

**A Report from the Joint Subcommittee on Toxicity and Food Additives  
concerning the Designation of Food Additives  
and the Revision of Standards for Use under the Food Sanitation Council**

January 6, 1999  
Food Chemistry Division

Today, the Joint Subcommittee on Toxicity and Food Additives under the Food Sanitation Council has compiled a report on the result of discussions conducted during the session held on December 18, 1998 on the adequacy of the designation of Sucralose as an approved additive. The session was based on the consultation made by the Minister of Health and Welfare to the Food Sanitation Council on June 15, 1998. The Food Chemistry Division hereby announces an outline of the report and work schedule for the designation of Sucralose.

1. Outline of the report

About the adequacy of the designation of Sucralose

- Sucralose may be designated as a food additive under the provisions of Article 6 of the Food Sanitation Law, based on the judgment that this additive does not harm human health.
- Standards for use and specifications for compositions must be established under Article 7, Paragraph 1 when this additive is designated.

2. Schedule

(1) Presentation to the Conference for Promotion of Food Import and Facilitation  
(Presentation to embassies and EU representative in Tokyo)

(2) Notification given to WTO

(Notification given to the member countries, based on the Marrakech Agreement to Establish the World Trade Organization)

(3) A final report from the Food Sanitation Council to the Minister of Health and Welfare

(4) Amendment of the Enforcement Regulations under the Food Sanitation Law, and announcement of the designation of Sucralose with newly added regulations

---

\* Translated by The San-Ei Gen Foundation for Food Chemical Research. Please refer to the Japanese version, if you find anything unclear on this translation.

---

Food Sanitation Council Notice, No.5  
January 6, 1999

Mr. Masaaki Terada, Chairman  
Food Sanitation Council

Masaru Tobe, Chairman  
The Subcommittee on Toxicity

Mikio Yamazaki, Chairman  
The Subcommittee on Food Additives

**A Report from the Joint Subcommittee on Toxicity and Food Additives  
concerning the Designation of Food Additives  
under the Food Sanitation Council**

Today, the Joint Subcommittee on Toxicity and Food Additives under the Food Sanitation Council has compiled a report on the result of discussions conducted during the session held on December 18, 1998 on the adequacy of the designation of Sucralose as an approved additive. The session was based on the consultation made by the Minister of Health and Welfare with the Food Sanitation Council on June 15, 1998, under Notice No. 109 issued by the Ministry of Health and Welfare. We hereby jointly report the result to the Chairperson of the Food Sanitation Council.

---

**The Joint Subcommittee on Toxicity and Food Additives  
under the Food Sanitation Council**

1. The Joint Subcommittee on Toxicity and Food Additives concerning the Designation of Food Additives under the Food Sanitation Council

- 1) Date of session    December 18, 1998
- 2) Members' list    Omitted

2. The Working Group on the Designation of Food Additives

- 1) Dates of sessions    1st August 6, 1998  
                              2nd October 6, 1998  
                              3rd November 13, 1998
  - 2) Members' list    Omitted
- 

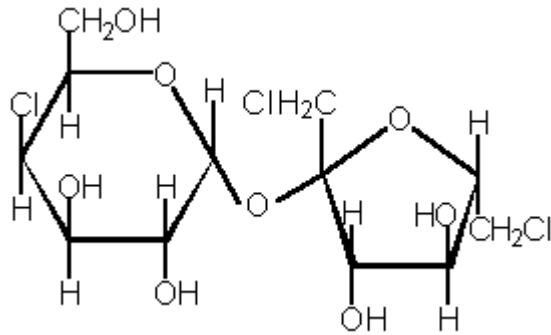
**Designation of Sucralose**

1. **Name:** sucralose

(Synonyms) trichlorogalactosucrose  
4,1',6'-trichlorogalactosucrose

2. **Structural formula:**

Chemical name : 1,6-dichloro-1,6-dideoxy-beta-D-fructofuranosyl-4-chloro-4-deoxy-alpha-D-garactopyranoside



Chemical formula:  $C_{12}H_{19}Cl_3O_8$

Molecular weight: 397.64

CAS No.: 56038-13-2

INS No.: 955

### 3. Use: Sweetening agent

Sucralose is used as a sweetening agent in more than 100 kinds of foods; e. g., drinks, desserts, and dressings.

### 4. Origin or details of development and use conditions

Sucralose is produced by selectively replacing three hydroxy groups with chlorine atoms.

Sucralose, which is 600 times sweeter than sucrose, was discovered during collaborative research between Queens Elizabeth College in London and a private company, Tate & Lyle, after an experiment involving chemical modification of sucrose conducted by the same collage in the 1970's.

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) evaluated the safety of sucralose. The JECFA allocated 0-3.5 mg/kg bw/day as a temporary ADI for sucralose in 1988 and 0-15 mg/kg bw/day as the ADI in 1990 at the 37th session.

### 5. Effectiveness

Sucralose will be able to be used in various foods as a sweetener.

Sucralose has few of the drawbacks in taste and stability exhibited by several of the previously approved sweeteners. Sodium saccharine, stevia extract, and licorice extract have characteristic bitterness and stringency. Aspartame is low in storage stability and heat stability in a neutral or alkaline aqueous solution. Sucralose is well examined in terms of these aspects. The attached document mentions that this sweetener has similar sweetness to sucrose and has no bitterness or metallic and other unpleasant tastes. In addition, it mentions the substance is superior in stability to other sweeteners (Attachment 1). For example, 97.1% of sucralose in a 1 % aqueous solution remains after a 336-day storage period under the condition of 30°C and pH 3.0.

(Note: Approved sweeteners include aspartame, xylitol, disodium glycyrrhizinate, saccharin, sodium saccharin, and D-sorbitol, which appear in Table 2 of the Enforcement Regulations under the Food Sanitation Law, and N-

acetyl glucosamine, licorice extract, D-xylose, and stevia extract, which appear in the List of Existing Food Additives (Ministry of Health and Welfare Announcement No. 120).

## 6. Safety

(1) Acute Toxicity Studies - Rats and mice received a single oral dose of sucralose at 10.0g/kg and 16.0g/kg, respectively. The administration was by gavage. No deaths were observed during the 14-day observation period. The LD<sub>50</sub> was estimated at more than 10.0g/kg for rats and more than 16.0g/kg for mice.

(2) Subacute Toxicity Studies - No deaths were observed of rats fed sucralose in the diet at levels of 10,000, 25,000 and 50,000 ppm for 4 weeks. Atrophy of lymph follicles in the spleen and thymus was observed in the 50,000 ppm group. Rats exposed to sucralose at dietary concentrations of 4 and 8% for 9 weeks exhibited a reduced growth rate and increased cecal weights. For rats exposed to oral (gavage) doses of 2,000, 3,000 and 4,000 mg/kg for 4, 9, and 13 weeks, increased cecal weights were observed in all groups, but there was no apparent toxicological significance. Increased cecal weights observed in these studies were reported in animals exposed to less-absorbable osmotically-active substances at high dose levels and toxicological significance was considered to be low. In addition, no remarkable changes were noted in an oral 34-day toxicity study in mice.

(3) Repeated Dose (Chronic) Toxicology and Carcinogenicity Studies - In a 26-week oral study, in which sucralose was fed to rats at doses of 1 and 3 %, there were no toxicological effects, except for reduction in body weight gain. In this study, dietary restriction groups were also investigated to elucidate the cause of the growth retardation. It was concluded that the decreased body weight gain in the 1% group was attributable to decrease in food intake. It was also concluded that the majority of the growth retardation in the 3% group could be attributed to reduction in food consumption, although some of the effect might be related to a physiological response to the high concentration of nondigestible sucralose in the diet. In a 12-month repeated dose toxicity study in Beagle dogs, no toxicological effect was observed at dietary levels of 0.3, 1 and 3%. In a combined chronic toxicity/carcinogenicity study in mice exposed to sucralose at dietary levels of 3,000, 10,000 and 30,000 ppm for 104 weeks, neither deaths nor any clinical signs related to the treatment were observed. The incidences of neoplastic lesions in treated and control groups were similar. In both sexes of the 30,000 ppm group, growth retardation, related to decreased food intake, was observed, and females given sucralose at dietary concentrations of 10,000 ppm or more showed increased relative liver weights. A decreased red blood cell count was noted for females of the 30,000ppm group. These changes were not considered to be of toxicological significance, since there were no associated histopathologic lesions. No carcinogenicity was observed in either sex of mice

exposed to sucralose at up to 30,000 ppm. In a combined chronic toxicity/carcinogenicity study in rats, animals were fed diets containing sucralose at concentrations of 3,000, 10,000 and 30,000 ppm for 104 weeks. Growth retardation related to decreased food intake was observed in all treated groups, but this was not considered to be of toxicological significance. The incidence of mild hyperplasia in the renal pelvis was significantly increased in females of all treated groups, accompanied by mineral deposition in 10,000 ppm and 30,000 ppm females. This was considered to have a causal relation, associated with a physiological response of caecum enlargement induced by diet containing high levels of poorly absorbable substances. Enlargement of the caecum and mineral deposition in the renal pelvis are reported to occur frequently in response to feeding poorly-absorbable, osmotically-active substances, such as xylitol, sorbitol or natural sugars, to rats\*1, 2), and it is considered that the toxicological significance of this might be minimal. The no-observed-adverse-effect level (NOAEL) in rats was estimated to be 30,000 ppm (1,500 mg/kg bw/day). No carcinogenicity was observed in either sex of rats.

\* 1 Leegwater, D. C., DE Groot, A. P. & VAN Kalmthout-Kuiper, M. *Fd. Cosmet. Toxicol.* (1974) The aetiology of caecal enlargement in the rat. 12: 687-697

2 Lord, G. H. & Newberne, P. M. *Fd. Chem. Toxic* (1990) Renal mineralization - a ubiquitous lesion in chronic rat studies (REVIEW). 28:449-455

(4) Reproduction Study - Repeated oral administration of sucralose to male rats at a dose level of 500 mg/kg/day for 28 days resulted in no changes in <sup>14</sup>CO<sub>2</sub> production or ATP concentration of sperm. In a two-generation reproduction study in rats, parents and offspring rats given sucralose in the diet at dose levels of 3,000, 10,000 and 30,000 ppm. No adverse effects on parameters concerned with reproduction, such as copulation rate, fertility rate, gestation rate, birth rate and birth numbers, were observed in the treated groups. Furthermore, in the derivation phase of a two-year chronic toxicity/carcinogenicity study with dietary levels of 3,000, 10,000 and 30,000 ppm, sucralose had no adverse effects on any reproductive parameter. Although slight extension of the pregnancy period was observed, this was not considered as biologically significant. In addition, no adverse effects were found on their offspring.

(5) Teratogenicity Study - Sucralose was administered by gavage to pregnant rats (days 6 to 15 of gestation) at dose levels of 500, 1,000 and 2,000 mg/kg/day. In this study, no adverse effects were observed on fetuses. No teratogenicity was noted and therefore the NOAEL was estimated to be over 2,000 mg/kg. In another teratogenicity study in rabbits, sucralose was administered to pregnant animals (days 6 to 19 of gestation) at dose levels of 175, 350 and 700 mg/kg/day. At the highest level of 700 mg/kg, the parent animals showed decreased body weights accompanied with gastrointestinal disturbance (diarrhea), and deaths

and abortions were observed. However, it was considered that this effect was related to a high sensitivity of rabbits to poorly-absorbable, osmotically-active substances. Sucralose at the dose level of 700 mg/kg did not affect the growth and development of fetuses. In this study, sucralose did not exert any teratogenic effects, and the NOAEL was estimated to be over 700 mg/kg.

(6) Antigenicity Study - In a study using guinea pigs, animals were first intradermally treated with Freund's Complete Adjuvant (FCA), 30% sucralose aqueous solution or 10% sucralose FCA emulsion as the first sensitization treatment, and 7 days later 50% sucralose solution was applied topically as the second sensitization treatment. No delayed contact hypersensitivity was found.

(7) Mutagenicity Study - In a reverse mutation test in *Salmonella typhimurium*, sucralose did not show any mutagenicity at levels of 16, 80, 400, 2,000 and 10,000 µg/plate. In a DNA repair test with *Escherichia coli*, no genotoxic effects were observed at doses of 0.5, 1, 10, 100, 500, and 1000 µg/plate under the test conditions. In a *in vitro* chromosome aberration test with human peripheral lymphocytes, no significant effects were found at levels of 8, 40 or 200 µg/ml. On the other hand, in an *in vitro* mutagenesis assay using mouse lymphoma cells, with sucralose at levels of 1,335, 1,780, 2,373, 3,164, 4,219, 5,625, 7,500 and 10,000 µg/ml, weak mutagenicity was demonstrated at the two highest doses. In a mouse bone marrow micronucleus assay, mice were given a single oral dose of sucralose at 1,000 and 5,000 mg/kg. There was no evidence of induced chromosomal damage leading to micronucleus formation. In addition, in a rat bone marrow cytogenetic assay, when rats were orally treated with sucralose at doses of 500, 1,000 and 2,000 mg/kg for five days, no chromosome aberrations were induced.

Thus, the positive result from the *in vitro* mutagenesis assay using mouse lymphoma cells was judged to be of no toxicological significance, since this adverse effect appeared only at very high concentrations, and all other mutagenesis bioassays gave negative results.

(8) General Pharmacological Studies - There were no adverse clinical signs or altered behavior exhibited by rats and mice in any of the relevant oral studies. Furthermore, no potential of sucralose to cause toxic effects to the central nervous system of mice, monkeys and humans was evident on neurological and/or histopathological examination. In addition, in clinical studies in human, sucralose did not affect the respiration rate, pulse, blood pressure, or electrocardiogram findings, and did not influence the respiratory or cardiovascular systems. In the gastrointestinal system, repeated administration of sucralose to rats caused increase in caecum weight. However, it was considered that the toxicological significance of this change was negligible, since no histopathological alterations were found. With regard to effects of sucralose on water and electrolyte metabolism, increase in water intake was noted, but no significant effects on electrolyte constituents or urine volume were observed.

(9) Other Toxicity Studies

The results from the studies, listed in attachment 1, were submitted.

No major adverse effects and signs were observed.

**7. Absorption, Distribution, Metabolism and Elimination**

(1) Absorption and Elimination - When sucralose was orally administered to mice, rats, dogs and humans, the results for absorption, elimination and kinetics were similar between animal species. Approximately 60 to 90% of the sucralose was excreted in the feces, while the remaining 10 to 30% was excreted in the urine. None was detected in the expired air. Maximal plasma levels in these species were observed 30 minutes to 3 hours after the administration. For example, when sucralose was orally administered to rats at a dose of 2,000 mg/kg, the plasma concentration reached the highest level of 10 to 15 µg/ml within an hour. The 'half-life' of sucralose in human was determined to 2.5 to 23 hours.

(2) Distribution - In studies of oral administration of radiolabeled sucralose to the rat, maximal levels were observed in the liver, kidney, and gastrointestinal tract, but those levels declined to under the plasma level within 24 hours. There was no indication of active transport across the blood brain barrier, judging from levels in the brain.

(3) Metabolism - In rats, dogs and humans, most of the excreted material in urine and feces following oral administration was unchanged sucralose, with a small amount of the glucuronic acid conjugate identified in the urine of dogs and humans.

(4) Others - In a human study, sucralose did not affect the absorption of sucrose, and did not increase the secretion of insulin.

**8. Determination of acceptable daily intake(ADI)**

Based on a accompanying documents, we evaluated as follows.

No-observed-adverse-effect-level (NOAEL) 1,500mg/kg bw/day

Animal species rat

Dose levels 3%(30,000ppm) into the diet

Duration of administration 104 weeks

Test species Combined toxicity / carcinogenicity study

Safety factor 100

In the rabbit teratogenicity study, some adverse effects were recognized in the parent animals at a dose level of 700 mg/kg. Rabbits are sensitive to substances with low absorbability and positive osmotic pressure activity, and are subject to diarrhea. Teratogenicity was not observed in fetal at a dose level 700mg/kg. Therefore, though the NOAEL of parent animal is estimated at 350mg/kg in this study, it is inappropriate to use the NOAEL as a basis for establishing the

ADI of sucralose.

As mentioned above, as sucralose  
ADI 15mg/kg bw/day

### 9. Estimation of daily intake

Sucralose is expected to be used in various foods as a sweetener. Based on food intakes according to food group obtained from the 1993 National Nutrition Survey, the daily intake of sweeteners is estimated at 35.0 g, converted into sucrose. Sucralose is 600 times sweeter than sucrose. Therefore, the estimated daily intake of sucralose is 58.3 g, when calculated by converting sucrose into sucralose. The estimated daily intake for the Japanese is 1.17 mg/kg, assuming that the Japanese average body weight is 50 kg.

### 10. Standards for use of sucralose

Additives	Major use	Standards for use		
		Foods	Maximum Limit of use	Limitation of use
Sucralose	Sweetener	Confectionery	1.8g/kg	The limits are not apply for foods approved for "special dietary use" labeling.
		Chewing gum	2.6g/kg	
		Jam	1.0g/kg	
		Nonalcoholic beverages "Sake"(rice wine) Wine Miscellaneous alcoholic beverages Milk drinks Lactic acid bacteria drinks	0.40g/kg (This limitation is applied to a diluted product in case of a concentrated product.)	
		Substitute for Sugar	12g/kg	
		Other foods	0.58g/kg	

### 11. Specifications

Specifications for components of sucralose should be established as given in Attachment 2. For information, Attachment 3 gives a table which compares the Japanese proposed specifications with those by JECFA and the Food Chemicals Codex (FCC).

The study results and other information mentioned here were given in the accompanying documents listed in Attachment 1.

## Attachment 1

### Contents of document

Contents	Reference	Document No	Vol.
1 Summary	San-Ei Gen F.F.I., Inc.	1	1

### 2 Chronology on origin or development and overseas use condition

2-1 Details of origin or development	San-Ei Gen F.F.I., Inc.	2-1	2
2-2 Overseas use condition	San-Ei Gen F.F.I., Inc.	2-2	2

### 3 Physicochemical characteristics and specifications

3-1 Name	San-Ei Gen F.F.I., Inc.	3-1	2
3-2 Structural formula or rational formula	San-Ei Gen F.F.I., Inc.	3-2	2
3-3 Molecular formula and molecular weight	San-Ei Gen F.F.I., Inc.	3-3	2
3-4 Assay	San-Ei Gen F.F.I., Inc.	3-4	2
3-5 Methods of manufacturing	San-Ei Gen F.F.I., Inc.	3-5	2
3-6 Description	San-Ei Gen F.F.I., Inc.	3-6	2
3-7 Identification	San-Ei Gen F.F.I., Inc.	3-7	2
3-8 Specific properties	San-Ei Gen F.F.I., Inc.	3-8	2
3-9 Purity tests	San-Ei Gen F.F.I., Inc.	3-9	2
3-10 Water	San-Ei Gen F.F.I., Inc.	3-10	2
3-11 Residues on ignition	San-Ei Gen F.F.I., Inc.	3-11	2
3-12 Method of assay	San-Ei Gen F.F.I., Inc.	3-12	2
3-13 Stability	Tate & Lyle Speciality Sweeteners	3-13	2
3-14 Analytical method for the food additives in food	Tate & Lyle Speciality Sweeteners and San-Ei Gen F.F.I., Inc.	3-14	2
3-15 Specification	San-Ei Gen F.F.I., Inc.	3-15	2
3-16 Overall judgement table	San-Ei Gen F.F.I., Inc.	3-16	2

### 4 Effectiveness

4-1 Effectiveness	Tate & Lyle Speciality	4-1	3
-------------------	------------------------	-----	---

	Sweeteners		
4-2 Comparison in the effects with other similar food additives	Tate & Lyle Speciality Sweeteners and San-Ei Gen F.F.I., Inc.	4-2	4
4-3 Stability in foods	Tate & Lyle Speciality Sweeteners and San-Ei Gen F.F.I., Inc.	4-3	4

## 5 Safety evaluation

### (1) Toxicity studies

5-1 Investigation of report on the safety of sucralose	San-Ei Gen F.F.I., Inc.	5-1	5
--	-------------------------	-----	---

### 5-2 Safety evaluation for sucralose

#### 5-2-1 Acute toxicity study

5-2-1-1 Acute oral toxicity studies in the rat.	Johnson & Johnson Research Foundation (1980)	5-2-1-1 (E002)	6
5-2-1-2 Acute oral toxicity to mice.	Life Science Research (1977)	5-2-1-2 (E001)	6

#### 5-2-2 Subacute toxicity study

5-2-2-1 8-week toxicity study in rat .	Life Science Research (1983)	5-2-2-1 (E031)	6
5-2-2-2 Dose range finding study in rat during lactation.	Johnson & Johnson Research Foundation (1984)	5-2-2-2 (E060)	6
5-2-2-3 9-weeks toxicity study in rat.	Hazleton Lab. America (1985)	5-2-2-3 (E098)	6
5-2-2-4 4, 9 and 13-week toxicity study in rat.	Inveresk Res. International (1988)	5-2-2-4 (E151)	6
5-2-2-5 Dose range finding study in mice (34 days).	Johnson & Johnson Research Foundation (1983)	5-2-2-5 (E062)	6

#### 5-2-3 Chronic toxicity study

5-2-3-1 Dietary administration study in rat (1)	Pharmaco-LSR (1993)	5-2-3-1 (E160)	6
5-2-3-2 Dietary administration study in	Pharmaco-LSR	5-2-3-2	6

rat (2)	(1994)	(E161)	
5-2-3-3 Oral toxicity study in dogs (12 months)	Hazleton Lab. America (1985)	5-2-3-3 (E051)	6

#### 5-2-4 Reproduction study

5-2-4-1 Anti-fertility screen in male rats.	Life Science Research (1978)	5-2-4-1 (E016)	7
5-2-4-2 The effect of sucralose on the glycolytic ability of rat spermatozoa.	University Whiteknights (1987)	5-2-4-2 (E107)	7
5-2-4-3 Two generation reproductive study in rats.	Life Science Research (1986)	5-2-4-3 (E056)	7
5-2-4-4 104-Week combined toxicity and oncogenicity study in rats. ; Breeding phase.	Life Science Research (1987)	5-2-4-4 (E057)	7

#### 5-2-5 Teratogenicity study

5-2-5-1 Effects of oral administration upon pregnancy in the rat.	Life Science Research (1983)	5-2-5-1 (E030)	7
5-2-5-2 Preliminary study in the pregnant rabbit.	Life Science Research (1987)	5-2-5-2 (E115)	7
5-2-5-3 Preliminary teratology study in the rabbit.	Life Science Research (1987)	5-2-5-3 (E129)	7
5-2-5-4 Teratology study in the rabbit.	Life Science Research (1987)	5-2-5-4 (E134)	7

#### 5-2-6 Carcinogenicity study

5-2-6-1 104-Week oncogenicity study in mice.	Life Science Research (1987)	5-2-6-1 (E055)	8
--	------------------------------	----------------	---

#### 5-2-7 Combined chronicl toxicity/carcinogenicity study

5-2-7-1 104-Week combined toxicity and oncogenicity study in rats.	Life Science Research (1986)	5-2-7-1 (E057)	9,10
--	------------------------------	----------------	------

#### 5-2-8 Antigenicity study

5-2-8-1 Delayed contact hypersensitivity study in guinea-pigs.	Life Science Research (1986)	5-2-8-1 (E113)	11
--	------------------------------	----------------	----

#### 5-2-9 Mutagenicity study

5-2-9-1 Reverse mutation test with <i>Salmonella typhimurium</i> . (1)	Life Science Research (1981)	5-2-9-1 (E015)	11
5-2-9-2 Reverse mutation test with <i>Salmonella typhimurium</i> . (2)	Litton Bionetics Inc. (1979)	5-2-9-2 (E011)	11
5-2-9-3 Gene mutation test in mouse lymphoma cells.	E & G Mason Research Institute (1981)	5-2-9-3 (E014)	11
5-2-9-4 Micronucleus test in mouse bone marrow erythrocytes. (1)	Life Science Research (1978)	5-2-9-4 (E010)	11
5-2-9-5 Micronucleus test in mouse bone marrow erythrocytes. (2)	Life Science Research (1986)	5-2-9-5 (E114)	11
5-2-9-6 Chromosome aberration test in the rat bone marrow.	Litton Bionetics Inc. (1981)	5-2-9-6 (E013)	11
5-2-9-7 Chromosome aberration test in cultured human peripheral lymphocytes.	Life Science Research (1981)	5-2-9-7 (E012)	11
5-2-9-8 DNA repair test in <i>Escherichia coli</i> .	Litton Bionetics Inc. (1979)	5-2-9-8 (E011)	11

#### 5-2-10 General pharmacological study

##### 5-2-10-1 Effects on general conditions

5-2-10-1-1 Acute oral toxicity studies in the rat.	Johnson & Johnson Research Foundation (1980)	5-2-10-1-1 (E002)	12
5-2-10-1-2 Acute oral toxicity to mice.	Life Science Research (1977)	5-2-10-1-2 (E001)	12
5-2-10-1-3 Neurotoxicity study in mice.	Life Science Research (1981)	5-2-10-1-3 (E008)	12
5-2-10-1-4 4, 9 and 13-week toxicity study in rat.	Inveresk Res. International (1988)	5-2-10-1-4 (E151)	12
5-2-10-1-5 Dietary administration study in rat (2) (26-week)	Pharmaco-LSR (1994)	5-2-10-1-5 (E161)	12
5-2-10-1-6 A study to observe the tolerance to orally administered single ascending doses of TGS followed by seven days administration in eight normal subjects.	Medical Science Research (1984)	5-2-10-1-6 (E047)	12
5-2-10-1-7 A tolerance study in normal subjects of varying doses of TGS administered continuously for a period	Medical Science Research (1986)	5-2-10-1-7 (E048)	12

of thirteen weeks.			
--------------------	--	--	--

#### 5-2-10-2 Effects on the central nervous system

5-2-10-2-1 Neurotoxicity study in mice.	Life Science Research (1981)	5-2-10-2-1 (E008)	12
5-2-10-2-2 Neurotoxicity study in marmoset monkeys.	Life Science Research (1981)	5-2-10-2-2 (E009)	12
5-2-10-2-3 A study to observe the tolerance to orally administered single ascending doses of TGS followed by seven days administration in eight normal subjects.	Medical Science Research (1984)	5-2-10-2-3 (E047)	12

#### 5-2-10-3 Effects on the respiratory and cardiovascular systems

5-2-10-3-1 A study to observe the tolerance to orally administered single ascending doses of TGS followed by seven days administration in eight normal subjects.	Medical Science Research (1984)	5-2-10-3-1 (E047)	12
5-2-10-3-2 A tolerance study in normal subjects of varying doses of TGS administered continuously for a period of thirteen weeks.	Medical Science Research (1986)	5-2-10-3-2 (E048)	12

#### 5-2-10-4 Effects on the gastrointestinal system

5-2-10-4-1 9-week toxicity study in rat.	Hazleton Lab. America (1985)	5-2-10-4-1 (E098)	12
5-2-10-4-2 4, 9 and 13-week toxicity study in rat.	Inveresk Res. International (1988)	5-2-10-4-2 (E151)	12
5-2-10-4-3 Dietary administration study in rat (2) (26-week)	Pharmaco-LSR (1994)	5-2-10-4-3 (E161)	12

#### 5-2-10-5 Effects on water and electrolyte metabolism

5-2-10-5-1 8-week toxicity study in rat.	Life Science Research (1983)	5-2-10-5-1 (E031)	13
5-2-10-5-2 9-week toxicity study in rat.	Hazleton Lab. America (1985)	5-2-10-5-2 (E098)	13
5-2-10-5-3 104-Week combined toxicity and oncogenicity study in rats.	Life Science Research (1986)	5-2-10-5-3 (E057)	13

### 5-2-11 Other toxicity study

5-2-11-1 Neurotoxicity study in mice.	Life Science Research (1981)	5-2-11-1 (E008)	14
5-2-11-2 Neurotoxicity study in marmoset monkeys.	Life Science Research (1981)	5-2-11-2 (E009)	14
5-2-11-3 Immunotoxicity study in rats.	TNO Nutrition and Food Research (1994)	5-2-11-3 (E162)	14
5-2-11-4 Eight-week palatability study in female rats.	Life Science Research (1985)	5-2-11-4 (E058)	14
5-2-11-5 14-week palatability study in rats.	Life Science Research (1988)	5-2-11-5 (E143)	14
5-2-11-6 An investigation of the acceptability of aqueous solutions of sucralose to rats.	Life Science Research (1987)	5-2-11-6 (E130)	14
5-2-11-7 An investigation of diet spillage among rats fed diet containing sucralose.	Life Science Research (1991)	5-2-11-7 (E154)	14
5-2-11-8 14-day palatability study in beagle dogs.	Life Science Research (1980)	5-2-11-8 (E007)	14

### 5-2-13 Clinical study

5-2-13-1 Glycemic effect of a single high oral dose of the novel sweetener sucralose in patients with diabetes.	Mezitis, N.M.E. <i>et al.</i> Diabetes Care, 19, 1004-1005, (1996)	5-2-13-1	22
5-2-13-2 A six-month study of the effect of sucralose vs placebo on glucose homeostasis in patients with non-insulin-dependent diabetes mellitus.	Mount Sinai Hospital (1997)	5-2-13-2 (E157)	22
5-2-13-3 An evaluation of specific clinical chemistry parameters and methods in Study E157 : A six-month study of the effect of sucralose vs placebo on glucose homeostasis in patients with non-insulin-dependent diabetes mellitus.	University of Missouri- Columbia (1996)	5-2-13-3 (E168)	22
5-2-13-4 A 12 week study of the effect of sucralose on glucose homeostasis and HbA1c in normal healthy volunteers.	Leicester Clinical Research Center Ltd. (1996)	5-2-13-4 (E169)	22
5-2-13-5 A three-month study of the effect of	University of California	5-2-13-5	22

sucralose versus placebo on glucose homeostasis in subjects with non-insulin-dependent diabetes mellitus.	San Diego, <i>et al.</i> (1997)	(E171)	
---	------------------------------------	--------	--

### 5-3 Safety evaluation for the hydrolysis products of sucralose and compounds related to sucralose

#### 5-3-1 Acute toxicity study

5-3-1-1 TGS-HP : Acute oral toxicity in the rat. (1)	Life Science Research (1982)	5-3-1-1 (E028)	18
5-3-1-2 TGS-HP : Acute oral toxicity in the rat. (2)	Johnson & Johnson Research Foundation (1980)	5-3-1-2 (E002)	18
5-3-1-3 TGS-HP : Acute oral toxicity in the mouse.	Life Science Research (1982)	5-3-1-3 (E029)	18
5-3-1-4 3/C334(6-CDG) : Acute oral toxicity in the rat.	Life science Research (1977)	5-3-1-4 (E050)	18
5-3-1-5 TCDS : Acute oral toxicity in the mouse.	Life science Research (1976)	5-3-1-5 (E069)	18

#### 5-3-2 Subacute toxicity study

5-3-2-1 TGS-HP : 13-week toxicity study in rats.	Life Science Research (1986)	5-3-2-1 (E054)	18
5-3-2-2 TGS-HP : Dose range finding/toxicity study in the dog.	Johnson & Johnson Research Foundation (1984)	5-3-2-2 (E061)	18

#### 5-3-3 Chronic toxicity study

5-3-3-1 TGS-HP : Twenty-six week oral toxicity study in dogs.	Litton Bionetics Inc. (1985)	5-3-3-1 (E068)	18
---	---------------------------------	-------------------	----

#### 5-3-4 Reproduction study

5-3-4-1 TGS-HP : Two generation reproductive study in rats.	Life Science Research (1986)	5-3-4-1 (E052)	18
5-3-4-2 1,6-DCF : Effect on male fertility in the rat.	Ortho Pharmaceutical Co. (1982)	5-3-4-2 (E090)	18
5-3-4-3 3/C-339, 3/C-340 : Anti-fertility screen in male rats.	Life science Research (1978)	5-3-4-3 (E016)	18
5-3-4-4 3/C-343~346, 3/C-348 : Anti-fertility screen in male rats.	Life science Research (1978)	5-3-4-4 (E038)	18

5-3-4-5 6-CF : Anti-fertility evaluation in the male rat.	Life science Research (1984)	5-3-4-5 (E037)	18
5-3-4-6 4,6'-DGS : Anti-fertility evaluation in the male rat.	Life science Research (1986)	5-3-4-6 (E100)	18
5-3-4-7 TCDS : The effect on the glycolytic ability of rat spermatozoa.	The University Whiteknights (1987)	5-3-4-7 (E107)	18
5-3-4-8 6-CDG, 6-CDM : The effects on male fertility and motor function in several species.	Ortho Pharmaceutical Co. (1981)	5-3-4-8 (E091)	18

#### 5-3-5 Teratogenicity study

5-3-5-1 TGS-HP : Effects of oral administration upon pregnancy in the rat.	Life Science Research (1983)	5-3-5-1 (E032)	18
--	------------------------------	----------------	----

#### 5-3-6 Carcinogenicity study

5-3-6-1 TGS-HP : 104-week oncogenicity study in rats.	Life Science Research (1987)	5-3-6-1 (E053)	19
---	------------------------------	----------------	----

#### 5-3-7 Antigenicity study

5-3-7-1 1,6-DCF : Primary skin irritation study.	Toxicol Laboratories Ltd. (1984)	5-3-7-1 (E080)	19
--	----------------------------------	----------------	----

#### 5-3-8 Mutagenicity study

5-3-8-1 TGS-HP : Reverse mutation test with <i>Salmonella typhimurium</i> .	Life Science Research (1981)	5-3-8-1 (E015)	20
5-3-8-2 TGS-HP : Dominant lethal test in mice.	Life Science Research (1983)	5-3-8-2 (E034)	20
5-3-8-3 1,6-DCF : Reverse mutation test with <i>Salmonella typhimurium</i> . (1)	Life Science Research (1980)	5-3-8-3 (E020)	20
5-3-8-4 1,6-DCF : Reverse mutation test with <i>Salmonella typhimurium</i> . (2)	EG & G Mason Research Institute (1981)	5-3-8-4 (E023)	20
5-3-8-5 1,6-DCF : Gene mutation test in mouse lymphoma cells. (1)	EG & G Mason Research Institute (1981)	5-3-8-5 (E022)	20
5-3-8-6 : Gene mutation test in mouse lymphoma cells. (2)	EG & G Mason Research Institute (1981)	5-3-8-6 (E024)	20

5-3-8-7 1,6-DCF : Assessment of its mutagenic potential in <i>Drosophila melanogaster</i> , using the sex-linked recessive lethal test.	Life Science Research (1981)	5-3-8-7 (E021)	20
5-3-8-8 1,6-DCF : Single exposure dose selection study for <i>in vivo</i> micronucleus assay in the mouse.	Hazleton Lab. America (1988)	5-3-8-8 (E152)	20
5-3-8-9 1,6-DCF : <i>In vivo</i> micronucleus assay in the mouse.	Hazleton Lab. America (1988)	5-3-8-9 (E149)	20
5-3-8-10 1,6-DCF : Investigation of effects on bone marrow chromosomes of the rat after acute and subacute oral administration.	Life Science Research (1981)	5-3-8-10 (E019)	20
5-3-8-11 1,6-DCF : <i>In vitro</i> assessment of the clastogenic action on mouse bone marrow erythrocytes in the micronucleus test.	Life Science Research (1981)	5-3-8-11 (E012)	20
5-3-8-12 1,6-DCF : <i>In vivo</i> sister chromatid exchange assay in the mouse.	Hazleton Lab. America (1988)	5-3-8-12 (E150)	20
5-3-8-13 1,6-DCF : Study to evaluate the potential of 1,6-dichlorofructose to induce unscheduled DNA synthesis (UDS) in isolated rat hepatocytes <i>in vitro</i> .	Hazleton Europe (1994)	5-3-8-13 (E165)	20
5-3-8-14 4-CG : Reverse mutation test with <i>Salmonella typhimurium</i> .	Life Science Research (1980)	5-3-8-14 (E025)	20
5-3-8-15 4-CG : Gene mutation test in mouse lymphoma cells.	EG & G Mason Research Institute (1981)	5-3-8-15 (E026)	20
5-3-8-16 4-CG : Mutagenicity evaluation in the rat bone marrow cytogenetic assay.	Litton Bionetics, Inc. (1981)	5-3-8-16 (E027)	20
5-3-8-17 4-CG : <i>In vitro</i> assessment of the clastogenic action on mouse bone marrow erythrocytes in the micronucleus test.	Life Science Research (1981)	5-3-8-17 (E012)	20
5-3-8-18 C/334(6-CDG) : The micronucleus test in mouse bone marrow erythrocytes..	Life Science Research (1978)	5-3-8-18 (E010)	20
5-3-8-19 C/337 : The micronucleus test in mouse bone marrow erythrocytes..	Life Science Research (1978)	5-3-8-19 (E010)	20
5-3-8-20 3/C340(1-CF) : Reverse mutation test with <i>Salmonella typhimurium</i> .	Life Science Research (1981)	5-3-8-20 (E074)	20

5-3-8-21 C/339 : The micronucleus test in mouse bone marrow erythrocytes.	Life Science Research (1978)	5-3-8-21 (E072)	20
5-3-8-22 C/338 : The micronucleus test in mouse bone marrow erythrocytes.	Life Science Research (1978)	5-3-8-22 (E072)	20
5-3-9 Other toxicity study			
5-3-9-1 TGS-HP : Neurotoxicity study in mice.	Life Science Research (1981)	5-3-9-1 (E008)	20
5-3-9-2 TGS-HP : Neurotoxicity study in marmoset monkeys.	Life Science Research (1981)	5-3-9-2 (E009)	20
5-3-9-3 TGS-HP : Palatability study in dogs.	Litton Bionetics Inc. (1984)	5-3-9-3 (E065)	20

(2) Metabolism and pharmacokinetic studies

5-2-12 Metabolism and pharmacokinetic studies (Sucralose)

5-2-12-1 Absorption, tissue distribution and excretion in the rat.	Life Science Research (1981)	5-2-12-1 (E004)	15
5-2-12-2 Dietary toxicity study in rat (8 weeks).-A study on the metabolism	Life Science Research (1981)	5-2-12-2 (E031)	15
5-2-12-3 104-Week combined toxicity and oncogenicity study in rats. -Mesurement of metabolic adaptation.	Life Science Research (1981)	5-2-12-3 (E057)	15
5-2-12-4 A study on the metabolism of sucralose after oral and intravenous administration to the rat.	University of Southampton (1987)	5-2-12-4 (E137)	15
5-2-12-5 Comparative pharmacokinetics after dietary and oral gavage administration to rats.	Huntingdon Research Centre Ltd. (1994)	5-2-12-5 (E163)	15
5-2-12-6 Pharmacokinetic studies after oral administration to pregnant rabbits and rats.	Huntingdon Research Centre Ltd. (1994)	5-2-12-6 (E164)	15
5-2-12-7 Studies of the absorption, excretion and metabolism in the mouse.	Huntingdon Research Centre Ltd. (1987)	5-2-12-7 (E146)	15
5-2-12-8 Pharmacokinetics in dogs following intravenous administration.	Life Science Research (1984)	5-2-12-8 (E049)	15
5-2-12-9 Intravenous-oral cross over dog metabolism study.	Huntingdon Research Centre Ltd. (1986)	5-2-12-9 (E123)	16
5-2-12-10 Isolation and identification of an	Huntingdon Research	5-2-12-10	16

unknown radioactive component present in urine after intravenous administration of sucralose.	Centre Ltd. (1987)	(E133)	
5-2-12-11 Studies of the metabolism in the rabbit.	Huntingdon Research Centre Ltd. (1987)	5-2-12-11 (E124)	16
5-2-12-12 Preliminary teratology study in the rabbit.	Life Science Research (1987)	5-2-12-12 (E129)	16
5-2-12-13 Urinary excretion in human after a single oral dose.	Tate & Lyle (1981)	5-2-12-13 (E003)	16
5-2-12-14 Absorption and excretion in human.	Life Science Research (1983)	5-2-12-14 (E033)	16
5-2-12-15 The examination of the radioactive material in the stored urine taken from three human volunteers given an oral dose of [14C]TGS.	Tate & Lyle (1986)	5-2-12-15 (E033a)	17
5-2-12-16 A randomized double-blind study in normal subjects to investigate the influence of TGS on the absorption of sucrose and the secretion of insulin.	Medical Science Research UK (1984)	5-2-12-16 (E046)	17
5-2-12-17 A study to observe the tolerance to orally administered single ascending doses of TGS followed by seven days administration in eight normal subjects.	Medical Science Research UK (1984)	5-2-12-17 (E047)	17
5-2-12-18 A tolerance study in normal subjects of varying doses of TGS administered continuously for a period of thirteen weeks.	Medical Science Research UK (1986)	5-2-12-18 (E048)	17
5-2-12-19 A study of the metabolism and pharmacokinetics following oral administration to healthy human volunteers.	Univ. Southampton (1986)	5-2-12-19 (E128)	17
5-2-12-20 A study of the metabolism of 14C-TGS following oral administration to healthy human volunteers.	Univ. Southampton (1988)	5-2-12-20 (E145)	17
5-2-12-21 Stability of chlorinated disaccharides to hydrolysis by microbial, plant and mammalian glycosidases.	Tate & Lyle Group Research & Development (1986)	5-2-12-21 (E104)	17
5-2-12-22 The effect of oral administration	University of Reading	5-2-12-22	17

on some aspects of the metabolism of D-glucose by tissues of the rat.	(1978)	(E005)	
5-2-12-23 The influence of sucralose on carbohydrate metabolism in the rat.	Med. Sch. St. George's Hospital, London	5-2-12-23 (E064)	17
5-2-12-24 Enzyme induction studies of TGS in the rat.	Huntingdon Research Centre Ltd. (1988)	5-2-12-24 (E144)	17

5-3-10 Metabolism and pharmacokinetic studies (the hydrolysis products of sucralose and compounds related to sucralose)

5-3-10-1 Enzyme induction studies of TGS-HP in the rat.	Huntingdon Research Centre Ltd. (1988)	5-3-10-1 (E144)	21
5-3-10-2 1,6-DCF : Distribution in blood, brain, testes and urine at intervals after oral dosing of male rats.	Life Science Research (1981)	5-3-10-2 (E017)	21
5-3-10-3 1,6-DCF : Metabolism and dechlorination in the rat.	University College, UK (1987)	5-3-10-3 (E116)	21
5-3-10-4 4-CG and 1,6-DCF : Metabolic disposition in the rat.	Life Science Research (1980)	5-3-10-4 (E018)	21
5-3-10-5 1,6-DCF : Metabolism in the rat.	University College, UK (1988)	5-3-10-5 (E147)	21
5-3-10-6 The cellular effects of 1,6-DCF : Preliminary studies.	Univ. Med. And Rent. New Jersey (1985)	5-3-10-6 (E085)	21
5-3-10-7 4-CG : Metabolism in the rat.	University College, UK (1987)	5-3-10-7 (E139)	21
5-3-10-8 In vitro studies on the hepatic metabolism of some chlorodeoxysugars.	University of Surrey (1980)	5-3-10-8 (E136)	21

(3) The daily intake of the food additive

5-4 The daily intake of sucralose.	San-Ei Gen F.F.I., Inc.	5-4	21
------------------------------------	-------------------------	-----	----

6 Standards for use

6-1 Documentation on the target foods and use.	San-Ei Gen F.F.I., Inc.	6-1	21
6-2 Documentation on the amount of use.	San-Ei Gen F.F.I., Inc.	6-2	21

## Attachment 2

### Specification for sucralose

	Specification
<b>Name</b>	Sucralose
<b>Chemical name</b>	Trichlorogalactosucrose (4,1',6'-trichlorogalactosucrose)
<b>Chemical structure</b>	<p>The chemical structure shows two pyranose rings connected by an oxygen bridge. The left ring is galactose in its pyranose form, with a chlorine atom at C2 and a hydroxyl group at C3. The right ring is sucrose in its pyranose form, with chlorine atoms at C1', C4', and C6'. The two rings are linked at C4 of the galactose ring and C1' of the sucrose ring.</p>
<b>Chemical formula</b>	$C_{12}H_{19}Cl_3O_8$
<b>Molecular weight</b>	397.64
<b>CAS No.</b>	56038-13-2
<b>Contents</b>	Sucralose, when dried, contains 98.0-102.0% of sucralose ( $C_{12}H_{19}Cl_3O_8$ )
<b>Description</b>	Sucralose occurs as a white to grayish-white crystalline powder. It is odorless*, has a strong sweet taste and is freely soluble in water, methanol and ethanol, and is slightly soluble in ethyl acetate.
<b>Identification</b>	<p>(1) The infrared absorption spectrum of a potassium bromide dispersion sample has a similar absorption bands to the standard spectrum of sucralose with a similar intensity at similar wavelength.</p> <p>(2) Dissolve 1.0g of sucralose in 10ml of methanol, apply 5l of this solution for thin-layer chromatography to the bottom of the chromatographic plate. Place the plate in mobile phase which contains mixture of sodium chloride (dissolve 1g in a solvesnt to make 20m) and acetonitrile (7:3), and allow the solvent front to ascend approximately 15cm. Remove the plate, allow it to dry,</p>

	and spray it with the solution which contains 15%(v/v) sulfuric acid in methanol. Heat the plate in an oven at 125°C for 10 min. Chromatographic plate coated with octadecyl silyl silica gel can be used in this methods. The R <sub>f</sub> value as a spot of sucralose is 0.4-0.6 under the conditions described above.
<b>Purity</b> (1) Clarity and color of solution	Clear (1.0g, in 10ml water)
(2) Specific rotation	$[\alpha]_D^{20} = +84.0 \sim +87.5$ (1.0g, in 10 ml water, calculated on the anhydrous basis)
(3) pH	pH= 3.0~6.0 (2.0g, in 20 ml water)
(4) Heavy metals	Not more than 10 µg/g (1.0g, method 2, 1.0ml lead standard solution as control solution)
(5) Arsenic	Not more than 4.0 µg/g as As <sub>2</sub> O <sub>3</sub> . (0.50g, method 2, apparatus B)
(6) Other chlorinated disaccharide	Not more than 0.5% Dissolve 1.0 g of sucralose in 10 ml of methanol (sample solution). Take 0.5ml of this sample solution and add methanol to make 100ml (standard solution). Apply 5l of sample or control solution to the bottom of the chromatographic plate for thin-layer chromatography as described on Identification(2). The spot of sample solution is only detected on same position to that of standard solution. If other spot in sample solution is detected, the detected spot in sample solution is not more intense in color than that in standard solution.
(7) Chlorinated monosaccharide	Not more than 0.16% as calculated on fructose. Dissolve 2.5 g of sucralose and add methanol to make 10ml exactly (sample solution). Take exactly 10.0g of D-mannitol and add water to make 100ml, exactly (standard [A] solution). Take exactly both 10.0g of D-mannitol and 40mg of fructose and add water to make 100ml, exactly (standard [B] solution). Apply 1l of sample, standard [A] or [B] solution to silicagel thin-layer plate of 0.25mm in thickness for thin-layer chromatography and dry. Repeat another 4 times this process. Spray the plate with the solution which contains <i>p</i> -anisidine phtalate. Heat the plate in an over at 98-102°C for 10min. The spot in sample solution is not more intense in color than that in standard [B] solution. The spot in standard [A] solution results from a overheating of the plate, and the test should be repeated again in use of another

	plate.
(8) Triphenylphosphine oxide	<p>Not more than 150µg/g</p> <p>Dissolve 100 mg of sucralose or triphenylphosphine oxide in mixture of acetonitrile and water (67:33) and make exact 10 ml solution, separately. Take exactly 1ml of triphenylphosphine oxide solution and add mixture of acetonitrile and water (67:33) to make 100 ml solution, exactly (standard solution). Take 25µl of sample solution or standard solution for liquid chromatography under the condition described below.</p> <p>System          Detector : UV-detector ( 220 nm)          Column packing material : 5 µm octadecyl silyl silica gel          Column : A stainless steel tube of 4.6 mm (internal diameter) τ15 cm (length)          Column temperature : 40πC          Mobile phase : a mixture of acetonitrile and water (67 : 33)          Flow rate : 1.5 ml/min.</p> <p>Record the mean peak areas for the standard and test solution as <math>A_s</math> and <math>A_t</math>, respectively. Calculate the concentration of triphenylphosphine oxide in the sample from the following formula.</p> $\text{triphenylphosphine oxide (C}_{18}\text{H}_{15}\text{OP)}(\mu\text{g/g}) = \frac{A_t}{A_s} \times \frac{10,000}{\text{Weight of sample(mg)}}$
(9) Methanol	<p>Not more than 0.1%</p> <p>Dissolve exactly 2.0 g of sucralose, add water to make 10 ml exactly and mix (sample solution). Take exactly 2 ml of methanol, add water to make 100 ml exactly and mix. Take exactly 1ml of this solution, add water to make 100 ml exactly and mix (standard solution). Take 1µl of sample solution or standard solution for liquid chromatography under the condition described below.</p> <p>System          Detector : Hydrogen flame ionization detector          Column packing material : 150~180 µm of porous polymer beads for gas chromatography          Column : glass column of 2~4 mm (internal diameter) τ about 2 m (length)          Column temperature : constant temperature at about 150πC</p>

	<p>Inlet temperature : 200°C          Detector temperature : 250°C          Carrier gas and flow rate : Use nitrogen or helium. Adjust flow rate or temperature to detect a peak of methanol in about 4 min.</p> <p>Record the mean peak areas for the standard and test solution as <math>S_A</math> and <math>A_s</math>, respectively. Calculate the concentration of methanol in the sample from the following formula.</p> $\text{Methanol}(\%) = \frac{S_A \times C_s \times \text{weight of reference standard (ml)}}{A_s \times \text{weight of sample (g)}}$ <p>where <math>C_s</math> is the concentration of methanol in the standard in percent.</p>
<b>Residue in Ignition</b>	Not more than 0.7%.
<b>Water</b>	Not more than 2.0% (1g, Direct titration)
<b>Method of assay</b>	<p>Dissolve 1g of sucralose add water to make 100ml, exactly. Take exactly 10ml of this solution, add 10ml of sodium hydroxide (dissolve 1g in a solvent to make 10ml), equip with a reflux condenser, boil gently for 30min, cool and neutralize it by diluted-nitric acid. Titrate with 0.1 mol/l of silver as electric indicator and silver-silver chloride as reference electrode. Perform a blank test in the same manner, make any necessary correction, and calculate on the dried basis.</p> <p>0.1mol/l Silver nitrate 1ml = 13.255mg <math>C_{12}H_{19}Cl_3O_8</math></p>

\*The term "odorless" means odorless or practically odorless on the Japanese Standards for Food Additives.

### Attachment 3

Comparison draft specification of sucralose  
 with specifications established by other international organizations

Definition		Specification (draft)	JECFA	FCC
Description	Description	White to grayish-white, crystalline powder.	White to off-white, crystalline powder.	White to off-white, crystalline powder.

	Odorless	Odorless*	Practically odorless	Practically odorless
	Sweet taste	Sweet taste	Sweet taste	Sweet taste
	Solubility	It is freely soluble in water, in methanol and ethanol and is slightly soluble in ethyl acetate.	It is freely soluble in water, in methanol and in alcohol and slightly soluble in ethyl acetate.	It is freely soluble in water, in methanol and in alcohol and slightly soluble in ethyl acetate.
Identification	Infrared absorption	The infrared absorption spectrum of a potassium bromide dispersion sample has a similar absorption bands to the standard spectrum with a similar intensity at similar wavelength.	The infrared absorption spectrum of a potassium bromide dispersion of the sample exhibits relative maxima at similar wavenumbers as those shown in the reference spectrum.	The infrared absorption spectrum of a potassium bromide dispersion of the sample exhibits relative maxima at similar wavelengths as those shown in Sucralose Standard for analytical use.
	Thin-layer chromatography	The Rf value is from 0.4 to 0.6.	The main spot has the same Rf value as that of the main spot of Standard Solution A.	The main spot has the same Rf value as that of the main spot of Standard Solution A.
Purity	Clarity	Clear (1.0g, in 10ml water)	-	-
	Specific rotation	+84.0~+87.5 $\pi$ (1.0g, in 10ml water, calculated on the anhydrous basis)	+84.0~+87.5 $\pi$ (10%w/v, calculated on the anhydrous basis.)	+84.0~+87.5 $\pi$ (1g, water, 100ml, calculated on the anhydrous basis.)

	pH	3.0~6.0 (2.0g, in 20ml water)	-	-
	Heavy metals	Not more than 10µg/g (1.0g, Method 2, 1.0ml lead standard solution as control solution)	Not more than 10mg/kg as Pb.	Not more than 10mg/kg as Pb.
	Arsenic	Not more than 4.0g/g as As <sub>2</sub> O <sub>3</sub> . (0.50g, method 2, apparatus B)	Not more than 3mg/kg as As.	Not more than 3mg/kg as As.
	Other chlorinated disaccharides	Not more than 0.5%	The main spot has the same Rf value as the main spot in Solution A. No other spot is more intense than the spot in Solution B.	The main spot has the same Rf value as the main spot in Solution A. No other spot is more intense than the spot in Solution B.
	Chlorinated monosaccharide	Not more than 0.16% as calculated on fructose	Not more colored than the spot from Reference solution B.	Not more colored than the spot from Reference solution B.
	Triphenylphosphine oxide	Not more than 150 µg/g	Not more than 150mg/kg	-
	Methanol	Not more than 0.1%	Not more than 0.1%	Not more than 0.1%.
	Residue in Ignition	Not more than 0.7%.	Not more than 0.7%.	Not more than 0.7%.
	Water	Not more than 2.0%.	Not more than 2.0%.	Not more than 2.0%.
	Content	98~102.0%	98~102%	98.0~102.0%

\*The term "odorless" means odorless or practically odorless on the Japanese Standards for