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Japan

Agricultural Situation

Japan proposes changes to MRLs and designation of food additives.

2007

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Report Highlights:
On September 6, Japan proposed establishment of maximum residue limits (MRL) for the pesticides Quinoxyfen and Fluopicolide in foods and designation of the food additives Polysorbates 20, 60, 65, and 80, Calcium Silicate, and Calcium L-Ascorbate.

Includes PSD Changes: No
Includes Trade Matrix: No
Trade Report
Tokyo [JA1]
[JA]

Executive Summary

On September 6, 2007 the Japanese Ministry of Health, Labour and Welfare (MHLW) proposed establishment of maximum residue limits (MRL) for the pesticides Quinoxyfen and Fluopicolide in foods and designation of the food additives Polysorbates 20, 60, 65, and 80, Calcium Silicate, and Calcium L-Ascorbate. The period for sending comments on these proposed changes ends September 20, 2007. However, MHLW will also notify these proposed changes to the WTO/SPS committee, which will provide another chance for public comments on this subject. After the closing of the comment period, the Pharmaceutical Affairs and Food Sanitation Council will meet to discuss any comments received and then a final report will be made based on the conclusions of the session. This report will constitute the final decision.

If you have any comments, please send them in Japanese or English directly to the Japanese Government at:

Standards and Evaluation Division, Department of Food Safety,
Pharmaceutical and Food Safety Bureau,
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Please also consider copying the U.S. Embassy, Tokyo at agtokyo@usda.gov on your comments in order for them to be considered as part of the official U.S. Government comments to the WTO.

Agenda 1. Establishment of Maximum Residue Limits for the Pesticides (Quinoxyfen and Fluopicolide) in Food

Purpose

This activity is to develop specifications and standards for foods. Under the provisions of Article 11, Paragraph 1 of the Food Sanitation Law, the Minister of Health, Labour, and Welfare may establish residue standards (maximum residue limits: MRLs) for pesticides, feed additives, and veterinary drugs (referred to as just "agricultural chemicals") that may remain in foods. Any food for which standards are established pursuant to the provisions is not permitted to be marketed unless such food complies with the established standards.

On May 29, 2006, the Ministry of Health, Labour and Welfare introduced the positive list system for agricultural chemicals in food.* Basically, all foods distributed in the Japanese marketplace are subject to regulation based on the system.

> *Note: The positive list system was established based on the 2003 amendment of the Food Sanitation Law. The system aims to prohibit the distribution of any food in the Japanese marketplace if it contains agricultural chemicals at amounts exceeding certain levels specified under the Law.*

Outline of the activity

Quinoxyfen (Fungicide): This chemical is not permitted for use in Japan. The MHLW has reviewed the existing MRLs, which had been provisionally established at the time of the introduction of the new system.

Fluopicolide (Fungicide): This chemical is not permitted for use in Japan. This time the Ministry of Agriculture, Forestry and Fisheries has decided to approve the chemical based on the Agricultural Chemicals Regulation Law. In addition, a foreign business has filed an application with the MHLW for the establishment of MRLs for the chemical based on the Guideline for Application for Establishment and Revision of Maximum Residue Limits for Agricultural Chemicals Used outside Japan, published on 5 February 2004. In response to MAFF's decision and the application, the MHLW has newly established MRLs for some crops. Currently, MRLs are not set for any crops.

The existing MRLs for quinoxyfen appear in either of the MRLs List (the Item 6, Section A "General Compositional Standards for Food," Part I "Food" in the Specifications and Standards for Food, Food Additives, Etc.) and Provisional MRLs List (Item 7, Section A), according to crops. These MRLs have been modified as necessary. Finalized MRLs for quinoxyfen will be placed on the MRLs List in Item 6, and the MRLs currently placed in Item 7 will be deleted. The MRLs for fluopicolide will be placed in Item 6. For draft MRLs, see Attachments 1-1 and 1-2.

Attachment 1-1

Quinoxyfen (Fungicide)

Commodity	MRL (draft) ppm	Current MRL ppm
Wheat	0.01	
Barley	0.01	
Sugar beet	0.03	
Lettuce (including cos lettuce and leaf lettuce)	20	
Pimiento (sweet pepper)	1	
Other solanaceous vegetables*	10	
Pumpkin (including squash)		0.3
Water melon	0.08	0.3
Melons	0.1	0.3
Muskmelon melon	0.1	0.3
Cherry	0.4	0.3
Strawberry	1	
Other berries[b]	1	
Grape	2	1
Hop	1	3
Cattle, muscle	0.01	0.01
Pig, muscle	0.01	0.01
Other terrestrial mammals[c], muscle	0.01	0.01
Cattle, fat	0.1	0.1
Pig, fat	0.1	0.1
Other terrestrial mammals, fat	0.1	0.1
Cattle, liver	0.01	0.01
Pig, liver	0.01	0.01
Other terrestrial mammals, liver	0.01	0.01
Cattle, kidney	0.01	0.01
Pig, kidney	0.01	0.01
Other terrestrial mammals, kidney	0.01	0.01
Cattle, edible offal[d]	0.01	0.01
Pig, edible offal	0.01	0.01
Other terrestrial mammals, edible offal	0.01	0.01
Milk	0.01	0.01
Chicken, muscle	0.01	
Other poultry[e], muscle	0.01	
Chicken, fat	0.02	
Other poultry, fat	0.02	
Chicken, liver	0.01	
Other poultry, liver	0.01	
Chicken, kidney	0.01	
Other poultry, kidney	0.01	
Chicken, edible offal	0.01	
Other poultry, edible offal	0.01	
Chicken, eggs	0.01	
Other poultry, eggs	0.01	

Note:
The uniform limit (0.01 ppm) will be applied to commodities for which draft MRLs are not given. Some limits in the column “MRL (draft)” remain unchanged from the current MRLs.
1. “Other solanaceous vegetables” refers to all solanaceous vegetables, except tomato, pimiento (sweet pepper), and egg plant.
2. “Other berries” refers to all berries, except strawberry, raspberry, blackberry, blueberry, cranberry, and huckleberry.
3. “Other terrestrial mammals” refers to all terrestrial mammals, except cattle and pig.
4. “Edible offal” refers to all edible offal, except muscle, fat, liver, and kidney.
5. “Other poultry” refers to all poultry, except chicken.

Agenda 2 . Designation of Food Additives

(Polysorbates 20, 60, 65, and 80, Calcium Silicate, and Calcium L-Ascorbate)

Purpose

This activity is to newly designate six substances (Polysorbates 20, 60, 65, and 80, Calcium Silicate, and Calcium L-Ascorbate) as authorized food additives.

Under Article 10 of the Food Sanitation Law, food additives may be used or marketed only when they are designated by the Minister of Health, Labour and Welfare. Where use standards or specifications are established for additives under Article 11 of the law, those additives may be marketed only when they meet the established standards or specifications.

In response to a request from the Minister, the Subcommittee on Food Additives under the Food Sanitation Committee under the Pharmaceutical Affairs and Food Sanitation Council has discussed the adequacy of the designation of these substances as food additives. The reports from the subcommittee are outlined as below.

Outline

The Minister should designate these substance under Article 10 of the Food Sanitation Law as food additives that are unlikely to injure human health. In addition, the Minister should establish compositional specifications and use standards for them under Article 11 of the law. See Attachment 2-1 for Polysorbates 20, 60, 65, and 80; Attachment 2-2 for Calcium Silicate; and Attachment 2-3 for Calcium L-Ascorbate.

Additional Information

Progress in the designation procedure of food additives that have been proven safe by JECFA (Joint FAO/WHO Expert Committee on Food Additives) and that are widely used in countries other than Japan (Attachment 2-4)

Attachment 2-1

Polysorbate 20

1. Use standards

Products	Maximum use level as polysorbate 80
Capsule- and tablet-form foods excluding confections	25 g/kg
Chewing gum	5.0 g/kg
Cocoa and chocolate products	
Milk-fat substitutes	
Sauces	
Seasonings for instant noodles	
Shortening	
Bakery confections	3.0 g/kg
Decorations for confections (Sugar coatings and icings)	
Dressing	
Ice creams	
Mayonnaise	
Mix powder for bakery confections and moist sweet cake	
Moist sweet cake, unbaked cake (Including fruit tart, cream cake, rare cheese cake, custard pudding, and like products)	
Sweetened yoghurt	
Candies	1.0 g/kg
Edible ices including sherbet	
Flour paste*	
Soup	
Pickled sea weed	0.50 g/kg
Pickled vegetables	
Chocolate drinks	
Unripened cheese	0.080 g/kg
Canned and bottled sea weed	0.030 g/kg
Canned and bottled vegetables	
Other foods	0.020 g/kg

If it is used together with one of polysorbate 60, 65, and 80, the sum of each amount used shall be not more than the corresponding maximum levels as polysorbate 80.

The above standards are not applied for products that are approved or recognized as foods for special dietary use.

Note

Flour paste is the hot flour paste is confectionery products of cocoa and chocolate that are prepared with sugar, fat and, powder milk, egg or sweet flour as secondary materials, and baked/steamed. They are used as filling or coatings of bread or bakery confectionery.

2. Compositional specifications

Substance name Polysorbate 20 (Polyoxyethylene (20) sorbitan monolaurate)

CAS number [9005-64-5]

Definition Polysorbate 20 is a mixture of laurate partial esters of sorbitol and sorbitol anhydrides, condensed with approximately 20 moles of ethylene oxide for each mole of sorbitol and its anhydrides.

Content It contains 70.0–74.0% of oxyethylene groups (- OCH_2CH_2 = 44.05).

Description It occurs as a colorless to orange-yellow oily liquid having a faint, characteristic odor.

Identification (1) Measure the absorption spectrum of Polysorbate 20 as directed in the Liquid Film Method under Infrared Spectrophotometry. Compare the obtained spectrum with the Reference Spectrum. Both spectra exhibit similar intensities of absorption at the same wavenumbers.
(2) Weigh 0.10 g of Polysorbate 20 in a flask, add 2 ml of a solution (1 in 50) of sodium hydroxide in methanol, and heat under a reflux condenser for 30 minutes in a water bath. Add 2 ml of boron trifluoride–methanol TS through the condenser, and heat for 30 minutes. Then add 4.0 ml of heptane through the condenser, and heat for 5 minutes. After cooling, add 10 ml of saturated sodium chloride solution, shake for about 15 seconds, then add saturated sodium chloride solution further to raise the liquid surface to the mouth of the flask. Take 2 ml of the upper layer, wash three times with 2 ml of water each time, and dehydrate with anhydrous sodium sulfate. Use the resultant solution as the test solution. Separately, prepare a control solution by weighing 0.05 g of methyl laurate, 0.05 g of methyl palmitate, 0.08 g of methyl stearate, and 0.10 g of methyl oleate in a 50-ml volumetric flask and adding heptane to make 50 ml. Perform Gas Chromatography on 1 µl each of the test solution and the control solution under the following conditions. The chromatogram from the test solution shows a peak corresponding to methyl laurate.

Operating conditions
Detector: Flame-ionization detector.
Column: A silicate glass capillary tube (0.25-mm internal diameter and 30-m length) coated with a 0.5-µm thickness of polyethylene glycol for gas chromatography.
Column temperature: Raise at 10°C/minute from 80°C to 220°C, and maintain for 40 minutes.
Inlet temperature: 250°C.
Detector temperature: 250°C.
Injection: Spritless (50:1).
Carrier gas: Helium or nitrogen.
Flow rate: Adjust so that the peak of methyl laurate appears 10 minutes after injection and the peaks of methyl stearate and methyl oleate are separated.

Purity (1) Saponification value 40–55 (2.0 g, Flavorings Substances Tests).
(2) Acid value Not more than 2.0 (Flavorings Substances Tests).
(3) Hydroxyl value 96–108 (Fats and Related Substances Tests).
(4) Lead Not more than 2.0 µg/g as Pb (5.0 g, Method 1).

(5) Arsenic Not more than 4.0 μg/g as As_2O_3 (0.50 g, Method 3, Apparatus B).
(6) Ethylene oxide and dioxane Not more than 1.0 μg/g for ethylene oxide.
Not more than 10 μg/g for dioxane.

Test Solution Weigh accurately about 1 g of Polysorbate 20 into a specified head space vial, and add exactly 1 ml of water.

Standard Solution To 2.5 ml of ethylene oxide–tetrahydrofuran TS for polysorbate, measured exactly, add water to make exactly 100 ml. Take exactly 1 ml of this solution, add water to make exactly 100 ml, and use the resultant solution as the ethylene oxide standard stock solution. To about 1 g of dioxane, weighed accurately, add water to make exactly 100 ml. Take 1ml of this solution, add water to make exactly 200 ml, and use the resultant solution as the dioxane standard stock solution. Prepare a standard solution by taking exactly 5 ml of ethylene oxide and exactly 10 ml of dioxane in a volumetric flask and diluting exactly to 50 ml with water.

Control Solution Weigh accurately about 1 g of Polysorbate 20 in a specified head space vial, and add exactly 1 ml of the standard solution.

Procedure Stopper the vials, shake them well while warming until they are uniform. Analyze by Head-Space Gas Chromatography under the following operating conditions. Measure the peak areas, (A_{Te} and A_{Td}) and (A_{Re} and A_{Re}), of ethylene oxide and dioxane for each of the test solution and control solution. Obtain the each amount of ethylene oxide and dioxane in the sample by the formula.

$$\text{Amount } (\mu g/g) \text{ of ethylene oxide} = \frac{A_{Te} \times C_e}{(A_{Re} \times W_T) - (A_{Te} \times W_R)},$$

$$\text{Amount } (\mu g/g) \text{ of dioxane} = \frac{A_{Td} \times C_d}{(A_{Rd} \times W_T) - (A_{Td} \times W_R)},$$

Where, W_T: Weighed amount (g) of the sample in the test solution.
W_R: Weighed amount (g) of the sample in the control solution.
C_e: Amount (μg/g) of ethylene oxide added to the control solution.
C_d: Amount (μg/g) of dioxaneadded to the control solution.

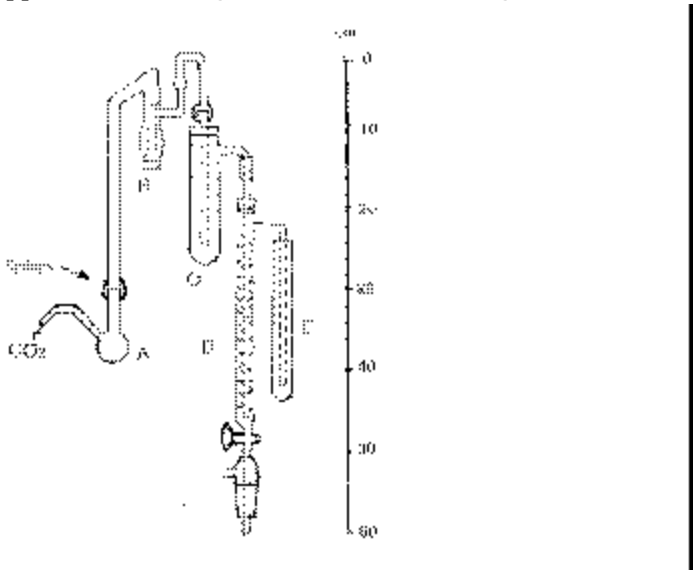
Operating conditions
Detector: Flame-ionization detector.
Column: A silicate glass or quartz capillary tube (0.25-mm internal diameter and 60-m length) coated with a 1.4-μm thickness of 25% diphenyl–75% dimethylpolysiloxane for gas chromatography.
Column temperature: Maintain at 40°C for 10 minutes, raise at 10°C/minute to 100°C, and maintain for 10 minutes. Then raise at 20°C/minute to 230°C.
Inlet temperature: A constant temperature at about 150°C.
Detector temperature: A constant temperature at about 250°C.
Injection: Spritless (20:1).
Carrier gas: Helium or nitrogen.
Flow rate: Adjust so that the peak of dioxane appears 22 minutes after injection.
Headspace sampler
Vial equilibration temperature: 70°C
Vial equilibration time: 45 minutes
Inlet-line temperature: 80°C
Injection amount: 1.0 ml
Column selection: Use a column capable of completely resolving peaks of acetaldehyde, ethylene oxide, and dioxane in that order, when the solution prepared as directed below is chromatographed using the above conditions.
Solution: Place 1.0 ml of the standard solution into a specified headspace vial, add 0.10

ml of 2 mg/L acetaldehyde solution, prepared fresh, tightly stopper, and shake until it is uniform.

Water Not more than 3.0% (1 g, back titration).

Residue on Ignition Not more than 0.25% (5 g, 800°C, 15 minutes).

Assay (1) Apparatus An arrangement is shown in the figure.



A: Side-arm reaction flask (28-mm diameter, 12/18 standard-taper joint, CO_2 inlet capillary: 1-mm internal diameter).
B: Condenser trap (condenser: 9-mm internal diameter; inlet to trap B: 2 mm-internal diameter; inlet to absorption tube C: 7/15 standard-taper joint, 2-mm internal diameter tube)
C: Absorption tube (14-mm internal diameter)
D: Absorption tube (inner tube: 8-mm external diameter; bottom of spiral: 2-mm opening; spiral: 1.75-mm rod, 23 turns, 8.5 mm rise per turn; outer tube: 12.5-mm internal diameter; side arm: 7 cm from the top of spiral, 3.5-mm internal diameter, 2-mm opening at bottom; the stopcock is lubricated with silicon grease)
E: Terminal absorption tube.

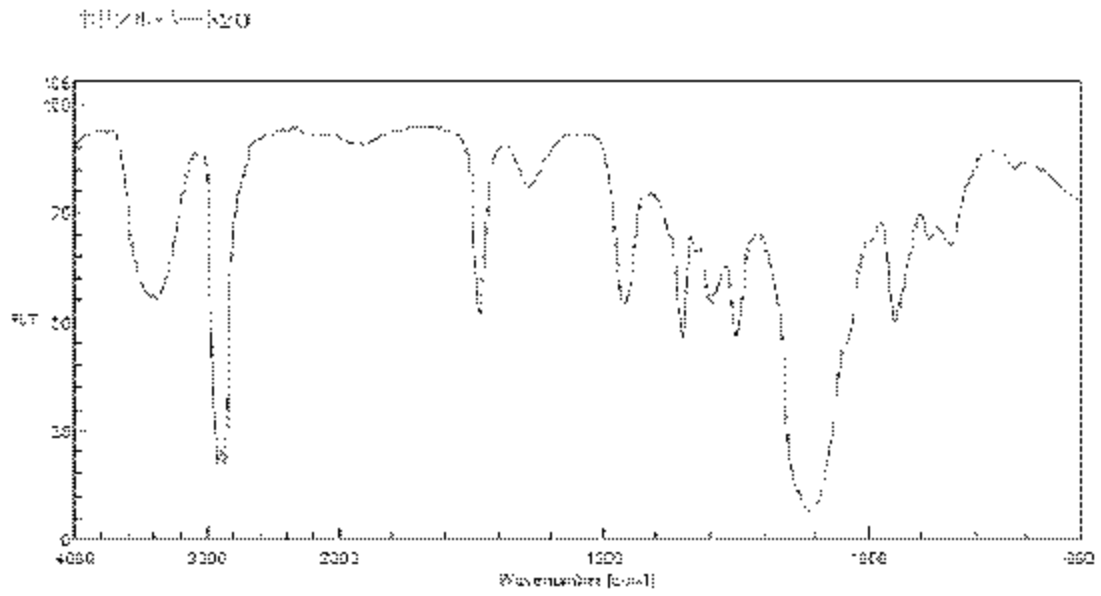
(2) *Procedure* Fill trap B with a suspension of 0.06 g of red phosphorus in 100 ml of water. Place exactly 10 ml of silver nitrate–ethanol TS in absorption tube C, exactly 15 ml bromine–potassium bromide TS for oxyethylene determination in absorption tube D, and exactly 10 ml of potassium iodide solution (1 in 10) in tube E. Place about 0.065 g of the sample, weighed accurately, in reaction flask A, together with 10 ml of hydriodic acid and boiling chips. Connect reaction flask A to trap/condenser B. Pass a slow stream of carbon dioxide through the apparatus at a rate allowing about one bubble to come out each second. Heat the flask gently in an oil bath to 140–150°C, and maintain at this temperature for at least 40 minutes to allow the mixture to react. Continue heating until there is no longer any cloudy reflux in the condenser B, and until the supernatant liquid in absorption tube C is clarified almost completely. Five minutes before the completion of the reaction, heat absorption tube C to 50–60°C in a hot water bath to drive out the dissolved olefin completely. On the completion of decomposition, carefully disconnect tubes D and C in that order, disconnect the carbon dioxide source, and remove the oil bath from flask A. Connect flask D, by its lower adapter, to a 500-ml iodine flask containing 150 ml of water and 10 ml of potassium iodide solution (1? 10). Disconnect tube E, rinse the side-arm of tube D with water

into tube E. Allow the solution in tube D to run into the iodine flask through the stopcock, and rinse the inner tube and spiral with water. Add the contents in tube E to the iodine flask, rinse the inside of tube E with water, stopper, and allow to stand for 5 minutes. Add 5 ml of dilute sulfuric acid, and immediately titrate with 0.05 mol/L sodium thiosulfate (indicator: 2 ml of starch TS). Separately, perform a blank test to make necessary correction. Transfer the liquid in tube C into a flask, rinse the inside of tube C with water, and add water to the flask to make 150 ml. Heat to boiling. After cooling to room temperature, titrate with 0.05 mol/L ammonium thiocyanate (indicator: 3 ml of iron (III) ammonium sulfate TS for oxyethylene determination). Perform a blank test to make necessary correction. Calculate the oxyethylene content in the sample by the following formula.

$$\text{Content (\%) of oxyethylene} = \frac{(B-S)\times 0.05\times 2.203}{W} - \frac{(B'-S')\times 0.05\times 4.405}{W}$$

where S = Amount (ml) of 0.05 mol/L sodium thiosulfate consumed in the test,
S' = Amount (ml) of 0.05 mol/L ammonium thiocyanate consumed in the test,
B = Amount (ml) of 0.05 mol/L sodium thiosulfate consumed in the blank test,
B' = Amount (ml) of 0.05 mol/L ammonium thiocyanate consumed in the blank test,
W = Weighed amount (g) of the sample.

Reference Spectrum of Polysorbate 20



<Reagents and test solutions (TS)>

Bromine–Potassium Bromide TS for Oxyethylene Determination
Add 1 ml of bromine to 300 ml of a solution of acetic acid saturated by 5 g of potassium bromide.

Iron (III) Ammonium Sulfate TS for Oxyethylene Determination

Dissolve 8 g of iron (III) ammonium sulfate•12H_2O in water to make 100 ml.

Silver Nitrate–Ethanol TS
Dissolve 15 of silver nitrate in 50 ml of water, add 400 ml of ethanol, mix, and add a few drops of nitric acid. Store in a brown bottle.

Methyl Oleate $C_{19}H_{36}O_2$ A colorless or pale-yellow liquid.

Refractive index n_D^{20}: 1.452.

Specific gravity 0.88

Deuterated Chloroform for Nuclear Magnetic Resonance Spectrum Measurement $CDCl_3$
Use a product produced exclusively for nuclear magnetic resonance spectrum measurement.

Ethylene Oxide–Tetrahydrofuran TS for Polysorbate A colorless, clear liquid.
Because it is highly volatile, use promptly after opening.
Content About 44.05 g of ethylene oxide (C_2H_4O) in 1,000 ml (1 mol/L)?
Assay Place oxethylene–tetrahydrofuran TS for polysorbate, cooled in methanol with dry ice, in a glass tube (2-mm external diameter), and seal the tube with a fluorine resin tape. Place deuterated chloroform for nuclear magnetic resonance spectrum measurement in a NMR tube (5-mm external diameter), and cool in methanol with dry ice. Transfer the tube containing the sample to the NMR tube, and seal tightly. Measure the ^1H nuclear magnetic resonance spectrum at once. Express the resonance intensity (approximate 3.95 ppm) of tetrahydrofuran as A when the resonance intensity (approximate 2.85 ppm) of the sample is normalized as 1. Obtain the content of ethylene oxide by the following formula.

$$\text{Content (g/L) of ethylene oxide } (C_2H_4O) = \frac{11.01}{12.24 + 20.26 \times A} \times 1{,}000$$

Methyl Stearate $C_{19}H_{38}O_2$ White or yellow crystalline lumps.
Melting point About 38°C.

Methyl Palmitate $C_{17}H_{34}O_2$ White or yellow crystalline lumps.

Refractive index n_D^{20}: 1.451.

Melting point About 30°C.

Methyl Laurate $C_{13}H_{26}O_2$ A colorless or yellow liquid.

Refractive index n_D^{20}: 1.431.
Specific gravity 0.87.
Melting point About 5°C.

<General Tests>

Nuclear Magnetic Resonance Spectrum Spectroscopy

Nuclear Magnetic Resonance (NMR) Spectroscopy is a spectroscopic technique based on the phenomenon that magnetic nuclei in a substance when placed in a static magnetic field absorb specific radio frequency energy, causing a resonance transition from the lower energy state to higher energy state.

From the NMR spectrum, the four parameters (chemical shift, spin-spin coupling constant, resonance intensity, and relaxation time) are obtained. These parameters are applicable to identification tests, purity tests, and assay. The targets nuclei include $_{1}H$, $_{13}C$, $_{15}N$, $_{19}F$, and $_{31}P$.

The chemicals shift is given by

$$\delta = \frac{\nu_S - \nu_R}{\nu_R} + \delta_R$$

where, ν_S: The resonance frequency of the observed signal,

ν_R: The resonance frequency of the reference signal,

d_R: The chemical shift of the reference signal (in the case of the value not being 0).

The chemical shifts are normally expressed in ppm, a dimensionless unit, by assuming the chemical shift of the reference compound (reference nucleus) as 0.

Spectrometers

There are two types of spectrometers.

(1) Fourier transform NMR (FT-NMR) spectrometers (Fig. 1)

Fig. 1

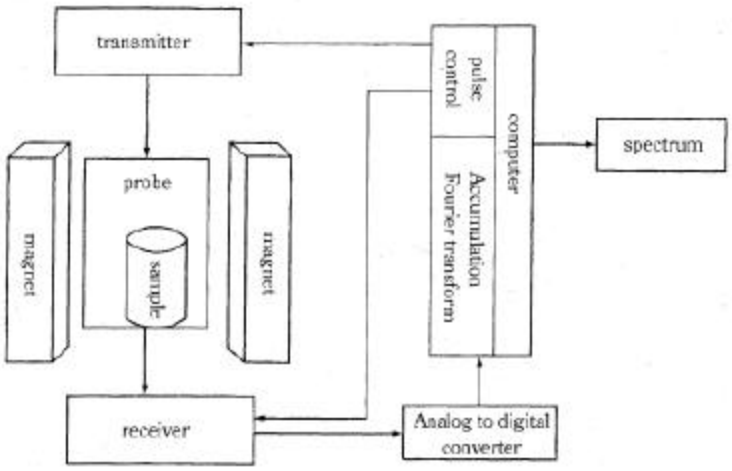


Fig. 1

(2) Continuous wave NMR (CW-NMR) spectrometers (Fig. 2)

Fig. 2

Measurement

The test solutions should be prepared as otherwise specified. Prior to measurement, the sensitivity and resolution of the instrument must be adjusted to the optimum levels using a standard sample (ethylbenzene, 1,2-dichlorobenzene, or acetaldehyde) dissolved in an appropriate deuterated NMR solvent.

(1) The sample dissolved in a suitable solvent is transferred to an NMR tube. The reference compound can be added directly to the sample solution (internal reference), or a sealed capillary tube containing the reference compound can be inserted into the NMR tube together with the test solution (external reference). The sample solutions should be completely homogenous. In particular, solid contaminants should be removed in order to obtain good spectra. Various deuterated NMR solvents are commonly used for NMR measurement. Solvent selection should ensure that (i) the solvent signals do not overlap with

the sample signals, (ii) the sample must be soluble in the solvent selected, and (iii) the solvent does not react with the sample. Furthermore, it should be noted that chemical shifts can depend upon the solvent employed, sample concentration and deuterium ion concentration, and that viscous solutions usually give rather broad, poorly resolve spectra.

(2) As reference compounds, reagents for nuclear magnetic resonance spectroscopy should be used. Specifically, for $_{1}$H and $_{13}$C spectra, tetramethylsilane (TMS) is usually used for samples dissolved in organic solvents, and sodium 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) or sodium 3-(trimethylsilyl)propionate (TSP) is used for samples dissolved in deuterium oxide. For other nuclei, nitromethane, trichlorofluoromethane, and phosphoric acid are used as reference compounds for $_{15}$N, $_{19}$F, and $_{31}$P, respectively. Furthermore, chemical shifts of residual protons in deuterated solvents and $_{13}$C in the solvent, instead of a reference compound, can be used for $_{1}$H and $_{13}$C NMR.

When the chemical shift of reference compound is not assumed to be 0 ppm, chemicals shifts of samples are corrected accordingly.

Polysorbate 60

1. Use standards

The same as Polysorbate 20

2. Compositional specifications

Substance name Polysorbate 60 (Polyoxyethylene (20) sorbitan monostearate)

Cas number [9005-67-8]

Definition Polysorbate 60 is a mixture of stearate and palmitate partial esters of sorbitol and sorbitol anhydrides, condensed with approximately 20 moles of ethylene oxide for each mole of sorbitol and its anhydrides.

Content It contains 65.0–69.5% of oxyethylene groups (- OCH_2CH_2 = 44.05).

Description It occurs as a colorless to orange oily liquid or semi-gel having a faint, characteristic odor.

Identification (1) If necessary, dissolve the sample by heating. Measure the absorption spectrum of Polysorbate 60 as directed in the Liquid Film Method under Infrared Spectrophotometry. Compare the obtained spectrum with the Reference Spectrum. Both spectra exhibit similar intensities of absorption at the same wavenumbers.
(2) Proceed as directed under Identification (2) for Polysorbate 20. The chromatogram from the test solution shows peaks corresponding to methyl stearate and methyl palmitate.

Purity (1) Saponification value 45–55 (2.0 g, Flavorings Substances Tests).
(2) Acid value Not more than 2.0 (Flavorings Substances Tests).
(3) Hydroxyl value 81–96 (Fats and Related Substances Tests).
(4) Lead Not more than 2.0 μg/g as Pb (5.0 g, Method 1).
(5) Arsenic Not more than 4.0 μg/g as As_2O_3 (0.50 g, Method 3, Apparatus B).
(6) Ethylene oxide and dioxane Not more than 1.0 μg/g for ethylene oxide.
Not more than 10 μg/g for dioxane.
Proceed as directed under Purity (6) for Polysorbate 20.

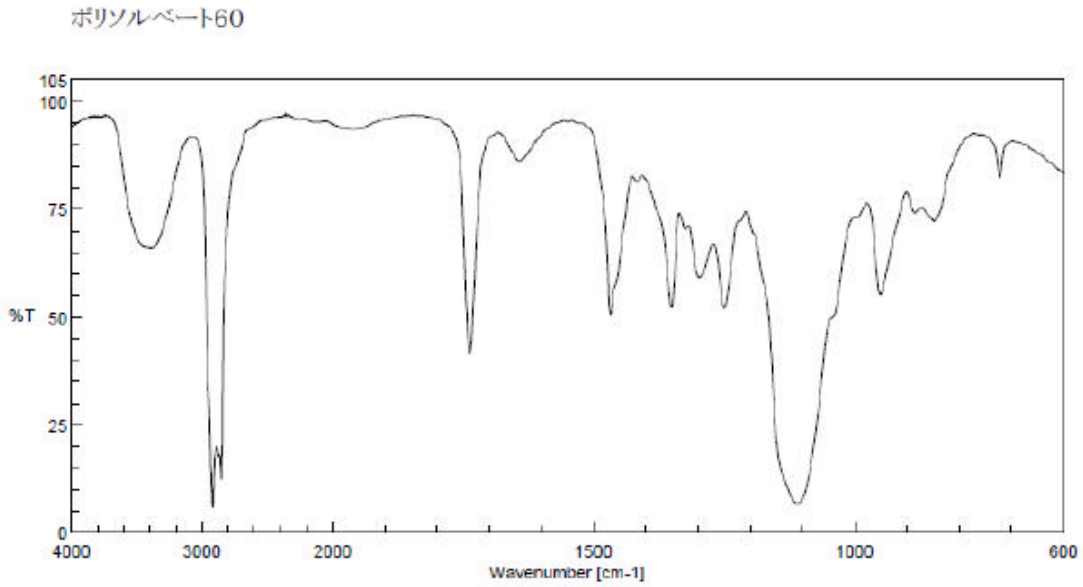
Water Not more than 3.0% (1 g, back titration).

Residue on Ignition Not more than 0.25% (5 g, 800°C, 15 minutes).

Assay Weigh accurately about 0.065 g of the sample, and proceed as directed under Assay for Polysorbate 20.

Reference Spectrum of Polysorbate 60

Reference Spectrum of Polysorbate 60



Polysorbate 65

1. Use standards

The same as Polysorbate 20

2. Compositional specifications

Substance name Polysorbate 65 (Polyoxyethylene (20) sorbitan tristearate)
Cas number [9005-71-4]

Definition Polysorbate 65 is a mixture of stearate and palmitate partial esters of sorbitol and sorbitol anhydrides, condensed with approximately 20 moles of ethylene oxide for each mole of sorbitol and its anhydrides.

Content It contains 46.0–50.0% of oxyethylene groups (- OCH_2CH_2 = 44.05).
Description It occurs as a white to yellow-brown solid having a faint, characteristic odor.
Identification (1) Dissolve the sample by heating. Measure the absorption spectrum of Polysorbate 65 as directed in the Liquid Film Method under Infrared Spectrophotometry. Compare the obtained spectrum with the Reference Spectrum. Both spectra exhibit similar intensities of absorption at the same wavenumbers.
(2) Proceed as directed under Identification (2) for Polysorbate 20. The chromatogram from the test solution shows peaks corresponding to methyl stearate and methyl palmitate.

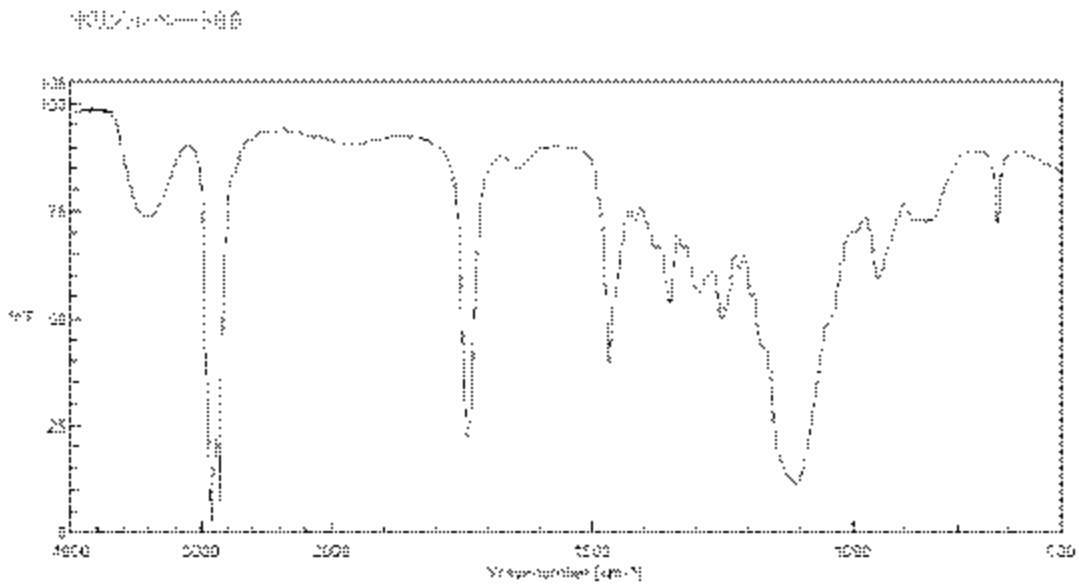
Purity (1) Congealing point 29–33°C
(2) Saponification value 88–98 (2.0 g, Flavorings Substances Tests).
(3) Acid value Not more than 2.0 (Flavorings Substances Tests).
(4) Hydroxyl value 40–60 (Fats and Related Substances Tests).
(5) Lead Not more than 2.0 μg/g as Pb (5.0 g, Method 1).
(6) Arsenic Not more than 4.0 μg/g as As_2O_3 (0.50 g, Method 3, Apparatus B).
(7) Ethylene oxide and dioxane Not more than 1.0 μg/g for ethylene oxide.
Not more than 10 μg/g for dioxane.
Proceed as directed under Purity (6) for Polysorbate 20.

Water Not more than 3.0% (1 g, back titration).

Residue on Ignition Not more than 0.25% (5 g, 800°C, 15 minutes).

Assay Weigh accurately about 0.09 g of the sample, and proceed as directed under Assay for Polysorbate 20.

Reference Spectrum of Polysorbate 65



Polysorbate 80

1. Use standards

The same as Polysorbate 20

2. Compositional specifications

Substance name Polysorbate 80 (Polyoxyethylene (20) sorbitan monooleate)

CAS number [9005-65-6]

Definition Polysorbate 65 is a mixture of oleate partial esters of sorbitol and sorbitol anhydrides, condensed with approximately 20 moles of ethylene oxide for each mole of sorbitol and its anhydrides.

Content It contains 65.0–69.5% of oxyethylene groups (- OCH_2CH_2 = 44.05).

Description It occurs as a colorless to orange-yellow oily liquid having a faint, characteristic odor.

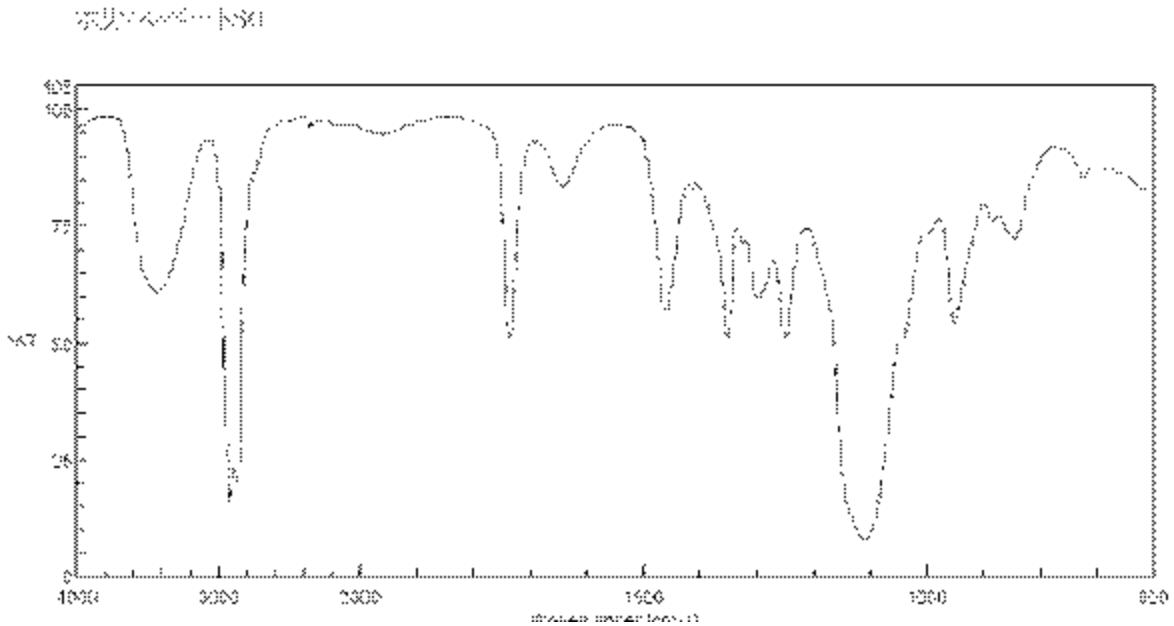
Identification (1) Measure the absorption spectrum of Polysorbate 80 as directed in the Liquid Film Method under Infrared Spectrophotometry. Compare the obtained spectrum with the Reference Spectrum. Both spectra exhibit similar intensities of absorption at the same wavenumbers.
(2) Proceed as directed under Identification (2) for Polysorbate 20. The chromatogram from the test solution shows a peak corresponding to methyl oleate.

Purity (1) Saponification value 44–55 (2.0 g, Flavorings Substances Tests).
(2) Acid value Not more than 2.0 (Flavorings Substances Tests).
(3) Hydroxyl value 65–80 (Fats and Related Substances Tests).
(4) Lead Not more than 2.0 μg/g as Pb (5.0 g, Method 1).
(5) Arsenic Not more than 4.0 μg/g as As_2O_3 (0.50 g, Method 3, Apparatus B).
(6) Ethylene oxide and dioxane Not more than 1.0 μg/g for ethylene oxide.
Not more than 10 μg/g for dioxane.

Proceed as directed under Purity (6) for Polysorbate 20.

Water Not more than 3.0% (1 g, back titration).
Residue on Ignition Not more than 0.25% (5 g, 800°C, 15 minutes).
Assay Weigh accurately about 0.065 g of the sample, and proceed as directed under Assay for Polysorbate 20.

Reference Spectrum of Polysorbate 80



Attachment 2-2

Calcium Silicate

1. Use standards

Calcium Silicate must not be used in human milk substitutes or weaning foods.
The use amount must be not more than 2.0% weight of each target food. When it is used together with fine silicon dioxide, the sum of each use amount must be not more than 2.0%.

2. Compositional specifications

Substance name Calcium Silicate

Chemical name, Cas number Calcium silicate [1344-95-2]

Definition Calcium Silicate is a compound of silicon dioxide and calcium oxide.

Content It contains 50.0–95.0% of silicon dioxide(SiO_2=60.08) and 3.0–35.0% of calcium oxide(CaO=56.08).

Description It occurs as a white to grayish-white, hygroscopic fine powder.

Identification (1) Mix 0.5 g of Calcium Silicate with 0.2 g of anhydrous sodium carbonate and 2 g of anhydrous potassium carbonate. Transfer the mixture into a platinum or nickel crucible, and heat until it melts completely. Cool, add 5 ml of water, and allow to stand for about 3 minutes. Heat the bottom of crucible gently to detach the melt, and transfer to a beaker with about 50 ml of water. Add gradually hydrochloric acid until no effervescence is observed, then add additional 10 ml of hydrochloric acid, and evaporate the mixture to dryness on a water bath. Cool, add 20 ml of water, boil, and filter the mixture. Transfer the gelatinous residue on the filter paper into a platinum dish, and add 5 ml of hydrofluoric acid. The precipitate dissolves. Heat and hold in the vapors a glass stirring rod with a drop of water on the tip. The drop becomes turbid.
(2) Neutralize the filtrate obtained in Identification (1) with ammonia TS using 2 drops of methyl red TS as an indicator. Then add dilute hydrochloric acid dropwise until the solution is acid. On the addition of ammonium oxalate solution (7? 200), a white granule precipitate of calcium forms. This precipitate is insoluble in acetic acid but dissolves in hydrochloric acid.

Purity (1) pH 8.4–12.5 (5% suspension)
(2) Lead Not more than 5.0 μg/g asPb.

Test Solution Weigh exactly 5.0 g of Calcium Silicate into a beaker, add 50 ml of diluted hydrochloric acid solution (1 in 4), and stir. Cover the beaker with a watch dish, and boil gently for 15 minutes. Filter the solution by suction through a quantitative filter paper (5C) into a 50-ml measuring flask. Rinse the beaker and the residue on the filter paper with hot water, and combine the filtrate with the washings. Cool, and add water to make exactly 50 ml.

Control Solution To 5 ml of Lead Standard Solution, exactly measured, add diluted hydrochloric acid (1 in 4) to make 100 ml.

Procedure Measure the absorbances of the test solution and control solution by Atomic Absorption Spectrophotometry (Flame Type) using the operating conditions given below. The absorbance of the test solution is not more than that of the control solution.

Operating conditions

Light source: Lead hollow cathode lamp.
Analytical line wavelength: 217 nm.

Supporting gas: Air.
Combustible gas: Acetylene.

(3) Arsenic Not more than 4.0 μg/g as As_2O_3.
Test Solution Use 5 ml of the test solution prepared in Purity (2).
Apparatus Use Apparatus B.
(4) Fluoride Not more than 50 μg/g as F.
Test Solution Weigh exactly 2 g of Calcium Silicate into a polyethylene beaker, add 40 ml of water, and stir for 15 minutes. Transfer the suspension to a 50 ml volumetric flask, and add water to volume. Centrifuge the suspension, transfer exactly 30 ml of the supernatant solution to a polyethylene beaker, and add 15 ml of EDTA–tris TS.
Control Solution Weigh exactly 2.210 g of sodium fluoride, previously dried at 110°C for 2 hours, into a polyethylene beaker, and dissolve in 200 ml of water with stirring. Transfer the solution to a 1,000-ml polyethylene volumetric flask, and add water to volume. Use this solution as the control stock solution. Store the stock solution in a polyethylene bottle. Prepare the control solution fresh before use. To 2 ml of the control stock solution, measured exactly, add water to make exactly 1,000 ml. Take exactly 30 ml of this solution into a polyethylene beaker, and add 15 ml of EDTA–tris TS, and use the resultant solution as the control solution.
Procedure Measure the electric potentials using a potentiometer connected to a reference electrode and a fluoride ion electrode. The potential of the test solution is not less than that of the control solution.

Loss of Drying Not more than 10.0% (105°C, 2 hours).

Loss on Ignition 5.0–14.0% (1,000°C, constant weight, dry basis).

Assay (1) Silicon dioxide Weigh accurately about 0.4 g of Calcium Silicate, dried previously, into a beaker, add 5 ml of water and 10 ml of perchloric acid, and heat until white fumes are evolved. Cover the beaker with a watch dish, and heat for additional 15 minutes. Cool, and add 30 ml of water, and filter the contents through a quantitative filter paper (5C). Rinse the residue on the filter paper with 200 ml of hot water, combine the washings with the filtrate, and refer to as solution A. Heat gently the residue with the filter paper in a platinum crucible until the filter paper is carbonized. Cool, add a few drops of sulfuric acid, and ignite at 1,300°C to constant weight. Weigh the crucible with the residue (W g). To the residue, add 5 drops of sulfuric acid and 15 ml of hydrofluoric acid, heat at 1,000°C to constant weight, and cool in a desiccator, and weigh the crucible (w g). Obtain the content of calcium silicate by the formula.

$$\text{Content (\%) of calcium silicate} = \frac{W\,(g) - w\,(g)}{\text{Weighed amount of the sample}\,(g)} \times 100$$

(2) Calcium oxide Neutralize solution A obtained in Assay (1) with sodium hydroxide solution (1 in 25), and add about 30 ml of 0.05 mol/L EDTA using a burette while stirring. Then add 15 ml of sodium hydroxide solution (1 in 25) and 0.3 g of NN indicator, and titrate with 0.05 mol/L EDTA. The end point is when the red-purple color of the solution completely disappears and changes to blue.
1 ml of 0.05 mol/L EDTA = 2.804 mg CaO
Reagents and Test Solutions (TS)
EDTA–tris TS Weigh exactly 18.6 g of disodium ethylenediaminetetraacetate and 6.05 g of 2-amino-2-hydroxymethylpropandiol into a 250-ml beaker, and dissolve in 200 ml of hot water with stirring. Adjust the pH to 7.5–7.6 with sodium hydroxide solution (1 in 5). Cool, then adjust the pH to 8.0 with sodium hydroxide solution (1 in 5), transfer the solution to a 250-ml of volumetric flask, and add water to volume. Mix well, and store in a plastic bottle.

Attachment 2-3

Calcium L-Ascorbate

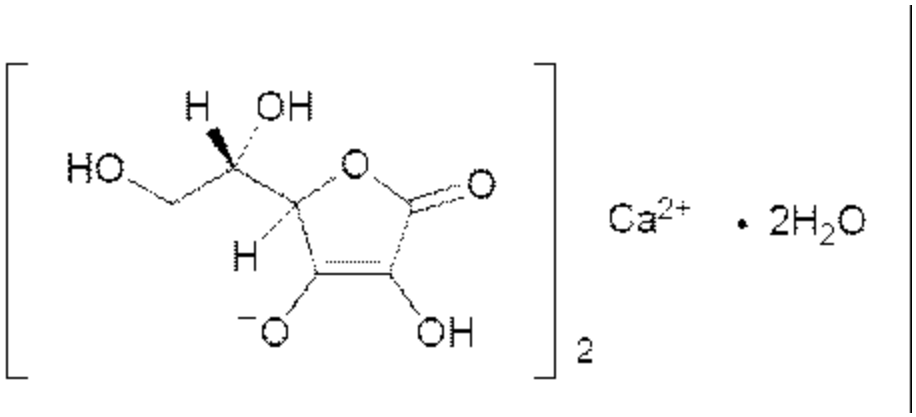
1. Use standards

Standards are not established.

2. Compositional specifications

Substance name Calcium L-Ascorbate

Structural formula



Molecular formula $C_{12}H_{14}CaO_{12}\bullet 2H_2O$

Mol. Weight. 426.34

Chemical name, CAS number

Monocalcium bis{(2R)-2-[(1S)-1,2-dihydroxyethyl]-4-hydroxy-5-oxo-2,5-dihydrofuran-3-olate} dihydrate [5743-28-2]

Content It contains not less than 98.0% of calcium L-ascorbate ($C_{12}H_{14}CaO_{12}\bullet 2H_2O$).

Description It occurs as a white to yellowish white crystalline powder. It has no or faint odor.

Idetification (1) To 10 ml of a solution (1 in 100) of Calcium L-Ascorbate, add 1 to 2 drops of sodium 2,6-dichlorophenolindophenol TS. The solution turns blue and disappears at once.
(2) A solution (1 in 10) of Calcium L-Ascorbate responds to all tests for Calcium Salts as directed in the Qualitative Tests.

Purity (1) Specific rotation $[a]_D^{25}$ =+95 to +97° (1 g, newly boiled and cooled water 20 ml).
(2) pH 6.7–7.5 (2.0 g, water 20 ml).
(3) Lead Not more than 2.0 µg/g as Pb (5.0 g, Method 1).
(4) Arsenic Not more than 4.0 µg/g as As_2O_3 (0.50 g, Method 1, Apparatus B).
(5) Fluoride Not more than 50 µg/g as F.

Test Solution Weigh exactly 1.00 g of Calcium L-Ascorbate into a beaker, and dissolve in 10 ml of water. Add gradually 20 ml of diluted hydrochloric acid (1 in 10), and boil for 1 minute. Transfer the hot solution to a polyethylene beaker, and immediately cool by ice. Then add 10 ml of a solution (1 in 40) of disodium ethylenediaminetetraacetate and 15 ml of sodium citrate solution (1 in 4), and mix. Adjust the pH to 5.4–5.6 with diluted hydrochloric acid (1 in

10) or sodium hydroxide solution (2 in 5), and transfer the solution to a 100-ml volumetric flask, add water to volume. Transfer 50 ml of this solution to a polyethylene beaker.

Control Solution Weigh exactly 2.210 g of sodium fluoride, previously dried at 110°C for 2 hours, into a polyethylene beaker, and dissolve in 200 ml of water with stirring. Transfer the solution to a 1,000-ml polyethylene volumetric flask, and add water to volume. Use this solution as the control stock solution. Store the stock solution in a polyethylene bottle. Prepare the control solution fresh before use. Place 1 ml of the control stock solution, measured exactly, into a 100-ml polyethylene volumetric flask, and add water to volume. Place 1 ml of this solution, exactly measured, into a polyethylene beaker, add 10 ml of a solution (1 in 40) of disodium ethylenediaminetetraacetate and 15 ml of sodium citrate solution (1 in 4), and mix. Adjust the pH to 5.4–5.6 with diluted hydrochloric acid (1 in 10) or sodium hydroxide solution (2 in 5), and transfer the solution to a 100-ml volumetric flask, add water to volume. Transfer 50 ml of the resultant solution to a polyethylene beaker.

Procedure Measure the electric potentials using a potentiometer connected to a reference electrode and a fluoride ion electrode. The potential of the test solution is not less than that of the control solution.

Assay Dissolve 0.2 g of Calcium L-Ascorbate, accurately weighed, in 50 ml of metaphosphoric acid solution (1 in 50), and titrate with 0.05 mol/L iodine using starch TS as an indicator.

1 ml of 0.05 mol/L iodine = 10.66 mg of $C_{12}H_{14}CaO_{12}\cdot 2H_2O$

Progress of evaluation of food additives that have been proven safe and are widely used in the world

Attachment 2-1
As of January 2007

Substance name	Request for evaluation	Food Safety Commission		MHLW		
		Evaluation by expert committee[1]	Notification of result[2]	Discussion by subcommittee[3]	Closing date for comments[4]	Date of designation as food additives
Isobutanol	22 Nov 2002	26 Mar 2004(Fin.)	27 May 2004	23 Apr 2004(Fin.)	19 Aug 2004	21 Dec 2004
2-Methylbutanol		9 Mar 2004(Fin.)	27 May 2004	8 Apr 2004(Fin.)	19 Aug 2004	21 Dec 2004
2,3,5,6-Tetramethylpyrazine		9 Mar 2004(Fin.)	27 May 2004	8 Apr 2004(Fin.)	19 Aug 2004	21 Dec 2004
Cellulose powder	8 Mar 2002	26 Mar 2004(Fin.)	29 Jul 2004	24 Sep 2004(Fin.)	21 Oct 2004	2 Dec 2004
Propanil	29 Nov 2002	26 Mar 2004 20 May 2004 28 Jul 2004(Fin.)	8 Sep 2004	22 Sep 2004(Fin.)	18 Dec 2004	24 Jan 2005
Methyl oxide	29 Oct 2003	17 Dec 2003 2 Oct 2004(Fin.)	9 Dec 2004	17 Dec 2004(Fin.)	3 Feb 2005	22 Mar 2005
Isopropanil	15 Dec 2003	26 Mar 2004 9 Sep 2004 1 Dec 2004 7 Oct 2004(Fin.)	9 Dec 2004	22 Oct 2004(Fin.)	4 Jan 2005	24 Mar 2005
Hydroxypropyl cellulose	15 Dec 2004	22 Mar 2005(Fin.)	12 May 2005	23 Sep 2005(Fin.)	14 Jan 2006	8 Mar 2006
Xylan-laurate						
Xylan-palmitate		24 Mar 2005(Fin.)	12 May 2005	24 Feb 2006(Fin.)	24 Jan 2007	9 Mar 2007
Xylan-stearate						
Natamycin	28 Oct 2003	9 Jun 2004 15 Nov 2004 26 Apr 2005(Fin.)	9 May 2005	24 Mar 2006(Fin.)	7 Sep 2006	28 Nov 2006
Acesulfame K	22 Nov 2002	9 Jun 2004 2 Sep 2004 21 Apr 2005 28 Nov 2005 16 Apr 2006(Fin.)	23 Jun 2006	22 Jun 2006(Fin.)	27 Jul 2006	15 May 2006
2'-Fucosyllactose	1 Apr 2005	14 Apr 2006(Fin.)	12 May 2006	29 Jun 2006(Fin.)	15 Dec 2006	16 Mar 2007
6'-Sialyllactose						
Pullulan		14 Apr 2005 28 Jul 2005(Fin.)	26 Sep 2005	21 Nov 2005 26 Nov 2006(Fin.)	30 Apr 2006	2 Sep 2006
Ammonium alginate	28 Mar 2002	2 Dec 2003 14 Dec 2006 (Fin.)	09 May 2006	29 Nov 2006(Fin.)	8 Sep 2006	26 Dec 2006
Potassium alginate						
Calcium alginate						

Substance name	Request for evaluation	Food Safety Commission		MHLW		
		Evaluation by expert committee[1]	Notification of result[2]	Discussion by subcommittee[3]	Closing date for comments[4]	Date of designation as food additives
2-Methylbutanol	19 Dec 2005	14 Jul 2006 11 Aug 2006(Fin.)	12 Oct 2006	8 Dec 2006 16 Jan 2007 (Fin.)	22 May 2007	3 Aug 2007
Isobutyraldehyde	19 Dec 2005	28 Jun 2006 14 Jul 2006 11 Aug 2006 13 Sep 2006 13 Oct 2006(fin.)	7 Dec 2006	8 Dec 2006 16 Jan 2007 (Fin.)	22 May 2007	3 Aug 2007
Butyraldehyde	19 Dec 2005	19 Dec 2006 26 Jan 2007(fin.)	22 Mar 2007	20 Mar 2007(fin.)	27 Aug 2007	
Polysorbate 20, 60, 65, 80	8 Oct 2003	29 Oct 2003 27 Apr 2004 28 Jul 2004 23 Mar 2007(fin.)	7 Jun 2007	4 Jul 2007 9 Aug 2007(fin.)		
Calcium silicate	15 Aug 2005	26 Feb 2007 23 Mar 2007 17 Apr 2007 29 May 2007(fin.)	26 Jul 2007	9 Aug 2007(fin.)		
Calcium ascorbate	3 Oct 2005	23 Mar 2007 17 Apr 2007 29 May 2007 22 Jun 2007(fin.)	23 Aug 2007	9 Aug 2007(fin.)		
Nisin	20 Oct 2003	9 Apr 2004 16 Nov 2004 26 Jan 2005 30 Jul 2007 27 Aug 2007(fin.)				
Acetylated distarch adipate Acetylated distarch phosphate Acetylated oxidized starch Starch sodium octenylsuccinate Hydroxypropyl starch Hydroxypropyl distarch phosphate Phosphated distarch phosphate Monostarch phosphate Distarch phosphate Oxidized starch Starch acetate	26 Nov 2004	23 Mar 2005 17 May 2005 27 Aug 2007(fin.)				

Substance name	Request for evaluation	Food Safety Commission		MHLW		
		Evaluation by expert committee [1]	Notification of results [2]	Discussion by subcommittee [3]	Closing date for comments [4]	Date of designation as food additives
Magnesium hydroxide	8 Mar 2006	22 Jan 2007 30 Jul 2007 27 Aug 2007 (under consideration)				
Dimagnesium phosphate	2? Mar 2006	18 May 2006 23 Jun 2006 14 Jul 2006 18 Aug 2006 15 Sep 2006 13 Oct 2006 28 Nov 2006 (under consideration)				
Polyvinylpyrrolidone	30 Jun 2006	15 Sep 2006 13 Oct 2006 28 Nov 2006 19 Dec 2006 26 Jan 2007 (under consideration)				
Magnesium silicate (synthetic)	15 Aug 2006	20 Feb 2007 20 Mar 2007 17 Apr 2007 (under consideration)				
Sodium aluminum silicate	15 Aug 2006	20 Feb 2007 (under consideration)				
Calcium aluminum silicate	15 Aug 2006	20 Feb 2007 (under consideration)				
Calcium stearate	22 May 2006	27 Aug 2007 (under consideration)				
Ammonium isovalerate	12 Mar 2006					
Sodium ferrous citrate	6 Feb 2007					
Potassium lactate	6 Apr 2007					
Calcium sorbate	10 Mar 2007					
Valeraldehyde	19 Mar 2007					
Isovaleraldehyde	[illegible]					

(Remaining figures)
1. Date when discussion was conducted by the expert committee.
2. Date when the evaluation result was filed with the MHLW
3. Date when discussion was conducted by the Subcommittee on Food Additives under the Pharmaceutical Affairs and Food Sanitation Council
4. Closing date for comment on WTO notification.