March 6, 2002

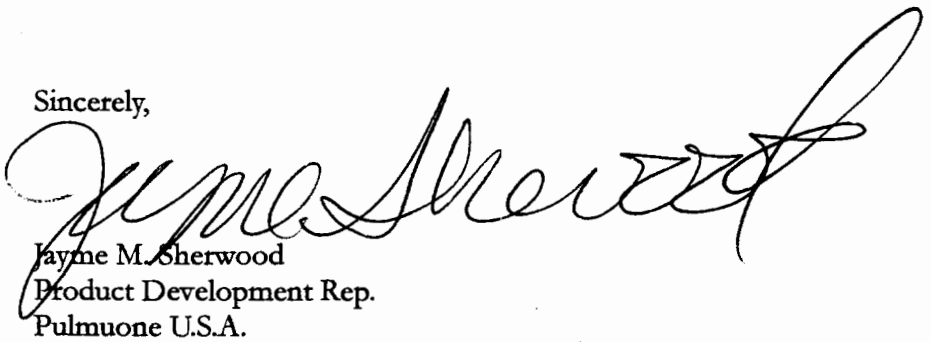
National Organic Standards Board
C/o Robert Pooler
Agricultural Marketing Specialist
USDA/AMS/Tm/NOP
Room 2510-So
Ag Stop 0268
P.O. Box 96456
Washington, D.C. 20090-6456

To Whom It May Concern:

Included you will find our petition for the substance **Glucono Delta Lactone**. GDL is a commonly used ingredient in combination with Magnesium Chloride and Calcium Sulfate for the production of tofu and other soy products. Since studies show no adverse affects to human health or the environment we are requesting the addition of **Glucono Delta Lactone** the National List.

Thank you for your time and assistance. If you have any questions please call me at (323) 564-3000 ext. 120 or (310) 663-6701.

Sincerely,



Jayme M. Sherwood
Product Development Rep.
Pulmuone U.S.A.

4567 FIRESTONE BLVD.
SOUTH GATE, CA 90280

# Glucono Delta Lactone

## Item A

- Category: Nonagricultural (non-organic) substances allowed in or on processed products labeled as " organic" or "made with organic (specified ingredients)."

## Item B

1. Glucono Delta Lactone
2. Yoshikawa Chemical Co., Ltd.
   - 1-18-6, Kojima Akasaki, Kurashiki, Okayama, 711, Japan
   - Tel: 086-472-2102 Fax: 086-472-2116
3. Use of substance as processing aid.
4. The agent is used as a soymilk-curdling agent.
5. See Attachment A
6. See Attachment B
7. See Attachment C
8. CAS# 90-80-2
9. See Attachment D
10. See Attachment D
11. See Attachment B
12. Justification Statement See Attachment E

ATTACHMENT : A

MARZEN **YOSHIKAWA CHEMICAL CO., LTD.** SINCE 1861
1-18-6, KOJIMA AKASAKI, KURASHIKI, OKAYAMA, 711, JAPAN.
TEL : 086-472-2102 FAX : 086-472-2116

# Production process

PRODUCT : GLUCONO DELTA LACTONE
(FOOD ADDITIVE)
Origin : Japan

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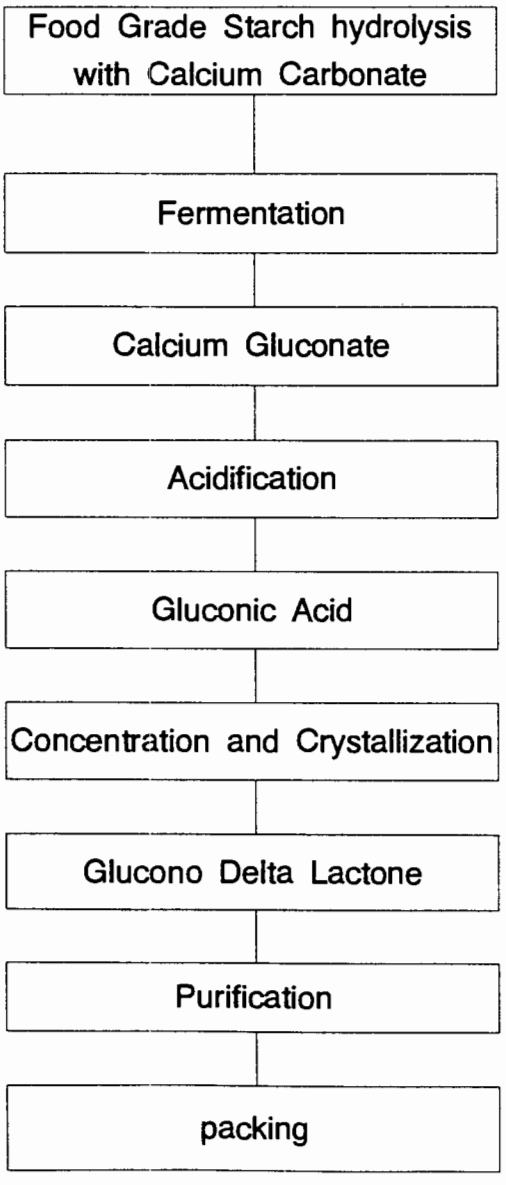

ATTACHMENT : B



GLUCONO DELTA-LACTONE

EXPLANATION

Glucono delta-lactone (GDL) was evaluated for acceptable daily intake at the tenth and eighteenth meetings of the Joint FAO/WHO Expert Committee on Food Additives (Annex 1, references 13 and 35). Toxicological monographs were published after both of these meetings (Annex 1, references 12 and 36).

Since the previous evaluation, at which time an ADI of 0-50 mg/kg b.w. was established, additional data have become available and are summarized and discussed in the following monograph. The previously-published monograph has been expanded and is reproduced in its entirety below.

BIOLOGICAL DATA

Biochemical aspects

GDL, in an aqueous medium, readily forms an equilibrium mixture of the lactone and gluconic acid. These are intermediates in the oxidation of glucose through the pentose phosphate cycle, which, while not the main pathway of glucose metabolism, is well recognized.

GDL was reported to inhibit competitively mannosidase and glucosidase isolated from rat epididymis and limpet tissue (Levvy et al., 1964). These findings were confirmed using acid alpha-glucosidase from rabbits (Palmer, 1971).

GDL is a non-competitive inhibitor of polysaccharide phosphorylase in in vitro assays (Tu et al., 1971).

The enzyme gluconolactonase (E.C. 3.1.1.17) has been isolated from porcine liver; it was found to catalyze the hydrolysis of GDL to gluconic acid with maximum activity at pH 7.5 (Roberts et al., 1978).

Groups of six rats were fed a diet in which the limiting factor was inadequate caloric value. When the basal diet was supplemented with either glucose or GDL, as a source of additional calories, increased growth rate was observed. Glucose and GDL were almost equally effective in the promotion of growth (Eyles & Lewis, 1943).

Sodium gluconate uniformly labelled with $^{14}C$ and $^{2}H$ was administered i.p. to normal rats for three successive days. Approximately 57% of the administered $^{14}C$ label appeared in expired $CO_2$. Only a small fraction of gluconate carbon could be recovered as urinary saccharate. When labelled gluconate was administered to phlorizinized rats, about 10% of the total $^{14}C$ label appeared in the expired $CO_2$. Urinary glucose from phlorizinized rats and liver glycogen from normal rats were shown to be uniformly labelled with respect to $^{14}C$ (Stetten & Stetten, 1950).

Radioactivity was measured in the blood of normal and alloxan-diabetic Wistar rats after the oral administration of (U-$^{14}C$)-GDL or (U-$^{14}C$)-gluconate. Radioactivity was also measured in the intestinal contents and faeces 5 hours after ingestion of the radioactive materials. The authors concluded that the lactone is better-absorbed from the intestine than is the gluconate anion. Because of enhanced membrane permeation and higher concentrations of the lactone in blood, the distribution space of the lactone is larger than that of gluconate (50 and 41% of the body weight, respectively); a higher retention in tissues and a greater loss in urine was also observed after administration of the lactone. Incorporation into liver

glycogen was higher after the administration of the lactone than after the administration of gluconate, particularly in diabetic animals. The initial deficit in the oxidation of gluconate compared to that of the lactone, caused by a lag period of 7 and 4 hours, respectively, was completely compensated for during the following 8–9 hours. The oxidative turnover of both compounds was significantly enhanced in diabetic animals. The better utilization in diabetic metabolism is in part explained by a rise of glycolytic intermediates in the liver, which are decreased in starvation and diabetes. Initial phosphorylation is the limiting step of gluconate metabolism (Tharandt et al., 1979.

When three men were given 10 g (167 mg/kg b.w.) of GDL orally as a 10% solution, the amounts recovered in the urine in 7 hours represented 7.7–15% of the dose. No pathological urine constituents were noted. When 5 g (84 mg/kg b.w.) was given orally, none was recovered in the urine. The largest dose given was 30 g (500 mg/kg b.w.) (Chenoweth et al., 1941).

## Toxicological studies

### Special study on mutagenicity

The mutagenic effects of GDL were assessed in Saccharomyces cerevisiae and Salmonella typhimurium strains TA1535 and TA1537, with and without metabolic actuation. GDL was not mutagenic in these assays at doses of 0.25 and 0.5% (Litton Bionetics, Inc., 1974).

### Special studies on teratogenicity

#### Mice

Six groups of 25 pregnant mice were given continuously from days 6–15 of gestation 0, 6.95, 32.5, 150, or 695 mg/kg b.w./day GDL by oral intubation. A positive control group that was administered 150 mg/kg b.w./day aspirin was included. No clearly-discernible

effects were seen on nidation or on maternal or fetal survival. The number of abnormalities seen in either soft or skeletal tissues of animals in the test groups did not differ from the number occurring spontaneously in the sham-treated controls (FDRL, 1974).

Rats

Six groups of 22 to 25 pregnant rats were given continuously from days 6-15 of gestation 0, 5.94, 27.6, 128, or 594 mg/kg b.w./day GDL by oral intubation. A positive control group that was administered 250 mg/kg b.w./day aspirin was included. No clearly-discernible effects were seen on nidation or on maternal or fetal survival. The number of abnormalities seen in either soft or skeletal tissues of animals in the test groups did not differ from the number occurring spontaneously in the sham-treated controls (FDRL, 1974).

Hamsters

Six groups of approximately 25 pregnant hamsters were given continuously from days 6-10 of gestation 0, 5.6, 26, 121, or 560 mg/kg b.w./day GDL by oral intubation. A positive control group that was administered 250 mg/kg b.w./day aspirin was included. No clearly-discernible effects were seen on nidation or on maternal or fetal survival. The number of abnormalities seen in either soft or skeletal tissues of animals in the test groups did not differ from the number occurring spontaneously in the sham-treated controls (FDRL, 1974).

Rabbits

Six groups of 10 pregnant rabbits were given continuously from days 6-18 of gestation 0, 7.8, 32.2, 168, or 780 mg/kg b.w./day GDL by oral intubation. A positive control group that was administered 2.5 mg/kg b.w./day 6-aminonicotinamide was included. No clearly-discernible effects were seen on nidation or on maternal or fetal survival. The number of abnormalities seen in either soft or skeletal

tissues of animals in the test groups did not differ from the number occurring spontaneously in the sham-treated controls (FDRL, 1974).

Acute toxicity

| Species | Compound | Route | $LD_{50}$ (mg/kg b.w.) | Reference |
|---|---|---|---|---|
| Rabbit | Sodium gluconate | i.v. | 7630 | Gajatto, 1939 |

Short-term studies

Rats

Groups of 20 male and 20 female rats were fed gluconic acid (as GDL) for 26 weeks at levels of 0 or 1% in the diet without ill-effects or demonstrable changes in the main organs on microscopic examination (Harper & Gaunt, 1962).

Cats and dogs

Gluconic acid was administered as a 10% solution by stomach tube to 5 cats and 3 dogs at a daily dose of 1.0 g/kg b.w. for 14 days. Urine was examined daily for protein, blood, casts, and sugar. Gross examination of lungs, heart, liver, kidneys, gastrointestinal tract, bladder, ureters, and spleen as well as histological examination of lungs, liver, and kidneys were performed. No evidence of toxicity was found. (Chenoweth et al., 1941).

Long-term study

Rats

Groups of 30 male and 30 female rats were fed diets containing

meat treated with 1% GDL (equivalent to feeding 0.4% GDL) or untreated meat for 29 months. Growth, food intake, and mortality were not affected. Haematology, clinical biochemistry, liver function tests, and histopathology revealed no differences between treated animals and controls (Van Logten et al., 1972).

Observations in man

Sixteen persons (7 with urologic conditions) were administered 5-g doses of GDL at 2-hour intervals, up to total doses of 15 to 25 g daily, and subsequently 10-g doses, up to total doses of 20 to 50 g daily. The pH and specific gravity of the urine from those on test and from the controls were determined. In g of the 16 patients, the urine became more acid, and in the other half it became more alkaline during the period of treatment. Eleven of the 16 patients developed diarrhoea without nausea during the course of the study (Gold & Civin, 1939).

The administration for 3 to 6 days of large oral doses (5-10 g/day) of gluconic acid to five normal humans did not produce any renal changes, as shown by the absence of blood, protein, casts, or sugar in the urine (Chenoweth et al., 1941).

Comments

GDL, in an aqueous medium, readily forms an equilibrium mixture of the lactone and gluconic acid. these are intermediates in the oxidation of glucose through the pentose phosphate cycle.

A single long-term test in rats with 1 level of GDL in the diet showed no evidence of carcinogenicity. Teratogenicity studies have shown no abnormalities in several species. GDL was not mutagenic in microbial tests.

GDL makes an insignificant contribution to the normal carbohydrate diet and is metabolized into normal body constituents. Single doses of GDL in excess of 20 grams exert a laxative effect in

man.

EVALUATION

**Estimate of acceptable daily intake for man**

ADI "not specified". The fact that high doses of GDL exert a laxative effect in man should be taken into account when considering its level of use.

REFERENCES


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Eyles, R. & Lewis, H.B. (1943). The utilization of d–glucono–delta–lactone by the organism of the young white rat. J. Nutr., 26, 309–317.

FDRL, (1974). Teratologic evaluation of FDA 71–72 (glucono delta–lactone). Prepared under Contract No. FDA 71–260 by Food and Drug Research Laboratories, Inc. 58 pp. Available from: National Technical Information Service, Springfield, VA, USA; No. PB–223,830.

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Levvy, G.A., Hay, A.J., & Conchie, J. (1964). Inhibition of glycosidases by aldonolactones of corresponding configuration. 4. Inhibitors of mannosidase and glucosidase. Biochem. J., 91, 378-384.

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Tu, J.I., Jacobson, G.R., & Graves, D.J. (1971). Isotopic effects and inhibition of polysaccharide phosphorylase by 1,5-glucono-lactone. Relationship to the catalytic mechanism. Biochemistry, 10, 1229-1236.

Van Logten, M.J., den Tonkelaar, E.M., Kroes, R., Berkvens, J.M., & van Esch, G.J. (1972). Long-term experiment with canned meat treated with sodium nitrite and glucono-delta-lactone in rats. Food Cosmet. Toxicol., 10, 475-488.

See Also:

Toxicological Abbreviations

Glucono delta-lactone (JECFA Evaluation)

ATTACHMENT : C



# Code of Federal Regulations

# Title 21 - Food and Drugs

# Revised as of April 1, 2001



[Code of Federal Regulations]
[Title 21, Volume 2]
[Revised as of April 1, 2001]
From the U.S. Government Printing Office via GPO Access
[CITE: 21CFR133.129]



TITLE 21--FOOD AND DRUGS

CHAPTER I--FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES--CONTINUED

PART 133--CHEESES AND RELATED CHEESE PRODUCTS--Table of Contents

Subpart B--Requirements for Specific Standardized Cheese and Related Products

Sec. 133.129 Dry curd cottage cheese.

(a) Cottage cheese dry curd is the soft uncured cheese prepared by the procedure set forth in paragraph (b) of this section. The finished food contains less than 0.5 percent milkfat. It contains not more than

80 percent of moisture, as determined by the method prescribed in Sec. 133.5(a).

(b)(1) One or more of the dairy ingredients specified in paragraph (b)(2) of this section is pasteurized; calcium chloride may be added in a quantity of not more than 0.02 percent (calculated as anhydrous calcium chloride) of the weight of the mix; thereafter one of the following methods is employed:

(i) Harmless lactic-acid-producing bacteria, with or without rennet and/or other safe and suitable milk-clotting enzyme that produces equivalent curd formation, are added and it is held until it becomes coagulated. The coagulated mass may be cut; it may be warmed; it may be stirred; it is then drained. The curd may be washed with water and further drained; it may be pressed, chilled, worked, seasoned with salt; or

(ii) Food grade phosphoric acid, lactic acid, citric acid, or hydrochloric acid, with or without rennet and/or other safe and suitable milk-clotting enzyme that produces equivalent curd formation, is added in such amount as to reach a pH of between 4.5 and 4.7; coagulation to a firm curd is achieved while heating to a maximum of 120 deg.F without agitation during a continuous process. The coagulated mass may be cut; it may be warmed; it may be stirred; it is then drained. The curd is washed with water, stirred, and further drained. It may be pressed, chilled, worked, seasoned with salt.

(iii) Food grade acids as provided in paragraph (b)(1)(ii) of this section, D-Glucono-delta-lactone with or without rennet, and/or other safe and suitable milk clotting enzyme that produces equivalent curd formation, are added in such amounts as to reach a final pH value in the range of 4.5-4.8, and it is held until it becomes coagulated. The coagulated mass may be cut; it may be warmed; it may be stirred; it is then drained. The curd is then washed with water, and further drained. It may be pressed, chilled, worked, and seasoned with salt.

(2) The dairy ingredients referred to in paragraph (b)(1) of this section are sweet skim milk, concentrated skim milk, and nonfat dry milk. If concentrated skim milk or nonfat dry milk is used, water may be added in a quantity not in excess of that removed when the skim milk was concentrated or dried.

(3) For the purposes of this section the term ``skim milk'' means the milk of cows from which the milk fat has been separated, and ``concentrated skim milk'' means skim milk from which a portion of the water has been removed by evaporation.

(c) The name of the food consists of the following two phrases which shall appear together:

(1) The words ``cottage cheese dry curd'' or alternatively ``dry curd cottage cheese'' which shall all appear in type of the same size and style.

(2) The words ``less than ₩1/2₩% milkfat'' which shall all appear in letters not less than one-half of the height of the letters in the phrase specified in paragraph (c)(1) of this section, but in no case less than one-eighth of an inch in height.

(d) When either of the optional processes described in paragraph (b)(1) (ii) or (iii) of this section is used to make cottage cheese dry curd, the label shall bear the statement ``Directly set'' or ``Curd set by direct acidification''. Wherever the name of the food appears on the label so conspicuously as to be seen under customary conditions of purchase, the statement specified in this paragraph, showing the optional process used, shall immediately and conspicuously precede or follow such name without intervening written, printed, or graphic matter.

(e) Each of the ingredients used in the food shall be declared on the label as required by the applicable sections



of parts 101 and 130 of this chapter, except that milk-clotting enzymes may be declared by the word ``enzymes''.

[42 FR 14366, Mar. 15, 1977, as amended at 47 FR 11826, Mar. 19, 1982; 49 FR 10093, Mar. 19, 1984; 58 FR 2892, Jan. 6, 1993]

ATTACHMENT : D

**** SECTION 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION ****

MSDS Name: Delta-Gluconolactone, 99%, Coarse Powder
Catalog Numbers:
AC271050000, AC271050010, AC271050050, AC271051000, AC271052500
Synonyms:
Company Identification (Europe): Acros Organics BVBA
Janssen Pharmaceuticalaan 3a
2440 Geel, Belgium
Company Identification (USA): Acros Organics
One Reagent Lane
Fairlawn, NJ 07410
For information in North America, call: 800-ACROS-01
For information in Europe, call: 0032(0) 14575211
For emergencies in the US, call CHEMTREC: 800-424-9300
For emergencies in Europe, call: 0032(0) 14575299

**** SECTION 2 - COMPOSITION, INFORMATION ON INGREDIENTS ****

| CAS# | Chemical Name | % | EINECS# |
|---|---|---|---|
| 90-80-2 | Delta-Gluconolactone, Coarse Powder | 99 | 202-016-5 |

Hazard Symbols: None Listed.
Risk Phrases: None Listed.

**** SECTION 3 - HAZARDS IDENTIFICATION ****

EMERGENCY OVERVIEW

Moisture sensitive.Light sensitive.

Potential Health Effects

Eye:

May cause eye irritation.

Skin:

May cause skin irritation.

Ingestion:

May cause gastrointestinal irritation with nausea, vomiting and diarrhea.

Inhalation:

May cause respiratory tract irritation.

Chronic:

Not available.

**** SECTION 4 - FIRST AID MEASURES ****

Eyes:

Flush eyes with plenty of water for at least 15 minutes, occasionally lifting the upper and lower eyelids. If irritation develops, get medical aid.

Skin:

Flush skin with plenty of soap and water for at least 15 minutes while removing contaminated clothing and shoes. Get medical aid if irritation develops or persists. Wash clothing before reuse.

Ingestion:

If victim is conscious and alert, give 2-4 cupfuls of milk or water. Never give anything by mouth to an unconscious person. Get medical aid if irritation or symptoms occur.

Inhalation:

Remove from exposure to fresh air immediately. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical aid if cough or other symptoms appear. Get medical aid.

Notes to Physician:

**** SECTION 5 - FIRE FIGHTING MEASURES ****

General Information:

As in any fire, wear a self-contained breathing apparatus in pressure-demand, MSHA/NIOSH (approved or equivalent), and full protective gear. During a fire, irritating and highly toxic gases may be generated by thermal decomposition or combustion.

Extinguishing Media:

Use agent most appropriate to extinguish fire. Use water spray, dry chemical, carbon dioxide, or appropriate foam.

**** SECTION 6 - ACCIDENTAL RELEASE MEASURES ****

General Information: Use proper personal protective equipment as indicated in Section 8.

Spills/Leaks:

Clean up spills immediately, observing precautions in the Protective

# Attachment E

## Petition Justification Statement

Glucono Delta Lactone (GDL) is a widely used substance in the manufacturing of tofu and soy products. In proprietary combination with Magnesium Chloride and Calcium Sulfate, Pulmuone tofu is made using GDL with the two other coagulating agents. The substance as documented in laboratory studies, shows no adverse affects to human health and to the environment. Therefore, we are earnestly requesting to include glucono delta lactone on the national list.


March 6, 2002

National Organic Standards Board
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Agricultural Marketing Specialist
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Thank you for your time and assistance. If you have any questions please call me at (323) 564-3000 ext. 120 or (310) 663-6701.

Sincerely,

Jayme Sherwood

Jayme M. Sherwood
Product Development Rep.
Pulmuone U.S.A.

4567 FIRESTONE BLVD.
SOUTH GATE, CA 90280