UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

July 13, 1998

MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Subject:

EPA Reg. No.:	3573-LO	Cleaning Magic I
DP Barcode:	D244086	
Case No:	062115	
EPA Reg. No.:	3573-AE	Cleaning Magic II
DP Barcode:	D244149	
Case No:	063348	
EPA Reg. No.:	3573-AR	Cleaning Care I
DP Barcode:	D244168	
Case No:	062119	
EPA Reg. No.:	3573-AN	Cleaning Care II
DP Barcode:	D244154	
Case No:	000439	

To: Velma Noble, PM 31
Regulatory Management Branch
Antimicrobials Division (7510W)

From: Ian Blackwell, Biologist
Team 2
Product Science Branch
Antimicrobials Division (7510W)

Through: Karen Hicks, Acting Team Leader
Toxicology & Chemistry Team
Product Science Branch
Antimicrobials Division (7510W)

Registrant: The Procter and Gamble Company

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Alkyl (C10-16) dimethyl amine oxide	4.81
Inert Ingredient(s):	95.19
Total:	100.00%

BACKGROUND: The Procter & Gamble Company has submitted acute toxicity information to support the registration of their products "Cleaning Magic I," "Cleaning Magic II," "Cleaning Care I" and "Cleaning Care II." According to information submitted by Procter & Gamble, Cleaning Magic I and II are also known as "Ultra Dawn Concentrated Dishwashing Detergent." The registrant also states that Cleaning Care I and II are also known as "Ultra Joy Concentrated Dishwashing Liquid." Procter & Gamble has been publicly selling products similar to these as household dishwashing liquids for a number of years. However, the Procter & Gamble Company now wishes to label these products as having antimicrobial properties. In order to do so, they must be registered with the EPA as pesticide products.

For this submission, Procter & Gamble have submitted an acute oral toxicity, dermal sensitization study, and three primary skin irritation studies. One of the primary skin irritation studies was conducted using rabbits. The other two studies were conducted using humans as the test species. The MRID numbers are 444347-06 through 444347-11.

This submission also requests the waiver of the acute dermal toxicity, acute inhalation and primary eye irritation studies. The identification of many of the test materials and the waiver requests for file symbol 3573-LO are found in Volume II, MRID number 444347-01.

RECOMMENDATIONS: ESSB findings are:

1. The acute oral toxicity, primary skin irritation (MRID number 444347-07) and dermal sensitization studies are acceptable.

2. The waiver of the acute dermal toxicity study is denied. Actually, this is not so much a request for a waiver as it is a request to cite incidence data. However, this denial is not final and will be reconsidered upon the receipt of some information. ESSB/AD would like for the registrant to submit the following information together in a new submission:

   a. CSFs of 3573-LO and each of amine oxide products to be cited.
   b. Reports of the acute dermal toxicity studies to be cited in support of 3573-LO. (These reports must have their materials identified.)
   c. Or, Reports of incidence data developed with chemically similar products. CSFs must be submitted for the cited products also.
   d. A letter stating the specific goals of the citation submission.

3. The waiver of the acute inhalation toxicity is granted. It is felt that it is extremely difficult to breathe dishwashing liquid or to generate an aerosol using diluted dishwashing liquid. Also, the diluted product does not readily form a breathable aerosol. It would be very difficult for a normal person to breathe aerosols from concentrated or diluted dishwashing liquid. There is the possibility of spraying the diluted product; however, this would be

unusual and does not agree with the directions for use. This product will be assigned toxicity category **IV** for acute inhalation toxicity.

4. The waiver of the primary eye irritation study is denied. Again, this is not so much a request for a waiver as it is a request to cite incidence data. However, this denial is not absolute at this point. This decision will be reconsidered upon the receipt of more conclusive information. ESSB/AD would like for the registrant to submit the following information together in a new submission:

   a. CSFs of 3573-LO and each of the amine oxide products to be cited for primary eye irritation.
   b. Reports of any primary eye irritation studies to be cited in support of 3573-LO.
   c. Reports of incidence data developed with chemically similar products. These similar products that are cited must have CSFs submitted.
   d. Explain why in the waiver request, Volume X (no MRID number), Table 1 gives incidence data on only **78%** of the reported cases.
   e. A letter stating the goals of that citation submission.

5. The primary skin irritation study conducted on humans (MRID number 444347-08) is not acceptable. The problems with this study are as follows:

   a. The test was conducted on humans. The Agency discourages human acute toxicity testing. EPA guidelines state that humans are not an acceptable test species.
   b. This study was not conducted in accordance with EPA Quality Assurance (QA) guidelines. The report did not define the ways in which the study did not conform to QAs. Quality Assurance is a very important facet of study conduct.
   c. The test material was applied first to the gauze patch. It should have been applied to the skin first, that is, unless the test material was too thin or was a light a liquid that would run off of the test site.
   d. The study employed an irritation control, Dodecyl Sulfate, sodium salt (SDS). ESSB would like to receive an explanation of the use of the irritation control in this study, i.e., is it a negative control?

6. The other primary skin irritation study (MRID number 444347-09) conducted on humans is not acceptable. The study difficulties are as follows:

   a. The study was <u>not</u> conducted using rabbits, but used humans. Humans are not a species accepted by the EPA.
   b. The test material is listed as "SIBTS-0132." It is not clear to ESSB what material SIBTS-0132 is.
   c. The study was not conducted using the Draize Method.

d. This study was not conducted in accordance with EPA Quality Assurance (QA) guidelines.
e. The report was unclear of the specific usage of the four irritancy controls.

The acute toxicity profile for reg. no. 3573-LO is currently:

acute oral toxicity	IV	acceptable
acute dermal toxicity		request denied/more information requested
acute inhalation toxicity	IV	waived
primary eye irritation		request denied/more information requested
primary skin irritation	II	acceptable/ more information requested to review request to change toxicity category
dermal sensitization	nonsensitizer	acceptable

LABELING:

Due to the absence of certain acute toxicity data, no precautionary labeling can be recommended for these products at this time.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§ 81-1, 870.1100)

Product Manager: 31
MRID No.: 444347-06

Reviewer: I. Blackwell
Study Completion Date: 4/24/97
SLI Study No.: 3029.2106

Testing Laboratory : Springborn Laboratories, Inc.
Authors : Todd N. Merriman, B.S.

Quality Assurance (40 CFR §160.12): Included

Test Material: SI0737.01; Cleaning Magic I, "clear blue liquid"

Species: Sprague Dawley rats
Age: young adult
Weight: males = 187-193 g; females = 205-221 g
Source: Charles River Laboratories, Inc.

Conclusion:

1. **LD_{50} (mg/kg):** **Males** > 5,000 mg/kg
Females > 5,000 mg/kg
Combined > 5,000 mg/kg

2. **The estimated LD_{50} is greater than 5,000 mg/kg of body weight.**

3. **Tox. Category**: IV **Classification**: Acceptable

Procedure (Deviations from §81-1): none

Results:

Dosage (mg/kg)	(Number Deaths/Number Tested)		
	Males	Females	Combined
5,000	0/5	0/5	0/10

Observations: salivation, rales, dark material around facial area, reddish urine, urine staining, rough defecation and decreased defecation.

Gross Necropsy: no significant gross internal findings.

DATA REVIEW FOR SKIN IRRITATION TESTING (§81-5, 870.2500)

Product Manager: 31
MRID No.: 444347-07

Reviewer: Ian Blackwell
Study Completion Date:
SLI Study No.: 3029.2107

Testing Laboratory: Springborn Laboratories, Inc.
Author: Todd N. Merriman

Quality Assurance (40 CFR §160.12): Included

Test Material: SI0737.01; Cleaning Magic I, "clear blue liquid"
Dosage: 0.5 mL under a 1 X 1 in. gauze patch
Species: New Zealand White rabbits
Age: adult
Sex: 6 males
Weight: 2.359-2.514 kg
Source: Myrtle's Rabbitry

Summary:

1. **Toxicity Category**: II

2. **Classification**: acceptable

Procedure (Deviations From §81-5):

Results: Well-defined erythema in 6/6, slight to moderate edema in 6/6 and focal and/or pinpoint blanching on 2/6 sites at one hour. The blanching increased in severity and incidence (blanching grade 2 in 3/6 test sites and focal and or pinpoint on an additional 2/6 test sites) over the course of the study. Focal and/or pinpoint eschar was also noted on 3/6 test sites by study day 7. The dermal irritation resolved completely in all animals by day 21. Additional finding included superficial lightening and desquamation which were both noted on 6/6 sites.

Special Comments:

☆ DATA REVIEW FOR SKIN IRRITATION TESTING (§81-5, 870.2500)

Product Manager: 31
MRID No.: 444347-08

Reviewer: Ian Blackwell
Study Completion Date: 8/13/97
Study No.: 97-018

Testing Laboratory: Proctor & Gamble, L&CP P&RS Skin Lab
Author: Sue A. Pitts

Quality Assurance (40 CFR §160.12): Study does NOT meet GLPs.

Test Material: SI0737.01; Cleaning Magic I; LDL-2EG
Dosage: 0.4 ml on a 5 cm^2 patch.

Species: human
Age: 18-65 years
Sex: not specified
Weight: not specified
Source: n/a

Summary:

1. **Toxicity Category**:
2. **Classification**: UNACCEPTABLE

Procedure (Deviations From §81-5):
☞An unacceptable test species, humans, was used for this study.
☞The study was not conducted in accordance with EPA Quality Assurance guidelines.
☞The test material was applied first to the gauze patch, not to the skin.
☞The ages of the test species was not reported.
☞This study employed an irritation control, Dodecyl Sulfate, Sodium salt (SDS).

Results: No erythema, edema, exudation, crust formation or any other irritation was reported.

Special Comments: This test was conducted using humans, not rabbits. The exposure times were not the same as the Draize test which is the Agency standard.

☆ DATA REVIEW FOR SKIN IRRITATION TESTING (§81-5, 870.2500)

Product Manager: 31
MRID No.: 444347-09

Reviewer: Ian Blackwell
Study Completion Date: 2/6/95
Study No.: 94-025

Testing Laboratory: The Procter & Gamble Company; L&CP P&RS Skin Lab
Author: C.K. Kappes

Quality Assurance (40 CFR §160.12): NOT included (Study does not meet GLPs.)

Test Material: SIBTS-0132
Dosage: 0.5 ml

Species: Human
Age: not specified
Sex: not specified
Source: n/a

Weight: not specified

Summary:

1. **Toxicity Category**:

2. **Classification**: UNACCEPTABLE

Procedure (Deviations From §81-5):
☞The identity of the test material is unclear.
☞Study does not meet GLPs.
☞The exposure was only for 15 minutes. (The Draize test exposure is four hours.)
☞The study employed four irritation control substances.

Results: The test substance (0.5 ml) was applied to the volar forearm surface, distributed for 10 seconds and applied for 15 minutes, once daily for four days. Observations were made one and twenty-four hours after exposure.

Special Comments: This study was conducted in humans, <u>not</u> in rabbits, rats or any Agency accepted lab animals.

DATA REVIEW FOR DERMAL SENSITIZATION TESTING (§81-6, 870.2600)

Product Manager: 31
MRID No.: 444347-11

Reviewer: I. Blackwell
Study Completion Date: 6/20/97
SLI Study No.: 3029.2108

Testing Laboratory: Springborn Laboratories, Inc. (SLI)
Author: Todd N. Merriman, B.S.

Quality Assurance (40 CFR §160.12): Included

Test Material: SI0737.01; Cleaning Magic I, "clear blue liquid"
Positive Control Material: DNCB; "yellow crystalline powder"

Species: Hartley-derived guinea pig
Weight: males = 371-412 g; females = 389-442 g
Age: young adult
Source: Harlan Sprague-Dawley, Inc.

Method: Modified Buehler Method

Summary:

1. **This Product is not a dermal sensitizer.**

2. **Classification**: acceptable

Procedure (Deviation From §81-6): none

Procedure: The test animals were induced with 0.3 ml of 10% SI0737.01 once per week for three weeks. Challenge of the test material-treated and naive control animals was conducted two weeks after the third induction treatment using 0.3 ml of 1.25% SI0737.01. The study referenced a historical positive control study that was conducted using DNCB at 0.1% for induction and 0.05% and 0.1% for challenge.

Results: Test material-treated animals displayed slight confluent erythema (1/10) and slight patchy erythema (2/10) 24-hours after the first induction treatment. Twenty-four hours after the third induction treatment, 1/10 test material-induced animals displayed moderate confluent erythema, 4/10 displayed slight confluent erythema, 5/10 slight patchy erythema, 1/10 graded 2 edema, 5/10 grade 1 edema, 1/10 superficial lightening and 1/10 grade 1 blanching. Twenty-four hours after challenge, 7/10 test material-induced and 8/10 naive control animals displayed slight patchy erythema.