 152–153), which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food as a nutrient supplement as defined in § 170.3(o)(20) of this chapter, with no limitation other than current good manufacturing practice. The ingredient may also be used in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 350a(g)) or with regulations promulgated under section 412(a)(2) of the act (21 U.S.C. 350a(2)).

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[53 FR 16867, May 12, 1988]

§ 184.1386 Isopropyl citrate.

(a) Isopropyl citrate is a mixture of the mono-, di-, and triisopropyl esters

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 49 of 100

of citric acid. It is prepared by esterifying citric acid with isopropanol.

(b) The Food and Drug Administration, in cooperation with the National Academy of Sciences, is developing food-grade specifications for isopropyl citrate. In the interim, this ingredient must be of a purity suitable for its intended use.

(c) In accordance with §184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an antioxidant as defined in §170.3(o)(3) of this chapter; a sequestrant as defined in §170.3(o)(26) of this chapter; and a solvent and vehicle as defined in §170.3(o)(27) of this chapter.

(2) The ingredient is used in margarine in accordance with §166.110 of this chapter; in nonalcoholic beverages as defined in §170.3(n)(3) of this chapter; and in fats and oils as defined in §170.3(n)(12) of this chapter at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section, or different from those set forth in part 181 of this chapter, do not exist or have been waived.

[59 FR 63896, Dec. 12, 1994]

§ 184.1387 Lactase enzyme preparation from Candida pseudotropicalis.

(a) This enzyme preparation is derived from the nonpathogenic, nontoxicogenic yeast *C. pseudotropicalis.* It contains the enzyme lactase (β-D-galactoside galactohydrolase, EC 3.2.1.23), which converts lactose to glucose and galactose. It is prepared from yeast that has been grown by a pure culture fermentation process.

(b) The ingredient meets the general requirements and additional requirements for enzyme preparations in the Food Chemicals Codex, 3d ed. (1981), pp. 107–110, which are incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Center for Food Safety and Applied Nutrition's Library, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) In accordance with §184.1(b)(1), the ingredient is used in food with no limitations other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an enzyme, as defined in §170.3(o)(9) of this chapter, to convert lactose to glucose and galactose.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice. Current good manufacturing practice is limited to use of this ingredient to reduce the lactose content in milk and milk-derived food products where food standards do not preclude such use.

[61 FR 7704, Feb. 29, 1996]

§ 184.1388 Lactase enzyme preparation from Kluyveromyces lactis.

(a) This enzyme preparation is derived from the nonpathogenic, nontoxicogenic yeast *Kluyveromyces lactis* (previously named *Saccharomyces lactis).* It contains the enzyme B-galactoside galactohydrase (CAS Reg. No. CBS 683), which converts lactose to glucose and galactose. It is prepared from yeast that has been grown in a pure culture fermentation and by using materials that are generally recognized as safe or are food additives that have been approved for this use by the Food and Drug Administration.

(b) The ingredient meets the general and additional requirements for enzyme preparations in the Food Chemicals Codex, 3d Ed. (1981), p. 107–110, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 50 of 100

Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an enzyme as defined in §170.3(o)(9) of this chapter to convert lactose to glucose and galactose.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice. Current good manufacturing practice is to use this ingredient in milk to produce lactase-treated milk, which contains less lactose than regular milk, or lactose-reduced milk, which contains at least 70 percent less lactose than regular milk.

[49 FR 47387, Dec. 4, 1984]

§ 184.1400 Lecithin.

(a) Commercial lecithin is a naturally occurring mixture of the phosphatides of choline, ethanolamine, and inositol, with smaller amounts of othe lipids. It is isolated as a gum following hydration of solvent-extracted soy, safflower, or corn oils. Lecithin is bleached, if desired, by hydrogen peroxide and benzoyl peroxide and dried by heating.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), pp. 166–167, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 51150, Nov. 7, 1983]

§ 184.1408 Licorice and licorice derivatives.

(a)(1) Licorice (glycyrrhiza) root is the dried and ground rhizome and root portions of *Glycyrrhiza glabra* or other species of *Glycyrrhiza*. Licorice extract is that portion of the licorice root that is, after maceration, extracted by boiling water. The extract can be further purified by filtration and by treatment with acids and ethyl alcohol. Licorice extract is sold as a liquid, paste (''block''), or spray-dried powder.

(2) Ammoniated glycyrrhizin is prepared from the water extract of licorice root by acid precipitation followed by neutralization with dilute ammonia. Monoammonium glycyrrhizinate ($C_{42}H_{61}O_{16}NH_4 5H_2O$, CAS Reg. No. 1407–03–0) is prepared from ammoniated glycyrrhizin by solvent extraction and separation techniques.

(b) The ingredients shall meet the following specifications when analyzed:

(1) *Assay*. The glycyrrhizin content of each flavoring ingredient shall be determined by the method in the Official Methods of Analysis of the Association of Official Analytical Chemists, 13th Ed., §§ 19.136–19.140, which is incorporated by reference, or by methods 19.CO1 through 19.CO4 in the *Journal of the Association of Official Analytical Chemists*, 65:471–472 (1982), which are also incorporated by reference. Copies of all of these methods are available from the Association of Official Analytical Chemists, 2200 Wilson Blvd., Suite 400, Arlington, VA 22201–3301, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(2) *Ash*. Not more than 9.5 percent for licorice, 2.5 percent for ammoniated glycyrrhizin, and 0.5 percent for monoammonium glycyrrhizinate on an anhydrous basis as determined by the method in the Food Chemicals Codex, 3d Ed. (1981), p. 466, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(3) *Acid unsoluble ash*. Not more than 2.5 percent for licorice on an anhydrous

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 51 of 100

basis as determined by the method in the Food Chemicals Codex, 3d Ed. (1981), p. 466, which is incorporated by reference.

(4) *Heavy metals (as Pb).* Not more than 40 parts per million as determined by method II in the Food Chemicals Codex, 3d Ed. (1981), p. 512, which is incorporated by reference.

(5) *Arsenic (As).* Not more than 3 parts per million as determined by the method in the Food Chemicals Codex. 3d Ed. (1981), p. 464, which is incorporated by reference.

(c) In accordance with § 184.1(b)(2), these ingredients are used in food only within the following specific limitations:

Category of food	Maximum level in food (percent glycyrrhizin content of food) (as served)	Functional use
Baked foods, §170.3(n)(1) of this chapter	0.05	Flavor enhancer, §170.3(o)(11) of this chapter; flavoring agent, §170.3(o)(12) of this chapter.
Alcoholic beverages, §170.3(n)(2) of this chapter	0.1	Flavor enhancer, §170.3(o)(11) of this chapter; flavoring agent, §170.3(o)(12) of this chapter; surface-active agent, §170.3(o)(29) of this chapter.
Nonalcoholic beverages, §170.3(n)(3) of this chapter	0.15	Do.
Chewing gum, §170.3(n)(6) of this chapter	1.1	Flavor enhancer, §170.3(o)(11) of this chapter; flavoring agent, §170.3(n)(12) of this chapter.
Hard candy, §170.3(n)(25) of this chapter	16.0	Do.
Herbs and seasonings, §170.3(n)(26) of this chapter	0.15	Do.
Plant protein products, §170.3(n)(33) of this chapter	0.15	Do.
Soft candy, §170.3(n)(38) of this chapter	3.1	Do.
Vitamin or mineral dietary supplements	0.5	Do.
All other foods except sugar substitutes, §170.3(n)(42) of this chapter. The ingredient is not permitted to be used as a nonnutritive sweetener in sugar substitutes.	0.1	Do.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[50 FR 21044, May 22, 1985, as amended at 54 FR 24899, June 12, 1989]

§ 184.1409 Ground limestone.

(a) Ground limestone consists essentially (not less than 94 percent) of calcium carbonate ($CaCO_3$) and is prepared by the crushing, grinding, and classifying of naturally occurring limestone.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 173, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 52442, Nov. 18, 1983]

§ 184.1415 Animal lipase.

(a) Animal lipase (CAS Reg. No. 9001–62–1) is an enzyme preparation obtained from edible forestomach tissue of calves, kids, or lambs, or from animal pancreatic tissue. The enzyme preparation may be produced as a tissue preparation or as an aqueous extract. Its characterizing enzyme activity is that of a triacylglycerol hydrolase (EC 3.1.1.3).

(b) The ingredient meets the general requirements and additional requirements for enzyme preparations in the Food Chemicals Codex, 3d ed. (1981), p. 110, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave., NW., Washington, DC 20418, or may be examined at the Office of Premarket Approval (HFS–200), Food and Drug Administration, 200 C St.,

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 52 of 100

SW., Washington, DC, and the Office of the Federal Register, 800 North Capitol St., NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as GRAS as a direct food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an enzyme as defined in § 170.3(o)(9) of this chapter to hydrolyze fatty acid glycerides.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

[60 FR 32911, June 26, 1995]

§ 184.1420 Lipase enzyme preparation derived from Rhizopus niveus.

(a) Lipase enzyme preparation contains lipase enzyme (CAS Reg. No. 9001–62–1), which is obtained from the culture filtrate resulting from a pure culture fermentation of a nonpathogenic and nontoxigenic strain of *Rhizopus niveus*. The enzyme preparation also contains diatomaceous earth as a carrier. The characterizing activity of the enzyme, which catalyzes the interesterification of fats and oils at the 1- and 3-positions of triglycerides, is triacylglycerol lipase (EC 3.1.1.3).

(b) The ingredient meets the general requirements and additional requirements for enzyme preparations in the monograph on Enzyme Preparations in the ''Food Chemicals Codex,'' 4th ed. (1996), pp. 133 and 134, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Center for Food Safety and Applied Nutrition's Library, 200 C St. SW., rm. 3321, Washington, DC, or the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an enzyme as defined in § 170.3(o)(9) of this chapter for the interesterification of fats and oils.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

[63 FR 24419, May 4, 1998]

§ 184.1425 Magnesium carbonate.

(a) Magnesium carbonate (molecular formula approximately $(MgCO_3)_4 \cdot Mg(OH)_2 \cdot 5H_2O$, CAS Reg. No. 39409–82–0) is also known as magnesium carbonate hydroxide. It is a white powder formed either by adding an alkaline carbonate (such as sodium carbonate) to a solution of magnesium sulfate or by carbonation of a slurry of magnesium hydroxide followed by boiling of the resulting magnesium carbonate.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 177, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an anticaking and free-flow agent as defined in § 170.3(o)(1) of this chapter; a flour treating agent as defined in § 170.3(o)(13) of this chapter; a lubricant and release agent as defined in § 170.3(o)(18) of this chapter; a nutrient supplement as defined in § 170.3(o)(20) of this chapter; a pH control agent as defined in § 170.3(o)(23) of this chapter; a processing aid as defined in § 170.3(o)(24) of this chapter; and a synergist as defined in § 170.3(o)(31) of this chapter.

(2) The ingredient is used in foods at levels not to exceed current good manufacturing practice.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 53 of 100

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[50 FR 13558, Apr. 5, 1985; 50 FR 16080, Apr. 24, 1985]

§ 184.1426 Magnesium chloride.

(a) Magnesium chloride ($MgC1_2 \cdot 6H_2O$, CAS Reg. No. 7786–30–3) is a colorless, deliquescent, crystalline material that occurs naturally as the mineral bischofite. It is prepared by dissolving magnesium oxide, hydroxide, or carbonate in aqueous hydrochloric acid solution and crystallizing out magnesium chloride hexahydrate.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 177, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter and a nutrient supplement as defined in § 170.3(o)(20) of this chapter.

(2) The ingredient is used in foods at levels not to exceed current good manufacturing practice. The ingredient also may be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) or with regulations promulgated under section 412(a)(2) of the act.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[50 FR 13559, Apr. 5, 1985; 50 FR 16080, Apr. 24, 1985]

§ 184.1428 Magnesium hydroxide.

(a) Magnesium hydroxide ($Mg(OH)_2$, CAS Reg. No. 1309–42–8) occurs naturally as the colorless, crystalline mineral brucite. It is prepared as a white precipitate by the addition of sodium hydroxide to a water soluble magnesium salt or by hydration of reactive grades of magnesium oxide.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 178, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a nutrient supplement as defined in § 170.3(o)(20) of this chapter; a pH control agent as defined in § 170.3(o)(23) of this chapter; and a processing aid as defined in § 170.3(o)(24) of this chapter.

(2) The ingredient is used in foods at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[50 FR 13559, Apr. 5, 1985, as amended at 64 FR 405, Jan. 5, 1999]

§ 184.1431 Magnesium oxide.

(a) Magnesium oxide (MgO, CAS Reg. No. 1309–48–4) occurs naturally as the colorless, crystalline mineral periclase. It is produced either as a bulky white powder (light) or a relatively dense white powder (heavy) by heating magnesium hydroxide or carbonate. Heating these magnesium salts under moderate conditions (400° to 900 °C for a few hours) produces light magnesium oxide. Heating the salts under more rigorous conditions (1200 °C for 12 hours) produces heavy magnesium

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 54 of 100

oxide. Light magnesium oxide is converted to heavy magnesium oxide by sustained heating at high temperatures.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 178, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an anticaking and free-flow agent as defined in § 170.3(o)(1) of this chapter; a firming agent as defined in § 170.3(o)(10) of this chapter; a lubricant and release agent as defined in § 170.3(o)(18) of this chapter; a nutrient supplement as defined in § 170.3(o)(20) of this chapter; and a pH control agent as defined in § 170.3(o)(23) of this chapter.

(2) The ingredient is used in foods at levels not be exceed current good manufacturing practice. The ingredient also may be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) or with regulations promulgated under section 412(a)(2) of the act.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[50 FR 13559, Apr. 5, 1985]

§ 184.1434 Magnesium phosphate.

(a) Magnesium phosphate includes both magnesium phosphate, dibasic, and magnesium phosphate, tribasic. Magnesium phosphate, dibasic ($MgHPO_4 \cdot 3H_2O$, CAS Reg. No. 7782–0975–094) occurs naturally as the white, crystalline mineral newberyite. It is prepared commercially as a precipitate formed by treating a solution of magnesium sulfate with disodium phosphate under controlled conditions. Magnesium phosphate, tribasic ($Mg_3(PO_4)2 \cdot xH_2O$, CAS Reg. No. 7727–0987–091) may contain 4, 5, or 8 molecules of water of hydration. It is produced as a precipitate from a solution of magnesite with phosphoric acid.

(b) Magnesium phosphate, dibasic, meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 179, which is incorporated by reference. Magnesium phosphate, tribasic, meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 180, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a nutrient supplement as defined in § 170.3(o)(20) of this chapter and a pH control agent as defined in § 170.3(o)(23) of this chapter.

(2) The ingredient is used in foods at levels not to exceed current good manufacturing practice. The ingredient also may be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) or with regulations promulgated under section 412(a)(2) of the Act.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[50 FR 13560, Apr. 5, 1985]

§ 184.1440 Magnesium stearate.

(a) Magnesium stearate ($Mg(C_{17}H_{34}COO)_2$, CAS Reg. No. 557–04–0) is the magnesium salt of stearic acid. It is produced as a white precipitate by the addition of an aqueous solution of magnesium chloride to an aqueous solution of sodium stearate derived from stearic acid that is obtained from edible sources and that conforms to the

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 55 of 100

requirements of § 172.860(b)(2) of this chapter.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 182, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a lubricant and release agent as defined in § 170.3(o)(18) of this chapter; a nutrient supplement as defined in § 170.3(o)(20) of this chapter; and a processing aid as defined in § 170.3(o)(24) of this chapter.

(2) The ingredient is used in foods at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[50 FR 13560, Apr. 5, 1985]

§ 184.1443 Magnesium sulfate.

(a) Magnesium sulfate ($MgSO_4 \cdot 7H_2O$, CAS Reg. No. 10034–99–8) occurs naturally as the mineral epsomite. It is prepared by neutralization of magnesium oxide, hydroxide, or carbonate with sulfuric acid and evaporating the solution to crystallization.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 183, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a flavor enhancer as defined in § 170.3(o)(11) of this chapter; a nutrient supplement as defined in § 170.3(o)(20) of this chapter; and a processing aid as defined in § 170.3(o)(24) of this chapter.

(2) The ingredient is used in foods at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[50 FR 13560, Apr. 5, 1985]

§ 184.1443a Malt.

(a) Malt is an enzyme preparation obtained from barley which has been softened by a series of steeping operations and germinated under controlled conditions. It is a brown, sweet, and viscous liquid or a white to tan powder. Its characterizing enzyme activities are α-amylase (EC 3.2.1.1.) and β-amylase (EC 3.2.1.2).

(b) The ingredient meets the general requirements and additional requirements for enzyme preparations in the Food Chemicals Codex, 3d ed. (1981), p. 110, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave., NW., Washington, DC 20418, or may be examined at the Office of Premarket Approval (HFS–200), Food and Drug Administration, 200 C St., SW., Washington, DC, and the Office of the Federal Register, 800 North Capitol St., NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as GRAS as a direct food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an enzyme as defined in § 170.3(o)(9) of this chapter to hydrolyze starch or starch-derived polysaccharides.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 56 of 100

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

[60 FR 32911, June 26, 1995]

§ 184.1444 Maltodextrin.

(a) Maltodextrin ($(C_6H_{10}O_5)_n$, CAS Reg. No. 9050–36–6) is a nonsweet nutritive saccharide polymer that consists of D-glucose units linked primarily by α-1-4 bonds and that has a dextrose equivalent (D.E.) of less than 20. It is prepared as a white powder or concentrated solution by partial hydrolysis of corn starch, potato starch, or rice starch with safe and suitable acids and enzymes.

(b)(1) Maltodextrin derived from corn starch must be of a purity suitable for its intended use.

(2) Maltodextrin derived from potato starch meets the specifications of the Food Chemicals Codex, 3d ed., 3d supp. (1992), p. 125, which are incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave., NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capital St. NW., suite 700, Washington, DC 20408, or at the Division of Petition Control (HFS–217), Center for Food Safety and Applied Nutrition, Food and Drug Administration, 200 C St. SW., Washington, DC 20204.

(3) Maltodextrin derived from rice starch meets the specifications of the Food Chemicals Codex, 4th ed. (1996), pp. 239 and 240, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Center for Food Safety and Applied Nutrition's Library, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 51911, Nov. 15, 1983; as amended at 60 FR 48893, Sept. 21, 1995; 63 FR 14611, Mar. 26, 1998]

§ 184.1445 Malt syrup (malt extract).

(a) Malt is the product of barley (*Hordeum vulgare* L.) germinated under controlled conditions. Malt syrup and malt extract are interchangeable terms for a viscous concentrate of water extract of germinated barley grain, with or without added safe preservative. Malt syrup is usually a brown, sweet, and viscous liquid containing varying amounts of amylolytic enzymes and plant constituents. Barley is first softened after cleaning by steeping operations and then allowed to germinate under controlled conditions. The germinated grain then undergoes processing, such as drying, grinding, extracting, filtering, and evaporating, to produce malt syrup (malt extract) with 75 to 80 percent solids or dried malt syrup with higher solids content.

(b) FDA is developing food-grade specifications for malt syrup (malt extract) in cooperation with the National Academy of Sciences. In the interim, the ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 51613, Nov. 10, 1983]

§ 184.1446 Manganese chloride.

(a) Manganese chloride ($MnCl_2 \cdot 4H_2O$, CAS Reg. No. 7773–01–5) is a pink, translucent, crystalline product. It is

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 57 of 100

also known as manganese dichloride. It is prepared by dissolving manganous oxide, pyrolusite ore (MnO_2), or reduced manganese ore in hydrochloric acid. The resulting solution is neutralized to precipitate heavy metals, filtered, concentrated, and crystallized.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 186, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a nutrient supplement as defined in § 170.3(o)(20) of this chapter.

(2) The ingredient may be used in infant formulas in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) or with regulations promulgated under section 412(a)(2) of the act.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[50 FR 19165, May 7, 1985]

§ 184.1449 Manganese citrate.

(a) Manganese citrate ($Mn_3(C_6H_5O_7)_2$, CAS Reg. No. 1002–46–65) is a pale orange or pinkish white powder. It is obtained by precipitating manganese carbonate from manganese sulfate and sodium carbonate solutions. The filtered and washed precipitate is digested first with sufficient citric acid solution to form manganous citrate and then with sodium citrate to complete the reaction.

(b) FDA is developing food-grade specifications for manganese citrate in cooperation with the National Academy of Sciences. In the interim, this ingredient must be of purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a nutrient supplement as defined in § 170.3(o)(20) of this chapter.

(2) The ingredient is used in the following foods at levels not to exceed current good manufacturing practice: baked goods as defined in § 170.3(n)(1) of this chapter; nonalcoholic beverages as defined in § 170.3(n)(3) of this chapter; dairy product analogs as defined in § 170.3(n)(10) of this chapter; fish products as defined in § 170.3(n)(13) of this chapter; meat products as defined in § 170.3(n)(29) of this chapter; milk products as defined in § 170.3(n)(31) of this chapter; and poultry products as defined in § 170.3(n)(34) of this chapter. The ingredient may be used in infant formulas in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) or with regulations promulgated under section 412(a)(2) of the act.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[50 FR 19166, May 7, 1985]

§ 184.1452 Manganese gluconate.

(a) Manganese gluconate ($C_{12}H_{22}MnO_{14}\cdot 2H_2O$, CAS Reg. No. 648–0953–0998) is a slightly pink colored powder. It is obtained by reacting manganese carbonate with gluconic acid in aqueous medium and then crystallizing the product.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 186, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 58 of 100

manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a nutrient supplement as defined in § 170.3(o)(20) of this chapter.

(2) The ingredient is used in the following foods at levels not to exceed current good manufacturing practice: baked goods as defined in § 170.3(n)(1) of this chapter; nonalcoholic beverages as defined in § 170.3(n)(3) of this chapter; dairy product analogs as defined in § 170.3(n)(10) of this chapter; fish products as defined in § 170.3(n)(13) of this chapter; meat products as defined in § 170.3(n)(29) of this chapter; milk products as defined in § 170.3(n)(31) of this chapter; and poultry products as defined in § 170.3(n)(34) of this chapter. The ingredient may be used in infant formulas in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) or with regulations promulgated under section 412(a)(2) of the act.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[50 FR 19166, May 7, 1985]

§ 184.1461 Manganese sulfate.

(a) Manganese sulfate ($MnSO_4 \cdot H_2O$, CAS Reg. No. 7785–0987–097) is a pale pink, granular, odorless powder. It is obtained by reacting manganese compounds with sulfuric acid. It is also obtained as a byproduct in the manufacture of hydroquinone. Other manufacturing processes include the action of sulfur dioxide on a slurry of manganese dioxide in sulfuric acid, and the roasting of pyrolusite (MnO_2) ore with solid ferrous sulfate and coal, followed by leaching and crystallization.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 188, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a nutrient supplement as defined in § 170.3(o)(20) of this chapter.

(2) The ingredient is used in the following foods at levels not to exceed current good manufacturing practice: baked goods as defined in § 170.3(n)(1) of this chapter; nonalcoholic beverages as defined in § 170.3(n)(3) of this chapter; dairy product analogs as defined in § 170.3(n)(10) of this chapter; fish products as defined in § 170.3(n(13) of this chapter; meat products as defined in § 170.3(n)(29) of this chapter; milk products as defined in § 170.3(n)(31) of this chapter; and poultry products as defined in § 170.3(n)(34) of this chapter.

The ingredient may be used in infant formulas in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) or with regulations promulgated under section 412(a)(2) of the act.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[50 FR 19166, May 7, 1985]

§ 184.1472 Menhaden oil.

(a) *Menhaden oil.* (1) Menhaden oil is prepared from fish of the genus *Brevoortia*, commonly known as menhaden, by cooking and pressing. The resulting crude oil is then refined using the following steps: Storage (winterization), degumming (optional), neutralization, bleaching, and deodorization. Winterization may separate the oil and produce a solid fraction.

(2) Menhaden oil meets the following specifications:

(i) *Color and state.* Yellow liquid to white solid.

(ii) *Odor.* Odorless to slightly fishy.

(iii) *Saponification value.* Between 180 and 200 as determined by the American Oil Chemists' Society Official Method

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 59 of 100

Cd 3–25—''Saponification Value'' (reapproved 1989), which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies of this publication are available from the Office of Premarket Approval, Center for Food Safety and Applied Nutrition (HFS–200), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, or available for inspection at the Center for Food Safety and Applied Nutrition's Library, Food and Drug Administration, 200 C St. SW., rm. 3321, Washington DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(iv) *Iodine number*. Not less than 120 as determined by the American Oil Chemists' Society Recommended Practice Cd 1d–92—''Iodine Value of Fats and Oils, Cyclohexane—Acetic Acid Method,'' which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. The availability of this incorporation by reference is given in paragraph (a)(2)(iii) of this section.

(v) *Unsaponifiable matter*. Not more than 1.5 percent as determined by the American Oil Chemists' Society Official Method Ca 6b–53—''Unsaponifiable Matter'' (reapproved 1989), which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. The availability of this incorporation by reference is given in paragraph (a)(2)(iii) of this section.

(vi) *Free fatty acids*. Not more than 0.1 percent as determined by the American Oil Chemists' Society Official Method Ca 5a–40—''Free Fatty Acids'' (reapproved 1989), which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. The availability of this incorporation by reference is given in paragraph (a)(2)(iii) of this section.

(vii) *Peroxide value*. Not more than 5 milliequivalents per kilogram of oil as determined by the American Oil Chemists' Society Official Method Cd 8–53—''Peroxide Value, Acetic Acid—Chloroform Method'' (updated 1992) or Recommended Practice Cd 8b–90—''Peroxide Value, Acetic Acid—Isooctane Method'' (updated 1992), which are incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. The availability of this incorporation by reference is given in paragraph (a)(2)(iii) of this section.

(viii) *Lead*. Not more than 0.1 part per million as determined by the American Oil Chemists' Society Official Method Ca 18c–91—''Determination of Lead by Direct Graphite Furnace Atomic Absorption Spectrometry'' (revised 1992), which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. The availability of this incorporation by reference is given in paragraph (a)(2)(iii) of this section.

(ix) *Mercury*. Not more than 0.5 part per million as determined by the method entitled ''Biomedical Test Materials Program: Analytical Methods for the Quality Assurance of Fish Oil,'' published in the ''NOAA Technical Memorandum NMFS–SEFC–211,'' F. M. Van Dolah and S. B. Galloway, editors, National Marine Fisheries Service, U. S. Department of Commerce, pages 71–88, November, 1988, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. The availability of this incorporation by reference is given in paragraph (a)(2)(iii) of this section.

(3) In accordance with § 184.1(b)(2), the ingredient may be used in food only within the following specific limitations:

Category of food	Maximum level of use in food (as served)
Cookies, crackers, § 170.3(n)(1) of this chapter.	5.0 percent
Breads, rolls (white & dark), § 170.3(n)(1) of this chapter.	1.0 percent
Fruit pies, custard pies, § 170.3(n)(1) of this chapter.	7.0 percent
Cakes, § 170.3(n)(1) of this chapter ..	10.0 percent
Cereals, § 170.3(n)(4) of this chapter	4.0 percent
Fats, oils, § 170.3(n)(12) of this chapter, but not in infant formula.	20.0 percent
Yogurt, § 170.3(n)(31) of this chapter	4.0 percent
Cheese products, § 170.3(n)(5) of this chapter.	5.0 percent
Frozen dairy products, § 170.3(n)(20) of this chapter.	5.0 percent
Meat products, § 170.3(n)(29) of this chapter.	10.0 percent
Egg products, § 170.3(n)(11) of this chapter.	5.0 percent
Fish products, § 170.3(n)(13) of this chapter.	20.0 percent
Condiments, § 170.3(n)(8) of this chapter.	5.0 percent
Soup mixes, § 170.3(n)(40) of this chapter.	3.0 percent
Snack foods, § 170.3(n)(37) of this chapter.	5.0 percent
Nut products, § 170.3(n)(32) of this chapter.	5.0 percent

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 60 of 100

Category of food	Maximum level of use in food (as served)
Gravies, sauces, § 170.3(n)(24) of this chapter.	5.0 percent

(b) *Hydrogenated and partially hydrogenated menhaden oils.* (1) Partially hydrogenated and hydrogenated menhaden oils are prepared by feeding hydrogen gas under pressure to a converter containing crude menhaden oil and a nickel catalyst. The reaction is begun at 150 to 160 ½C and after 1 hour the temperature is raised to 180 ½C until the desired degree of hydrogenation is reached. Hydrogenated menhaden oil is fully hydrogenated.

(2) Partially hydrogenated and hydrogenated menhaden oils meet the following specifications:

(i) *Color.* Opaque white solid.

(ii) *Odor.* Odorless.

(iii) *Saponification value.* Between 180 and 200.

(iv) *Iodine number.* Not more than 119 for partially hydrogenated menhaden oil and not more than 10 for fully hydrogenated menhaden oil.

(v) *Unsaponifiable matter.* Not more than 1.5 percent.–

(vi) *Free fatty acids.* Not more than 0.1 percent.

(vii) *Peroxide value.* Not more than 5 milliequivalents per kilogram of oil.

(viii) *Nickel.* Not more than 0.5 part per million.

(ix) *Mercury.* Not more than 0.5 part per million.

(x) *Arsenic* (*as As*). Not more than 0.1 part per million.

(xi) *Lead.* Not more than 0.1 part per million.

(3) Partially hydrogenated and hydrogenated menhaden oils are used as edible fats or oils, as defined in § 170.3(n)(12) of this chapter, in food at levels not to exceed current good manufacturing practice.

(4) If the fat or oil is fully hydrogenated, the name to be used on the label of a product containing it shall include the term ''hydrogenated,'' or if it is partially hydrogenated, the name shall include the term ''partially hydrogenated,'' in accordance with § 101.4(b)(14) of this chapter.

[62 FR 30756, June 5, 1997]

§ 184.1490 Methylparaben.

(a) Methylparaben is the chemical methyl *p*-hydroxybenzoate. It is produced by the methanol esterification of *p*-hydroxybenzoic acid in the presence of sulfuric acid, with subsequent distillation.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), p. 199, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as an antimicrobial agent as defined in § 170.3(o)(2) of this chapter.

(d) The ingredient is used in food at levels not to exceed good manufacturing practices. Current good manufacturing practice results in a maximum level of 0.1 percent in food.

(e) Prior sanctions for this ingredient different from the uses established in this regulation do not exist or have been waived.

[42 FR 14653, Mar. 15, 1977, as amended at 49 FR 5612, Feb. 14, 1984]

§ 184.1498 Microparticulated protein product.

(a) Microparticulated protein product is prepared from egg whites or milk protein or a combination of egg whites and milk protein. These protein sources may be used alone or in combination with other safe and suitable ingredients to form the microparticulated product. The mixture of ingredients is high-shear heat processed to achieve a smooth and creamy texture similar to that of fat. Safe and suitable ingredients used in the preparation of the microparticulated protein product must be used in compliance with the limitations of the appropriate regulations in parts 172, 182, and 184 of this chapter.

(b) The ingredient is used in food in accordance with § 184.1(b)(2) at levels not to exceed current good manufacturing practice. The affirmation of the use of this ingredient as generally recognized as safe (GRAS) as a direct

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 61 of 100

human food ingredient is based upon the following conditions of use:

(1) The ingredient is used in food as a thickener as defined in § 170.3(o)(28) of this chapter or as a texturizer as defined in § 170.3(o)(32) of this chapter.

(2) The ingredient is used in frozen dessert-type products except that the ingredient may not be used to replace the milk fat required in standardized frozen desserts.

(3) The name of the ingredient used in the ingredient statement on both bulk and packaged food must include the source of the protein (e.g., ''microparticulated egg white protein''), followed by a parenthetical listing of each of the ingredients in the microparticulated protein product, in descending order of predominance. Microparticulated protein product must be used in accordance with this requirement or its addition to food will be considered by FDA to constitute the use of an unapproved food additive (see § 184.1(b)(2)).

[55 FR 6391, Feb. 23, 1990]

§ 184.1505 Mono- and diglycerides.

(a) Mono- and diglycerides consist of a mixture of glyceryl mono- and diesters, and minor amounts of triesters, that are prepared from fats or oils or fat-forming acids that are derived from edible sources. The most prevalent fatty acids include lauric, linoleic, myristic, oleic, palmitic, and stearic. Mono- and diglycerides are manufactured by the reaction of glycerin with fatty acids or the reaction of glycerin with triglycerides in the presence of an alkaline catalyst. The products are further purified to obtain a mixture of glycerides, free fatty acids, and free glycerin that contains at least 90 percent-by-weight glycerides.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 201, which is incorporated by reference in accordance with 5 U.S.C. 552(a). Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20005.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used in food as a dough strengthener as defined in § 170.3(o)(6) of this chapter; an emulsifier and emulsifier salt as defined in § 170.3(o)(8) of this chapter; a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter; a formulation aid as defined in § 170.3(o)(14) of this chapter; a lubricant and release agent as defined in § 170.3(o)(18) of this chapter; a solvent and vehicle as defined in § 170.3(o)(27) of this chapter; a stabilizer and thickener as defined in § 170.3(o)(28) of this chapter; a surface-active agent as defined in § 170.3(o)(29) of this chapter; a surface-finishing agent as defined in § 170.3(o)(30) of this chapter; and a texturizer as defined in § 170.3(o)(32) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[54 FR 7403, Feb. 21, 1989, as amended at 57 FR 10616, Mar.27, 1992]

§ 184.1521 Monosodium phosphate derivatives of mono- and diglycerides.

(a) Monosodium phophate derivatives of mono- and diglycerides are composed of glyceride derivatives formed by reacting mono- and diglycerides that are derived from edible sources with phosphorus pentoxide (tetraphosphorus decoxide) followed by neutralization with sodium carbonate.

(b) FDA is developing food-grade specifications for monosodium phosphate mono- and diglycerides in cooperation with the National Academy of Sciences. In the interim, this ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 62 of 100

human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used in food as an emulsifier and emulsifier salt as defined in § 170.3(o)(8) of this chapter, a lubricant and release agent as defined in § 170.3(o)(18) of this chapter, and as a surface-active agent as defined in § 170.3(o)(29) of this chapter.

(2) The ingredient is used in the following foods at levels not to exceed current good manufacturing practice: dairy product analogs as defined in § 170.3(n)(10) of this chapter and soft candy as defined in § 170.3(n)(38) of this chapter.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[54 FR 7404, Feb. 21, 1989]

§ 184.1530 Niacin.

(a) Niacin ($C_6H_5NO_2$, CAS Reg. No. 59–67–6) is the chemical 3-pyridinecarboxylic acid (nicotinic acid). It is a non-hygroscopic, stable, white, crystalline solid that sublimes without decomposition at about 230 °C. It is soluble in water and alcohol. It is insoluble in ether.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 4th ed. (1996), p. 264, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, Box 285, 2101 Constitution Ave. NW., Washington, DC 20055 (Internet address ''http://www.nap.edu''), or may be examined at the Center for Food Safety and Applied Nutrition's Library, Food and Drug Administration, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a nutrient supplement as defined in § 170.3(o)(20) of this chapter.

(2) The ingredient is used in foods at levels not to exceed current good manufacturing practice. The ingredient may also be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the Act) or with regulations promulgated under section 412(a)(2) of the Act.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 52033, Nov. 16, 1983; 48 FR 54336, Dec. 2, 1983, as amended at 64 FR 1760, Jan. 12, 1999]

§ 184.1535 Niacinamide.

(a) Niacinamide ($C_6H_6N_2O$, CAS Reg. No. 98–92–0) is the chemical 3-pyridinecarboxylic acid amide (nicotinamide). It is a white crystalline powder that is soluble in water, alcohol, ether, and glycerol. It melts between 128° and 131 °C.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 205, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a nutrient supplement as defined in § 170.3(o)(20) of this chapter.

(2) The ingredient is used in foods at levels not to exceed current good manufacturing practice. The ingredient may also be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) or with regulations promulgated under section 412(a)(2) of the Act.

(d) Prior sanctions for this ingredient different from the uses established in

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 63 of 100

this section do not exist or have been waived.

[48 FR 52033, Nov. 16, 1983; 48 FR 54336, Dec. 2, 1983]

§ 184.1537 Nickel.

(a) Elemental nickel (CAS Reg. No. 7440–02–0) is obtained from nickel ore by transforming it to nickel sulfide (Ni_3S_2). The sulfide is roasted in air to give nickel oxide (NiO). The oxide is then reduced with carbon to give elemental nickel.

(b) The Food and Drug Administration is developing food-grade specifications for nickel in cooperation with the National Academy of Sciences. In the interim, this ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a catalyst as defined in § 170.3(o)(24) of this chapter.

(2) The ingredient is used in the hydrogenation of fats and oils as defined in § 170.3(n)(12) of this chapter at levels not to exceed current good manufacturing practice. Current good manufacturing practice includes the removal of nickel from fats and oils following hydrogenation.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 51618, Nov. 10, 1983]

§ 184.1538 Nisin preparation.

(a) Nisin preparation is derived from pure culture fermentations of certain strains of Streptococcus lactis Lancefield Group N. Nisin preparation contains nisin (CAS Reg. No. 1414–45–5), a group of related peptides with antibiotic activity.

(b) The ingredient is a concentrate or dry material that meets the specifications that follow when it is tested as described in ''Specifications for Identity and Purity of Some Antibiotics,'' World Health Organization, FAO Nutrition Meeting Report Series, No. 45A, 1969, which is incorporated by reference. Copies are available from the Dockets Management Branch (HFA–305), Food and Drug Administration, rm. 1–23, 12420 Parklawn Dr., Rockville, MD 20857, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(1) Nisin content, not less than 900 international units per milligram.

(2) Arsenic, not more than 1 part per million.

(3) Lead, not more than 2 parts per million.

(4) Zinc, not more than 25 parts per million.

(5) Copper, zinc plus copper not more than 50 parts per million.

(6) Total plate count, not more than 10 per gram.

(7) *Escherichia coli,* absent in 10 grams.

(8) *Salmonella,* absent in 10 grams.

(9) Coagulase positive staphylococci, absent in 10 grams.

(c) The ingredient is used as an antimicrobial agent as defined in § 170.3(o)(2) of this chapter to inhibit the outgrowth of *Clostridium botulinum* spores and toxin formation in pasteurized cheese spreads and pasteurized process cheese spreads listed in § 133.175; pasteurized cheese spread with fruits, vegetables, or meats as defined in § 133.176; pasteurized process cheese spread as defined in § 133.179; pasteurized process cheese spread with fruits, vegetables, or meats as defined in § 133.180 of this chapter.

(d) The ingredient is used at levels not to exceed good manufacturing practice in accordance with § 184.1(b)(1) of this chapter. The current good manufacturing practice level is the quantity of the ingredient that delivers a maximum of 250 parts per million of nisin in the finished product as determined by the British Standards Institution Methods, ''Methods for the Estimation and Differentiation of Nisin in Processed Cheese,'' BS 4020 (1974), which is incorporated by reference. Copies are available from the Dockets Management Branch (HFA–305), Food and Drug Administration, rm. 1–23, 12420 Parklawn Dr., Rockville, MD

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 64 of 100

20857, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

[53 FR 11250, Apr. 6, 1988, as amended at 59 FR 14364, Mar. 28, 1994]

§ 184.1540 Nitrogen.

(a) Nitrogen (empirical formula N_2, CAS Reg. No. 7727–37–9) is a colorless, odorless, flavorless gas that is produced commercially by the fractionation of liquid air.

(b) The Food and Drug Administration is developing food-grade specifications for nitrogen in cooperation with the National Academy of Sciences. In the interim, the ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitations other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a propellant, aerating agent, and gas as defined in § 170.3(o)(25) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 57270, Dec. 29, 1983]

§ 184.1545 Nitrous oxide.

(a) Nitrous oxide (empirical formula N_2O, CAS Reg. No. 10024–97–2) is also known as dinitrogen monoxide or laughing gas. It is a colorless gas, about 50 percent heavier than air, with a slightly sweet smell. It does not burn but will support combustion. Nitrous oxide is manufactured by the thermal decomposition of ammonium nitrate. Higher oxides of nitrogen are removed by passing the dry gas through a series of scrubbing towers.

(b) The Food and Drug Administration is developing food-grade specifications for nitrous oxide in cooperation with the National Academy of Sciences. In the interim, the ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitations other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a propellant, aerating agent, and gas as defined in § 170.3(o)(25) of this chapter.

(2) The ingredient is used in dairy product analogs as defined in § 170.3(n)(10) of this chapter at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 57270, Dec. 29, 1983]

§ 184.1553 Peptones.

(a) Peptones are a variable mixture of polypeptides, oligopeptides, and amino acids that are produced by partial hydrolysis of casein, animal tissue, soy protein isolate, gelatin, defatted fatty tissue, egg albumin, or lactalbumin (whey protein). Peptones are produced from these proteins using proteolytic enzymes that either are considered to be generally recognized as safe (GRAS) or are regulated as food additives. Peptones are also produced by denaturing any of the proteins listed in this paragraph with safe and suitable acids or heat.

(b) FDA is developing food-grade specifications for peptones in cooperation with the National Academy of Sciences. In the interim, these ingredients must be of a purity suitable for their intended use.

(c) In accordance with § 184.1(b)(1), these ingredients are used in food with no limitation other than current good manufacturing practice. The affirmation of these ingredients as GRAS as direct human food ingredients is based upon the following current good manufacturing practice conditions of use:

(1) These ingredients are used as nutrient supplements as defined in § 170.3(o)(20) of this chapter; as processing aids as defined in § 170.3(o)(24) of

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 65 of 100

this chapter; and as surface-active agents as defined in § 170.3(o)(29) of this chapter.

(2) These ingredients are used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for these ingredients different from the uses established in this section do not exist or have been waived.

[49 FR 25430, June 21, 1984, as amended at 50 FR 49536, Dec. 3, 1985]

§ 184.1555 Rapeseed oil.

(a) *Fully hydrogenated rapeseed oil.* (1) Fully hydrogenated rapeseed oil is a mixture of triglycerides in which the fatty acid composition is a mixture of saturated fatty acids. The fatty acids are present in the same porportions which result from the full hydrogenation of fatty acids occurring in natural rapeseed oil. The rapeseed oil is obtained from the *napus* and *campestris* varieties of *Brassica* of the family Cruciferae. It is prepared by fully hydrogenating refined and bleached rapeseed oil at 310–375 °F, using a catalyst such as nickel, until the iodine number is 4 or less.

(2) The ingredient meets the following specifications: Acid value not more than 6, arsenic not more than 3 parts per million, free glycerin not more than 7 percent, heavy metals (as Pb) not more than 10 parts per million, iodine number not more than 4, residue on ignition not more than 0.5 percent.

(3) The ingredient is used as a stabilizer and thickener as defined in § 170.3(o)(28) of this chapter in peanut butter. The use level of the ingredient is limited by good manufacturing practice (GMP) to the minimum amount required to produce the intended effect. Current good manufacturing practices result in a maximum level of 2 percent in peanut butter.

(b) *Superglycerinated fully hydrogenated rapeseed oil.* (1) Superglycerinated fully hydrogenated rapeseed oil is a mixture of mono- and diglycerides with triglycerides as a minor component. The fatty acid composition is a mixture of saturated fatty acids present in the same proportions as those resulting from the full hydrogenation of fatty acids in natural rapeseed oil. It is made by adding excess glycerol to the fully hydrogenated rapeseed oil and heating, in the presence of a sodium hydroxide catalyst, to 330 °F under partial vacuum and steam sparging agitation.

(2) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), p. 201, relating to mono- and diglycerides, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408. An additional specification requires the iodine number to be 4 or less.

(3) The ingredient is used as an emulsifier as defined in § 170.3(o)(8) of this chapter in shortenings for cake mixes. The use level of the ingredient is limited by good manufacturing practice (GMP) to the minimum amount required to produce the intended effect. Current good manufacturing practices result in a maximum level, as served, of 4 percent of the shortening or 0.5 percent of the total weight of the cake mix.

(c) *Low erucic acid rapeseed oil.* (1) Low erucic acid rapeseed oil, also known as canola oil, is the fully refined, bleached, and deodorized edible oil obtained from certain varieties of *Brassica Napus* or *B. Campestris* of the family *Cruciferae.* The plant varieties are those producing oil-bearing seeds with a low erucic acid content. Chemically, low erucic acid rapeseed oil is a mixture of triglycerides, composed of both saturated and unsaturated fatty acids, with an erucic acid content of no more than 2 percent of the component fatty acids.

(2) Low erucic acid rapeseed oil as defined in paragraph (c)(1) of this section may be partially hydrogenated to reduce the proportion of unsaturated fatty acids. When the partially hydrogenated low erucic acid rapeseed oil is used, it shall be referred to as partially hydrogenated low erucic acid rapeseed oil.

(3) In addition to limiting the content of erucic acid to a level not exceeding 2 percent of the component fatty acids, FDA is developing other food-grade specifications for low erucic

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 66 of 100

acid rapeseed oil and partially hydrogenated low erucic acid rapeseed oil in cooperation with the National Academy of Sciences. In the interim, the ingredients must be of a purity suitable for their intended use.

(4) Low erucic acid rapeseed oil and partially hydrogenated low erucic acid rapeseed oil are used as edible fats and oils in food, except in infant formula, at levels not to exceed current good manufacturing practice.

[42 FR 48336, Sept. 23, 1977, as amended at 49 FR 5613, Feb. 14, 1984; 50 FR 3755, Jan. 28, 1985; 53 FR 52682, Dec. 29, 1988]

§ 184.1560 Ox bile extract.

(a) Ox bile extract (CAS Reg. No. 8008–63–7), also known as purified oxgall or sodium choleate, is a yellowish green, soft solid, with a partly sweet, partly bitter, disagreeable taste. It is the purified portion of the bile of an ox obtained by evaporating the alcohol extract of concentrated bile.

(b) Food-grade ox bile extract shall meet the specifications of the U.S. Pharmacopeia (USP), XIV, 1950, p. 410.[1]

(c) The ingredient is used as a surfactant as defined in § 170.3 (o)(29) of this chapter.

(d) The ingredient is used in food in accordance with § 184.1(b)(1) at levels not to exceed good manufacturing practice. Current good manufacturing practice results in a maximum level, as served, of 0.002 percent for cheese as defined in § 170.3(n)(5) of this chapter.

(e) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[43 FR 36064, Aug. 15, 1978. Redesignated and amended at 50 FR 49537, Dec. 3, 1985]

§ 184.1563 Ozone.

(a) Ozone (O_3, CAS Reg. No. 10028–15–6) is an unstable blue gas with a pungent, characteristic odor, which occurs freely in nature, It is produced commercially by passing electrical discharges or ionizing radiation through air or oxygen.

(b) The ingredient must be of a purity suitable for its intended use in accordance with § 170.30(h)(1) of this chapter.

(c) In accordance with § 184.1(b)(2), the ingredient is used to treat food only within the following specific limitations:

Category of food	Maximum treatment level in food	Functional use
Bottled water that prior to ozonation meets the microbiological, physical, chemical, and radiological quality standards of § 165.110 (b)(2) through (b)(5) of this chapter.	Not to exceed current good manufacturing practice. Current good manufacturing practice results in a maximum residual level at the time of bottling of 0.4 milligram of ozone per liter of bottled water.	Antimicrobial agent, § 170.3 (o)(2) of this chapter.

[47 FR 50210, Nov. 5, 1982, as amended at 60 FR 57130, Nov. 13, 1995]

§ 184.1583 Pancreatin.

(a) Pancreatin (CAS Reg. No. 8049–47–6) is an enzyme preparation obtained from porcine or bovine pancreatic tissue. It is a white to tan powder. Its characterizing enzyme activity that of a peptide hydrolase (EC 3.4.21.36).

(b) The ingredient meets the general requirements and additional requirements in the Food Chemicals Codex, 3d ed. (1981), p. 110, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of Premarket Approval (HFS–200), Food and Drug Administration, 200 C St. SW., Washington, DC, and the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as GRAS as a direct food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an enzyme as defined in § 170.3(o)(9) of this chapter to hydrolyze proteins or polypeptides.

[1] Copies may be obtained from: U.S. Pharmacopeial Convention, Inc., 12601 Twinbrook Parkway, Rockville, MD 20852.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 67 of 100

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

[60 FR 32911, June 26, 1995]

§ 184.1585 Papain.

(a) Papain (CAS Reg. No. 9001–73–4) is a proteolytic enzyme derived from *Carica papaya* L. Crude latex containing the enzyme is collected from slashed unripe papaya. The food-grade product is obtained by repeated filtration of the crude latex or an aqueous solution of latex or by precipitation from an aqueous solution of latex. The resulting enzyme preparation may be used in a liquid or dry form.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), pp. 107–110, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than currect good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing conditions of use:

(1) The ingredient is used as an enzyme as defined in § 170.3(o)(9) of this chapter; processing aid as defined in § 170.3(o)(24) of this chapter; and texturizer as defined in § 170.3(o)(32) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 48806, Oct. 21, 1983]

§ 184.1588 Pectins.

(a) The pectins (CAS Reg. No. 9000–69–5) are a group of complex, high molecular weight polysaccharides found in plants and composed chiefly of partially methylated polygalacturonic acid units. Portions of the carboxly group occur as methyl esters, and the remaining carboxyl groups exist in the form of the free acid or as its ammonium, potassium, or sodium (CAS Reg. No. 9000–59–8) salts, and in some types as the acid amide. Thus, the pectins regulated in this section are the high-ester pectins, low-ester pectins, amidated pectins, pectinic acids, and pectinates. Pectin is produced commercially by extracting citrus peel, apple pomace, or beet pulp with hot dilute acid (pH 1.0 to 3.5, 70° to 90 °C). The extract is filtered, and pectin is then precipitated from the clear extract with ethanol or isopropanol, or as the copper or aluminum salt. The acid extract is sometimes spray- or roller-dried, or it is concentrated to be sold as liquid pectin.

(b) The ingredients meet the specifications of the Food Chemical Codex, 3d Ed. (1981), p. 215, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredients are used in food with no limitation other than current good manufacturing practice. The affirmation of these ingredients as generally recognized as safe (GRAS) as direct human food ingredients is based upon the following current good manufacturing practice conditions of use:

(1) The ingredients are used as emulsifiers as defined in § 170.3(o)(8) of this chapter and as stabilizers and thickeners as defined in § 170.3(o)(28) of this chapter.

(2) The ingredients are used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for these ingredients different from the uses established in this section do not exist or have been waived.

[48 FR 51149, Nov. 7, 1983]

§ 184.1595 Pepsin.

(a) Pepsin (CAS Reg. No. 9001–75–6) is an enzyme preparation obtained from the glandular layer of hog stomach. It is a white to light tan powder, amber paste, or clear amber to brown liquid.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 68 of 100

Its characterizing enzyme activity is that of a peptide hydrolase (EC 3.4.23.1).

(b) The ingredient meets the general requirements and additional requirements for enzyme preparations in the Food Chemicals Codex, 3d ed. (1981), p. 110, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of Premarket Approval (HFS–200), Food and Drug Administration, 200 C St. SW., Washington, DC, and the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as GRAS as a direct food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an enzyme as defined in § 170.3(o)(9) of this chapter to hydrolyze proteins or polypeptides.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

[60 FR 32911, June 26, 1995]

§ 184.1610 Potassium alginate.

(a) Potassium alginate (CAS Reg. No. 9005–36–1) is the potassium salt of alginic acid, a natural polyuronide constituent of certain brown algae. Potassium alginate is prepared by the neutralization of purified alginic acid with appropriate pH control agents.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 239, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(2), the ingredient is used in food only within the following specific limitations:

Category of food	Maximum level of use in food (as served) (percent)	Functional use
Confections and frostings, § 170.3(n)(9) of this chapter.	0.1	Stabilizer, thickener, § 170.3(o)(28) of this chapter
Gelatins and puddings, § 170.3(n)(22) of this chapter.	0.7	Do.
Processed fruits and fruit juices, § 170.3(n)(35) of this chapter.	0.25	Do.
All other food categories.	0.01	Do.

(d) Prior sanctions for potassium alginate different from the uses established in this section do not exist or have been waived.

[47 FR 29951, July 9, 1982]

§ 184.1613 Potassium bicarbonate.

(a) Potassium bicarbonate ($KHCO_3$, CAS Reg. No. 298–14–6) is made by the following processes:

(1) By treating a solution of potassium hydroxide with carbon dioxide;

(2) By treating a solution of potassium carbonate with carbon dioxide.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 239, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a formulation aid as defined in § 170.3(o)(14) of this chapter; nutrient supplemlent as defined in § 170.3(o)(20) of this chapter; pH control agent as defined in § 170.3(o)(23) of this chapter; and processing aid as defined in § 170.3(o)(24) of this chapter.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 69 of 100

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 52442, Nov. 18, 1983]

§ 184.1619 Potassium carbonate.

(a) Potassium carbonate (K_2CO_3, CAS Reg. No. 584–08–7) is produced by the following methods of manufacture:

(1) By electrolysis of potassium chloride followed by exposing the resultant potassium to carbon dioxide;

(2) By treating a solution of potassium hydroxide with excess carbon dioxide to produce potassium carbonate;

(3) By treating a solution of potassium hydroxide with carbon dioxide to produce potassium bicarbonate, which is then heated to yield potassium carbonate.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 240, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, D.C. 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. the affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used in food as a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter; nutrient supplement as defined in § 170.3(o)(20) of this chapter; pH control agent as defined in § 170.3(o)(23) of this chapter; and processing aid as defined in § 170.3(o)(24) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 52442, Nov. 18, 1983]

§ 184.1622 Potassium chloride.

(a) Potassium chloride (KCl, CAS Reg. No. 7447–40–7) is a white, odorless solid prepared from source minerals by fractional crystallization or flotation. It is soluble in water and glycerol and has a saline taste at low concentration levels.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 241, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a flavor enhancer as defined in § 170.3(o)(11) of this chapter; as a flavoring agent as defined in § 170.3(o)(12) of this chapter; as a nutrient supplement as defined in § 170.3(o)(20) of this chapter; as a pH control agent as defined in §170.3(o)(23) of this chapter; and as a stabilizer or thickener as defined in § 170.3(o)(28) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice. Potassium chloride may be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the Act) or with regulations promulgated under section 412(a)(2) of the Act.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 51614, Nov. 10, 1983]

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 70 of 100

§ 184.1625 Potassium citrate.

(a) Potassium citrate ($C_6H_5K_3O_7 \cdot H_2O$, CAS Reg. No. 006100–0905–096) is the potassium salt of citric acid. It is prepared by neutralizing citric acid with potassium hydroxide or potassium carbonate. It occurs as transparent crystals or a white granular powder, is odorless and deliquescent, and contains one mole of water per mole of potassium citrate.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d ed. (1981), p. 242, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, and the Center for Food Safety and Applied Nutrition (HFS–200), 200 C St. SW., Washington, DC 20204, or may be examined at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section, or different from those set forth in part 181 of this chapter, do not exist or have been waived.

[59 FR 63896, Dec. 12, 1994]

§ 184.1631 Potassium hydroxide.

(a) Potassium hydroxide (KOH, CAS Reg. No. 1310–58–3) is also known as caustic potash, potash lye, and potassa. The empirical formula is KOH. It is a white, highly deliquescent caustic solid, which is marketed in several forms, including pellets, flakes, sticks, lumps, and powders. Potassium hydroxide is obtained commercially from the electrolysis of potassium chloride solution in the presence of a porous diaphragm.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available from inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a formulation aid as defined in § 170.3(o)(14) of this chapter; a pH control agent as defined in § 170.3(o)(23) of the chapter; a processing aid as defined in § 170.3(o)(24) of this chapter; and a stabilizer and thickener as defined in § 170.3(o)(28) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 52444, Nov. 18, 1983]

§ 184.1634 Potassium iodide.

(a) Potassium iodide (KI, CAS Reg. No. 7681–11–0) is the potassium salt of hydriodic acid. It occurs naturally in sea water and in salt deposits, but can be prepared by reacting hydriodic acid (HI) with potassium bicarbonate ($KHCO_3$).

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), pp. 246–247, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as a nutrient supplement as defined in § 170.3(o)(20) of this chapter.

(d) The ingredient is used in table salt in accordance with § 184.1(b)(2) of this chapter as a source of dietary iodine at a maximum level of 0.01 percent.

(e) Prior sanctions for this ingredient different from the uses established in

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 71 of 100

this section do not exist or have been waived.

[43 FR 11699, Mar. 21, 1978, as amended at 49 FR 5613, Feb. 14, 1984; 61 FR 14247, Apr. 1, 1996]

§ 184.1635 Potassium iodate.

(a) Potassium iodate (KIO_3, CAS Reg. No. 7758–05–6) does not occur naturally but can be prepared by reacting iodine with potassium hydroxide.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), pp. 245–246, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as a dough strengthener as defined in § 170.3(o)(6) of this chapter.

(d) The ingredient is used in the manufacture of bread in accordance with § 184.1(b)(2) of this chapter in an amount not to exceed 0.0075 percent based on the weight of the flour.

(e) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[43 FR 11699, Mar. 21, 1978, as amended at 49 FR 5613, Feb. 14, 1984]

§ 184.1639 Potassium lactate.

(a) Potassium lactate ($C_3H_5O_3K$, CAS Reg. No. 996–31–6) is the potassium salt of lactic acid. It is a hydroscopic, white, odorless solid and is prepared commercially by the neutralization of lactic acid with potassium hydroxide.

(b) FDA is developing food-grade specifications for potassium lactate in cooperation with the National Academy of Sciences. In the interim, this ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. This regulation does not authorize its use in infant foods and infant formulas. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a flavor enhancer as defined in § 170.3(o)(11) of this chapter; a flavoring agent or adjuvant as defined in § 170.3(o)(12) of this chapter; a humectant as defined in § 170.3(o)(16) of this chapter; and a pH control agent as defined in § 170.3(o)(23) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[52 FR 10886, Apr. 6, 1987]

§ 184.1643 Potassium sulfate.

(a) Potassium sulfate (K_2SO_4, CAS Reg. No. 7778–80–5) occurs naturally and consists of colorless or white crystals or crystalline powder having a bitter, saline taste. It is prepared by the neutralization of sulfuric acid with potassium hydroxide or potassium carbonate.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), p. 252, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter.

(d) The ingredient is used in food at levels not to exceed good manufacturing practice in accordance with § 184.1(b)(1). Current good manufacturing practice results in a maximum level, as served, of 0.015 percent for nonalcoholic beverages as defined in § 170.3(n)(3) of this chapter.

(e) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[45 FR 6086, Jan. 25, 1980, as amended at 49 FR 5613, Feb. 14, 1984]

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 72 of 100

§ 184.1655 Propane.

(a) Propane (empirical formula C_3H_8, CAS Reg. No. 74–98–6) is also known as dimethylmethane or propyl hydrid. It is a colorless, odorless, flammable gas at normal temperatures and pressures. It is easily liquefied under pressure at room temperature and is stored and shipped in the liquid state. Propane is obtained from natural gas by fractionation following absorption in oil, adsorption to surface-active agents, or refrigeration.

(b) The Food and Drug Administration is developing food-grade specifications for propane in cooperation with the National Academy of Sciences. In the interim, the ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitations other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a propellant, aerating agent, and gas as defined in § 170.3(o)(25) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 57271, Dec. 29, 1983]

§ 184.1660 Propyl gallate.

(a) Propyl gallate is the *n*-propylester of 3,4,5-trihydroxybenzoic acid ($C_{10}H_{12}O_5$). Natural occurrence of propyl gallate has not been reported. It is commercially prepared by esterification of gallic acid with propyl alcohol followed by distillation to remove excess alcohol.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), pp. 257–258, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as an antioxidant as defined in § 170.3(o)(3) of this chapter.

(d) The ingredient is used in food at levels not to exceed good manufacturing practice in accordance with § 184.1(b)(1). Good manufacturing practice results in a maximum total content of antioxidants of 0.02 percent of the fat or oil content, including the essential (volatile) oil content, of the food.

(e) Prior sanctions for this ingredient different from the uses established in this section, or different from that stated in part 181 of this chapter, do not exist or have been waived.

[42 FR 14653, Mar. 15, 1977, as amended at 44 FR 52826, Sept. 11, 1979; 49 FR 5613, Feb. 14, 1984]

§ 184.1666 Propylene glycol.

(a) Propylene glycol ($C_3H_8O_2$, CAS Reg. No. 57–55–6) is known as 1,2-propanediol. It does not occur in nature. Propylene glycol is manufactured by treating propylene with chlorinated water to form the chlorohydrin which is converted to the glycol by treatment with sodium carbonate solution. It is also prepared by heating glyercol with sodium hydroxide.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 255, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418. It is also available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as an anticaking agent as defined in § 170.3(o)(1) of this chapter; antioxidant as defined in § 170.3(o)(3) of this chapter; dough strengthener as defined in § 170.3(o)(6) of this chapter; emulsifier as defined in § 170.3(o)(8) of this chapter; flavor agent as defined in § 170.3(o)(12) of this chapter; formulation aid as defined in § 170.3(o)(14) of this chapter; humectant as defined in § 170.3(o)(16) of this chapter; processing aid as defined in § 170.3(o)(24) of this chapter; solvent and vehicle as defined

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 73 of 100

in § 170.3(o)(27) of this chapter; stabilizer and thickener as defined in § 170.3(o)(28) of this chapter; surface-active agent as defined in § 170.3(o)(29) of this chapter; and texturizer as defined in § 170.3(o)(32) of this chapter.

(d) The ingredient is used in foods at levels not to exceed current good manufacturing practice in accordance with § 184.1(b)(1). Current good manufacturing practice results in maximum levels, as served, of 5 percent for alcoholic beverages, as defined in § 170.3(n)(2) of this chapter; 24 percent for confections and frostings as defined in § 170.3(n)(9) of this chapter; 2.5 percent for frozen dairy products as defined in § 170.3(n)(20) of this chapter; 97 percent for seasonings and flavorings as defined in § 170.3(n)(26) of this chapter; 5 percent for nuts and nut products as defined in § 170.3(n)(32) of this chapter; and 2.0 percent for all other food categories.

(e) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[47 FR 27812, June 25, 1982]

§ 184.1670 Propylparaben.

(a) Propylparaben is the chemical propyl *p*-hydroxybenzoate. It is produced by the *n*-propanol esterification of *p*-hydroxybenzoic acid in the presence of sulfuric acid, with subsequent distillation.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), p. 258, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as an antimicrobial agent as defined in § 170.3(o)(2) of this chapter.

(d) The ingredient is used in food at levels not to exceed good manufacturing practices. Current good manufacturing practice results in a maximum level of 0.1 percent in food.

(e) Prior sanctions for this ingredient different from the uses established in this regulation do not exist or have been waived.

[42 FR 14653, Mar. 15, 1977, as amended at 49 FR 5613, Feb. 14, 1984]

§ 184.1676 Pyridoxine hydrochloride.

(a) Pyridoxine hydrochloride ($C_8H_{11}NO_3 \cdot HCl$, CAS Reg. No. 58–56–0) is the chemical 3-hydroxy–4,5-dihydroxymethy–2-methylpyridine hydrochloride that is prepared by chemical synthesis.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 260, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a nutrient supplement as defined in § 170.3(o)(20) of this chapter.

(2) The ingredient is used in the following foods at levels not to exceed current good manufacturing practice: baked goods as defined in § 170.3(n)(1) of this chapter; nonalcoholic beverages and beverage bases as defined in § 170.3(n)(3) of this chapter; breakfast cereals as defined in § 170.3(n)(4) of this chapter; dairy product analogs as defined in § 170.3(n)(10) of this chapter; meat products as defined in § 170.3(n)(29) of this chapter; milk products as defined in § 170.3(n)(31) of this chapter; plant protein products as defined in § 170.3(n)(33) of this chapter; and snack foods as defined in § 170.3(n)(37) of this chapter. Pyridoxine hydrochloride may be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the Act) or with regulations promulgated under section 412(a)(2) of the Act.

(d) Prior sanctions for this ingredient different from the uses established in

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 74 of 100

this section do not exist or have been waived.

[48 FR 51615, Nov. 10, 1983]

§ 184.1685 Rennet (animal-derived) and chymosin preparation (fermentation-derived).

(a)(1) Rennet and bovine rennet are commercial extracts containing the active enzyme rennin (CAS Reg. No. 9001–98–3), also known as chymosin (International Union of Biochemistry Enzyme Commission (E.C.) 3.4.23.4). Rennet is the aqueous extract prepared from cleaned, frozen, salted, or dried fourth stomachs (abomasa) of calves, kids, or lambs. Bovine rennet is the product from adults of the animals listed above. Both products are called rennet and are clear amber to dark brown liquid preparations or white to tan powders.

(2) Chymosin preparation is a clear solution containing the active enzyme chymosin (E.C. 3.4.23.4). It is derived, via fermentation, from a nonpathogenic and nontoxigenic strain of *Escherichia coli* K–12 containing the prochymosin gene. The prochymosin is isolated as an insoluble aggregate that is acid-treated to destroy residual cellular material and, after solubilization, is acid-treated to form chymosin. It must be processed with materials that are generally recognized as safe, or are food additives that have been approved by the Food and Drug Administration for this use.

(3) Chymosin preparation is a clear solution containing the active enzyme chymosin (E.C. 3.4.23.4). It is derived, via fermentation, from a nonpathogenic and nontoxigenic strain of *Kluyveromyces marxianus* variety *lactis*, containing the prochymosin gene. The prochymosin is secreted by cells into fermentation broth and converted to chymosin by acid treatment. All materials used in the processing and formulating of chymosin must be either generally recognized as safe (GRAS), or be food additives that have been approved by the Food and Drug Administration for this use.

(4) Chymosin preparation is a clear solution containing the active enzyme chymosin (E.C. 3.4.23.4). It is derived, via fermentation, from a nonpathogenic and nontoxigenic strain of *Aspergillus niger* van Tieghem variety *awamori* (Nakazawa) Al-Musallam (synonym *A. awamori* Nakazawa) containing the prochymosin gene. Chymosin is recovered from the fermentation broth after acid treatment. All materials used in the processing and formulating of chymosin preparation must be either generally recognized as safe (GRAS) or be food additives that have been approved by the Food and Drug Administration for this use.

(b) Rennet and chymosin preparation meet the general and additional requirements for enzyme preparations of the ''Food Chemicals Codex,'' 3d Ed. (1981), pp. 107–110, which is incorporated by reference in accordance with 5 U.S.C. 552(a). Copies are available from the National Academy Press, 2101 Constitution Avenue NW., Washington, DC 20418, or are available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an enzyme as defined in § 170.3(o)(9) of this chapter; a processing aid as defined in § 170.3(o)(24) of this chapter; and a stabilizer and thickener as defined in § 170.3(o)(28) of this chapter.

(2) The ingredient is used in the following foods at levels not to exceed current good manufacturing practice: In cheeses as defined in § 170.3(n)(5) of this chapter; frozen dairy desserts and mixes as defined in § 170.3(n)(20) of this chapter; gelatins, puddings, and fillings as defined in § 170.3(n)(22) of this chapter; and milk products as defined in § 170.3(n)(31) of this chapter.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[55 FR 10935, Mar. 23, 1990, as amended at 57 FR 6479, Feb. 25, 1992; 58 FR 27202, May 7, 1993]

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 75 of 100

§ 184.1695 Riboflavin.

(a) Riboflavin ($C_{17}H_{20}N_4O_6$, CAS Reg. No. 83–88–5) occurs as yellow to orange-yellow needles that are crystallized from 2*N* acetic acid, alcohol, water, or pyridine. It may be prepared by chemical synthesis, biosynthetically by the organism *Eremothecium ashbyii*, or isolated from natural sources.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 262, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a nutrient supplement as defined in § 170.3(o)(20) of this chapter.

(2) The ingredient is used in foods at levels not to exceed current good manufacturing practice. The ingredient may also be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the Act) or with regulations promulgated under section 412(a)(2) of the Act.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 51148, Nov. 7, 1983]

§ 184.1697 Riboflavin–5′-phosphate (sodium).

(a) Riboflavin-5′-phosphate (sodium) ($C_{17}H_{20}N_4O_9PNa{\cdot}2H_2O$, CAS Reg. No 130–40–5) occurs as the dihydrate in yellow to orange-yellow crystals. It is prepared by phosphorylation of riboflavin with chlorophosphoric acid, pyrophosphoric acid, metaphosphoric acid, or pyrocatechol cyclic phosphate.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 263, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a nutrient supplement as defined in § 170.3(o)(20) of this chapter.

(2) The ingredient is used in milk products, as defined in § 170.3(n)(31) of this chapter, at levels not to exceed current good manufacturing practice. The ingredient may also be used in infant formulas in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the Act) or with regulations promulgated under section 412(a)(2) of the Act.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 51148, Nov. 7, 1983]

§ 184.1698 Rue.

(a) Rue is the perennial herb of several species of *Ruta* (*Ruta montana* L., *Ruta graveolens* L., *Ruta bracteosa* L., and *Ruta calepensis* L.). The leaves, buds, and stems from the top of the plant are gathered, dried, and then crushed in preparation for use, or left whole.

(b) The ingredient is used in all categories of food in accordance with § 184.1(b)(2) of this chapter at concentrations not to exceed 2 parts per million.

(c) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[43 FR 3705, Jan. 27, 1978]

§ 184.1699 Oil of rue.

(a) Oil of rue is the natural substance obtained by steam distillation of the

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 76 of 100

fresh blossoming plants of rue, the perennial herb of several species of *Ruta—Ruta montana* L., *Ruta graveolens* L., *Ruta bracteosa* L., and *Ruta calepensis* L.

(b) Oil of rue meets the specifications of the ''Food Chemicals Codex,'' 4th ed. (1996), pp. 342–343, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, Box 285, 2101 Constitution Ave. NW., Washington, DC 20055 (Internet address ''http://www.nap.edu''), or may be examined at the Center for Food Safety and Applied Nutrition's Library, Food and Drug Administration, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) The ingredient is used in food under the following conditions:

MAXIMUM USAGE LEVELS PERMITTED

Food (as served)	Parts per million	Function
Baked goods and baking mixes, § 170.3(n)(1), of this chapter.	10	Flavoring agent and adjuvant, § 170.3(o)(12) of this chapter.
Frozen dairy desserts and mixes, § 170.3 (n)(20) of this chapter.	10	Do.
Soft candy, § 170.3(n)(38) of this chapter	10	Do.
All other food categories	4	Do.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[42 FR 14653, Mar. 15, 1977, as amended at 49 FR 5613, Feb. 14, 1984; 64 FR 1760, Jan. 12, 1999]

§ 184.1702 Sheanut oil.

(a) Sheanut oil is produced from sheanuts derived from the Shea tree *Butyrospermum parkii* and is composed principally of triglycerides containing an oleic acid moiety at the 2-position and saturated fatty acids, usually stearic or palmitic acids, at the 1- and 3-positions.

(b) The ingredient meets the following specifications when tested using any appropriate validated methodology:

(1) Saponification value of 185 to 195,

(2) Iodine value of 28 to 43,

(3) Unsaponifiable matter not to exceed 1.5 percent,

(4) Free fatty acids not more than 0.1 percent as oleic acid,

(5) Peroxide value not more than 10 milliequivalents/equivalent (meq/eq),

(6) Lead not more than 0.1 part per million (ppm),

(7) Copper not more than 0.1 ppm.

(c) In accordance with § 184.1(b)(3), the ingredient is used in the following food categories at levels not to exceed current good manufacturing practice, except that the ingredient may not be used in a standardized food unless permitted by the standard of identity: Confections and frostings as defined in § 170.3(n)(9) of this chapter, coatings of soft candy as defined in § 170.3(n)(38) of this chapter, and sweet sauces and toppings as defined in § 170.3(n)(43) of this chapter.

[63 FR 28895, May 27, 1998]

§ 184.1721 Sodium acetate.

(a) Sodium acetate ($C_2H_3O_2Na$, CAS Reg. No. 127–09–3 or $C_2H_3O_2Na{\cdot}3H_2O$, CAS Reg. No. 6131–90–4) is the sodium salt of acetic acid and occurs naturally in plant and animal tissues. Sodium acetate may occur in either the anhydrous or trihydrated form. It is produced synthetically by the neutralization of acetic acid with sodium carbonate or by treating calcium acetate with sodium sulfate and sodium bicarbonate.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), pp. 272, 273 which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 77 of 100

(c) The ingredient is used as a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter; and as a pH control agent as defined in § 170.3(o)(23) of this chapter.

(d) The ingredient is used in food at levels not to exceed current good manufacturing practice in accordance with 184.1(b)(1). Current good manufacturing practice results in a maximum level, as served, of 0.007 percent for breakfast cereals as defined in § 170.3(n)(4) of this chapter; 0.5 percent for fats and oils as defined in § 170.3(n)(12) of this chapter; 0.6 percent for grain products and pastas as defined in § 170.3(n)(23) of this chapter and snack foods as defined in § 170.3(n)(37) of this chapter; 0.15 percent for hard candy as defined in § 170.3(n)(25) of this chapter; 0.12 percent for jams and jellies as defined in § 170.3(n)(28) of this chapter and meat products as defined in § 170.3(n)(29) of this chapter; 0.2 percent for soft candy as defined in § 170.3(n)(38) of this chapter; 0.05 percent for soups and soup mixes as defined in § 170.3(n)(40) of this chapter and sweet sauces as defined in § 170.3(n)(43) of this chapter.

(e) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[47 FR 27815, June 25, 1982]

§ 184.1724 Sodium alginate.

(a) Sodium alginate (CAS Reg. No. 9005–38–3) is the sodium salt of alginic acid, a natural polyuronide constituent of certain brown algae. Sodium alginate is prepared by the neutralization of purified alginic acid with appropriate pH control agents.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 274, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(2), the ingredient is used in food only within the following specific limitations:

Category of food	Maximum level of use in food (as served) (percent)	Functional use
Condiments and relishes, § 170.3(n)(8) of this chapter, except pimento ribbon for stuffed olives.	1.0	Texturizer, § 170.3(o)(32) of this chapter, formulation aid § 170.3(o)(14) of this chapter, stabilizer, thickener, § 170.3(o)(28) of this chapter.
Pimento ribbon for stuffed olives	6.0	Do.
Confections and frostings, § 170.3(n)(9) of this chapter	0.3	Stabilizer, thickener, § 170.3(o)(28) of this chapter.
Gelatins and puddings, § 170.3(n)(22) of this chapter	4.0	Firming agent, § 170.3(o)(10) of this chapter; flavor adjuvant, § 170.3(o)(12) of this chapter; stabilizer, thickener, § 170.3(o)(28) of this chapter.
Hard candy, § 170.3(n)(25) of this chapter	10.0	Stabilizer, thickener, § 170.3(o)(28) of this chapter.
Processed fruits and fruit juices, § 170.3(n)(35) of this chapter.	2.0	Formulation aid, § 170.3(o)(14) of this chapter; texturizer, § 170.3(o)(32) of this chapter.
All other food categories	1.0	Emulsifier, § 170.3(o)(8) of this chapter; firming agent, § 170.3(o)(10) of this chapter; flavor enhancer, § 170.3(o)(11) of this chapter; flavor adjuvant, § 170.3(o)(12) of this chapter; processing aid, § 170.3(o)(24) of this chapter; stabilizer and thickener, § 170.3(o)(28) of this chapter; surface active agent, § 170.3(o)(29) of this chapter.

(d) Prior sanctions for sodium alginate different from the uses established in this section do not exist or have been waived.

[47 FR 29951, July 9, 1982, as amended at 48 FR 52448, Nov. 18, 1983]

§ 184.1733 Sodium benzoate.

(a) Sodium benzoate is the chemical benzoate of soda ($C_7H_5NaO_2$), produced by the neutralization of benzoic acid with sodium bicarbonate, sodium carbonate, or sodium hydroxide. The salt is not found to occur naturally.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 78 of 100

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), p. 278, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as an antimicrobial agent as defined in § 170.3(o)(2) of this chapter, and as a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter.

(d) The ingredient is used in food at levels not to exceed good manufacturing practice. Current usage results in a maximum level of 0.1 percent in food. (The Food and Drug Administration has not determined whether significally different conditions of use would be GRAS.)

(e) Prior sanctions for this ingredient different from the uses established in this section, or different from that set forth in part 181 of this chapter, do not exist or have been waived.

[42 FR 14653, Mar. 15, 1977, as amended at 49 FR 5613, Feb. 14, 1984]

§ 184.1736 Sodium bicarbonate.

(a) Sodium bicarbonate ($NaHCO_3$, CAS Reg. No. 144–55–8) is prepared by treating a sodium carbonate or a sodium carbonate and sodium bicarbonate solution with carbon dioxide. As carbon dioxide is absorbed, a suspension of sodium bicarbonate forms. The slurry is filtered, forming a cake which is washed and dried.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 278, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 52442, Nov. 18, 1983]

§ 184.1742 Sodium carbonate.

(a) Sodium carbonate (Na_2CO_3, CAS Reg. No. 497–19–8) is produced (1) from purified trona ore that has been calcined to soda ash; (2) from trona ore calcined to impure soda ash and then purified; or (3) synthesized from limestone by the Solvay process.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 280, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used in food as an antioxidant as defined in § 170.3(o)(3) of this chapter; curing and pickling agent as defined in § 170.3(o)(5) of this chapter; flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter; pH control agent as defined in § 170.3(o)(23) of this chapter; and processing aid as defined in § 170.3(o)(24) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 52442, Nov. 18, 1983, as amended at 50 FR 49536, Dec. 3, 1985]

§ 184.1751 Sodium citrate.

(a) Sodium citrate ($C_6H_5Na_3O_7 \cdot 2H_2O$, CAS Reg. No. 68–0904–092) is the sodium salt of citric acid. It is prepared by neutralizing citric acid with sodium hydroxide or sodium carbonate. The product occurs as colorless crystals or

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 79 of 100

a white crystalline powder. It may be prepared in an anhydrous state or may contain two moles of water per mole of sodium citrate.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d ed. (1981), pp. 283–284, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, and the Center for Food Safety and Applied Nutrition (HFS–200), 200 C St. SW., Washington, DC 20204, or may be examined at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section, or different from those set forth in part 181 of this chapter, do not exist or have been waived.

[59 FR 63896, Dec. 12, 1994]

§ 184.1754 Sodium diacetate.

(a) Sodium diacetate ($C_4H_7O_4Na \cdot xH_2O$, CAS Reg. No. 126–96–5) is a molecular compound of acetic acid, sodium acetate, and water of hydration. The technical grade is prepared synthetically by reacting sodium carbonate with acetic acid. Special grades are produced by reacting anhydrous sodium acetate and acetic acid.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 284, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as an antimicrobial agent as defined in § 170.3(o)(2) of this chapter; flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter; and pH control agent as defined in § 170.3(o)(23) of this chapter.

(d) The ingredient is used in food at levels not to exceed current good manufacturing practice in accordance with § 184.1(b)(1). Current good manufacturing practice results in a maximum level, as served, 0.4 percent for baked goods as defined in § 170.3(n)(1) of this chapter; 0.1 percent for fats and oils as defined in § 170.3(n)(12) of this chapter, meat products as defined in § 170.3(n)(29) of this chapter and soft candy as defined in § 170.3(n)(38) of this chapter; 0.25 percent for gravies and sauces as defined in § 170.3(n)(24) of this chapter; and 0.05 percent for snack foods as defined in § 170.3(n)(37) of this chapter and soups and soup mixes as defined in § 170.3(n)(40) of this chapter.

(e) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[47 FR 27815, June 25, 1982]

§ 184.1763 Sodium hydroxide.

(a) Sodium hydroxide (NaOH, CAS Reg. No. 1310–73–2) is also known as sodium hydrate, soda lye, caustic soda, white caustic, and lye. The empirical formula is NaOH. Sodium hydroxide is prepared commercially by the electrolysis of sodium chloride solution and also by reacting calcium hydroxide with sodium carbonate.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a pH control agent as defined in § 170.3(o)(23) of this chapter and as a processing aid as defined in § 170.3(o)(24) of this chapter.

(2) The ingredient is used in foods at levels not to exceed current good manufacturing practice.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 80 of 100

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 52444, Nov. 18, 1983]

§ 184.1764 Sodium hypophosphite.

(a) Sodium hypophosphite (NaH_2PO_2, CAS Reg. No. 7681–53–0) is a white, odorless, deliquescent granular powder with a saline taste. It is also prepared as colorless, pearly crystalline plates. It is soluble in water, alcohol, and glycerol. It is prepared by neutralization of hypophosphorous acid or by direct aqueous alkaline hydrolysis of white phosphorus.

(b) FDA is developing food-grade specifications for sodium hypophosphite in cooperation with the National Academy of Sciences. In the interim, the ingredient must be of a suitable purity for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitations other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an emulsifier or stabilizer, as defined in §§ 170.3(o)(8) and 170.3(o)(28) of this chapter.

(2) The ingredient is used in cod-liver oil emulsions at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the use established in this section do not exist or have been waived.

[47 FR 38277, Aug. 31, 1982]

§ 184.1768 Sodium lactate.

(a) Sodium lactate ($C_3H_5O_3N_a$, CAS Reg. No. 72–17–3) is the sodium salt of lactic acid. It is prepared commercially by the neutralization of lactic acid with sodium hydroxide.

(b) FDA is developing food-grade specifications for sodium lactate in cooperation with the National Academy of Sciences. In the interim, this ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. This regulation does not authorize its use in infant foods and infant formulas. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an emulsifier as defined in § 170.3(o)(8) of this chapter; a flavor enhancer as defined in § 170.3(o)(11) of this chapter; a flavoring agent or adjuvant as defined in § 170.3(o)(12) of this chapter; a humectant as defined in § 170.3(o)(16) of this chapter; and a pH control agent as defined in § 170.3(o)(23) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[52 FR 10886, Apr. 6, 1987]

§ 184.1769a Sodium metasilicate.

(a) Sodium metasilicate (CAS Reg. No. 6834–92–0) is a strongly alkaline white powder. It does not occur naturally but rather is synthesized by melting sand with sodium carbonate at 1400 °C. The commercially available forms of sodium metasilicate are the anhydrous form (Na_2SiO_3), the pentahydrate ($Na_2SiO_3 \cdot 5H_2O$), and the nonahydrate ($Na_2SiO_3 \cdot 9H_2O$).

(b) FDA is developing food-grade specifications for sodium metasilicate in cooperation with the National Academy of Sciences. In the interim, the ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a processing aid as defined in § 170.3(o)(24) of this chapter.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 81 of 100

(2) The ingredient is used to treat the following foods at levels not to exceed current good manufacturing practice: for use in washing and lye peeling of fruits, vegetables, and nuts when used in accordance with § 173.315 of this chapter; for use as a denuding agent in tripe; for use as a hog scald agent in removing hair; and for use as a corrosion preventative in canned and bottled water when used in accordance with § 103.35 of this chapter.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[50 FR 38781, Sept. 25, 1985; 50 FR 42011, Oct. 17, 1985]

§ 184.1784 Sodium propionate.

(a) Sodium propionate ($C_3H_5NaO_2$, CAS Reg. No. 137–40–6) is the sodium salt of propionic acid. It occurs as colorless, transparent crystals or a granular crystalline powder. It is odorless, or has a faint acetic-butyric acid odor, and is deliquescent. It is prepared by neutralizing propionic acid with sodium hydroxide.

(b) The ingredients meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 296, which is incorporated by reference. Copies are available from the the National Academy Press, 2101 Constitution Ave. NW., Washington DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an antimicrobial agent as defined in § 170.3(o)(2) of this chapter and a flavoring agent as defined in § 170.3(o)(12) of this chapter.

(2) The ingredient is used in the following foods at levels not to exceed current good manufacturing practice: baked goods as defined in § 170.3(n)(1) of this chapter; nonalcoholic beverages as defined in § 170.3(n)(3) of this chapter; cheeses as defined in § 170.3(n)(5) of this chapter; confections and frostings as defined in § 170.3(n)(9) of this chapter; gelatins, puddings, and fillings as defined in § 170.3(n)(22) of this chapter; jams and jellies as defined in § 170.3(n)(28) of this chapter; meat products as defined in § 170.3(n)(29) of this chapter; and soft candy as defined in § 170.3(n)(38) of this chapter.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[49 FR 13142, Apr. 3, 1984]

§ 184.1792 Sodium sesquicarbonate.

(a) Sodium sesquicarbonate ($Na_2CO_3 \cdot NaHCO_3 \cdot 2H_2O$, CAS Reg. No. 533–96–0) is prepared by: (1) Partial carbonation of soda ash solution followed by crystallization, centrifugation, and drying; (2) double refining of trona ore, a naturally occurring impure sodium sesquicarbonate.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 299, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a pH control agent as defined in § 170.3(o)(23) of this chapter.

(2) The ingredient is used in cream at levels not to exceed current good manufacturing practice. Current good manufacturing practice utilizes a level of the ingredient sufficient to control lactic acid prior to pasteurization and churning of cream into butter.

(d) Prior sanctions for this ingredient different from the uses established in

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 82 of 100

this section do not exist or have been waived.

[48 FR 52443, Nov. 18, 1983]

§ 184.1801 Sodium tartrate.

(a) Sodium tartrate ($C_4H_4Na_2O_6 \cdot 2H_2O$, CAS Reg. No. 868–18–8) is the disodium salt of L−(+)−tartaric acid. It occurs as transparent, colorless, and odorless crystals. It is obtained as a byproduct of wine manufacture.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 303, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an emulsifier as defined in § 170.3(o)(8) of this chapter and as a pH control agent as defined in § 170.3(o)(23) of this chapter.

(2) The ingredient is used in the following foods at levels not to exceed current good manufacturing practice: cheeses as defined in § 170.3(n)(5) of this chapter; fats and oils as defined in § 170.3(n)(12) of this chapter; and jams and jellies as defined in § 170.3(n)(28) of this chapter.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 52447, Nov. 18, 1983]

§ 184.1804 Sodium potassium tartrate.

(a) Sodium potassium tartrate ($C_4H_4KNaO_6 \cdot 4H_2O$, CAS Reg. No. 304–59–6) is the sodium potassium salt of L−(+)−tartaric acid and is also called the Rochelle salt. It occurs as colorless crystals or as a white, crystalline powder and has a cooling saline taste. It is obtained as a byproduct of wine manufacture.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 296, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an emulsifier as defined in § 170.3(o)(8) of this chapter and as a pH control agent as defined in § 170.3(o)(23) of this chapter.

(2) The ingredient is used in the following foods at levels not to exceed current good manufacturing practice: cheeses as defined in § 170.3(n)(5) of this chapter and jams and jellies as defined in § 170.3(n)(28) of this chapter.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 52447, Nov. 18, 1983]

§ 184.1807 Sodium thiosulfate.

(a) Sodium thiosulfate ($Na_2S_2O_3 \cdot 5H_2O$, CAS Reg. No. 010102–0917–097) is also known as sodium hyposulfite. It is prepared synthetically by the reaction of sulfides and sulfur dioxide (SO_2), the reaction of sulfur and sulfite, or the oxidation of metal sulfides and hydrosulfides.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), p. 304, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as a formulation aid as defined in § 170.3(o)(14) of this chapter and reducing agent as defined in § 170.3(o)(22) of this chapter.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 83 of 100

(d) The ingredient is used in alcoholic beverages and table salt in accordance with § 184.1(b)(1) at levels not to exceed good manufacturing practice. Current good manufacturing practice results in a maximum level, as served, of 0.00005 percent for alcoholic beverages as defined in § 170.3(n)(2) of this chapter and 0.1 percent for table salt as defined in § 170.3(n)(26) of this chapter.

(e) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[43 FR 22938, May 30, 1978, as amended at 49 FR 5613, Feb. 4, 1984]

§ 184.1835 Sorbitol.

(a) Sorbitol is the chemical 1,2,3,4,5,6-hexanehexol ($C_6H_{14}O_6$), a hexahydric alcohol, differing from mannitol principally by having a different optical rotation. Sorbitol is produced by the electrolytic reduction, or the transition metal catalytic hydrogenation of sugar solutions containing glucose or fructose.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), p. 308, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as an anticaking agent and free-flow agent as defined in § 170.3(o)(1) of this chapter, curing and pickling agent as defined in § 170.3(o)(5) of this chapter, drying agent as defined in § 170.3(o)(7) of this chapter, emulsifier and emulsifier salt as defined in § 170.3(o)(8) of this chapter, firming agent as defined in § 170.3(o)(10) of this chapter, flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter, formulation aid as defined in § 170.3(o)(14) of this chapter, humectant as defined in § 170.3(o)(16) of this chapter, lubricant and release agent as defined in § 170.3(o)(18) of this chapter, nutritive sweetener as defined in § 170.3(o)(21) of this chapter, sequestrant as defined in § 170.3(o)(26) of this chapter, stabilizer and thickener as defined in § 170.3(o)(28) of this chapter, surface-finishing agent as defined in § 170.3(o)(30) of this chapter, and texturizer as defined in § 170.3(o)(32) of this chapter.

(d) The ingredient is used in food at levels not to exceed good manufacturing practices. Current good manufacturing practice in the use of sorbitol results in a maximum level of 99 percent in hard candy and cough drops as defined in § 170.3(n)(25) of this chapter, 75 percent in chewing gum as defined in § 170.3(n)(6) of this chapter, 98 percent in soft candy as defined in § 170.3(n)(38) of this chapter, 30 percent in nonstandardized jams and jellies, commercial, as defined in § 170.3(n)(28) of this chapter, 30 percent in baked goods and baking mixes as defined in § 170.3(n)(1) of this chapter, 17 percent in frozen dairy desserts and mixes as defined in § 170.3(n)(20) of this chapter, and 12 percent in all other foods.

(e) The label and labeling of food whose reasonably foreseeable consumption may result in a daily ingestion of 50 grams of sorbitol shall bear the statement: ''Excess consumption may have a laxative effect.''

(f) Prior sanctions for this ingredient different from the uses established in this regulation do not exist or have been waived.

[42 FR 14653, Mar. 15, 1977, as amended at 49 FR 5613, Feb. 14, 1984]

§ 184.1845 Stannous chloride (anhydrous and dihydrated).

(a) Stannous chloride is anhydrous or contains two molecules of water of hydration. Anhydrous stannous chloride ($SnCl_2$, CAS Reg. No. 7772–99–8) is the chloride salt of metallic tin. It is prepared by reacting molten tin with either chlorine or gaseous tin tetrachloride. Dihydrated stannous chloride ($SnCl_2 \cdot 2H_2O$, CAS Reg. No. 10025–0969–091) is the chloride salt of metallic tin that contains two molecules of water. It is prepared from granulated tin suspended in water and hydrochloric acid or chlorine.

(b) Both forms of the ingredient meet the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 312, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 84 of 100

Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as an antioxidant as defined in § 170.3(o)(3) of this chapter.

(d) The ingredient is used in food at levels not to exceed current good manufacturing practice in accordance with § 184.(b)(1). Current good manufacturing practice results in a maximum level, as served, of 0.0015 percent or less; calculated as tin, for all food categories.

(e) Prior sanctions for this ingredient different from those uses established in this section do not exist or have been waived.

[47 FR 27816, June 25, 1982]

§ 184.1848 Starter distillate.

(a) Starter distillate (butter starter distillate) is a steam distillate of the culture of any or all of the following species of bacteria grown on a medium consisting of skim milk usually fortified with about 0.1 percent citric acid: *Streptococcus lactis, S. cremoris, S. lactis subsp. diacetylactis, Leuconostoc citrovorum,* and *L. dextranicum.* The ingredient contains more than 98 percent water, and the remainder is a mixture of butterlike flavor compounds. Diacetyl is the major flavor component, constituting as much as 80 to 90 percent of the mixture of organic flavor compounds. Besides diacetyl, starter distillate contains minor amounts of acetaldehyde, ethyl formate, ethyl acetate, acetone, ethyl alcohol, 2-butanone, acetic acid, and acetoin.

(b) FDA is developing food-grade specifications for starter distillate in cooperation with the National Academy of Sciences. In the interim, this ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 51907, Nov. 15, 1983]

§ 184.1851 Stearyl citrate.

(a) Stearyl citrate is a mixture of the mono-, di-, and tristearyl esters of citric acid. It is prepared by esterifying citric acid with stearyl alcohol.

(b) The Food and Drug Administration, in cooperation with the National Academy of Sciences, is developing food-grade specifications for stearyl citrate. In the interim, this ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an antioxidant as defined in § 170.3(o)(3) of this chapter; an emulsifier and emulsifier salt as defined in § 170.3(o)(8) of this chapter; a sequestrant as defined in § 170.3(o)(26) of this chapter; and a surface-active agent as defined in § 170.3(o)(29) of this chapter.

(2) The ingredient is used in margarine in accordance with § 166.110 of this chapter; in nonalcoholic beverages as defined in § 170.3(n)(3) of this chapter; and in fats and oils as defined in § 170.3(n)(12) of this chapter at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section, or different from those set forth in part 181 of this chapter, do not exist or have been waived.

[59 FR 63897, Dec. 12, 1994]

§ 184.1854 Sucrose.

(a) Sucrose ($C_{12}H_{22}O_{11}$, CAS Reg. No. 57–50–11–1) sugar, cane sugar, or beet sugar is the chemical β-D-fructofuranosyl-α-D-glucopyranoside.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 85 of 100

Sucrose is obtained by crystallization from sugar cane or sugar beet juice that has been extracted by pressing or diffusion, then clarified and evaporated.

(b) FDA is developing food-grade specifications for sucrose in cooperation with the National Academy of Sciences. In the interim, this ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[53 FR 44876, Nov. 7, 1988; 54 FR 228, Jan. 4, 1989]

§ 184.1857 Corn sugar.

(a) Corn sugar ($C_6H_{12}O_6$, CAS Reg. No. 50–99–7), commonly called D-glucose or dextrose, is the chemical α-D-glucopyranose. It occurs as the anhydrous or the monohydrate form and is produced by the complete hydrolysis of corn starch with safe and suitable acids or enzymes, followed by refinement and crystallization from the resulting hydrolysate.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), pp. 97–98 under the heading ''Dextrose,'' which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 1. Copies are available from the National Academy Press, 2101 Constitution Ave., NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[53 FR 44876, Nov. 7, 1988]

§ 184.1859 Invert sugar.

(a) Invert sugar (CAS Reg. No. 8013–17–0) is an aqueous solution of inverted or partly inverted, refined or partly refined sucrose, the solids of which contain not more than 0.3 percent by weight of ash. The solution is colorless, odorless, and flavorless, except for sweetness. It is produced by the hydrolysis or partial hydrolysis of sucrose with safe and suitable acids or enzymes.

(b) FDA is developing food-grade specifications for invert sugar in cooperation with the National Academy of Sciences. In the interim, this ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[53 FR 44876, Nov. 7, 1988; 54 FR 228, Jan. 4, 1989]

§ 184.1865 Corn syrup.

(a) Corn syrup, commonly called ''glucose sirup'' or ''glucose syrup,'' is obtained by partial hydrolysis of corn starch with safe and suitable acids or enzymes. It may also occur in the dehydrated form (dried glucose sirup). Depending on the degree of hydrolysis, corn syrup may contain, in addition to glucose, maltose and higher saccharides.

(b) The ingredient meets the specifications as defined and determined in § 168.120(b) or § 168.121(a) of this chapter, as appropriate. FDA, in cooperation with the National Academy of Sciences, is undertaking a study to determine if additional food-grade specifications for corn syrup are necessary.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[53 FR 44876, Nov. 7, 1988]

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 86 of 100

§ 184.1866 High fructose corn syrup.

(a) High fructose corn syrup, a sweet, nutritive saccharide mixture containing either approximately 42 or 55 percent fructose, is prepared as a clear aqueous solution from high dextrose-equivalent corn starch hydrolysate by partial enzymatic conversion of glucose (dextrose) to fructose using an insoluble glucose isomerase enzyme preparation described in § 184.1372. The product containing more than 50 percent fructose (dry weight) is prepared through concentration of the fructose portion of the mixture containing less than 50 percent fructose.

(b) The ingredient shall conform to the identity and specifications listed in the monograph entitled ''High-Fructose Corn Syrup'' in the Food Chemicals Codex, 4th ed. (1996), pp. 191–192, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the Office of Premarket Approval, Center for Food Safety and Applied Nutrition (HFS–200), Food and Drug Administration, 200 C St. SW., Washington, DC 20204–0001, or may be examined at the Center for Food Safety and Applied Nutrition's Library, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice.

[61 FR 43450, Aug.23, 1996]

§ 184.1875 Thiamine hydrochloride.

(a) Thiamine hydrochloride ($C_{12}H_{17}C1N_4OS{\cdot}HCl$, CAS Reg. No. 67–03–8) is the chloride-hydrochloride salt of thiamine. It occurs as hygroscopic white crystals or a white crystalline powder. The usual method of preparing this substance is by linking the preformed thiazole and pyrimidine ring systems.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 324, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter or as a nutrient supplement as defined in § 170.3(o)(20) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice. Thiamine hydrochloride may be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the Act) or with regulations promulgated under section 412(a)(2) of the Act.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 55124, Dec. 9, 1983]

§ 184.1878 Thiamine mononitrate.

(a) Thiamine mononitrate ($C_{12}H_{17}N_5O_4S$, CAS Reg. No. 532–43–4) is the mononitrate salt of thiamine. It occurs as white crystals or a white crystalline powder and is prepared from thiamine hydrochloride by dissolving the hydrochloride salt in alkaline solution followed by precipitation of the nitrate half-salt with a stoichiometric amount of nitric acid.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 325, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 87 of 100

the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a nutrient supplement as defined in § 170.3(o)(20) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice. Thiamine mononitrate may be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the Act) or with regulations promulgated under section 412(a)(2) of the Act.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 55124, Dec. 9, 1983]

§ 184.1890 α-Tocopherols.

(a) The α-tocopherols that are the subject of this GRAS affirmation regulation are limited to the following:

(1) *d*-α-Tocopherol (CAS Reg. No. 59–02–9) is the chemical [2R,4′R,8prime;R]-2,5,7,8-tetramethyl-2-(4′,8′,12′-trimethyltridecyl)-6-chromanol. It occurs commercially as a concentrate and is a red, nearly odorless, viscous oil. It is obtained by vacuum steam distillation of edible vegetable oil products.

(2) *dl*-α-Tocopherol (CAS Reg. No. 10191–41–0) is a mixture of stereoisomers of 2,5,7,8-tetramethyl-2-(4′,8′,12′-trimethyl-tridecyl)-6-chromanol. It is chemically synthesized by condensing racemic isophytol with trimethyl hydroquinone. It is a pale yellow viscous oil at room temperature.

(b) The ingredients meet the specifications of the Food Chemicals Codex, 3d Ed. (1981), pp. 330–331, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(3), the affirmation of the ingredients as generally recognized as safe is limited to the following conditions of use while the agency concludes the general evaluation of all food uses of tocopherols:

(1) The ingredients are used as inhibitors of nitrosamine formation.

(2) The ingredients are used in pump-cured bacon at levels not to exceed current good manufacturing practice.

[49 FR 13348, Apr. 4, 1984]

§ 184.1901 Triacetin.

(a) Triacetin ($C_8H_{14}O_6$, CAS Reg. No. 102–76–1), also known as 1,2,3,-propanetriol triacetate or glyceryl triacetate, is the triester of glycerin and acetic acid. Triacetin can be prepared by heating glycerin with acetic anhydride alone or in the presence of finely divided potassium hydrogen sulfate. It can also be prepared by the reaction of oxygen with a liquid-phase mixture of allyl acetate and acetic acid using a bromide salt as a catalyst.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), pp. 337–338, as revised by the First Supplement to the 3d Ed., which is incorporated by reference in accordance with 5 U.S.C. 552(a). Copies are available from the National Academy Press, 2102 Constitution Ave., NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20005.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used in food as a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter; a formulation aid as defined in § 170.3(o)(14) of this chapter; and humectant as defined in § 170.3(o)(16) of this chapter; and a solvent and vehicle as defined in § 170.3(o)(27) of this chapter.

(2) The ingredient is used in the following foods at levels not to exceed current good manufacturing practice: baked goods and baking mixes as defined in § 170.3(n)(1) of this chapter, alcoholic beverages as defined in § 170.3(n)(2) of this chapter; nonalcoholic beverages and beverage bases as defined in § 170.3(n)(3) of this chapter; chewing gum as defined in § 170.3(n)(6) of this chapter; confections and frostings as defined in § 170.3(n)(9)

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 88 of 100

of this chapter; frozen dairy dessert and mixes as defined in § 170.3(n)(20) of this chapter; gelatins, puddings, and fillngs as defined in § 170.3(n)(22) of this chapter; hard candy as defined in § 170.3(n)(25) of this chapter; and soft candy as defined in § 170.3(n)(38) of this chapter.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[54 FR 7404, Feb. 21, 1989]

§ 184.1903 Tributyrin.

(a) Tributyrin ($C_{15}H_{26}O_6$, CAS Reg. No. 60–01–5), also known as butyrin or glyceryl tributyrate, is the triester of glycerin and butyric acid. It is prepared by esterification of glycerin with excess butyric acid.

(b) The ingredient meets the specification of the Food Chemicals Codex, 3d Ed. (1981), p. 416, which is incorporated by reference in accordance with 5 U.S.C. 552(a). Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20005.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generaly recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used in food as a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter.

(2) The ingredient is used in the following foods at levels not to exceed current good manufacturing practice; baked goods as defined in § 170.3(n)(1) of this chapter; alcoholic beverages as defined in § 170.3(n)(2) of this chapter; nonalcoholic beverages as defined in § 170.3(n)(3) of this chapter; fats and oils as defined in § 170.3(n)(12) of this chapter; frozen dairy desserts and mixes as defined in § 170.3(n)(20) of this chapter; gelatins, puddings and fillngs as defined in § 170.3(n)(22) of this chapter; and soft candy as defined in § 170.3(n)(38) of this chapter.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[54 FR 7404, Feb. 21, 1989; 54 FR 10482, Mar. 13, 1989]

§ 184.1911 Triethyl citrate.

(a) Triethyl citrate ($C_{12}H_{20}O_7$, CAS Reg. No. 77–93–0) is the triethyl ester of citric acid. It is prepared by esterifying citric acid with ethyl alcohol and occurs as an odorless, practically colorless, oily liquid.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d ed. (1981), p. 339, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, and the Center for Food Safety and Applied Nutrition (HFS–200), 200 C St. SW., Washington, DC 20204, or may be examined at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a flavoring agent as defined in § 170.3(o)(12) of this chapter; a solvent and vehicle as defined in § 170.3(o)(27) of this chapter; and a surface-active agent as defined in § 170.3(o)(29) of this chapter.

(2) The ingredient is used in foods at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section, or different from those set forth in part 181 of this chapter, do not exist or have been waived.

[59 FR 63897, Dec. 12, 1994]

§ 184.1914 Trypsin.

(a) Trypsin (CAS Reg. No. 9002–07–7) is an enzyme preparation obtained from purified extracts of porcine or bovine pancreas. It is a white to tan

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 89 of 100

amorphous powder. Its characterizing enzyme activity is that of a peptide hydrolase (EC 3.4.21.4).

(b) The ingredient meets the general requirements and additional requirements for enzyme preparations in the Food Chemicals Codex, 3d ed. (1981), p. 110, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of Premarket Approval (HFS–200), Food and Drug Administration, 200 C St. SW., Washington, DC, and the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as GRAS as a direct food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an enzyme as defined in § 170.3(o)(9) of this chapter to hydrolyze proteins or polypeptides.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

[60 FR 32911, June 26, 1995]

§ 184.1923 Urea.

(a) Urea ($CO(NH_2)_2$, CAS Reg. No. 57–13–6) is the diamide of carbonic acid and is also known as carbamide. It is a white, odorless solid and is commonly produced from CO_2 by ammonolysis or from cyanamide by hydrolysis.

(b) FDA is developing food-grade specifications for urea in cooperation with the National Academy of Sciences. In the interim, this ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a formulation aid as defined in § 170.3(o)(14) of this chapter and as a fermentation aid.

(2) The ingredient is used in yeast-raised bakery products; in alcoholic beverages as defined in § 170.3(n)(2) of this chapter; and in gelatin products.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 51616, Nov. 10, 1983, as amended at 49 FR 19816, May 10, 1984]

§ 184.1924 Urease enzyme preparation from Lactobacillus fermentum.

(a) This enzyme preparation is derived from the nonpathogenic, nontoxicogenic bacterium *Lactobacillus fermentum*. It contains the enzyme urease (CAS Reg. No. 9002–13–5), which facilitates the hydrolysis of urea to ammonia and carbon dioxide. It is produced by a pure culture fermentation process and by using materials that are generally recognized as safe (GRAS) or are food additives that have been approved for this use by the Food and Drug Administration (FDA).

(b) The ingredient meets the general and additional requirements for enzyme preparations in the ''Food Chemicals Codex,'' 3d ed. (1981), pp. 107–110, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as GRAS as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used in wine, as defined in 27 CFR 2.5 and 4.10, as an enzyme as defined in § 170.3(o)(9) of this chapter to convert urea to ammonia and carbon dioxide.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice. Current good manufacturing practice is limited to use of

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 90 of 100

this ingredient in wine to inhibit formation of ethyl carbamate.

[57 FR 60473, Dec. 21, 1992]

§ 184.1930 Vitamin A.

(a)(1) Vitamin A (retinol; CAS Reg. No. 68–26–8) is the alcohol 9,13-dimethyl-7-(1,1,5-trimethyl-6-cyclohexen-5-yl)-7,9,11,13-nonatetraen-15-ol. It may be nearly odorless or have a mild fishy odor. Vitamin A is extracted from fish liver oils or produced by total synthesis from β-ionone and a propargyl halide.

(2) Vitamin A acetate (retinyl acetate; CAS Reg. No. 127–47–9) is the acetate ester of retinol. It is prepared by esterifying retinol with acetic acid.

(3) Vitamin A palmitate (retinyl palmitate; CAS Reg. No. 79–81–2) is the palmitate ester of retinol. It is prepared by esterifying retinol with palmitic acid.

(b) The ingredient meets the specifications for vitamin A in the Food Chemicals Codex, 3d Ed. (1981), p. 342, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used in food as a nutrient supplement as defined in § 170.3(o)(20) of this chapter.

(2) The ingredient is used in foods at levels not to exceed current good manufacturing practice. Vitamin A may be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) or with regulations promulgated under section 412(a)(2) of the Act.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 51610, Nov. 10, 1983]

§ 184.1945 Vitamin B_{12}.

(a) Vitamin B_{12}, also known as cyanocobalamin ($C_{63}H_{88}CoN_{14}O_{14}P$, CAS Reg. No. 68–0919–099), is produced commercially from cultures of *Streptomyces griseus*.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 343, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a nutrient supplement as defined in § 170.3(o)(20) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice. Vitamin B_{12} also may be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) or with regulations promulgated under section 412(a)(2) of the act.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[50 FR 6341, Feb. 15, 1985]

§ 184.1950 Vitamin D.

(a) Vitamin D is added to food as the following food ingredients:

(1) Crystalline vitamin D_2 ($C_{28}H_{44}O$, CAS Reg. No. 50–14–6), also known as ergocalciferol, is the chemical 9,10-seco(5Z,7E,22E)-5,7,10(19),22-ergostatetraen-3-ol. The ingredient is produced by ultraviolet irradiation of ergosterol isolated from yeast and related fungi and is purified by crystallization.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 91 of 100

(2) Crystalline vitamin D_3 ($C_{27}H_{44}O$, CAS Reg. No. 67–97–0), also known as cholecalciferol, is the chemical 9,10-seco(5Z,7E,)-5,7,10(19)-cholestatrien-3-ol. Vitamin D_3 occurs in, and is isolated from, fish liver oils. It is also manufactured by ultraviolet irradiation of 7-dehydrocholesterol produced from cholesterol. It is purified by crystallization. Vitamin D_3 is the vitamin D form that is produced endogenously in humans through sunlight activation of 7-dehydrocholesterol in the skin.

(3) Vitamin D_2 resin and vitamin D_3 resin are the concentrated forms of irradiated ergosterol (D_2) and irradiated 7-dehydrocholesterol (D_3) that are separated from the reacting materials in paragraphs (a) (1) and (2) of this section. The resulting products are sold as food sources of vitamin D without further purification.

(b) Vitamin D_2 and vitamin D_3 as crystals meet the specifications of the Food Chemicals Codex, 3d Ed. (1981), pp. 344 and 345, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408. FDA is developing food-grade specifications for vitamin D_2 resin and vitamin D_3 resin in cooperation with the National Academy of Sciences. In the interim, these resins must be of a purity suitable for their intended use.

(c)(1) In accordance with § 184.1(b)(2), the ingredients are used in food as the sole source of added vitamin D only within the following specific limitations:

Category of food	Maximum levels in food (as served)	Functional use
Breakfast cereals, § 170.3(n)(4) of this chapter.	350 (IU/100 grams).	Nutrient supplement, § 170.3(o)(20) of this chapter.
Grain products and pastas, § 170.3(n)(23) of this chapter.	90(IU/100 grams)	Do.
Milk, § 170.3(n)(30) of this chapter.	42 (IU/100 grams)	Do.
Milk products, § 170.3(n)(31) of this chapter.	89 (IU/100 grams)	Do.

(2) Vitamin D may be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) or with regulations promulgated under section 412(a)(2) of the act.

(3) Vitamin D may be used in margarine in accordance with § 166.110 of this chapter.

(d) Prior sanctions for these ingredients different from the uses established in this section do not exist or have been waived.

[50 FR 30152, July 24, 1985]

§ 184.1973 Beeswax (yellow and white).

(a) Beeswax (CAS Reg. No. 8012–89–3) is a secretory product of honey bees used as a structural material in honeycombs. Beeswax is prepared from honeycombs after removal of the honey by draining or centrifuging. The combs are melted in hot water or steam or with solar heat, and strained. The wax is refined by melting in hot water to which sulfuric acid or alkali may be added to extract impurities. The resulting wax is referred to as yellow beeswax. White beeswax is produced by bleaching the constituent pigments of yellow beeswax with peroxides, or preferably it is bleached by sun light.

(b) The ingredient meets the specifications of the ''Food Chemicals Codex,'' 3d Ed. (1981), pp. 34–35, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredient is used as a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter, as a lubricant as defined in § 170.3(o)(18) of this chapter, and as a surface-finishing agent as defined in § 170.3(o)(30) of this chapter.

(d) The ingredient is used in food, in accordance with § 184.1(b)(1) of this chapter, at levels not to exceed good manufacturing practice. Current good manufacturing practice results in a maximum level, as served, of: 0.065 percent for chewing gum as defined in § 170.3(n)(6) of this chapter; 0.005 percent for confections and frostings as defined in § 170.3(n)(9) of this chapter;

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 92 of 100

0.04 percent for hard candy as defined in § 170.3(n)(25) of this chapter; 0.1 percent for soft candy as defined in § 170.3(n)(38) of this chapter; and 0.002 percent or less for all other food categories.

[43 FR 14644, Apr. 7, 1978, as amended at 49 FR 5613, Feb. 14, 1984; 50 FR 49536, Dec. 3, 1985]

§ 184.1976 Candelilla wax.

(a) Candelilla wax (CAS Reg. No. 8006–44–8) is obtained from the candelilla plant. It is a hard, yellowish-brown, opaque-to-translucent wax. Candelilla wax is prepared by immersing the plants in boiling water containing sulfuric acid and skimming off the wax that rises to the surface. It is composed of about 50 percent hydrocarbons with smaller amounts of esters and free acids.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 67, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a lubricant as defined in § 170.3(o)(18) of this chapter and as a surface-finishing agent as defined in § 170.3(o)(30) of this chapter.

(2) The ingredient is used in the following foods at levels not to exceed current good manufacturing practice: in chewing gum as defined in § 170.3(n)(6) of this chapter and in hard candy as defined in § 170.3(n)(25) of this chapter.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 51617, Nov. 10, 1983]

§ 184.1978 Carnauba wax.

(a) Carnauba wax (CAS Reg. No. 008–015–869) is obtained from the leaves and buds of the Brazilian wax palm *Copernicia cerifera* Martius. The wax is hard, brittle, sparingly soluble in cold organic solvents and insoluble in water. It is marketed in five grades designated No. 1 through No. 5. Grades No. 4 and No. 5 represent the bulk of the commercial trade volume. These commercial grades consist chiefly of C_{24} to C_{32} normal saturated monofunctional fatty acids and normal saturated monofunctional primary alcohols.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 73, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an anticaking agent as defined § 170.3(o)(1) of this chapter; as a formulation aid as defined in § 170.3(o)(14) of this chapter; as a lubricant and release agent as defined in § 170.3(o)(18) of this chapter; and as a surface-finishing agent as defined in § 170.3(o)(30) of this chapter.

(2) The ingredient is used in the following foods at levels not to exceed current good manufacturing practice: baked goods and baking mixes as defined in § 170.3(n)(1) of this chapter; chewing gun as defined in § 170.3(n)(6) of this chapter; confections and frostings as defined in § 170.3(n)(9) of this chapter; fresh fruits and fruit juices as defined in § 170.3(n)(16) of this chapter; gravies and sauces as defined in § 170.3(n)(24) of this chapter; processed fruits and fruit juices as defined in § 170.3(n)(35) of this chapter; and soft candy as defined in § 170.3(n)(38) of this chapter.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 93 of 100

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 51147, Nov. 7, 1983]

§ 184.1979 Whey.

(a)(1) *Whey.* Whey is the liquid substance obtained by separating the coagulum from milk, cream, or skim milk in cheesemaking. Whey obtained from a procedure, in which a significant amount of lactose is converted to lactic acid, or from the curd formation by direct acidification of milk, is known as acid whey. Whey obtained from a procedure in which there is insignificant conversion of lactose to lactic acid is known as sweet whey. Sweet whey has a maximum titratable acidity of not more than 0.16 percent, calculated as lactic acid, and an alkalinity of ash of not more than 225 milliliters of 0.1*N* hydrochloric acid per 100 grams. The acidity of whey, sweet or acid, may be adjusted by the addition of safe and suitable pH-adjusting ingredients.

(2) *Concentrated whey.* Concentrated whey is the liquid substance obtained by the partial removal of water from whey, while leaving all other constituents in the same relative proportions as in whey.

(3) *Dry or dried whey.* Dry or dried whey is the dry substance obtained by the removal of water from whey, while leaving all other constituents in the same relative proportions as in whey.

(b) The ingredients meet the following specifications:

(1) The analysis of whey, concentrated whey, and dry (dried) whey, on a dry product basis, based on analytical methods in the referenced sections of ''Official Methods of Analysis of the Association of Official Analytical Chemists,'' 13th ed. (1980), which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51, is given in paragraphs (b)(1)(i) through (b)(1)(vii) of this section. Copies may be obtained from the Association of Official Analytical Chemists International, 481 North Frederick Ave., suite 500, Gaithersburg, MD 20877–2504, or may be examined at the Center for Food Safety and Applied Nutrition's Library, Food and Drug Administration, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(i) Protein content, 10 to 15 percent—as determined by the methods prescribed in section 16.036 (liquid sample), entitled ''Total Nitrogen—Official Final Action'' under the heading ''Total Solids,'' or in section 16.193 (dry sample), entitled ''Kjeldahl Method'' under the heading ''Protein—Official Final Action.''

(ii) Fat content, 0.2 to 2.0 percent—as determined by the methods prescribed in section 16.059 (liquid sample), ''Reese-Gottlieb Method [Reference Method] (11)—Official Final Action'' under the heading ''Fat,'' or in section 16.199 (dry sample), entitled ''Fat in Dried Milk (45)—Official Final Action.''

(iii) Ash content, 7 to 14 percent—as determined by the methods prescribed in section 16.035 (liquid sample), entitled ''Ash (5)—Official Final Action'' under the heading ''Total Solids,'' or in section 16.196 (dry sample), entitled ''Ash—Official Final Action'' under the heading ''Dried Milk, Nonfat Dry Milk, and Malted Milk.''

(iv) Lactose content, 61 to 75 percent—as determined by the methods prescribed in section 16.057 (liquid sample), entitled ''Gravimetric Method—Official Final Action'' under the heading ''Lactose,'' or in section 31.061 (dry sample), entitled ''Lane-Eynon General Volumetric Method'' under the heading ''Lactose—Chemical Methods—Official Final Action.''

(v) Moisture content, 1 to 8 percent—as determined by the methods prescribed in section 16.192, entitled ''Moisture (41)—Official Final Action'' under the heading ''Dried Milk, Nonfat Dry Milk, and Malted Milk.''

(vi) Solids content, variable—as determined by the methods prescribed in section 16.032, entitled ''Method I—Official Final Action'' under the heading ''Total Solids.''

(vii) Titratable Acidity, variable—as determined by the methods prescribed in section 16.023, entitled ''Acidity (2)—Official Final Action'' under the heading ''Milk,'' or by an equivalent potentiometric method.

(2) Limits of impurities are: Heavy metals (as lead). Not more than 10

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 94 of 100

parts per million (0.001 percent) as determined by the method described in the ''Food Chemicals Codex,'' 4th ed. (1996), pp. 760–761, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, Box 285, 2101 Constitution Ave. NW., Washington, DC 20055 (Internet address ''http://www.nap.edu''), or may be examined at the Center for Food Safety and Applied Nutrition's Library, Food and Drug Administration, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(3) The whey must be derived from milk that has been pasteurized, or the whey and modified whey product must be subjected to pasteurization techniques or its equivalent before use in food.

(c) Whey, concentrated whey, and dry (dried) whey may be used in food in accordance with good manufacturing practice as indicated in § 184.1(b)(1).

(d) The label on the whey form sold to food manufacturers shall read as follows:

(1) For whey: ''(Sweet or acid) whey'' or ''whey (____% titratable acidity).

(2) For concentrated whey: ''Concentrated (sweet or acid) whey, ____% solids'' or ''Concentrated whey (____% titratable acidity), ____% solids''.

(3) For dry (dried) whey: ''Dry (dried) (sweet or acid) whey'' or ''dry (dried) whey, (____% titratable acidity)''.

(e) Whey, concentrated whey, or dry (dried) whey in a finished food product shall be listed as ''whey.''

[46 FR 44439, Sept. 4, 1981; 47 FR 7410, Feb. 19, 1982, as amended at 54 FR 24899, June 12, 1989; 64 FR 1760, Jan. 12, 1999]

§ 184.1979a Reduced lactose whey.

(a) Reduced lactose whey is the substance obtained by the removal of lactose from whey. The lactose content of the finished dry product shall not exceed 60 percent. Removal of the lactose is accomplished by physical separation techniques such as precipitation, filtration, or dialysis. As with whey, reduced lactose whey can be used as a fluid, concentrate, or a dry product form. The acidity of reduced lactose whey may be adjusted by the addition of safe and suitable pH-adjusting ingredients.

(b) The reduced lactose whey meets the following specifications:

(1) The analysis of reduced lactose whey, on a dry product basis, based on analytical methods in the referenced sections of ''Official Methods of Analysis of the Association of Official Analytical Chemists,'' 13th ed. (1980), which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51, is given in paragraphs (b)(1)(i) through (b)(1)(vii) of this section. Copies may be obtained from the Association of Official Analytical Chemists International, 481 North Frederick Ave., suite 500, Gaithersburg, MD 20877–2504, or may be examined at the Center for Food Safety and Applied Nutrition's Library, Food and Drug Administration, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(i) Protein content, 16 to 24 percent—as determined by the methods prescribed in section 16.036 (liquid sample), entitled ''Total Nitrogen—Official Final Action'' under the heading ''Total Solids,'' or in section 16.193 (dry sample), entitled ''Kjeldahl Method'' under the heading ''Protein—Official Final Action.''

(ii) Fat content, 1 to 4 percent—as determined by the methods prescribed in section 16.059 (liquid sample), ''Reese-Gottlieb Method [Reference Method] (11)—Official Final Action'' under the heading ''Fat,'' or in section 16.199 (dry sample), entitled ''Fat in Dried Milk (45)—Official Final Action.''

(iii) Ash content, 11 to 27 percent—as determined by the methods prescribed in section 16.035 (liquid sample), entitled ''Ash (5)—Official Final Action'' under the heading ''Total Solids,'' or in section 16.196 (dry sample), entitled ''Ash—Official Final Action'' under the heading ''Dried Milk, Nonfat Dry Milk, and Malted Milk.''

(iv) Lactose content, not more than 60 percent—as determined by the methods prescribed in section 16.057 (liquid sample), entitled ''Gravimetric Method—Official Final Action'' under the heading ''Lactose,'' or in section 31.061 (dry sample), entitled ''Lane–Eynon General Volumetric Method'' under the

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 95 of 100

heading ''Lactose—Chemical Methods—Official Final Action.''

(v) Moisture content, 1 to 6 percent—as determined by the method prescribed in section 16.192, entitled ''Moisture (41)—Official Final Action'' under the heading ''Dried Milk, Nonfat Dry Milk, and Malted Milk.''

(vi) Solids content, variable—as determined by the methods prescribed in section 16.032, entitled ''Method I—Official Final Action'' under the heading ''Total Solids.''

(vii) Titratable Acidity, variable—as determined by the methods prescribed in section 16.023, entitled ''Acidity (2)—Official Final Action'' under the heading ''Milk,'' or by an equivalent potentiometric method.

(2) Limits of impurities are: Heavy metals (as lead). Not more than 10 parts per million (0.001 percent), as determined by the method described in the ''Food Chemicals Codex,'' 4th ed. (1996), pp. 760–761, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, Box 285, 2101 Constitution Ave. NW., Washington, DC 20055 (Internet address ''http://www.nap.edu''), or may be examined at the Center for Food Safety and Applied Nutrition's Library, Food and Drug Administration, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(3) The reduced lactose whey shall be derived from milk that has been pasteurized, or the reduced lactose whey shall be subjected to pasteurization techniques or its equivalent before use in food.

(c) Reduced lactose whey may be used in food in accordance with good manufacturing practice as indicated in § 184.1(b)(1).

(d) The percent of lactose present on a dry product basis, i.e., ''reduced lactose whey (____% lactose),'' shall be declared on the label of the package sold to food manufacturers. The percent of lactose may be declared in 5-percent increments, expressed as a multiple of 5, not greater than the actual percentage of lactose in the product, or as a actual percentage provided that an analysis of the product on which the actual percentage is based is supplied to the food manufacturer.

(e) The presence of reduced lactose whey in a finished food product shall be listed as ''reduced lactose whey.''

[46 FR 44440, Sept. 4, 1981, as amended at 54 FR 24899, June 12, 1989; 64 FR 1760, Jan. 12, 1999]

§ 184.1979b Reduced minerals whey.

(a) Reduced minerals whey is the substance obtained by the removal of a portion of the minerals from whey. The dry product shall not contain more than 7 percent ash. Reduced minerals whey is produced by physical separation techniques such as precipitation, filtration, or dialysis. As with whey, reduced minerals whey can be used as a fluid, concentrate, or a dry product form. The acidity of reduced minerals whey may be adjusted by the additional of safe and suitable pH-adjusting ingredients.

(b) The reduced minerals whey meets the following specifications:

(1) The analysis of reduced minerals whey, on a dry product basis, based on analytical methods in the referenced sections of ''Official Methods of Analysis of the Association of Official Analytical Chemists,'' 13th ed. (1980), which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51, is given in paragraphs (b)(1)(i) through (b)(1)(vii) of this section. Copies may be obtained from the Association of Official Analytical Chemists International, 481 North Frederick Ave., suite 500, Gaithersburg, MD 20877–2504, or may be examined at the Center for Food Safety and Applied Nutrition's Library, Food and Drug Administration, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(i) Protein content, 10 to 24 percent—as determined by the methods prescribed in section 16.036 (liquid sample), entitled ''Total Nitrogen—Official Final Action'' under the heading ''Total Solids,'' or in section 16.193 (dry sample), entitled ''Kjeldahl Method'' under the heading ''Protein—Official Final Action.''

(ii) Fat content, 1 to 4 percent—as determined by the methods prescribed in section 16.059 (liquid sample), ''Reese-

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 96 of 100

Gottlieb Method [Reference Method] (11)—Official Final Action'' under the heading ''Fat,'' or in section 16.199 (dry sample), entitled ''Fat in Dried Milk (45)—Official Final Action.''

(iii) Ash content, maximum 7 percent—as determined by the methods prescribed in section 16.035 (liquid sample), entitled ''Ash (5)—Official Final Action'' under the heading ''Total Solids,'' or in section 16.196 (dry sample), entitled ''Ash—Official Final Action'' under the heading ''Dried Milk, Nonfat Dry Milk, and Malted Milk.''

(iv) Lactose content, maximum 85 percent—as determined by the methods prescribed in section 16.057 (liquid sample), entitled ''Gravimetric Method—Official Final Action'' under the heading ''Lactose,'' or in section 31.061 (dry sample), entitled ''Lane-Eynon General Volumetric Method'' under the heading ''Lactose—Chemical Methods—Official Final Action.''

(v) Moisture content, 1 to 6 percent—as determined by the methods prescribed in section 16.192, entitled ''Moisture (41)—Official Final Action'' under the heading ''Dried Milk, Nonfat Dry Milk, and Malted Milk.''

(vi) Solids content, variable—as determined by the methods prescribed in section 16.032, entitled ''Method I—Official Final Action'' under the heading ''Total Solid.''

(vii) Titratable Acidity, variable—as determined by the methods prescribed in section 16.023, entitled ''Acidity (2)—Official Final Action'' under the heading ''Milk,'' or by an equivalent potentiometric method.

(2) Limits of impurities are: Heavy metals (as lead). Not more than 10 parts per million (0.001 percent), as determined by the method described in the ''Food Chemicals Codex,'' 4th ed. (1996), pp. 760–761, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, Box 285, 2101 Constitution Ave. NW., Washington, DC 20055 (Internet address ''http://www.nap.edu''), or may be examined at the Center for Food Safety and Applied Nutrition's Library, Food and Drug Administration, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(3) The reduced minerals whey shall be derived from milk that has been pasteurized, or the reduced minerals whey shall be subjected to pasteurization techniques or its equivalent before use in food.

(c) The reduced minerals whey may be used in food in accordance with good manufacturing practice as indicated in § 184.1(b)(1).

(d) The percent of minerals present on a dry product basis, i.e., ''reduced minerals whey (____% minerals),'' shall be declared on the label of the package sold to food manufacturers. The percent of minerals may be declared in 2-percent increments expressed as a multiple of 2, not greater than the actual percentage of minerals in the product, or as an actual percentage provided that an analysis of the product on which the actual percentage is based is supplied to the food manufacturer.

(e) The presence of reduced minerals whey in a finished food product shall be listed as ''reduced minerals whey''.

[46 FR 44441, Sept. 4, 1981, as amended at 54 FR 24899, June 12, 1989; 64 FR 1761, Jan. 12, 1999]

§ 184.1979c Whey protein concentrate.

(a) Whey protein concentrate is the substance obtained by the removal of sufficient nonprotein constituents from whey so that the finished dry product contains not less than 25 percent protein. Whey protein concentrate is produced by physical separation techniques such as precipitation, filtration, or dialysis. As with whey, whey protein concentrate can be used as a fluid, concentrate, or dry product form. The acidity of whey protein concentrate may be adjusted by the addition of safe and suitable pH-adjusting ingredients.

(b) The whey protein concentrate meets the following specifications:

(1) The analysis of whey protein concentrate, on a dry product basis, based on analytical methods in the referenced sections of ''Official Methods of Analysis of the Association of Official Analytical Chemists,'' 13th ed. (1980), which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51, is given in paragraphs (b)(1)(i) through (b)(1)(vii)

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 97 of 100

of this section. Copies may be obtained from the Association of Official Analytical Chemists International, 481 North Frederick Ave., suite 500, Gaithersburg, MD 20877–2504, or may be examined at the Center for Food Safety and Applied Nutrition's Library, Food and Drug Administration, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(i) Protein content, minimum 25 percent—as determined by the methods prescribed in section 16.036 (liquid sample), entitled ''Total Nitrogen—Officials Final Action'' under the heading ''Total Solids,'' or in section 16.193 (dry sample), entitled ''Kjeldahl Method'' under the heading ''Protein—Official Final Action.''

(ii) Fat content, 1 to 10 percent—as determined by the methods prescribed in section 16.059 (liquid sample), ''Reese-Gottlieb Method [Reference Method] (11)—Official Final Action'' under the heading ''Fat,'' or in section 16.199 (dry sample), entitled ''Fat in Dried Milk (45)—Official Final Action.''

(iii) Ash content, 2 to 15 percent—as determined by the methods prescribed in section 16.035 (liquid sample), entitled ''Ash (5)—Official Final Action'' under the heading ''Total Solids,'' or in section 16.196 (dry sample), entitled ''Ash—Official Final Action'' under the heading ''Dried Milk, Nonfat Dry Milk, and Malted Milk.''

(iv) Lactose content, maximum 60 percent—as determined by the methods prescribed in section 16.057 (liquid sample), entitled ''Gravimetric Method—Official Final Action'' under the heading ''Lactose,'' or in section 31.061 (dry sample), entitled ''Lane-Eynon General Volumetric Method'' under the heading ''Lactose—Chemical Methods—Official Final Action.''

(v) Moisture content, 1 to 6 percent—as determined by the methods prescribed in section 16.192, entitled ''Moisture (41)—Official Final Action'' under the heading ''Dried Milk, Nonfat Dry Milk, and Malted Milk.''

(vi) Solids content, variable—as determined by the methods prescribed in section 16.032, entitled ''Method I—Official Final Action'' under the heading ''Total Solids.''

(vii) Titratable Acidity, variable—as determined by the methods prescribed in section 16.023, entitled ''Acidity (2)—Official Final Action'' under the heading ''Milk,'' or by an equivalent potentiometric method.

(2) Limits of impurities are: Heavy metals (as lead). Not more than 10 parts per million (0.001 percent), as determined by the method described in the ''Food Chemicals Codex,'' 4th ed. (1996), pp. 760–761, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, Box 285, 2101 Constitution Ave. NW., Washington, DC 20055 (Internet address ''http://www.nap.edu''), or may be examined at the Center for Food Safety and Applied Nutrition's Library, Food and Drug Administration, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(3) The whey protein concentrate shall be derived from milk that has been pasteurized, or the whey protein concentrate shall be subjected to pasteurization techniques or its equivalent before use in food.

(c) The whey protein concentrate may be used in food in accordance with good manufacturing practice as indicated in § 184.1(b)(1).

(d) The percent of protein present on a dry product basis, i.e., ''whey protein concentrate (____% protein),'' shall be declared on the label of the package sold to food manufacturers. The percent of protein may be declared in 5-percent increments, expressed as a multiple of 5, not greater than the actual percentage of protein in the product, or as an actual percentage provided that an analysis of the product on which the actual percentage is based is supplied to the food manufacturer.

(e) The presence of whey protein concentrate in a finished food product shall be listed as ''whey protein concentrate''.

[46 FR 44441, Sept. 4, 1981, as amended at 54 FR 24899, June 12, 1989; 64 FR 1761, Jan. 12, 1999]

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 98 of 100

§ 184.1983 Bakers yeast extract.

(a) Bakers yeast extract is the food ingredient resulting from concentration of the solubles of mechanically ruptured cells of a selected strain of yeast, *Saccharomyces cerevisiae*. It may be concentrated or dried.

(b) The ingredient meets the following specifications on a dry weight basis: Less than 0.4 part per million (ppm) arsenic, 0.13 ppm cadmium, 0.2 ppm lead, 0.05 ppm mercury, 0.09 ppm selenium, and 10 ppm zinc.

(c) The viable microbial content of the finished ingredient as a concentrate or dry material is:

(1) Less than 10,000 organisms/gram by aerobic plate count.

(2) Less than 10 yeasts and molds/gram.

(3) Negative for *Salmonella, E. coli,* coagulase positive *Staphylococci, Clostridium perfringens, Clostridium botulinum,* or any other recognized microbial pathogen or any harmful microbial toxin.

(d) The ingredient is used as a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter at a level not to exceed 5 percent in food.

(e) This regulation is issued prior to general evaluation of use of this ingredient in order to affirm as GRAS the specific use named.

§ 184.1984 Zein.

(a) Zein (CAS Reg. No. 9010–66–6) is one of the components of corn gluten. It is produced commercially by extraction from corn gluten with alkaline aqueous isopropyl alcohol containing sodium hydroxide. The extract is then cooled, which causes the zein to precipitate.

(b) FDA is developing food-grade specifications for zein in cooperation with the National Academy of Sciences. In the interim, the igredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a surface-finishing agent as defined in § 170.3(o)(30) of this chapter.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[50 FR 8999, Mar. 6, 1985]

§ 184.1985 Aminopeptidase enzyme preparation derived from lactococcus lactis.

(a) Aminopeptidase enzyme preparation is derived from the nonpathogenic and nontoxicogenic bacterium *Lactococcus lactis* (previously named *Streptococcus lactis*). The preparation contains the enzyme aminopeptidase (CAS Reg. No. 9031–94–1; EC 3.4.11.1) and other peptidases that hydrolyze milk proteins. The preparation is produced by pure culture fermentation.

(b) The ingredient meets the specifications for enzyme preparations in the Food Chemicals Codex, 3d ed. (1981), pp. 107–110, which are incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Division of Petition Control (HFS–215), Center for Food Safety and Applied Nutrition, Food and Drug Administration, 1110 Vermont Ave. NW., suite 1200, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitations other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an enzyme, as defined in § 170.3(o)(9) of this chapter, as an optional ingredient for flavor development in the manufacture of cheddar cheese, in accordance with § 133.113 of this chapter, and in the preparation of protein hydrolysates.

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 99 of 100

(2) The ingredient is used at levels not to exceed current good manufacturing practice.

[60 FR 54193, Oct. 20, 1995]

PART 186—INDIRECT FOOD SUBSTANCES AFFIRMED AS GENERALLY RECOGNIZED AS SAFE

Subpart A—General Provisions

Sec.
186.1 Substances added indirectly to human food affirmed as generally recognized as safe (GRAS).

Subpart B—Listing of Specific Substances Affirmed as GRAS

186.1093 Sulfamic acid.
186.1256 Clay (kaolin).
186.1275 Dextrans.
186.1300 Ferric oxide.
186.1316 Formic acid.
186.1374 Iron oxides.
186.1551 Hydrogenated fish oil.
186.1555 Japan wax.
186.1557 Tall oil.
186.1673 Pulp.
186.1750 Sodium chlorite.
186.1756 Sodium formate.
186.1770 Sodium oleate.
186.1771 Sodium palmitate.
186.1797 Sodium sulfate.
186.1839 Sorbose.

AUTHORITY: 21 U.S.C. 321, 342, 348, 371.

SOURCE: 42 FR 14658, Mar. 15, 1977, unless otherwise noted.

Subpart A—General Provisions

§ 186.1 Substances added indirectly to human food affirmed as generally recognized as safe (GRAS).

(a) The indirect human food ingredients listed in this part have been reviewed by the Food and Drug Administration and determined to be generally recognized as safe (GRAS) for the purposes and under the conditions prescribed, providing they comply with the purity specifications listed in this part or, in the absence of purity specifications, are of a purity suitable for their intended use in accordance with § 170.30(h)(1) of this chapter. Certain ingredients in this part may also be used in food-contact surfaces in accordance with parts 174, 175, 176, 177, 178 or § 179.45 of this chapter. Ingredients affirmed as GRAS for direct use in part 184 of this chapter are also GRAS as indirect human food ingredients in accordance with § 184.1(a) of this chapter.

(b) The regulations in this part do not authorize direct addition of any food ingredient to a food. They authorize only the use of these ingredients as indirect ingredients of food, through migration from their immediate wrapper, container, or other food-contact surface. Any ingredient affirmed as GRAS in this part shall be used in accordance with current good manufacturing practice. For the purpose of this part, current good manufacturing practice includes the requirements that an indirect human food ingredient be of a purity suitable for its intended use, and that it be used at a level no higher than reasonably required to achieve its intended technical effect in the food-contact article.

(1) If the ingredient is affirmed as GRAS with no limitations on its conditions of use other than current good manufacturing practice, it shall be regarded as GRAS if its conditions of use are consistent with the requirements of paragraphs (b), (c), and (d) of this section. When the Food and Drug Administration (FDA) determines that it is appropriate, the agency will describe one or more current good manufacturing practice conditions of use in the regulation that affirms the GRAS status of the indirect ingredient. For example, when the safety of an ingredient has been evaluated on the basis of limited conditions of use, the agency will describe in the regulation that affirms the GRAS status of the indirect ingredient, one or more of these limited conditions of use, which may include the category of food-contact surface(s), technical effect(s) or functional use(s) of the indirect ingredient, and the level(s) of use. If the ingredient is used under conditions that are significantly different from those described in the regulation, such use of a substance may not be GRAS. In such a case, a manufacturer may not rely on the regulation as authorizing that use but shall independently establish that the use is GRAS or shall use the ingredient in accordance with a food additive regulation. Persons seeking FDA approval of an independent determination that a

NOVARTIS EXHIBIT 1031
Novartis v. Regents, IPR2023-01346
Page 100 of 100