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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

January 8, 1998

MEMORANDUM

Subject: EPA Reg. No.: 675-LL / Lysol Brand Disinfectant S.A. Cleaner
DP Barcode: D239690
Case No: 062161

From: Ian Blackwell, Biologist IBB
Team 2
Risk Assessment and Science Support Branch
Antimicrobials Division (7510W)

Through: Norm Cook, Branch Chief
Risk Assessment and Science Support Branch
Antimicrobials Division (7510W) 01-20-98

Laura E. Morris, Team Leader Laura E. Morris
Team 3
Risk Assessment and Science Support Branch
Antimicrobials Division (7510W)

To: Adam Heyward, PM 34
Regulatory Management Branch II
Antimicrobials Division (7510W)

Applicant: Reckitt and Coleman, Inc.
225 Summit Avenue
Montvale, NJ 07645

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
citric acid	2.5
Inert Ingredient(s):	97.5
Total:	100.0%

BACKGROUND: Reckitand Coleman has submitted an acute oral study, an acute dermal toxicity study, a primary eye irritation study, two dermal sensitization studies and requests for the waiver of the acute inhalation toxicity, primary skin irritation and dermal sensitization studies. The studies submitted were conducted by MB Research Laboratories, Inc. The MRID numbers are 443868-02 through 443868-06.

Although the product is named "Lysol Brand S.A. (Superior Acid) Disinfectant Cleaner", the test material is "Hard Surface Cleaner #428-177." Bruce Paolella of Reckitt & Coleman, Inc., clarified this discrepancy by noting that the test material is "Hard Surface Cleaner #428-177" and the CSF lists the product as "Formula #428-177." This identification is sufficient for RASSB

The registrant has submitted a request for the waiver of the acute inhalation toxicity study for file symbol 675-LL. This waiver request includes tables and charts demonstrating the particle size distribution for Formula 428-177.

The registrant has requested the waiver of the primary skin (dermal) irritation study. The reasons given are the lack of irritation observed in the acute dermal toxicity study with references to USEPA OPPTS Health Effects Guideline 870.2500 and Conduct of Acute Toxicity Studies. The registrant also references the lack of irritation observed in the Human Repeat Insult Patch Test (dermal sensitization) conducted in humans.

RECOMMENDATIONS: TRB findings are:

1. The actue oral and dermal toxicity studies are acceptable and sufficient to support the registration of this product.

2. RASSB denies the waiver of the acute inhalation toxicity study. Although the data presented with this waiver appears to demonstrate an MMAD near 300 microns, the registrant to present more information. RASSB would like additional information for the following reasons:

   a. The product consists of approximately [redacted] water has a "water-like consistency." As demonstrated by the submitted data, it is apparently thin enough to be sprayed.
   b. The waiver request does not state how the study was conducted, how the aerosol was generated or what attempts, if any, were made to reduce the particle size.
   c. The registrant did not state who (which laboratory) conducted this particle size distribution.

RASSB will reconsider the waiver of the acute inhalation toxicity study for this product if the registrant will submit the following information:

a. Specific information on the viscosity of this product. It is preferred that this information be related in centipoise.
b. Information on the particle size determination conducted on this product. This should include the testing facility, the equipment used, attempts to reduce the particle size, etc.
c. It would be a good idea to have a particle size distribution conducted by an approved testing laboratory. (The registrant may contact the American Council Of Independent Laboratories, 202-887-5872, for a list of testing facitilities.)

3. The primary eye irritation study is classified as supplementary data and is currently not acceptable to support the registration of this product. The problem with this study is that the report states that the animals' eyes were examined "Using a hand held auxilliary source of illumination." This is extremely vague. Not all hand-held sources of illumination are adequate for observations in the primary eye irritation study. In order to have this study reconsidered, the registrant must specify what types of illumination were used at each of the ocular observations.

4. RASSB waives the primary skin irritation study. The skin irritation study is waived because there was no more than slight erythema reported in the acute dermal toxicity study. This waiver is in accordance with the Conduct of Acute Toxicity Studies and the Agency's proposed USEPA OPPTS Health Effects Guideline 870.2500.

5. The dermal sensitization study (the Local Lymph Node Assay conducted by Huntingdon Life Sciences) did not receive a full review, but is unacceptable. This study (MRID number 443868-05) did not receive a full review for three reasons:

a. The LLNA is not actually a study that the Agency accepts in determining sensitization potential of pesticide products.
b. In glancing through this report, it became apparent that this study identified the product as being a nonsensitizer.
c. An additional sensitization study conducted on file symbol 675-LL was included in this submission.

The Local Lymph Node Assay (LLNA) is not one of the types of dermal sensitization studies that is listed as being accepted by the Agency in Subdivision F Guidelines, the Conduct of Acute Toxicity Studies or in the Agency's proposed Health Effects Test Guidelines, OPPTS 870.2600, Skin Sensitization (it is very unusual to receive and LLNA study). However, the Health Effects Test Guidelines do list it as being acceptable in screeening for positive controls. That is, the LLNA has a problem in identifying weak sensitizers when compared to the Guinea Pig Maximization Test and, thus, it is not considered to be able to accurately distinguish a weak sensitizer from a nonsensitizer.

6. The dermal sensitization sensitization study conducted by Consumer Product Testing Co. is acceptable although it has some deficiencies/idiocyncrasies. The problems with this study (MRID number 443868-06) are as follows:

a. The study was conducted using humans. The Agency discourages the use of humans in "acute toxicity" studies (it is recognized that the dermal sensitization study does not actually measure toxicity) or other studies in series 870 of the Agency's Health Effects Test Guidelines.
b. No positive control study was conducted. However, as this study was conducted in humans (some as old as 71 years of age) RASSB will excuse the lack of a positive control.

RASSB will accept this study due to the fact it was conducted in over 100 human test subjects, had ten induction treatments and used undiluted test material. It is actually a better *real world* judgement of sensitization than are the studies conducted in guinea pigs. Still, the Agency discourages the use of humans in acute toxicity studies.

The acute toxicity profile for file symbol 675-LL is currently:

Study	MRID	Category	Grade
acute oral toxicity	443868-02	IV	acceptable
acute dermal toxicity	443868-03	III	acceptable
acute inhalation toxicity	not submitted		REQUESTED
primary eye irritation	443868-04		supplementary
primary skin irritation	not submitted	IV	WAIVED
dermal sensitization	443868-06	nonsensitizer	acceptable

LABELING:

RASSB is currently unable to recomment labeling for this product due to the outstanding acute inhalation and primary eye irritation studies.

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

Product Manager: 34
MRID No.: 443868-02

Reviewer: I. Blackwell
Study Completion Date: 6/12/97
Project No.: MB 97-5864

Testing Laboratory: MB Research Laboratories, Inc.
Authors: Daniel R. Cerven, M.S.

Quality Assurance (40 CFR §160.12): Included (Conducted by Bonnie Cerven)

Test Material: Hard Surface Cleaner; formula 428-177; "Clear yellow liquid"

Species: Wistar albino rabbits
Age: 7-10 weeks
Weight: males = 210-232 grams; females = 203-223 grams
Source: Ace Animals

Conclusion:

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

Results:

Dosage (mg/kg)	(Number Deaths/Number Tested)		
	Males	Females	Combined
5000	0/5	0/5	0/10

Observations: There was dyspnea in two animals.

Gross Necropsy: No abnormalities were observed.

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DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2, 870.1200)

Product Manager: 34
MRID No.: 443868-03

Reviewer: Ian Blackwell
Study Completion Date: 4/16/97
Report No.: MB 96-5550.02

Testing Laboratory: MB Research Laboratories, Inc.
Author: Daniel R. Cerven, M.S.

Quality Assurance (40 CFR §160.12): Included

Test Material: Hard Surface Cleaner; formula 428-177; "clear yellow liquid"

Species: New Zealand White rabbits
Weight: males = 2.0-2.3 kg; females = 2.0-2.2 kg
Age: not specified
Source: Ace Animals

Summary:

1. **LD_{50} (mg/kg)**: **Males** > 2,000 mg/kg
   Females > 2,000 mg/kg
   Combined > 2,000 mg/kg

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

3. **Tox. Category**: III **Classification**: acceptable

Procedure (Deviation From §81-2):

Results:

Reported Mortality

DOSAGE	(NUMBER DEATHS/NUMBER TESTED)		
	Males	Females	Combined
2000 mg/kg	0/5	0/5	0/10

Observations: Diarrhea, anogenital soiling, lack of feces, very slight erythema.

Gross Necropsy Findings: Anogenital soiling and mottled kidneys.

DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (§81-4, 870.2400)

Product Manager: 34
MRID No.: 443868-04

Reviewer: Ian Blackwell
Study Completion Date: 4/16/97
Research Project No.: MB 96-5550.04

Testing Laboratory: MB Research Laboratories, Inc.
Author(s): Daniel R. Cerven, M.S.

Quality Assurance (40 CFR §160.12): Included

Test Material: Hard Surface Cleaner; formula 428-177; "clear yellow liquid"
Dosage: 0.1 mL
Species: New Zealand White rabbits
Sex: three males
Weight: 2.2-2.5 kg **Age**: 11-13 weeks
Source: Ace Animals, Inc.

Summary:

1. **Toxicity Category**:

2. **Classification**: supplementary

Procedure (Deviations From §81-4):
☞The report states that the eyes were examined only with a "hand held auxilliary source of illumination."

Results:

Observations	(number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	14	21
Corneal Opacity	0/3	0/3	0/3	0/3	---	0/3	0/3	---
Iritis	0/3	2/3	1/3	0/3	---	0/3	0/3	---
Conjunctivae								
Redness	3/3	3/3	3/3	2/3	---	0/3	0/3	---
Chemosis	3/3	3/3	1/3	0/3	---	0/3	0/3	---
Discharge	3/3	3/3	1/3	1/3	---	0/3	0/3	---

--- = no observations at this point

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

Product Manager: 34
MRID No.: 443868-06

Reviewer: I. Blackwell
Study Completion Date: 6/4/97
Study No.: 97.0077

Testing Laboratory: Consumer Product Testing Co.
Author: Richard R. Eisenberg, Robert W. Shanahan and Joy Frank

Quality Assurance (40 CFR §160.12): Included

Test Material: Hard Surface Cleaner a#428-177; EPA file symbol 675-LL
Positive Control Material: none

Species: human
Weight: not specified
Source: not applicable

Age: 18-71 years

Method: "Repeat Patch Insult Test" (Buehler Method)

Summary:

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

2. **Classification**: acceptable

Procedure (Deviation From §81-6):
☞No positive control study was conducted.
☞The weights of the test subjects were not reported.

Procedure: The area of the back between the scapulae was the treatment site. Approximately 0.2 mL of the indiluted test article was applied to a 1" x 3/4" gauze patch attached to a clear adhesive dressing and applied for twenty-four hours. This dosage was applied three times a week for a total of ten applications.

Results: 102/112 subjects finished this study. 5/112 subjects had reactions including well-defined erythema, very slight erythema and dryness. None of the 112 test subjects displayed any irritation at twenty-four or forty-eight hours after challenge at either the original or virgin test sites.

ACUTE TOX ONE-LINER

1. PC CODE: 021801

2. CURRENT DATE: January 8, 1998

3. TEST MATERIAL: citric acid 2.5%; file symbol 675-LL

Study/Species/Lab/ Study#/Date	MRID No.	Results	Tox. Cat.	Grade
acute oral toxicity /rat / MB Research Labs / MB 97-5864.01 / 6-12-97	443868-02			
acute dermal toxicity/ rabbit / MB Research Labs / MB 96-5550.02 / 4-16-97	443868-03			
primary eye irritation / rabbit / MB Research Labs / MB 96-5550.04 / 4-16-97	443868-04			
dermal sensitization/ guinea pigs / Huntingdon Life Sciences/ 96.0244/ 4-2-97	443868-05		---	U
dermal sensitization/ human / Consumer Product Testing Co. / 97.0077 / 6-4-97	443868-06	Not a dermal sensitizer.	---	A

Core Grade Key:

A = Acceptable
S = Supplementary (upgradeable)
U = Unacceptable
V = self-Validated