MCNEIL SPECIALTY
PRODUCTS COMPANY

RICHARD R. REO
ASSOCIATE DIRECTOR
REGULATORY AFFAIRS

501 GEORGE STREET
P.O. BOX 2400
NEW BRUNSWICK, NJ 08903-2400
(732) 524-0771
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EMAIL: rreo@mspus.jnj.com

December 7, 1998

Ms. Blondell Anderson
Novel Ingredients Branch HFS-207
Food and Drug Administration
200 C Street, S.W.
Washington, D.C. 20204

Subject: Sucralose (FAP 8A4624)

Dear Ms. Anderson:

Enclosed is an amendment to the Environmental Assessment (Exhibit H) for McNeil's pending petition, which seeks general purpose use for sucralose.

McNeil sought exclusion from the need to provide an environmental assessment. We took this approach since no changes to the conditions reported in the December 5, 1997, update to FAP 7A3987 have occurred.

However, during our October 20, 1998, phone conversation, you advised of the agency's need to publish information on the environmental impact of sucralose as part of a Federal Register notice announcing acceptance of the pending petition.

Accordingly, we have enclosed five copies of an amended Environmental Assessment for the pending petition, FAP 8A4624.

Sincerely,

Richard R. Reo

Richard R. Reo

1998 DEC -8 P 5:31

Enclosures

99F-0001

EA 1

SUCRALOSE

McNeil Specialty Products Company
501 George Street
New Brunswick, New Jersey 08903-2400

SUCRALOSE

FAP 8A4624

GENERAL PURPOSE SWEETENER USE

ENVIRONMENTAL ASSESSMENT

AMENDMENT

ENVIRONMENT
ASSESSMENT

December 2, 1998

SUCRALOSE

ENVIRONMENTAL ASSESSMENT AMENDMENT (FAP 8A4624)

McNeil Specialty Products Company amends its pending sucralose petition by providing the enclosed updated environmental assessment, prepared in accordance with FDA's *"Recommendations for Preparing an Environmental Assessment"*.

Where appropriate, we have incorporated data and information from the environmental assessment, and its amendments, submitted as part of the original sucralose petition (FAP 7A3987). Based on that assessment, FDA concluded that sucralose would have no significant impact on the environment. A copy of the cross referenced materials are appended. Information in this assessment which we deem to be confidential is clearly marked as such.

Exhibit H: Environmental Assessment

1. **Date:** December 2, 1998

2. **Name of Petitioner:** McNeil Specialty Products Company

3. **Address:** 501 George Street
New Brunswick, NJ 08903-2400

4. **Description of the Proposed Action:**

a. Requested approval:

McNeil proposes to amend the sucralose regulation to permit its use as a general purpose sweetener in accordance with good manufacturing practices.

As provided in 21CFR §172.831, sucralose is permitted for use as a sweetening ingredient in fifteen food and beverage categories. The pending petition (FAP 8A4624) contains data that support its use as a general purpose sweetener. Accordingly, McNeil proposes that 21CFR §172.831 be amended to designate sucralose as a general purpose sweetener, with elimination of the individual category listings specified in the current regulation.

b. Need for action:

Sucralose is intended for use as a non-nutritive sweetener. Its safety, sugar-like sensory attributes, and its stability to a wide variety of food processing and storage conditions make it an ideal choice for use as a sugar replacement.

c. Locations of use:

Sucralose will be sold to food and beverage manufacturers, in whose facilities sucralose will be incorporated into finished products. Similarly, sucralose may be sold to manufacturers of pharmaceuticals, dietary supplements, and medical foods, etc., for use in preparing finished dosage forms. Sucralose may also be sold as a bulk ingredient to bakeries, restaurants, etc., for use in preparing sugar-reduced foods and beverages.

Subsequent to manufacture, sucralose-sweetened products may be

4. Description of proposed action, cont.:

c. Locations of use, cont.

warehoused prior to distribution. Ultimately, sucralose-sweetened products will be consumed as components of the human diet in patterns corresponding to the national population density.

d. Locations of disposal:

Following consumption, disposal/elimination of sucralose and its excretion products is expected to occur nationwide, where it will enter publicly owned treatment works (POTW) or septic systems.

5. Identification of Chemical Substances That Are the Subject of the Proposed Action:

Common or Usual Name: SUCRALOSE

Synonyms: 4,1',6'trichlorogalactosucrose

Chemical Name:

IUPAC: 1,6-DICHLORO-1,6-DIDEOXY-β-D-FRUCTOFURANOSYL-4-CHLORO-4-DEOXY-α-D-GALACTOPYRANOSIDE

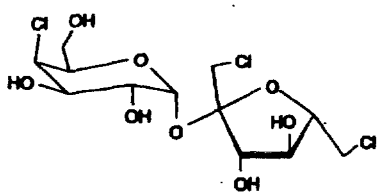
CAS: α-D-GALACTOPYRANOSIDE-1,6-DICHLORO-1,6-DIDEOXY-β-D-FRUCTOFURANOSYL-4-CHLORO-4-DEOXY

CAS Reg. Number: 56038-13-2

Molecular Weight: **397.64**

Molecular Formula: $C_{12}H_{19}Cl_3O_8$

Structural Formula:



Physical Description: White to off-white crystalline powder having an intensely sweet taste. Freely soluble in water, methanol, ethanol and slightly soluble in ethyl acetate.

6. Introduction of Substances into the Environment

a. Introduction of substances into the environment as a result of manufacture.

No extraordinary circumstances apply to the production of sucralose. In this regard, we incorporate the attachment, dated December 5, 1997, and submitted to FAP 7A3987, to update the environmental assessment prior to approval of the original sucralose petition on April 3, 1998.

b. Introduction of substances into the environment as a result of use:

There will be little introduction of sucralose into the environment as a result of its use. Sucralose will be almost completely incorporated into foods and beverages destined for consumption by the U.S. population.

Sucralose will enter the environment, in diluted form, through direct release into sewage systems, where it will undergo additional dilution. We calculate that the maximal likely concentration of sucralose in surface water, assuming a ten-fold dilution of sewage effluent and full utilization of production capacity, to be 0.003 mg/L. By contrast, sensory analysis shows that the threshold sucralose concentration for sweetness perception to be 5 mg/L, more than 1600 times the projected environmental maximum.

Ultimately, there will be a negligible sucralose concentration in the marine environment. However, because of its demonstrated low toxicity to both freshwater and marine species, its low octanol/water partition coefficient, and its intrinsic biodegradability, environmental accumulation of sucralose is unlikely.

c. Introduction of substances into the environment as a result of disposal:

We incorporate our amended environmental assessment, submitted to FAP 7A3987 (see attached) on June 10, 1987, for information related to the introduction of substances into the environment as a result of disposal. The projections contained in the June 1987 amendment continue to represent a **"worst case"** scenario. We also attach the November 1, 1990, update to the June 1987 assessment, which reported upon the decreases achieved in the quantity of substances introduced into the environment as an outcome of sucralose production, use, and disposal.

7. **Fate of substances released into the environment:**

Refer to the attached copies of the amended assessments submitted June 10, 1987, and November 1, 1990, to FAP 7A3987.

8. **Environmental effects of released substances:**

Refer to the attached copies of the amended assessments submitted June 10, 1987, and November 1, 1990, to FAP 7A3987.

9. **Use of resources and energy:**

Refer to the attached copies of the amended assessments submitted June 10, 1987, and November 1, 1990, to FAP 7A3987.

10. **Mitigation measures:**

Refer to the attached copies of the amended assessments submitted June 10, 1987, and November 1, 1990, to FAP 7A3987.

11. **Alternatives to the proposed action:**

Refer to the attached copies of the amended assessments submitted June 10, 1987, and November 1, 1990, to FAP 7A3987.

12. **List of preparers:**

Refer to the attached copies of the amended assessments submitted June 10, 1987, and November 1, 1990, to FAP 7A3987.

13. **Certification:**

December 7, 1998
(Date)

R. Reo for L. A. Goldsmith
(Signature of responsible official)

Leslie A. Goldsmith, Ph.D., V.M.D., Vice President, Product Safety and Regulatory Affairs

14. References:

Refer to the attached copies of the amended assessments submitted June 10, 1987, and November 1, 1990, to FAP 7A3987.

15. Attachments:

The following materials are attached to this assessment:

a. Amended Environmental Assessment submitted to sucralose FAP 7A3987 on June 10, 1987*.

b. Envrionmental Assessment update submitted to sucralose FAP 7A3987 on November 1, 1990.

c. Envrionmental Assessment update submitted to sucralose FAP 7A3987 on December 5, 1997.

*Copies of the reports submitted with the assessment amendment can be provided on request.

JUNE 10, 1987
ASSESSMENT

McNEIL

McNEIL SPECIALTY PRODUCTS COMPANY PO BOX 3000 GRANDVIEW ROAD SKILLMAN NJ 08558-3000 (201) 874-2700
Facsimile Number (201) 874-1120
Telex Number 219907

June 10, 1987

Ms. Blondell Anderson
Direct Additives Branch HFF-334
Division of Food and Color Additives
Food and Drug Administration
200 C Street, S.W.
Washington, DC 20204

Re: FAP 7A3987
Sucralose Food Additive Petition

Dear Ms. Anderson:

As discussed with you and Dr. Michael Harrass, the environmental assessment (Exhibit H and Appendix H) of the sucralose food additive petition contains six reports that require replacement because of errors in the analytical data. These six reports, prepared by ICI Brixham Laboratory, relate to the physico-chemical characteristics and acute aquatic toxicity of TOSPA, an intermediate in the manufacture of sucralose.

After McNeil Specialty Products Company had submitted the sucralose petition to FDA, ICI Brixham Laboratory discovered that it had mis-read the peak representing the constituent solvent in TOSPA as being the peak representing TOSPA itself. ICI Brixham has now repeated the six studies and issued new reports. In turn, McNeil Specialty has corrected the environmental assessment where references were made to the invalid data and to the old report numbers.

The resulting "Amendment to Exhibit H: Environmental Assessment" is enclosed, in quadruplicate, for Agency review. Also enclosed is a fifth copy, bound in green, which has been purged of confidential information to facilitate the Agency's handling of Freedom of Information requests.

According to the results of these six studies, TOSPA has a water solubility of 7.8 mg/l at 20° C, an octanol/water partition coefficient of 984, and a half-life at 25° C in sterile systems of 3.9 hours at pH 9 and 319 hours at pH 7. TOSPA exhibits no toxicity at its limit of water solubility in Daphnia magna, rainbow trout, and bluegill sunfish. While the octanol/water partition coefficient of TOSPA is higher than erroneously reported in the petition, the bioconcentration factors for TOSPA are very low, as calculated from the empirical correlations (Kenaga and Goring, 1980) of bioconcentration factors with water solubility.

As reported in the petition, TOSPA converts rapidly to sucralose in biodegradation studies. Furthermore, the potential for introduction of TOSPA into the environment will be very limited, since TOSPA will be produced at one site and shipped in sealed containers to a second site for conversion to sucralose.

In summary, the complete data base on TOSPA continues to support the conclusion set forth in the petition that "the potential environmental effect of TOSPA is judged to be negligible."

Sincerely,

Franta J. Broulik

Franta J. Broulik
Senior Manager, Regulatory Affairs

FJB/vls

Enclosures: 5 copies of Amendment to Exhibit H: Environmental Assessment

AMENDMENT TO EXHIBIT H: ENVIRONMENTAL ASSESSMENT

Sucralose Food Additive Petition, FAP 7A3987

June 9, 1987

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Freshwater Quarry, Overgang,
Brixham, Devon, TQ5 8BA.

Telephone Brixham 6411-5
Telex 42812

Fax (08045) 59437

Industries
PLC

TO WHOM IT MAY CONCERN

9 June 1987

TOSPA : Environmental Assessment

The Brixham Laboratory of ICI plc was commissioned by McNeil Specialty Products Company to conduct six studies on TOSPA as part of the environmental assessment programme. These studies were reported and included in a submission for F.D.A. approval. However, it was subsequently discovered that an error had been made in analysing the concentrations of TOSPA in all six studies. This error, which invalidated the analytical data, but not the toxicity test results, has now been rectified and action has been taken to minimise the possibility of a recurrence.

As a result of this, the six studies that were affected have been repeated and replacement reports issued. In accordance with Brixham Laboratory policy, the defective reports are being recalled and will be destroyed with the exception of a single authenticated copy which will be kept in the Brixham Laboratory archive.

The studies that were affected and the relevant report numbers are as follows:

			Brixham Report Numbers	
			Recalled Report	Re-issued Report
1.	TOSPA:	Determination of octanol-water partition co-efficient	BL/B/2960	BL/B/3040
2.	TOSPA:	Determination of water solubility	BL/B/2992	BL/B/3044
3.	TOSPA:	Determination of hydrolysis as a function of pH	BL/B/3008	BL/B/3069
4.	TOSPA:	Acute toxicity to rainbow trout (*Salmo gairdneri*)	BL/B/2947	BL/B/3045
5.	TOSPA:	Acute toxicity to bluegill sunfish (*Lepomis macrochirus*)	BL/B/2944	BL/B/3046
6.	TOSPA:	Determination of the acute toxicity to *Daphnia magna*	BL/B/2963	BL/B/3047

Registered in England No 218019 Registered Office: Imperial Chemical House, Millbank, London, SW1P 3JF

In addition, report number BL/B/3010 (TOSPA: Determination of ready biodegradability) refers to reports 2 and 3 above. An erratum sheet has been issued which indicates the revised reference.

J R Street
(Study Director)

Sucralose Food Additive Petition

EXHIBIT H: ENVIRONMENTAL ASSESSMENT

McNeil Specialty Products Company
One Johnson & Johnson Plaza
New Brunswick, NJ 08933

Amended June 8, 1987

SUMMARY

EXHIBIT H: ENVIRONMENTAL ASSESSMENT

Description of the Proposed Action

McNeil Specialty Products Company proposes to produce and market sucralose, a unique non-nutritive, high-intensity sweetener that is made from sugar and that can be used in a wide variety of products. The chemical name of sucralose is 1,6-dichloro-1,6-dideoxy-β-D-fructo-furanosyl-4-chloro-4-deoxy-α-D-galactopyranoside.

Sucralose production will take place at an existing Johnson & Johnson manufacturing site in Athens, Georgia. The key raw material for the production of sucralose, referred to as TOSPA, will be produced in an existing manufacturing facility in Newport, Tennessee.

Introduction of Substances into the Environment from Production

The production processes at both sites will generate wastes in liquid, gaseous, and solid forms. The liquid wastes or effluents will be biologically treated. Existing treatment facilities will be used at the Georgia site, and additional treatment facilities will be constructed at the Tennessee site. Atmospheric emissions will be controlled such that each site will retain its present status as a small generator (under 100 tons per year of organics). The solid wastes and non-aqueous liquid wastes will be small in quantity. These sites will be operated within the limits and permits imposed by the Environmental Protection Agency and the state and local authorities. Both plants will operate within the requirements of the Occupational Safety and Health Act (OSHA).

Fate and Effects of TOSPA in the Environment

The potential for introduction of TOSPA into the environment will be limited, since TOSPA will be produced at one site and then shipped in sealed containers to a second site for conversion to sucralose.

TOSPA has a relatively low octanol/water partition coefficient (984) and therefore is not expected to accumulate in organisms. It is rapidly converted to sucralose in water.

TOSPA is classified as being of "low oral toxicity" from results of an acute toxicity study in rats. TOSPA exhibits no toxicity in Daphnia, rainbow trout, and bluegill sunfish at the limit of its water solubility.

The potential environmental effect of TOSPA is judged to be negligible.

Fate of Sucralose in the Environment

Sucralose is characterized by high water solubility (28 g/100 ml at 20°C), low octanol/water partition coefficient (0.3), negligible volatility, and resistance in some tests simulating environmental degradation. These properties indicate a tendency for sucralose to enter and remain in the aquatic environment.

Sucralose is resistant to biodegradation in the usual tests simulating environmental degradation, but in some tests it is inherently biodegradable, with a slow rate of acclimation. Certain soil extracts and mixtures of organisms are able to degrade sucralose. Because of its low octanol/water partition coefficient and its inherent biodegradability, sucralose is not expected to accumulate adversely in the environment.

Effects of Sucralose Use and/or Disposal

Sucralose will enter the environment, in diluted form, through direct release into sewage systems, where additional dilution will take place. The maximal likely concentration of sucralose in surface water, assuming ten-fold dilution of sewage effluent and full utilization of the initial production capacity, is estimated to be approximately 0.003 mg/l. The threshold sweetness concentration of sucralose is 5 mg/l, which is 1,667 times the estimated concentration. Ultimately, sucralose will be diluted to negligible levels in the marine environment.

Sucralose exhibits extremely low toxicity to freshwater aquatic organisms. In general, marine species are no more sensitive than freshwater species. Sucralose does not inhibit either aerobic or anaerobic microorganisms.

The potential effect of sucralose on the environment is judged to be negligible.

EXHIBIT H: ENVIRONMENTAL ASSESSMENT

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-> Contains trade secret, privileged or confidential commercial information which is exempt from disclosure under FOI.

EXHIBIT H: ENVIRONMENTAL ASSESSMENT

1. **Date**: June 8, 1987

2. **Name of Petitioner**: McNeil Specialty Products Company

3. **Address**: One Johnson & Johnson Plaza
New Brunswick, New Jersey 08933

4. **Description of the Proposed Action**

McNeil proposes to produce and market sucralose, a unique non-nutritive, high-intensity sweetener. Sucralose is made from sugar and tastes like sugar and can be used in a wide variety of food products.

Because sucralose will be used by consumers throughout the U.S., a diverse set of environments will be encountered. Investigations of the fate and effect of sucralose in the environment are described in this assessment and have shown that sucralose will have no adverse effect on the environment.

Sucralose production will take place at an existing Johnson & Johnson manufacturing site in Athens, Georgia. The key raw material for the production of sucralose, referred to as TOSPA, will be produced in an existing manufacturing facility in Newport, Tennessee.

5. **Identification of Chemical Substances That Are the Subject of the Proposed Action**

Common or usual name: sucralose

Synonyms: TGS; 4,1',6'trichlorogalactosucrose

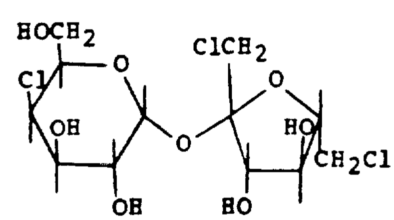
Chemical Name: 1,6-dichloro-1,6-dideoxy-b-D-fructofuranosyl-4-chloro-4-deoxy-a-D-galactopyranoside (IUPAC nomenclature)

CAS Reg. No: 56038-13-2

Molecular weight: 397.64

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

Structural formula:



Physical description: White to off-white, practically odorless, crystalline solid having a sweet taste. Freely soluble in water, methanol and ethanol and slightly soluble in ethyl acetate.

Additives: None.

Impurities: Composition of sucralose batch 167002 is as follows:

Sucralose	97.7 %
4,6'-Dichlorogalactosucrose	0.12 %
4,1'-Dichlorogalactosucrose	0.06 %
1',6'-Dichlorosucrose	0.03 %
Sucralose-anhydro	0.09 %
Sucralose-6-acetate	0.25 %
6,1',6'-Trichlorosucrose	0.02 %
1,6-Dichlorofructose	≤0.06 %
4-Chlorogalactose	≤0.02 %
Triphenylphosphine oxide	0.04 %
Ethyl acetate	0.49 %
Methanol	0.03 %
Water	0.21 %
Residue on ignition	0.49 %
Heavy metals	≤20 ppm
Arsenic	≤ 3 ppm
Adjusted sucralose assay	98.9 %

6. Introduction of Substances into the Environment

A. Introduction into Environment at Sucralose Production Site

The production process for sucralose at Athens, Georgia, will generate wastes in solid, liquid and gaseous forms, which will be disposed of in accordance with all applicable regulations.

The wastes have been estimated by scale-up calculations from pilot plant studies, and they will fall into the following three categories:

(a) Aqueous effluent streams referred to as "effluents".

(b) Solids and nonaqueous liquid effluents referred to as "solid wastes".

(c) Atmospheric gaseous emissions referred to as "atmospheric emissions".

(1) Effluents

The effluent load will arise from the following sources: (a) sanitary effluent; (b) surface water; (c) segregated surface water; and (d) process effluent.

(a) Sanitary Effluent

Sanitary effluent will not exceed 16 m^3/day based on an estimate of the number of people to be employed at the site. Sanitary effluent will be sent to the Publicly Owned Treatment Works (POTW) of the City of Athens. This quantity will be small and environmentally insignificant.

(b) Surface Water

Surface water runoff such as roof water and roadway gullies will discharge directly to the site storm drainage system.

(c) Segregated Surface Water

Surface water entering the tank farm dike can be diverted to the onsite waste treatment plant. Any other areas where spillages or contamination might occur also can be handled in this manner.

(d) Process Effluent

Three major process streams will be generated: two aqueous distillate streams and a mother liquor bleed stream.

A listing of these streams is given in Table 1. The total volume of raw effluent streams will be 5.1 m^3/day. This assumes 20% bleed of the mother liquor. A conservative estimate of the BOD is 1005 kg/day and 193,000 mg/l. The total inorganic dissolved solids (TIDS) will be approximately 32 mg/l.

Treatability studies of a simulated composite stream (Appendix H001) showed that it was biologically treatable but the biodegradation process was inefficient and unstable. Since the total volume of the process streams will be quite small (5.1 m^3/day), additional studies on biological treatment will be performed when these streams are blended with other waste streams from the manufacturing site, and/or alternate treatment methods will be explored to assure meeting all discharge requirements.

Operation of the onsite waste treatment plant will conform to the Athens Sewer Use Ordinance and the plant agreement with the Athens POTW. The treated effluent will be discharged as a very small portion of the Athens POTW effluent into the North Oconee River.

(2) Solid Wastes

The solid waste load will arise from the following sources: (a) general office waste and refuse; (b) inert solids; and (c) treatment plant sludges.

(a) General Office Waste and Refuse

The quantities of general office waste and refuse generated by this project will not be large and can be disposed of with local services in a manner similar to domestic refuse.

(b) Inert Solids

Inert solids will consist of filter-aid, resin and waste activated carbon. The quantity is estimated to be less than one cubic meter/day. The solids will be treated to ensure that no hazardous materials are present. They will be disposed of in a municipal landfill that is in current use for other materials from the plant. Any non-inert or hazardous solids will be disposed of in accordance with the applicable hazardous waste regulations.

(c) Treatment Plant Sludges

If all the process streams are treated at an onsite biological oxidation plant, the quantity of activated sludge generated would be an estimated 526 kg/day dry weight. This is equivalent to less than 3 m^3/day @ 20% solids. The sludge would be incinerated.

(3) Atmospheric Emissions

Emissions to the atmosphere will arise from the following sources: (a) process building and (b) fugitive emissions from the tank farm.

Table 2 summarizes the non-boiler emissions and identifies the controls utilized. The total normal emissions for the existing facilities at the site, including boiler vents, are currently 24 tons of organics per year (calculated as carbon). The site will still be a small generator (under 100 tons/year) of organic emissions once the sucralose facilities are in operation, including operation of the incinerator.

B. Introduction into Environment at TOSPA Production Site

TOSPA is the intermediate that will be converted into sucralose at the Athens, Georgia, site.

The structure, some basic properties, and the assay of a typical batch of TOSPA used in determining its properties are given in Table 3.

TOSPA will be produced in an existing facility in Newport, Tennessee. The specific process equipment for TOSPA will be added to the site.

The production process will generate wastes in solid, liquid and gaseous forms, which will be disposed of in accordance with all applicable regulations. These wastes will fall into the following three categories:

(a) Aqueous effluent streams referred to as "effluents".

(b) Solids and non-aqueous liquid effluents referred to as "solid wastes".

(c) Atmospheric gaseous emissions referred to as "atmospheric emissions".

(1) Effluents

The effluent load will arise from the following sources: (a) sanitary effluent; (b) surface water; (c) segregated surface water; and (d) process effluent.

(a) Sanitary effluent

Sanitary effluent will be approximately 40 m^3/day based on an estimate of the number of people to be employed. Sanitary effluent will be either pretreated onsite or sent directly to the Newport Utilities Board (NUB) waste water treatment plant.

(b) Surface Water

Surface water runoff such as roof water and roadway gullies will discharge directly to the storm drainage system.

(c) Segregated Surface Water

Surface water entering the tank farm dike can be diverted to the effluent treatment plant. Any other areas where spillages or contamination might occur also can be handled in this manner.

(d) Process Effluent

Twelve process streams will be generated, mostly consisting of residues from recovery operations and intermediate and product wash steps. The streams will be characterized generally by high BOD and high salt (TIDS) levels.

A listing of these streams is given in Table 4. The total volume of raw effluent streams will be 151.6 m^3/day, containing 20,000 kg of BOD and 38,200 kg of inorganic salts per day. Dilution water may be used to lower the salt concentration so that the final effluent will be approximately 1700 m^3/day.

Additional treatment facilities will be constructed either on the production site or in conjunction with the NUB facility. Treatment also will be provided to insure the salts level meets water quality standards.

Treatability studies (Appendix H002) showed that a simulated composite stream is biologically treatable to a high level. Over 99 percent BOD reduction and 94 percent COD reduction were achieved in these tests. No adverse effects on the activated sludge processes were observed.

(2) Solid Wastes

The solid waste load will arise from the following sources: (a) general office waste and refuse; (b) inert solids; and (c) treatment plant sludges.

(a) General Office Waste and Refuse

The quantities of general office waste and refuse generated by this project will not be large and can be disposed of in a manner similar to domestic refuse.

(b) Inert Solids

There will be essentially no inert solid wastes.

Any non-inert or hazardous solids will be disposed of in accordance with the applicable hazardous waste regulations.

(c) Treatment Plant Sludges

If all the process streams are treated at an onsite biological oxidation plant, the quantity of activated sludge generated will be an estimated 10500 kg/day dry weight. This is equivalent to 53 m^3/day @ 20% solids. The sludge will be incinerated.

(3) Atmospheric Emissions

Emissions to atmosphere will arise from the following sources: (a) process building; (b) solvent incineration; and (c) fugitive emissions from tank farm and solvent recovery.

The existing facilities at this site are emitting 25 tons/year of organics.

Table 5 contains a list of the non-boiler emissions for this process area with the controls for each area identified. The site will still be a small generator (under 100 tons/year) of organic emissions once these new process facilities are in operation, including controlled emissions from the incinerator.

C. Regulations and Compliance

(1) Sucralose Production Site

The following is a list of regulations covering the various aspects of the plant operations:

The U. S. Environmental Protection Agency

1. Hazardous Waste & Consolidated Permit Regulations (40 CFR 260-265), May 19, 1980, and as amended.

The U. S. Environmental Protection Agency (continued)

2. Regulations on Oil Pollution Prevention (40 CFR 112), December 11, 1973, and as amended.

3. Regulations on Determination of Reportable Quantities for Hazardous Substances (40 CFR 117), August 29, 1979, and as amended.

4. Pretreatment Standards (40 CFR 403), June 26, 1978, and as amended.

5. Effluent Guidelines and Standards for Pharmaceutical Manufacturing (40 CFR 439), November 17, 1976, and as amended.

The Georgia Department of Natural Resources, Environmental Protection Division

1. Georgia Hazardous Waste Management Rules (Chapter 391-3-11), August 28, 1980, and as amended.

2. Georgia Water Quality Control Regulations and Standards (Chapter 391-3-6), June 30, 1974, and as amended.

3. Georgia Air Quality Control Rules and Regulations (Chapter 391-3-1), September 26, 1973, and as amended.

4. Permit no. 28230298726, issued October 14, 1983, for construction and operation of a waste incinerator. The permit has no expiration date as long as monitoring requirements are being met.

The City of Athens, Georgia

1. Sewer Use Ordinance, December 1984.

2. Letter of Agreement with Athens POTW.

The date for each above-listed rule and/or regulation is the original date of promulgation, not the most recent date or amendment.

Noise

The plant will operate within the requirements of the Occupational Safety and Health Act (OSHA).

(2) TOSPA Production Site

See above for summary of U. S. Environmental Protection Agency regulations.

The Tennessee regulations that are applicable are:

1. Newport Utilities Board Contract: Treatability tests will be required before new waste can be sent to the NUB plant. Non-toxicity to the bacteria in the aeration basin will also be required.

2. Solid Hazardous Waste: Tennessee Department of Public Health, Division of Solid Waste Management rules, Chapter 1200, Hazardous Waste Management, adopted January 14, 1981, effective March 2, 1981, and as amended.

3. Air pollution: Chapter 1200-3-1 through 1200-3-22 effective June 16, 1974, and as amended.

4. Tennessee Air Pollution Control Board: Permit no. 021207 P, issued August 6, 1984; expires February 1, 1990, for boilers #1 and #2.

Noise

The plant will operate within OSHA requirements.

(3) Compliance

Both plants will comply with all the required limitations and regulations. Any additional or alternative sites and facilities that might be selected will be operated in compliance with all applicable Federal, state and local regulations.

D. Sucralose Use and/or Disposal

(1) Use

Human consumption and excretion of sucralose will result in its introduction to the environment in sewage effluent.

Following are estimates of environmental concentration of sucralose based on production capacity:

(a) At initial capacity

Maximal environmental concentration of sucralose = 0.0024 mg/l

(b) At four times initial capacity

Maximal environmental concentration
of sucralose = 0.25 mg/l

The assumptions and calculations for these estimates appear in Table 6. Since the sucralose intake values used in the assumptions directly correspond with production capacity, these values are confidential commercial information which is exempt from disclosure under the Freedom of Information Act.

Thus, at initial production capacity, the maximal likely concentration of sucralose in the aquatic environment will be less than 0.003 mg/l. (The threshold sweetness concentration of sucralose is 5 mg/l.) This concentration will be reduced further by additional site-specific dilution in receiving waters. Ultimately, a negligible concentration will be reached in the marine environment.

The major anticipated route of sucralose introduction to land will be via sludge from sewage treatment facilities. However, testing has shown that sucralose adsorbs only minimally to activated sludge; thus, only approximately 0.5% of the total sucralose is expected to remain with sludge.

(2) Transportation

Sucralose will be transported in sealed drums fitted with plastic bags for containment. In the event of an accident that involves a fire, test burning of sucralose (H003) has shown that the products of combustion will be carbon dioxide, hydrogen, methane, aliphatic hydrocarbons, aromatic hydrocarbons (mainly benzene) and hydrogen chloride. This information will be included in the sucralose Material Safety Data Sheet that will accompany each shipment.

(3) Disposal

Ordinarily, sucralose will not need to be discarded. An exception would occur in the case where some of the product might need to be recalled. In this event, a safe disposal method, e.g., incineration, will be chosen, such that sucralose will be prevented from introduction into the environment.

E. TOSPA Use and/or Disposal

The potential for loss of TOSPA into the environment will be very limited.

TOSPA will be made in a closed system through crystallization, recrystallization, and drying. Then it will be packaged in sealed drums fitted with plastic bags for containment.

TOSPA will be shipped in these closed containers 200 miles distant. Each truck shipment will be 40,000 pounds, and it is unlikely that more than one truck would be on the road or that more than one truck would be involved in an accident at any given time.

In the event of a truck accident, it is reasonable to assume that no more than one-fourth of the drums would burst, which would release 10,000 pounds of TOSPA. Thus, the maximum potential exposure in the event of an accident would be 10,000 pounds of TOSPA.

If the accident involved a fire, test burning of TOSPA (H004) has shown that the products of combustion will be carbon dioxide, hydrogen, methane, aliphatic hydrocarbons, aromatic hydrocarbons (mainly benzene), and hydrogen chloride. This information will be included in the TOSPA Material Safety Data Sheet that will accompany each truck shipment.

7. Fate of Emitted Substances in the Environment

A. Fate of Sucralose in the Environment

Table 7 (part A) summarizes the environmental fate data on sucralose. Fate data determinations are found in Exhibit A and Appendices H005 - H013.

Sucralose is characterized by high water solubility (28 g/100 ml at $20^{o}C$), low octanol/water partition coefficient (0.3), negligible volatility, and resistance in some tests simulating environmental degradation. These properties indicate a tendency for the compound to enter and remain in the aquatic environment.

Practically all the sucralose that will enter the environment will be released directly into water. Dilution will further reduce the concentration. Ultimately, sucralose will be diluted to negligible levels in the marine environment.

Any sucralose released to land will be readily dissolved by rainfall; if sorbed to soil, it would be readily released to an aqueous phase. Only in extremely dry (desert) environment would sucralose remain associated with soil.

Further discussion of the three potential environments (air, aquatic, and terrestrial) is as follows:

(1) Air: Due to its negligible volatility, sucralose is not expected to enter the air as vapor. Plus, with its high water solubility, any that should become airborne as particulate would be readily washed out by rain.

(2) Freshwater, Estuarine and Marine Ecosystems: The high water solubility of sucralose indicates its preference for the aqueous phase. Calculated values of its soil sorption coefficient (log Koc = 0.64-1.09) indicate that, while some sorption onto sediment might occur, the amount would be low relative to many other man-made substances found in the environment.

Sucralose has a very low octanol/water partition coefficient, 0.3, which indicates that it will tend to remain in the aqueous phase, rather than accumulating in biota.

Sucralose was not a preferred food for organisms in both "ready" and "inherent" biodegradability tests (H008, H009, and H010). Subsequently, it was found to be inherently biodegradable in a sediment/water system when inoculated with organisms extracted from soil (H009 and H013).

(3) Terrestrial: The extent of sucralose presence in the terrestrial environment is expected to be negligible relative to aquatic systems due to (a) its relatively minor rate of introduction, (b) its high solubility, and (c) its calculated low soil sorption coefficient.

Certain soil extracts and mixtures of organisms were found to degrade sucralose (H013). Thus, its fate in a terrestrial environment would be a relatively rapid transfer to the aquatic environment, with the rate and extent of degradation depending on location and/or conditions.

B. Fate of TOSPA in the Environment

Table 8 (part A) summarizes the environmental fate data on TOSPA. Fate data determinations are found in Appendices H019 - H025.

TOSPA exhibits a relatively low octanol/water partition coefficient (984) and therefore is not expected to accumulate in organisms. In addition, TOSPA converts rapidly to sucralose in water (H025). The potential for introduction into the environment is very limited.

8. Environmental Effects of Released Substances

A. Effects of Sucralose Waste Stream

As reported in Part 6, A, above, a simulated composite of sucralose waste stream did not maintain a stable condition during treatability tests. Therefore, a representative sample of an adequately treated waste stream could not be obtained, and the toxicity of the treated stream to aquatic species could not be determined. If biological treatment is chosen for this waste stream, its toxicity will be evaluated in the following freshwater aquatic species: Daphnia magna, rainbow trout and bluegill sunfish. Other methods of handling this small amount of waste will also be considered.

B. Effects of Sucralose Use and/or Disposal

Table 7 (part B) summarizes the environmental effects data on sucralose. Effects data determinations are found in Appendices H014 - H018.

A test was undertaken to determine the toxicity of sucralose to the green alga, Selenastrum capricornutum. There were no significant effects on the growth of the alga, compared with the control, at 1800 mg/l, the maximum sucralose concentration tested (H014).

Tests were also performed to determine the effects of sucralose on freshwater aquatic species, with the following results:

Daphnia magna: 48-hour EC_{50} > 1800 mg/l (H015)
Rainbow trout: 96-hour LC_{50} > 2400 mg/l (H016)
Bluegill sunfish: 96-hour LC_{50} > 3200 mg/l (H017)

In each case, due to the very low toxicity of sucralose, only partial kills were obtained. Therefore, precise LC_{50}'s could not be determined.

The three species used are standard test species. Daphnia have been widely used in toxicological testing and are sensitive to pollutants. Rainbow trout and bluegill sunfish, a cold water and a warm water species, respectively, have generally been the most sensitive to previously tested man-made substances (Verschueren, 1983).

A 21-day test was also performed to study the effects of sucralose on the survival and reproduction of _Daphnia magna_. No effect was observed at 1800 mg/l, the maximum sucralose concentration tested (H018).

In other tests, it has been shown that sucralose does not inhibit either aerobic or anaerobic microorganisms (H011 and H012).

Thus, the environmental effect of sucralose on freshwater ecosystems is predicted to be negligible.

The environmental effect of sucralose on estuarine and marine ecosystems is also predicted to be negligible by analogy with freshwater test data. It has been found that marine species generally are no more sensitive than freshwater species, although toxic effects can be modified by water chemistry (Verschueren, 1983). In addition, the additional dilution that will occur as sucralose is transported to the ocean will reduce the concentrations to below even the low levels present in freshwater.

The effect of sucralose on terrestrial ecosystems is also predicted to be negligible, since, as discussed above, it will be only minimally introduced to land and will then rapidly transfer into rainwater runoff. The exception would be very dry areas, in which sucralose would spend more time in the terrestrial environment; however, this situation would account for at most a small fraction of the total sucralose entering the environment and is therefore negligible.

As noted above, sucralose is not expected to enter the atmosphere; thus, there will be no environmental effect due to airborne concentrations.

In summary, the environmental fate and effects data summarized in Table 8 demonstrate that the potential effect of sucralose on the environment will be negligible.

C. _Effects of TOSPA Waste Stream_

The residual toxicity of the treated effluent from treatability studies of a simulated composite TOSPA waste stream has been determined using _Daphnia magna_ (H030), bluegill sunfish (H031) and rainbow trout (H032). The results of the tests are summarized as follows:

Daphnia magna:	48-hour EC_{50} = 74.8% (v/v)
Rainbow trout:	96-hour LC_{50} > 32% (v/v)
Bluegill sunfish:	96-hour LC_{50} > 32% (v/v)

D. Environmental Effects of TOSPA

The environmental effects data for TOSPA are summarized in Table 8 (part B). Effects data determinations are found in Appendices H026 - H028.

TOSPA is classified as being of "low oral toxicity" from results of an acute study in rats (H029). The animals were dosed at the maximum practicable level of 5000 mg/kg. No systemic signs of reaction to treatment were observed.

TOSPA exhibited no toxicity to *Daphnia*, rainbow trout, or bluegill sunfish at the limit of its water solubility. Its potential for introduction into the environment is limited. Other than the potential for loss during production, the only other potential for exposure is during shipment from one site to another (in sealed drums).

Thus, it is reasonable to conclude that the environmental fate and effects data summarized in Table 8 demonstrate that the potential effect of TOSPA on the environment will be negligible.

9. Use of Resources and Energy

A. Production of Sucralose and TOSPA

For the production of the quantities of sucralose and TOSPA given in Tables 1 and 3, respectively, following are the resources that will be used at both locations, inclusive of the resources required for waste disposal:

Sucrose -------->		TOSPA
Land:		22 Acres (8.9 Hectares)
Water:		1,700 m^3/day
Electricity:	Max demand	3.0 MW
	Annual usage	12.0×10^6 KW HR/year
Natural Gas:		18.0×10^6 m^3/year
(or other fossil fuel)		(methane)

TOSPA --------->		Sucralose
Land:		Located in existing building (approx. 1 acre)
Water:		120 m^3/day
Electricity:	Max demand	0.75×10^6 MW
	Annual usage	5.0×10^6 KW HR/year
Natural Gas:		3.0×10^6 m^3/year
(or other fossil fuel)		(methane)

B. Special Environmental Considerations

There will be no adverse effect on endangered or threatened species, historic places or national monuments.

C. Transportation, Use and Disposal

The use of resources and energy to transport, use, and dispose of sucralose is expected to be no greater than for other products already on the market.

10. Mitigation Measures

A. Production

The establishment of these production facilities does not entail any adverse environmental effects. As such, no mitigation measures are required.

B. Use and/or Disposal

As discussed under Part 8, no adverse environmental effects are expected; therefore, no additional mitigation measures are required.

11. Alternatives to the Proposed Action

A. Production

The establishment of these production facilities does not entail any adverse environmental effects. As such, no alternatives are required.

B. Use and/or Disposal

Since no potential adverse environmental effects have been identified, no assessment of alternatives is required.

12. List of Preparers

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13. Certification

The undersigned official certifies that the information presented is true, accurate, and complete to the best of the knowledge of the firm or agency responsible for preparation of the environmental assessment.

Date: June 8, 1987

Signature: Raymond J. Stratmeyer
(Raymond J. Stratmeyer)

Title: Vice President, International
Johnson & Johnson

14. References

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Table 7: Summary of Sucralose Environmental Fate and Effect Data, Compared with FDA Draft Environmental Assessment Guideline

PARAMETER	EXISTING INFORMATION DATA VALUE	 APPENDIX #	COMMENTS
A. Environmental Fate			
1. Water Solubility	28.3 g/100 ml @ 20°C	-	See Petition Exhibit A.
2. n-Octanol/Water Partition Coefficient (Kow)	0.3 @ 20°C	H005	Measured by a shaken flask method.
3. Vapor Pressure	Negligible	-	Note (1). See Exhibit A.
4. Dissociation Constant	Not applicable	-	-
5. Ultraviolet-Visible Absorption Spectrum	< 290 nm	-	Weak maximum absorption at 204 nm. See Exhibit A.
6. Melting Temperature	114.5 to 125.5°C	-	Depends on heating rate.(Exhibit A
7. Density/Relative Density	0.18 g/ml, bulk 0.36 g/ml, compacted	-	See Exhibit A.
8. Sorption/Desorption	Not adsorbed on activated sludge. Calculated Koc = 4.4 to 12.4 for soils (based on soil organic carbon).	H006	Note (2).
9. Hydrolysis	None detectable at pH 4.0, 6.0, or 7.5 over 1 year at 30°C.	B001	See Exhibit B.
10. Photodegradation	None	-	Note (3).
11. Biodegradation in Water	Negligible BOD in five day test. Minimal degradation in other tests.	H007-H012	Note (4).
12. Biodegradation in Soil	Three of ten soils tested in aerobic study caused breakdown. Combinations of two organisms from soil extracts effected breakdown.	H013	Note (5).

Table 7 (continued)
Summary of Sucralose Environmental Fate and Effect Data,
Compared with FDA Draft Environmental Assessment Guideline

PARAMETER	EXISTING INFORMATION		COMMENTS
	DATA VALUE	APPENDIX #	
B. Environmental Effects			
1. Algal Assay	NOEC 1800 mg/l	H014	Note (6).
2. Microbial Growth Inhibition	Does not inhibit either aerobic or anaerobic microorganisms.	H011, H012	Note (4).
3-5 (Reserved)			
6. Seed Germination	-	-	Note (7).
7. Seedling Growth	-	-	Note (7).
8. *Daphnia* Acute Toxicity	> 1800 mg/l	H015	Note (8).
9. Freshwater Fish Acute LC50	> 2400 mg/l (Trout) > 3200 mg/l (Bluegill)	H016 H017	Note (9).
10. LC50 (EC50) and Confidence Calculations	-	-	Note (10).
11. Hyalella Azteca Acute Toxicity	-	-	Note (11).
12. *Daphnia* Chronic Toxicity	NOEC 1800 mg/l	H018	Note (12).
13. Earthworm Subacute Toxicity	-	-	Note (7).

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Notes to Table 7

(1) Sucralose melts at 115 to 125°C and shows no evidence of sublimation. Thus, at normal environmental temperatures, it has negligible vapor pressure. See Exhibit A, Part 11, K, for melting point data.

(2) Adsorption onto sludge was measured by modified OECD method 106 (H006).

Calculated sorption onto soil is based upon solubility (S) and octanol/water partition coefficient (K_{ow}) using binary correlations derived by Kenaga (1980), from data for 170 chemicals. These chemicals ranged in solubility from .0001 to 2,100,000 ppm; in K_{ow} from .0001 to 3,700,000; and in K_{oc} from 0 to 1,200,000. K_{oc}, the soil sorption coefficient, is the concentration of chemical sorbed by the soil, expressed on a soil organic carbon basis, divided by the concentration of chemical in the soil water.

Resulting values of log K_{oc} for sucralose, with 95% confidence limits, are:

0.64 +/- 1.23, based on S, and 1.09 +/- 1.37 based on K_{ow}.

(3) Per A(5) in the table, sucralose does not absorb above 290 nm, which is the cutoff for solar radiation reaching Earth's surface (Verschueren, 1983). Thus no photodegradation is expected.

(4) Sucralose Biodegradability (Sewage Organisms)

(a) Biochemical oxygen demand (BOD) (H007)

Five-day test at 20°C.
BOD = 0.008 mg O_2/mg sucralose; i.e., negligible.

(b) Modified OECD screening test for ready biodegradability (H008)

28-day test using 30 mg/l actived sludge.
Sucralose concentration 10 mg/l as carbon.
Removal of sucralose 5%.

(c) Biodegradability in sediment/water (H009)

Inherent biodegradability test using microorganisms extracted from soil: 63.0 and 45.2% biodegradation were determined in 130 days. Approximately 56 days were required for microbial adaptation to sucralose.

Notes to Table 7 (continued)

No breakdown of sucralose observed over 34 days in a ready biodegradability test using either adapted or non-adapted micro-organisms.

(d) Semi-continuous activated sludge (SCAS) test for inherent biodegradability (H010)

Three-month test using sucralose at 4 and 10 mg/l (as carbon).
No degradation detected.

(e) Anaerobic sludge digestion (H011)

52-day test using ^{14}C sucralose, run at 35°C.
Sucralose not toxic to anaerobic organisms.
The bulk of sucralose (85 - 93%) remained in aqueous phase; less than 2% of radioactivity recovered as evolved gas.

(f) Toxicity to aerobic microorganisms in sewage treatment (H012)

No inhibition of respiration of activated sludge observed at sucralose concentrations of 10 - 320 mg/l.

(5) Biodegradability (Soil Organisms) (H013)

Three soils out of ten garden, woodland, and park soils in the United Kingdom caused some breakdown of sucralose.

A series of enrichments using sucralose and soil extract medium resulted in breakdown of sucralose.

Another study of sucralose breakdown yielded one positive culture out of forty tested. This culture was also isolated from garden soil.

These studies provide strong evidence that sucralose is unlikely to accumulate in the environment. The breakdown products suggest that the molecule is vulnerable to microbial attack at two positions, the disaccharide bond and the 6-position.

(6) Algal Assay (H014)

Sucralose had no significant effects on the growth of the green alga, <u>Selenastrum</u> <u>capricornutum</u>, when the alga was cultured in a range of concentrations of sucralose at 24 ± 1°C for 96 hours. The no-observed effect concentration (NOEC) ($P = <0.05$) was 1800 mg/l, also the maximum concentration tested.

Notes to Table 7 (continued)

(7) FDA has determined that these data are not required based on review of following results:

- Minimal introduction of sucralose to soils.
- Minimal toxicity to Daphnia, trout, and bluegill.

(8) Acute toxicity to Daphnia magna (H015)

- 48-hour static test at sucralose concentrations of 180 - 1800 mg/l by OECD method 202.
- No immobilization observed.
- Hence $EC_{50} > 1800$ mg/l.

(9) Fish Acute Toxicity

(a) Acute toxicity to rainbow trout (Salmo gairdneri) (H016)

- 96-hour static test at sucralose concentrations of 560-2400 mg/l, by OECD Method 203
- No significant mortalities.
- Hence $LC_{50} > 2400$ mg/l.

(b) Acute toxicity to bluegill sunfish (Lepomis macrochirus) (H017)

- 96-hour static test at sucralose concentrations of 320-3200 mg/l, by U.S. EPA Office of Toxic Substances guidelines for testing chemicals.
- No significant mortalities.
- Hence $LC_{50} > 3200$ mg/l.

(10) Due to the very low toxicity of sucralose, only partial kills were obtained. Therefore, precise LC_{50}'s could not be calculated.

(11) FDA has determined that these data are not required based on minimal toxicity to Daphnia.

Generalized criteria have been suggested (Maki and Bishop, 1985) to determine the need for additional toxicity testing in performing an environmental assessment. These criteria, and their applications to sucralose, are as follows:

"The first step in an environmental effects assessment is determining the acute toxicity of the chemical to one or more species of fish. The ratio of the LC_{50} to the estimated surface water concentration (Csw) is used to indicate the need for additional acute toxicity testing. Some possible decisions include:

$LC_{50}/Csw > 100$: No further tests unless there is information indicating that specific tests should be run.

$LC_{50}/Csw = 1$: Material too toxic to be used except with restriction.

$LC_{50}Csw > 1 < 100$: Further tests should be done on appropriate organisms to more closely estimate this ratio."

Per sucralose data:

LC_{50} > 2400 mg/l for rainbow trout

Csw = 0.004 mg/l to 0.7 mg/l max

so LC_{50}/Csw = 3400 to 600,000.

This is much greater than 100. Consequently, acute testing of Hyalella azteca or of additional freshwater fish species does not appear to be necessary.

(12) Effect of sucralose on the survival and reproduction of Daphnia magna (H018)

The no-observed effect concentration (NOEC) was greater than 1800 mg/l on the survival and reproduction of Daphnia under semi-static conditions, at 20°C for 21 days.

Table 8: Summary of TOSPA Environmental Fate and Effect Data
Compared with FDA Draft Environmental Assessment Guideline

	PARAMETER	EXISTING INFORMATION		COMMENTS
		DATA VALUE	APPENDIX #	
A.	Environmental Fate			-
1.	Water Solubility	7.8 ± 0.3 mg/1 @ 20°C	H019	
2.	n-Octanol/Water partition coefficient (Kow)	984 ($\log_{10}$ Kow=3.0)	H020	See note (1).
3.	Vapor pressure	Negligible	-	See note (2).
4.	Dissociation constant	Not applicable	-	-
5.	Ultraviolet-visible absorption spectrum	Strong maxima at 213 nm and 258 nm	H021	See note (3).
6.	Melting temperature	98.2 to 99.6°C	H022	See note (2).
7.	Density/relative density	Bulk density 0.59 ± 0.1 g/ml. Compacted bulk density 0.72 ± 0.01g/ml	H023	-
8.	Sorption/desorption	Measurement not planned.		See note (4).
9.	Hydrolysis	Half-life at 25° C = 3.9 hrs. at pH 9, 319 hrs. at pH 7	H024	See note (5).
10.	Photodegradation	Negligible	H021	See note (6).
11.	Biodegradation in water	Rapid conversion to sucralose	H025	See note (7).
12.	Biodegradation in soils			See note (7).

Table 8 (continued)
Summary of TOSPA Environmental Fate and Effect Data
Compared with FDA Draft Environmental Assessment Guideline

PARAMETER	EXISTING INFORMATION		COMMENTS
	DATA VALUE	APPENDIX #	
8. <u>Environmental Effects</u>			
1. Algal assay	-	-	See note (8).
2. Microbial growth inhibition	-	-	See note (9).
3-5 (Reserved)			
6. Seed germination	-	-	See note (10).
7. Seedling growth	-	-	See note (10).
8. *Daphnia* acute toxicity	No toxicity at limit of water solubility	H026	See note (11).
9. Freshwater fish	No toxicity to rainbow trout and bluegill sunfish at limit of water solubility	H027, H028	See note (11).
10. LC50 (EC50) and Confidence calculations	No toxicity at limit of solubility	-	See note (12).
11. Hyalella azteca acute toxicity	-	-	See note (13).
12. Earthworm subacute toxicity	-	-	See note (13).

Notes to Table 8

(1) Water to organism testing is not needed based on:

- Very limited potential for distribution into the environment.
- Solubility significantly higher than the 1 mg/l guideline cited by Kimerle (1978).
- The octanol/water partition coefficient of 984 is higher than the guideline of 500 cited by Kimerle (1978) for considering water to organism testing. However, the bioconcentration factors, BCF(f) (flowing water ecosystem) and BCF(t) (terrestrial-aquatic ecosystem), estimated from the empirical correlations of Kenaga and Goring (1980),

  $\log BCF(f) = 2.791 - 0.564 \times \log WS$
  and
  $\log BCF(t) = 2.183 - 0.629 \times \log WS$

  are 194 and 42 and significantly lower than the guideline of 1000 cited by Kimerle (1978) for considering organism to organism testing.

(2) The melting point of TOSPA, when heated from 10°C below its melting point at a rate of heating 1°C per minute and 3°C per minute, is 98.2°C and 99.6°C, respectively. A wide melting range was observed, and the melting point shows a marked dependence on the rate and duration of heating. There is no evidence of sublimation and thus negligible vapor pressure (H022).

(3) The spectrum for TOSPA exhibits strong absorption maxima at 213 nm and 258 nm. However, due to levels of solvents, the absorption maximum for TOSPA (at 211 nm) is not well resolved (H021).

(4) FDA has determined that sorption/desorption measurements are not required based on:

- Limited potential for distribution onto soil.
- Solubility an order of magnitude greater than 1 mg/l, as cited by Kimerle (1978).
- General low toxicity.

Sorption onto soil can be estimated from binary correlations developed by Kenaga and Goring (1980):

$\log K_{oc} = 3.64 - 0.55 \times \log WS$
and $\log K_{oc} = 1.377 + 0.54 \times \log K_{ow}$

where K_{oc} is the concentration of chemical sorbed onto the soil divided by the concentration in the soil water. Using WS = 7.8 mg/l and K_{ow} = 984, the estimated values of $\log K_{oc}$ are 3.15 ± 1.23 (95% confidence limits) and 2.98 ± 1.37. Based on these estimates, preferential distribution onto soil is indicated,

Notes to Table 8 (continued)

although the practical amounts would be limited due to very limited potential for TOSPA to be released to the environment. These estimates indicate a tendency for TOSPA to absorb preferentially to activated sludge.

(5) At 25°C in sterile systems, the half-life of TOSPA is 3.9 hours at pH 9 and 319 hours at pH 5 (H024). The rate of conversion of TOSPA to sucralose was found to be rapid under non-sterile conditions in biodegradation studies (H025).

(6) TOSPA does not absorb above 290 nm, the cutoff for solar radiation reaching the Earth's surface (Verschueren, 1983). Thus no photodegradation is expected.

(7) TOSPA is rapidly broken down to sucralose in water, probably by a combination of hydrolysis and biodegradation. While there are no data on the biodegradation of TOSPA in soil, it can be expected to convert slowly to sucralose (H025).

(8) FDA has determined that algal assay data are not required based on review of following results:

- No toxicity to Daphnia, rainbow trout, and bluegill sunfish at limit of solubility.
- Limited potential for distribution into the environment.

(9) Microbial growth inhibition is not expected. Treatability studies of TOSPA waste stream showed no adverse effects on activated sludge processes (H002).

(10) FDA has determined that these data are not required based on review of following results:

- No toxicity to Daphnia, rainbow trout, and bluegill sunfish at limit of solubility.
- Limited potential for distribution into the environment.

(11) A maximum nominal concentration of 10 mg/l was used in batch toxicity tests. After 48 hours, the mean measured concentration of TOSPA sample in the Daphnia test was >3.8 mg/l; and after 96 hours in the rainbow trout and bluegill sunfish tests, the actual measured concentrations of TOSPA sample were 8.5 and 5.7 mg/l, respectively (H026, H027, and H028).

(12) Since no toxicity was observed at limit of solubility, precise numbers cannot be presented. Also, the concentration varied during the experiments.

(13) FDA has determined that these data are not required based on review of following results:

- No toxicity to Daphnia, rainbow trout, and bluegill sunfish at limit of solubility.
- Limited potential for distribution into the environment.

McNEIL

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November 1, 1990

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Direct Additives Branch HFF-334
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Food and Drug Administration
200 C Street, S.W.
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Re: Sucralose FAP 7A3987

Dear Ms. Anderson:

As discussed with Dr. Harrass, McNeil Specialty has just conducted a thorough review of the environmental assessment submitted as part of the sucralose food additive petition in 1987. We can now provide the Agency with updated projections of waste materials and further details on the effluent treatment facilities and emission controls at the two manufacturing sites. Based on this updated information, we continue to believe that the production of sucralose will have no adverse effect on the environment.

In the 1987 assessment, we identified the nature and levels of anticipated waste materials based on theoretical engineering designs for the two planned manufacturing sites: a facility in Newport, TN, that would produce the key intermediate, TOSPA; and a second facility in Athens, GA, that would convert TOSPA to sucralose. Even though the basic chemical manufacturing process has not changed from that set forth in the petition, we have modified both sites' engineering designs not only to facilitate greater efficiencies in the process but also to mitigate any potential effects on the environment.

We have prepared the enclosed tables to delineate the differences between the 1987 information and our current information. We must emphasize that our current projections for the quantities of expected waste materials are still estimates and not actual data generated from commercial manufacturing. Also, please note that Tables 2 and 3 contain site-specific proprietary information that we deem to be exempt from public disclosure under the Freedom of Information Act.

Table 1 is a list of all federal, state, and local regulations and permits applicable to each site's operations. We have denoted those citations that are revised or updated with an asterisk (*) and those that are new with a double asterisk (**). Both sites are complying and will continue to comply with all regulations and permits.

Athens, GA, Site

Table 2 shows that, although the Athens facility will generate more wastewater, an onsite aerobic wastewater treatment plant and an added solvent recovery system will greatly reduce the BOD level. Operation of the treatment plant will conform to the requirements of the Athens sewer use ordinance. The treated effluent will be discharged as a very small portion of the Athens Publicly Owned Treatment Works (POTW) effluent into the North Oconee River. Also, a second waste stream, containing mostly waste solvent, will be diverted for use as fuel in an onsite boiler, which meets the existing air emissions permit.

The solid wastes at the Athens facility will be significantly lower than originally projected, while the non-boiler stack emissions to the atmosphere may increase minimally. We have incorporated extensive controls (vacuum jet condensers, catalytic fume incinerator, bag house, vent condensers, and conservation vents) to keep emissions as low as possible.

Newport, TN, Site

As shown in Table 3, the Newport facility will generate less wastewater and salts (totally dissolved solids), with a significantly reduced BOD level, after processing in the new onsite anaerobic treatment facility. The solvent removal system is designed to minimize discharge of solvent in the wastewater and will produce a new waste stream (70% water) for offsite disposal by a licensed handler under RCRA. We intend to recycle this material once it has been characterized in actual operation and a suitable recovery scheme has been installed.

The new onsite anaerobic treatment system for wastewater will greatly reduce the level of sludge, although the neutralization/filtration system will at the same time produce a new calcium-based solid that will be disposed of in a non-hazardous industrial landfill. Furthermore, the non-boiler stack emissions will be significantly lower than originally projected with the installation of a thermal oxidizer.

<u>Summary</u>

Through modifications in engineering design and the addition of waste treatment facilities and emission controls at both manufacturing sites, we have worked to further control the potential for introducing substances into the environment. We have achieved marked improvement in our 1987 waste projections and have identified appropriate disposal methods for some new waste materials. Based on this update to our 1987 environmental assessment, we maintain our original conclusion that the production of sucralose will have no adverse effect on the environment.

Sincerely,

Franta J. Broulik

Franta J. Broulik
Director, Regulatory Affairs
and Information Services

Enclosures

November 1, 1990

TABLE 1: APPLICABLE ENVIRONMENTAL REGULATIONS
Update to Environmental Assessment, Sucralose FAP 7A3987

Following are the environmental regulations applicable to the plant operations at the two sites. Revised/updated citations are denoted by an asterisk (*) and new citations by a double asterisk (**). Both plants will comply with all regulations and permits.

SUCRALOSE PRODUCTION SITE, ATHENS, GA

THE U.S. ENVIRONMENTAL PROTECTION AGENCY

* 1. Resource Conservation and Recovery Act of 1976 and subsequent regulations (40 CFR 260-266), October 21, 1976, and as amended.

2. Regulations on Oil Pollution Prevention (40 CFR 112), December 11, 1973, and as amended.

3. Regulations on Determination of Reportable Quantities for Hazardous Substances (40 CFR 117), August 29, 1979, and as amended.

4. Pretreatment Standards (40 CFR 403), June 26, 1978, and as amended.

5. Effluent Guidelines and Standards for Pharmaceutical Manufacturing (40 CFR 439), November 17, 1976, and as amended.

** 6. Emergency Planning and Community Right-to-Know Act of 1986, and subsequent regulations (40 CFR 302-305, 311-313, 355, 370, 372).

THE GEORGIA DEPARTMENT OF NATURAL RESOURCES,
ENVIRONMENTAL PROTECTION DIVISION

1. Georgia Hazardous Waste Management Rules (Chapter 391-3-11), August 28, 1980, and as amended.

2. Georgia Water Quality Control Regulations and Standards (Chapter 391-3-6), June 30, 1974, and as amended.

3. Georgia Air Quality Control Rules and Regulations (Chapter 391-3-1), September 26, 1973, and as amended.

* 4. Permit No. 286902910005, issued October 6, 1988, for operation of this manufacturing facility.

THE CITY OF ATHENS, GEORGIA

1. Sewer Use Ordinance, December 1984.

TABLE 1: APPLICABLE ENVIRONMENTAL REGULATIONS (continued)

EMPLOYEE EXPOSURES

The plant will operate within the requirements of the Occupational Safety and Health Act (OSHA).

TOSPA PRODUCTION SITE, NEWPORT, TN

See above for list of U.S. Environmental Protection Agency regulations.

THE STATE OF TENNESSEE

* 1. Newport Utilities Board Contract: Discharge to the Newport Board wastewater treatment facility will not cause NUB to be out of compliance with its NPDES permit, TN-0020702, June 22, 1990.

2. Solid Hazardous Waste: Tennessee Department of Health, Division of Solid Waste Management rules, Chapter 1200, Hazardous Waste Management, adopted January 14, 1981, effective March 2, 1981, and as amended.

3. Air Pollution: Chapter 1200-3-1 through 1200-3-22, effective June 26, 1974, and as amended.

* 4. Tennessee Air Pollution Control Board: Operating Permit Nos. 028220P, 028221P, 028219F for boilers, tank farm, and production process.

** 5. Tennessee Hazardous Waste Reduction Act, January 1, 1990.

EMPLOYEE EXPOSURES

The plant will operate within OSHA requirements.