

Report Title: Up And Down Procedure For Estimating Acute Oral Toxicity (LD50) in Rats of G0506.01

Test Type: Acute Oral Toxicity (LD50)

Conducting Laboratory and Location: Hazelton-Madison Laboratories, Madison, Wisconsin

Test Substance (s): 0.3% Octopirox (G0506.01) in conditioner formula. Undiluted material was used for dosing.

Species: Rat

of Animals: 3 males and 3 females given initial dose

Test Conditions: Dosed orally (gavage) with initial dose of 20.0 g/kg.

Results: Female: LD₅₀ > 21.1 g/kg
Male: LD₅₀ > 20.6 g/kg

Study #: 50106723

Report Date: 2/28/85

QA report/GLP compliance: Yes

Accession #: 30620



HAZLETON

LABORATORIES AMERICA, INC

Chemical & BioMedical Sciences Division

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#2

(1)

REPORT OF ANALYSIS

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THE PROCTER & GAMBLE COMPANY
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SAMPLE NUMBER: 50106723
DATE ENTERED: 01/25/85
REPORT PRINTED: 02/28/85

VISCOUS LIQUID: G0506.01
ORD# BYCR 0372; C1B; ISSUE DATE 5-1-84
PURCHASE ORDER NUMBER: C1B-G0506.01-0372

UP AND DOWN PROCEDURE FOR ESTIMATING
ACUTE ORAL TOXICITY (LD50) IN RATS OF G0506.01

ENCLOSED: METHOD, PAGES 2 AND 3
SUMMARY, PAGES 4 TO 6
PATHOLOGY, PAGES 6 TO 8
OAU REPORT, PAGE 9
RAW DATA APPENDIX
PROTOCOL APPENDIX

INITIATION: 01/28/85
COMPLETION: 02/19/85 (In-life)

SIGNED: *Steven M. Glaza*
STEVEN M. GLAZA
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ACUTE TOXICOLOGY

Wayne A. Madison
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STUDY DIRECTOR
ACUTE TOXICOLOGY

BY AND FOR HAZLETON LABORATORIES AMERICA, INC.
RAW DATA FOR THIS STUDY ARE KEPT ON FILE AT HAZLETON LABORATORIES
AMERICA, INC., MADISON, WISCONSIN.

RECEIVED BY
MAR 7 1985
OPERATIONS SECTION



SAMPLE NUMBER: 50106723

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VISCIOUS LIQUID: G0506.01

DRD# BYCR 0372: C1B: ISSUE DATE 5-1-84

ACUTE ORAL TOXICITY

Objective: To estimate the lethality (LD50 value) and acute symptoms to a test substance by using a small number of rats.

Test Material: G0506.01

Physical Description: Blue viscous liquid

Stability of Test Material: Sponsor assumes responsibility for stability determination.

Test Animal: Young adult male and female albino rats (approximately 7 weeks of age) of the Sprague-Dawley strain were procured, maintained in group cages in temperature- and humidity-controlled rooms, provided continuous access to Purina Rodent Chow and water and held for an acclimation period of at least 7 days.

Animals were chosen at random from the acclimated animals and weighed between 210 and 299 grams prior to fasting. Food and water were available ad libitum throughout the study period except for a fasting period of approximately 18 to 20 hours prior to test material administration when food, but not water, was withheld. Following fasting, the animals weighed between 196 and 282 grams. Test animals were individually housed and identified by animal number and corresponding ear tag.

Preparation and Administration of Test Material: An individual dose was calculated for each animal based upon its fasted body weight and administered undiluted by gavage. The dose volume varied per dosage level based upon the average bulk density of 0.89 g/ml.

Selection of Dose Levels: Testing utilizing the up and down procedure (Protocol C1B) was conducted. One male and one female animal was administered an initial dose of 20.0 g/kg of body weight. This dose level was selected based upon the sponsor's estimate. Subsequent dose levels for each sex either decreased or increased based upon the mortality result of the previous level, i.e., if the animal survived, the dose increased and if death occurred or imminent death was indicated, the dose was decreased. One male and/or one female animal was used each time a dosage level was administered. Once the initial point of reversal in the survival rate had been determined, five additional levels for the males and three additional levels for the females were dosed using the above procedure.



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ACUTE ORAL TOXICITY

(CONTINUED)

Observations: The animals were observed for clinical signs and mortality at 1/2, 2 and 4 hours following test material administration. The animals were observed daily thereafter for 7 days for clinical signs and mortality.

Body weights were taken before fasting and just prior to test material administration. Body weights of all surviving animals were taken 7 days following test material administration.

Pathology: At study termination, surviving animals were euthanatized. All animals, whether dying on study or euthanatized, were subjected to a gross necropsy examination and abnormalities were recorded.



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ACUTE ORAL TOXICITY

(CONTINUED)

SUMMARY

Test Animal: Albino rats - Sprague-Dawley strain
 Source: Harlan Sprague-Dawley, Madison WI
 Date Animals Received: 12/12, 12/24/84 and 01/22/85
 Temperature and Humidity of Animal Room: 21 to 26 Degrees C.;
 36 to 56% Relative Humidity

Method of Administration: Oral Gavage

Test Material: G0506.01

Date Test Started: 01/28/85

Date Test Completed: 02/19/85 (In-life)

Estimated Oral LD50: Male - 20.6 g/kg of body weight
 95% Confidence Limits of 15.8 to 26.9 g/kg
 Female - 21.1 g/kg of body weight
 95% Confidence Limits of 15.3 to 29.0 g/kg

MORTALITY SUMMARY (NUMBER OF DEATHS)

Dosage Level (G/KG)	Number of Animals Dosed	Hours 0 - 4	Days							Total Dead
			1	2	3	4	5	6	7	
MALES										
15.4	1	0	0	0	0	0	0	0	0	0
17.3	1	0	0	0	0	0	0	0	1	-
20.0	3	0	0	1	0	0	0	0	0	0
22.3	2	0	0	0	1	0	0	0	0	0
FEMALES										
15.4	1	0	0	0	0	0	0	0	0	0
20.0	3	0	0	0	1	0	0	0	0	0
22.3	1	0	0	0	0	1	-	-	-	-



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ACUTE ORAL TOXICITY

(CONTINUED)

DOSING SEQUENCE

ANIMAL NUMBER	DOSE LEVEL (G/KG)	DATE DOSED	RESULTS
MALES			
C23307	20.0	01/28/85	Died Day 2.
C23294	15.4	01/30/85	Survived to termination.
C23315	20.0	01/31/85	Survived to termination.
C23257	22.3	02/01/85	Died Day 3.
C23274	17.3	02/04/85	Died Day 6.
C23246	20.0	02/05/85	Survived to termination.
C27599	22.3	02/08/85	Survived to termination.

FEMALES

C23241	20.0	01/28/85	Survived to termination.
C23369	22.3	01/30/85	Died Day 4.
C23367	20.0	02/05/85	Died Day 2.
C28332	15.4	02/08/85	Survived to termination.
C28383	20.0	02/12/85	Survived to termination.

AVERAGE BODY WEIGHTS (G)

Dosage Level (g/kg)	No. of Animals Dosed	Pre-fast	Initial	Terminal
Males				
15.4	1	293	268	300
17.3	1	252	241	---
20.0	3	291	268	281
22.3	2	275	253	243
Females				
15.4	1	217	201	224
20.0	3	238	220	229
22.3	1	241	228	---



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ACUTE ORAL TOXICITY

(CONTINUED)

Comments:

Clinical signs seen during the study included diarrhea, hypoactivity, ataxia, red-stained nose and mouth or face, brown- or dark-stained anal area, hypothermic to touch, possible respiratory congestion, piloerection, reddish discharge from nose and mouth, and death. All deaths occurred within six days following test material administration.

Deviations from the protocol: During the study period the temperature of the animal room ranged from 21 to 26 degrees C. Once the initial point of reversal in the survival rate had been determined, five additional males and three additional females were dosed instead of four additional animals as required by the protocol. These deviations are not considered to have had an effect on the validity of the study.

PATHOLOGY

DOSAGE LEVEL: 15.4 g/kg of body weight

Animal Number	Sex	Died	Test Day Sacrificed	Necropsy Comments
Date Dosed: 01/30/85				
C23294	M	-	7	No visible lesions.

Date Dosed: 02/08/85				
C28332	F	-	7	No visible lesions.

DOSAGE LEVEL: 17.3 g/kg of body weight

Animal Number	Sex	Died	Test Day Sacrificed	Necropsy Comments
Date Dosed: 02/04/85				
C23274	M	6	-	Perinasal discharge, dark red and crusted; perineum/perianal area stained brown; stomach - entire intestinal tract contains dark brown, red semifluid.



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ACUTE ORAL TOXICITY

(CONTINUED)

PATHOLOGY (CONTINUED)

DOSAGE LEVEL: 20.0 g/kg of body weight

Animal Number	Sex	Test Day Died	Test Day Sacrificed	Necropsy Comments
Date Dosed: 01/28/85				
C23307	M	2	-	Stomach - glandular mucosa diffusely red, with multiple brown areas, up to 3 mm in diameter.
C23241	F	-	7	No visible lesions.
Date Dosed: 01/31/85				
C23315	M	-	7	No visible lesions.
Date Dosed: 02/05/85				
C23246	M	-	7	No visible lesions.
C23367	F	2	-	Stomach - contains thick, mint-green material.
Date Dosed: 02/12/85				
C28383	F	-	7	No visible lesions.



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ACUTE ORAL TOXICITY

(CONTINUED)

PATHOLOGY (CONTINUED)

DOSAGE LEVEL: 22.3 g/kg of body weight

Animal Number	Sex	Test Day		Necropsy Comments
		Died	Sacrificed	

Date Dosed: 01/30/85

C23369	F	4	-	Entire intestinal tract filled with tan/yellow, creamy fluid; stomach - contains yellow, granular material.
--------	---	---	---	---

Date Dosed: 02/01/85

23257	M	3	-	Stomach - contains mint-green, creamy material.
-------	---	---	---	---

Date Dosed: 02/08/85

C27599	M	-	7	No visible lesions.
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QUALITY ASSURANCE STATEMENT

Up and Down Procedure for Estimating
Acute Oral Toxicity (LD₅₀) in Rats

Study No. 50106723

The report as herein attached for the above-mentioned study has been reviewed by the assigned Quality Assurance Unit of Hazleton Laboratories America, Inc. in accordance with the Good Laboratory Practice Regulations as set forth in 21 CFR 58.35 (b) (6) (7). It has been found to accurately identify and/or describe the authorized methods and standard operating procedures followed in the conduct of the study and that the reported data accurately reflect the raw data of the laboratory study. Furthermore, the Quality Assurance Unit has conducted the following inspections of the testing facilities utilized in the conduct of this study and has submitted written reports of said inspections to the study director and/or management.

<u>Date of Inspection</u>	<u>Type of Inspection</u>	<u>Date Issued to Management</u>
1/23-25/85	Process Audit	1/25/85
2/26/85	Report Review	2/26/85

Diana E. Skalitzky
Diana E. Skalitzky
Inspector, Quality Assurance Unit

2/27/85
Date

ACUTE ORAL TOXICITY (UP AND DOWN) PROCEDURE

Test Article: G0506.01 RT No. 50106723
 Dosage Level: 15.4 g/kg Vehicle: NA
 Species Rat Source Hurlan Date Received 12-24-84
 Fasted: Date 1-29-85 Time 3:00 p.m. Tech. smm Room No. 3 Sex ♂

CLINICAL OBSERVATIONS

Observations	Hours			DAYS							
	1/2	2	4	1	2	3	4	5	6	7	
Appeared normal	1	1	0	0	0	0	0	1	1	1	
Diarrhea	0	0	1	0	1	1	0	0	0	0	
Brown stained anal region	0	0	1	1	1	1	1	0	0	0	
Reddish stained nose & mouth	0	0	0	0	1	1	1	0	0	0	
/											
Deaths											
Technician	smm	smm	smm	smm	smm	ck	ck	ck	ck	ck	
Date	1985	1/30	1/30	1/30	1/31	2/1	2/2	2/3	2/4	2/5	2/6

DOSAGE CALCULATIONS

Ave. Bulk Density 0.89 g/ml
 Temp. of Test Material 23 C
 Dose Level = Dose / Bulk Density = Volume
 $15.4 \text{ g/kg} = \frac{17.3 \text{ ml/kg}}{0.89 \text{ g/ml}}$
 Tech. SMAM 1-30-85
 See Dosage Calculation Sheets.

Dosage	<u>15.4 (g/kg)</u>	Dose Time: <u>9:00 a.m.</u>				
Dose Volume	<u>17.3 (ml/kg)</u>	Tech	<u>smm</u>	Date	<u>1-29-85</u>	Scale Used:
Animal No./Ear Tag No.	<u>C-2-3286</u>	<u>3294</u>	<u>smm</u>	<u>1-29</u>	<u>NA</u>	
Prefasted Body Weight (g)	<u>298</u>	<u>293</u>	<u>smm</u>	<u>1-29</u>	<u>KTRON 5228</u>	
Fasted Body Weight (g)	<u>265</u>	<u>268</u>	<u>smm</u>	<u>1-30</u>	<u>KTRON 5228</u>	
Actual Dose (ml)	<u>4.6</u>	<u>4.6</u>	<u>smm</u>	<u>1-30</u>	<u>NA</u>	
Day 7 Body Weight (g)	<u>*</u>	<u>300</u>	<u>ck</u>	<u>2/6</u>	<u>KTRON 5228</u>	

① ENTRY ERROR 1-30-85 smm

Verified By flb 1-30-85

NA = Not applicable
 NE = Not evident

*-Dosage calculated but not administered
 unused animal returned to stock.

Reviewed By MW 2-19-85

ACUTE ORAL TOXICITY (UP AND DOWN) PROCEDURE

Test Article: G0506.01 RT No. 50106723
 Dosage Level: 15.4 g/kg Vehicle: NA
 Species Rat Source Havlan Date Received 12-24-84
 Fasted: Date 2-7-85 Time 4:21 Tech. CK Room No. 3 Sex ♀

CLINICAL OBSERVATIONS

Observations	Hours			DAYS						
	1/2	2	4	1	2	3	4	5	6	7
Appeared normal	1	0	0	0	0	0	1	1	1	1
Red stained face	0	1	1	1	1	1	0	0	0	0
Diarrhea	0	0	0	0	1	1	0	0	0	0
Dark stained anal area	0	0	0	0	1	1	0	0	0	0
/										
Deaths										
Technician	SPM	SPM	SPM	SPM	SPM	SPM	SPM	SPM	SPM	SPM
Date	1985 2/9	2/9	2/9	2/9	2/10	2/11	2/12	2/13	2/14	2/15

DOSAGE CALCULATIONS

Ave. Bulk Density
0.99 g/ml
 Temp. of Test Material
23 C
 Dose Level = Dose
 Bulk Density = Volume

$$\frac{15.4 \text{ g/kg}}{0.99 \text{ g/ml}} = \underline{17.3 \text{ ml/kg}}$$

 Tech. SPM 2-9-85
 See Dosage Calculation Sheets.

Dosage	15.4 (g/kg)	Dose Time: 10:55 a.m.			
Dose Volume	17.3 (ml/kg)	Tech	Date	Scale Used:	
Animal No./Ear Tag No.	G2-8333 8396	CK	2/7	NA	
Prefasted Body Weight (g)	217 211	CK	2/7	KTRON 5228	
Fasted Body Weight (g)	201 200	SPM	2/8	KTRON 5228	
Actual Dose (ml)	3.5 3.5	SPM	2/8	NA	
Day 7 Body Weight (g)	224 *	SPM	2/15	KTRON 5228	

Verified By dlb 2/8/85

NA = Not applicable
 NE = Not evident

*-Doseage calculated but not administered
 unused animal returned to stock.

Reviewed By MW 2-19-85

ACUTE ORAL TOXICITY (UP AND DOWN) PROCEDURE

Test Article: 60506.01 RT No. 5D106723
 Dosage Level: 17.3 g/kg Vehicle: NA
 Species Rat Source Hanford Date Received 12-24-84
 Fasted: Date 2-3-85 Time 2:30pm Tech. CK Room No. 3 Sex ♂

CLINICAL OBSERVATIONS

Observations	Hours			DAYS						
	1/2	2	4	1	2	3	4	5	6	7
Appeared normal	1	1	0	0	0	0	0	0	0	0
Possible Respiratory Congestion	0	0	1	0	0	0	1	1	0	
Hypoaactive	0	0	0	1	1	1	1	1	0	
Brown staining around anus	0	0	0	1	1	1	1	1	0	
Red stained face	0	0	0	0	1	1	1	1	0	
Hypothermic to touch	0	0	0	0	0	0	1	1	0	
Deaths	0	0	0	0	0	0	0	0	1	
Technician	ALH	SP	SP	ALH	CK	CK	MM	MM	MM	MM
Date	1985	2/4	2/4	2/4	2/5	2/6	2/7	2/8	2/9	2/10

DOSAGE CALCULATIONS

Ave. Bulk Density 0.89 g/ml
 Temp. of Test Material 23 C
 Dose Level = Dose Bulk Density * Volume
 $\frac{17.3 \text{ g/kg}}{0.89 \text{ g/ml}} = 19.44 \text{ ml/kg}$
 Tech. ALH 2/4/85

See Dosage Calculation Sheets.

Dosage	17.3 (g/kg)	Dose Time: <u>2:30pm 1985</u>				
Dose Volume	10.44 (ml/kg)	Tech	Date	Scale Used:		
Animal No./Ear Tag No.	3292 3274	CK	2/3	NA		
Prefasted Body Weight (g)	276 252	CK	2/3	KHM 5228		
Fasted Body Weight (g)	260 241	ALH	2/4	KHM 1348		
Actual Dose (ml)	5.1 4.7	ALH	2-4	NA		
Day 7 Body Weight (g)	* NA					

0122
 2-10-85 Verified By 2-4-85 MM
 1-20-85

NA = Not applicable
 NE = Not evident

*-Dosage calculated but not administered unused animal returned to stock.

Reviewed By MM 2-19-85

@Recording number 2-4-85

ACUTE ORAL TOXICITY (UP AND DOWN) PROCEDURE

Test Article: GO50(6.0) RT No. 50106723
 Dosage Level: 20g/kg Vehicle: NA
 Species Rat Source HARLAN Date Received 12-12-84
 Fasted: Date 1-27-85 Time 1:00pm Tech. jm Room No. 3 Sex ♂

CLINICAL OBSERVATIONS

Observations	Hours			DAYS						
	1/2	2	4	1	2	3	4	5	6	7
Appeared normal	X ⁰	0	0	0	0					
Brown stained anal area	0	1	1	1	0					
Diarrhea	0	1	1	1	0					
Res. Dis. nose Discharge from end of mouth	0	0	1	1	0					
Deaths	0	0	0	0	1					
Technician	SM	SM	SM	SM	SM					
Date	1985	1/28	1/28	1/29	1/30					

DOSAGE CALCULATIONS

Ave. Bulk Density _____ g/ml
 Temp. of Test Material _____ C
 Dose Level = Dose / Bulk Density = Volume
 _____ g/kg = _____ ml/kg
 _____ g/ml
 Tech. _____
 See Dosage Calculation Sheets.

Dosage	200g/kg		Dose Time: 10:30 a.m.		
Dose Volume	22.47 (ml/kg)		Tech	Date	Scale Used:
Animal No./Ear Tag No.	33c7	33c8	jm	1/27	NA
Prefasted Body Weight (g)	297	230	jm	1/27	Vitron 134B
Fasted Body Weight (g)	263	237	SM	1-28	KTEON 1345
Actual Dose (ml)	5.9	5.3	SM	1-28	NA
Day 7 Body Weight (g)	NA	*	NA		

Died 1/30/85
 MH 2/20/85
 Verified By deb 1-28-85

NA = Not applicable
 NE = Not evident

*-Dosage calculated but not administered
 unused animal returned to stock.

① writing error 1-30-85 SM

Reviewed By MW 2-19-85

ACUTE ORAL TOXICITY (UP AND DOWN) PROCEDURE

Test Article: GO 506.01 RT No. 50106723
 Dosage Level: 20g/kg Vehicle: NA
 Species Rat Source HAELAN Date Received 12-12-84
 Fasted: Date 1-27-85 Time 1:00 pm Tech. jm Room No. 3 Sex ♀

CLINICAL OBSERVATIONS

Observations	Hours			DAYS						
	1/2	2	4	1	2	3	4	5	6	7
Appeared normal	X ²	0	0	0	0	0	0	0	1	1
Brown stained anal area	0	1	1	1	1	1	1	1	0	0
Diarrhea	0	1	1	0	0	1	1	0	0	0
Reddish Discharge from nose and mouth	0	0	1	1	0	0	0	0	0	0
/										
Deaths										
Technician	Sam	Sam	Sam	Sam	Sam	Sam	Sam	Sam	ck	ck
Date	1985	1/28	1/29	1/29	1/30	1/31	2/1	2/2	2/3	2/4

DOSAGE CALCULATIONS

NA Ave. Bulk Density _____ g/ml
 Temp. of Test Material _____ C
 $\frac{\text{Dose Level}}{\text{Bulk Density}} = \frac{\text{Dose}}{\text{Volume}}$
 _____ g/kg = _____ ml/kg
 g/ml
 Tech. _____
 See Dosage Calculation Sheets.

Dosage	20.0 (g/kg)		Dose Time: 10:30 a.m.			
Dose Volume	22.47 (ml/kg)		Tech	Date	Scale Used:	
Animal No./Ear Tag No.	021	3241	3242	jm	1/27	NA
Prefasted Body Weight (g)	260	251	251	jm	1/27	KTRON 1348
Fasted Body Weight (g)	233	233	233	Sam	1-28	KTRON 1345
Actual Dose (ml)	5.30	5.2	5.2	Sam	1-28	NA
Day 7 Body Weight (g)	250	*	*	ck	2/4	KTRON 1345

Verified By ck 1-28-85

NA = Not applicable
 NE = Not evident

*-Dosage calculated but not administered
 unused animal returned to stock.

- ① recording error 1-28-85 Sam
- ② writing error 2-19-85 Sam

Reviewed By MMW 2-19-85

ACUTE ORAL TOXICITY (UP AND DOWN) PROCEDURE

Test Article: G0506.01 KI No. 50106723
 Dosage Level: 20.0g/kg Vehicle: NA
 Species Rat Source Harlan Date Received 12-24-84
 Fasted: Date 1-30-85 Time 2:30pm Tech. Samm Room No. 3 Sex ♂

CLINICAL OBSERVATIONS

Observations	Hours			DAYS						
	1/2	2	4	1	2	3	4	5	6	7
Appeared normal	0	0	0	0	0	0	0	0	0	0
Diarrhea	1	1	1	0	1	1	1	0	0	0
Brown stained anal region	0	1	1	1	1	1	1	1	1	1
Face Red stained	0	0	0	0	1	1	1	1	1	1
Hypn Active	0	0	0	0	1	1	1	1	1	1
/										
Deaths										
Technician	KAM	SAM	SAM	SAM	CK	CK	dh	CK	CK	SAM
Date	1985	1/31	1/31	2/1	2/2	2/3	2/4	2/5	2/6	2/7

DOSAGE CALCULATIONS

Ave. Bulk Density 0.89 g/ml
 Temp. of Test Material 23 C
 $\frac{\text{Dose Level}}{\text{Bulk Density}} = \frac{\text{Dose}}{\text{Volume}}$
 $\frac{20.0 \text{ g/kg}}{0.89 \text{ g/ml}} = \underline{22.47 \text{ ml/kg}}$
 Tech. Samm 1-31-85
 See Dosage Calculation Sheets.

Dosage	<u>20.0 (g/kg)</u>	Dose Time: <u>10:25 a.m.</u>				
Dose Volume	<u>22.47 (ml/kg)</u>	Tech	<u>SAM</u>	Date	<u>1-30</u>	Scale Used:
Animal No./Ear Tag No.	<u>C2-3315</u>	<u>3274</u>	<u>SAM</u>	<u>1-30</u>	<u>NA</u>	
Prefasted Body Weight (g)	<u>299</u>	<u>298</u>	<u>SAM</u>	<u>1-30</u>	<u>KTRON 5228</u>	
Fasted Body Weight (g)	<u>292</u>	<u>264</u>	<u>SAM</u>	<u>1-31</u>	<u>KTRON 5228</u>	
Actual Dose (ml)	<u>6.3</u>	<u>5.9</u>	<u>SAM</u>	<u>1-31</u>	<u>NA</u>	
Day 7 Body Weight (g)	<u>282</u>	<u>*</u>	<u>SAM</u>	<u>2-7</u>	<u>KTRON 5228</u>	

Verified By dh 1-31-85

NA = Not applicable
 NE = Not evident

*-Dosage calculated but not administered
 unused animal returned to stock.

Reviewed By MMA 2-19-85

Test Article: 60506.01 RT No. 50106723
 Dosage Level: 20.0 g/kg Vehicle: NA
 Species Rat Source Harlan Date Received 12-24-84
 Fasted: Date 2-4-85 Time 3:15 PM Tech. SP Room No. 3 Sex ♂

CLINICAL OBSERVATIONS

Observations	Hours			DAYS						
	1/2	2	4	1	2	3	4	5	6	7
Appeared normal	1	1	1	0	0	0	0	0	0	0
Red stained face	0	0	0	1	1	1	1	1	1	1
Diarrhea	0	0	0	0	1	1	1	1	1	0
Hypocactive	0	0	0	0	1	1	1	1	0	0
Brown stained anal area	0	0	0	0	1	1	1	1	1	1
/										
Deaths										
Technician	dlb	dlb	dlb	ck	SP	SP	SP	SP	SP	SP
Date	1/5	2/5	2/5	2/6	2/7	2/8	2/9	2/10	2/11	2/12

DOSAGE CALCULATIONS

Ave. Bulk Density
0.89 g/ml
 Temp. of Test Material
23 C
 Dose Level = Dose
 Bulk Density = Volume
 $\frac{20.0 \text{ g/kg}}{0.89 \text{ g/ml}} = 22.47 \text{ ml/kg}$
 Tech. dlb 2/5/85

See Dosage Calculation Sheets.

Dosage	<u>20.0 (g/kg)</u>	Dose Time: <u>10:15 a.m.</u>				
Dose Volume	<u>22.47 (ml/kg)</u>	Tech	Date	Scale Used:		
Animal No./Ear Tag No.	<u>C2-3246</u>	<u>SP</u>	<u>2/4</u>	<u>NA</u>		
Prefasted Body Weight (g)	<u>276</u>	<u>SP</u>	<u>2/4</u>	<u>KTRON 5228</u>		
Fasted Body Weight (g)	<u>258</u>	<u>dlb</u>	<u>2/5</u>	<u>KTRON 5228</u>		
Actual Dose (ml)	<u>5.8</u>	<u>dlb</u>	<u>2/5</u>	<u>NA</u>		
Day 7 Body Weight (g)	<u>279</u>	<u>SP</u>	<u>2/12</u>	<u>KTRON 1349</u>		

Verified By SP 2/12/85

NA = Not applicable
 NE = Not evident

*-Dosage calculated but not administered
 unused animal returned to stock.

Reviewed By MW 2-19-85

ACUTE ORAL TOXICITY (UP AND DOWN) PROCEDURE

17

Test Article: 60506-01 RT No. 50106723
 Dosage Level: 20.0 g/kg Vehicle: NA
 Species: Rat Source: Harlan Date Received: 12-24-84
 Fasted: Date 2-4-85 Time 3:15 PM Tech. SP Room No. 3 Sex ♀

CLINICAL OBSERVATIONS

Observations	Hours			DAYS						
	1/2	1	4	1	2	3	4	5	6	7
Appeared normal	1	1	0	0	0	0				
Hyporeactive	0	0	1	1	1	0				
Red stained face	0	0	0	1	1	0				
Brown stained Anal Area	0	0	0	1	1	0				
diarrhea	0	0	0	1	1	0				
Hypothermic to touch	0	0	0	0	1	0				
Deaths	0	0	0	0	0	0	1			
Technician	deb	deb	ebck	smm	smm					
Date	1985	2/5	2/5	2/5	2/6	2/7	2/8			

DOSAGE CALCULATIONS

Ave. Bulk Density
0.89 g/ml
 Temp. of Test Material
23 C
 Dose Level Dose
 Bulk Density = Volume
 $\frac{20.0 \text{ g/kg}}{0.89 \text{ g/ml}} = 22.47 \text{ ml/kg}$
 Tech. deb 2/5/85

See Dosage Calculation Sheets.

Dosage	20.0 (g/kg)		Dose Time: 10:15 a.m.		
Dose Volume	22.47 (ml/kg)		Tech	Date	Scale Used:
Animal No./Ear Tag No.	C1-3367	3355	SP	2/4	NA
Prefasted Body Weight (g)	245	243	SP	2/4	Ktron 5228
Fasted Body Weight (g)	227	224	deb	2/5	Ktron 5228
Actual Dose (ml)	5.1	5.0	deb	2/5	NA
Day 7 Body Weight (g)	* NA				

Verified By msr 2/12/85

NA = Not applicable
 NE = Not evident

*-Doseage calculated but not administered
 unused animal returned to stock.

① Animal died 2-7-85, 2-27-85 smm

Reviewed By MW 2-19-85

ACUTE ORAL TOXICITY (UP AND DOWN) PROCEDURE

Past Article: G0506.01 ET No. 50106723
 Dosage Level: 20.0 g/kg Vehicle: NA
 Species Rat Source Harlan Date Received 1-22-85
 Fasted: Date 2-11-85 Time 2:45 Tech. smm Room No. 3 Sex F

CLINICAL OBSERVATIONS

Observations	Hours			DAYS						
	1/2	2	4	1	2	3	4	5	6	7
Appeared normal	1	0	0	0	0	0	1	1	1	1
Diarrhea	0	1	1	1	1	1	0	0	0	0
Hyporeactive	0	0	1	0	0	0	0	0	0	0
Red stained face	0	0	0	1	1	1	0	0	0	0
Dark stained anal area	0	0	0	0	1	1	0	0	0	0
/										
Deaths										
Technician	smm	smm	smm	smm	smm	smm	smm	smm	smm	smm
Date	1985 2/12	2/12	2/12	2/13	2/14	2/15	2/16	2/17	2/18	2/19

DOSAGE CALCULATIONS

Ave. Bulk Density 0.89 g/ml
 Temp. of Test Material 23 C
 Dose Level Dose
 Bulk Density = Volume
 $\frac{20.0 \text{ g/kg}}{0.89 \text{ g/ml}} = 22.47 \text{ ml/kg}$
 Tech. smm 2/12/85
 See Dosage Calculation Sheets.

Dosage	20.0 (g/kg)		Dose Time: 11:00 a.m.			
Dose Volume	22.47(ml/kg)		Tech	Date	Scale Used:	
Animal No./Ear Tag No.	C2-9290	9393	smm	2-11	NA	
Prefasted Body Weight (g)	209	210	smm	2-11	LTPON 1349	
Fasted Body Weight (g)	195	196	smm	2-12	KTRON 1349	
Actual Dose (ml)	44	44	smm	2-12	NA	
Day 7 Body Weight (g)	*	208	smm	2-19	KTRON 5224	

Verified By pyr 2/12/85

NA = Not applicable
 NE = Not evident

*-Dosage calculated but not administered unused animal returned to stock.

Reviewed By MW 2-19-85

ACUTE ORAL TOXICITY (UP AND DOWN) PROCEDURE

Test Article: G0506.01 RT No. 50106723
 Dosage Level: 22.3g/kg Vehicle: NA
 Species Rat Source Harlan Date Received 12-24-84
 Fasted: Date 1-29-85 Time 3:00 AM Tech. SPM Room No. 3 Sex ♀

CLINICAL OBSERVATIONS

Observations	Hours			DAYS						
	1/2	2	4	1	2	3	4	5	6	7
Appeared normal	1	0	0	0	0	0	0			
Purrrhea	0	1	1	1	1	1	0			
Brown stained anal region	0	0	1	1	1	1	0			
Red stained nose and mouth	0	0	0	1	1	1	0			
Ataxic gait	0	0	0	0	0	1	0			
Ataxia	0	0	0	0	0	1	0			
Piloerection	0	0	0	0	0	1	0			
Deaths	0	0	0	0	0	0	1			
Technician	SPM	SPM	SPM	SPM	SPM	CK	CK			
Date	1985	1/30	1/30	1/30	1/31	2/1	2/2	2/3		

DOSAGE CALCULATIONS

Ave. Bulk Density
0.89 g/ml
 Temp. of Test Material
23 C
 Dose Level = Dose
 Bulk Density = Volume
 $\frac{22.3 \text{ g/kg}}{0.89 \text{ g/ml}} = \frac{25.1 \text{ ml/kg}}$
 Tech. SPM 1-30-85

See Dosage Calculation Sheets.

Dosage	<u>22.3 (g/kg)</u>	Dose Time: <u>9:00 a.m.</u>			
Dose Volume	<u>25.1 (ml/kg)</u>	Tech	Date	Scale Used:	
Animal No./Ear Tag No.	<u>3370</u>	<u>3369</u>	<u>SPM</u>	<u>1-29</u>	<u>NA</u>
Prefasted Body Weight (g)	<u>256</u>	<u>241</u>	<u>SPM</u>	<u>1-29</u>	<u>KTRCN 5228</u>
Fasted Body Weight (g)	<u>239</u>	<u>228</u>	<u>SPM</u>	<u>1-30</u>	<u>KTRCN 5228</u>
Actual Dose (ml)	<u>6.0</u>	<u>5.7</u>	<u>SPM</u>	<u>1-30</u>	<u>NA</u>
Day 7 Body Weight (g)	<u>*</u>	<u>NA</u>			

0.22 2-3-85
 ml Verified By deb 1-30-85
 2-20-85

NA = Not applicable
 NE = Not evident

*-Dose calculated but not administered
 unused animal returned to stock.

Reviewed By MH 2-19-85

① Diagonal line on day 4 - entry error. MH 2/19/85

ACUTE ORAL TOXICITY (UP AND DOWN) PROCEDURE

Test Article: G0586.01 RT No. 50106723
 Dosage Level: 22.3 g/kg Vehicle: NA
 Species Rat Source Harlan Date Received 12-24-84
 Fasted: Date 1-31-85 Time 2:00 Tech. SPM Room No. 3 Sex ♂

CLINICAL OBSERVATIONS

Observations	Hours			DAYS						
	1/2	2	4	1	2	3	4	5	6	7
Appeared normal	1	0	0	0	0	0				
Diarrhea	0	1	1	1	1	0				
Brown fecal material	0	0	1	1	1	0				
Hyperactive	0	0	1	1	1	0				
Red stained face	0	0	0	0	1	0				
Deaths	0	0	0	0	0	1				
Technician	SPM	SPM	SPM	CK	CK	ML				
Date	1985	2/1	2/1	2/1	2/2	2/3	2/4			

DOSAGE CALCULATIONS

Ave. Bulk Density
0.89 g/ml
 Temp. of Test Material
23 C
 Dose Level Dose
 Bulk Density = Volume
22.3 g/kg = 25.1 ml/kg
0.89 g/ml
 Tech. SPM 2-1-85
 See Dosage Calculation Sheets.

Dosage	<u>22.3 (g/kg)</u>	Dose Time: <u>8:50 a.m.</u>				
Dose Volume	<u>25.1 (ml/kg)</u>	Tech	Date	Scale Used:		
Animal No./Ear Tag No.	<u>02-3257 3270</u>	<u>SPM</u>	<u>1-31</u>	<u>NA</u>		
Prefasted Body Weight (g)	<u>291 290</u>	<u>SPM</u>	<u>1-31</u>	<u>KTCN 1343</u>		
Fasted Body Weight (g)	<u>267 265</u>	<u>SPM</u>	<u>2-1</u>	<u>KTCNS229</u>		
Actual Dose (ml)	<u>6.7 6.7</u>	<u>SPM</u>	<u>2-1</u>	<u>NA</u>		
Day 7 Body Weight (g)	<u>NA *</u>	<u>NA</u>				

Verified By SG 2-1-85

NA = Not applicable
 NZ = Not evident

*-Dosage calculated but not administered
 unused animal returned to stock.

Reviewed By MMH 2-19-85

ACUTE ORAL TOXICITY (UP AND DOWN) PROCEDURE

Test Article: G0506.01 RT No. 50106723
 Dosage Level: 22.3 g/kg Vehicle: NA
 Species Rat Source Harlan Date Received 12-24-84
 Fasted: Date 2-7-85 Time 4:19 Tech. CK Room No. 3 Sex ♂

CLINICAL OBSERVATIONS

Observations	Hours			DAYS						
	1/2	2	4	1	2	3	4	5	6	7
Appeared normal	1	0	0	0	0	0	0	0	1	1
Red stained on face	0	1	1	0	1	1	1	1	0	0
Diarrhea	0	1	1	0	1	1	1	1	0	0
Dark stained anal area	0	0	0	1	1	1	1	1	0	0
Hypoactive	0	0	0	0	0	1	1	0	0	0
/										
Deaths										
Technician	SP	SP	SP	SP	SP	SP	SP	SP	SP	SP
Date	1985 2/3	2/9	2/5	2/9	2/10	2/11	2/12	2/13	2/14	2/15

Dumping error 2:5-55gpm

DOSAGE CALCULATIONS

Ave. Bulk Density
0.89 g/ml
 Temp. of Test Material
23 C
 Dose Level Dose
 Bulk Density = Volume
22.3 g/kg = 25.1 ml/kg
0.89 g/ml
 Tech. SPM 2-9-85

See Dosage Calculation Sheets.

Dosage	22.3 (g/kg)	Dose Time: 10:50 a.m.			
Dose Volume	25.1 (ml/kg)	Tech	Date	Scale Used:	
Animal No./Ear Tag No.	62-7600 / 7599	CK	2/7	NA	
Prefasted Body Weight (g)	238 / 258	CK	2/7	KTRON 5229	
Fasted Body Weight (g)	221 / 239	SPM	2/8	KTRON 5229	
Actual Dose (ml)	5.5 / 6.0	SPM	2/8	NA	
Day 7 Body Weight (g)	* / 243	SPM	2/15	KTRON 5229	

Verified By ALB 2-8-85

NA = Not applicable
 NE = Not evident

*-Dosage calculated but not administered
 unused animal returned to stock.

Reviewed By MAH 2-19-85

PROTOCOL NO. C1B

UP AND DOWN PROCEDURE FOR ESTIMATING
ACUTE ORAL TOXICITY (LD₅₀) IN RATS

Issue Date: May 1, 1984
Supersedes Issue Dated: May 4, 1983

Test Substance Identification Number (TSIN) # E 0506101

Divisional Request Document Number (DRD # BYU0372

Sponsor: The Procter & Gamble Company
Cincinnati, Ohio

Testing Facility: Hazleton Laboratories America, Inc. Study # 50106723
(To be filled in by Operations Section) P. O. Box 7545 (To be filled in by Testing Facility)
Madison, Wisconsin 53707

Purpose: To estimate the lethality (LD₅₀ value) and acute symptoms to a test substance by using a small number of rats.

Justification for Selection of Test System: The rat is the animal classically used for toxicity testing due to its small size, ready availability, and the large amount of back-ground data.

Route of Administration of Test Substance and Reason for Choice: By gavage. This is a method for administering a known quantity of test substance and has been the historically chosen route.

Diet and/or Water Analyses Required: None (no known contaminants expected which would interfere with this study).

Records to be Maintained: All records that would be required to reconstruct the study and demonstrate adherence to protocol.

PROTOCOL C1BUP AND DOWN PROCEDURE FOR ESTIMATING
ACUTE ORAL TOXICITY (LD₅₀) IN RATS

Issue Date: May 1, 1984

Test Substance(s)

<u>TSIN #</u>	<u>DRD Number</u>	<u>Description</u>		<u>Expiration Date</u>
		<u>Color</u>	<u>Physical Form</u>	
G0506.01	81CR0372	azura blue	viscous liquid	1/9/86

Storage Conditions: (Check one)

Room temperature Refrigerator Freezer
 Other

Hazards: (Check one)

None known. Take ordinary precautions in handling.
 As follows:

Special Instructions: (Check one)

None
 As follows: *If the first animal (dosed at 20g/kg) lives,
 contact the Divisional Toxicologist for instructions.*

Animals:

A sufficient number of female rats, Sprague-Dawley (CD), 190-300 grams prefasted weight. (See Options, page 4)

Animal Care and Diet:

Follow the approved Standard Operating Procedures of the Test Facility.

Environmental
Conditions:

Follow the approved Standard Operating Procedures of the Test Facility.

AnimalIdentification:

Follow the approved Standard Operating Procedures of the Test Facility.

Animal Selection:

Determine prefasted body weights and select animals weighing 190-300 grams for study.

PROTOCOL C1B

UP AND DOWN PROCEDURE FOR ESTIMATING
ACUTE ORAL TOXICITY (LD₅₀) IN RATS

Issue Date: May 1, 1984

Dose Preparation:

(Check appropriate box)

- Dose test substance undiluted.
 Dose as a freshly prepared _____ % (w/w)
solution/suspension of test substance in _____
 Dose as a freshly prepared _____ % (w/v)
solution/suspension of test substance in _____
 Dose per Special Instructions (see page 2)
 Save solution for dosing.

Note

A concentration analysis of the test substance-vehicle mixture(s) will ; will not be required.

If a concentration analysis is required.

- Prepare a sufficient quantity of the test substance - vehicle mixture(s) so that a portion can be returned to the Sponsor's Divisional Toxicologist. Store solution/mixture at room temperature; refrigerator; freezer; other _____

Shipping Instructions

Send approximately _____ ml. Send frozen; under ambient conditions; other _____

- Analyze the test substance - vehicle mixtures(s) for test substance concentration using the analytical method in Appendix _____.

Dosing Instructions:

Deprive the animals of food for 18-20 hours before administering the test substance. Determine fasted body weights. Calculate the dose for each animal according to fasted body weight to give the specified quantities of test substance per unit of body weight.

The test substance, at the concentration specified under "Dose Preparation", will be gavaged following the Test Facility's Standard Operating Procedures. Record all information necessary to document animal weights and volume of test substance administered to each animal. If high dose levels require dose volumes which exceed 25 ml/kg, contact Sponsor's Divisional Toxicologist for further instructions.

PROTOCOL C1BUP AND DOWN PROCEDURE FOR ESTIMATING
ACUTE ORAL TOXICITY (LD₅₀) IN RATS

Issue Date: May 1, 1984

Dosing Instructions
(Cont'd):Estimated LD₅₀ value of the undiluted test substance:
20 g/kg

Dose one animal at a time starting at estimated LD₅₀. Observe each animal for a minimum of 24 hours. (A longer observation time may result when a weekend intervenes before the next animal is dosed.) If the animal dies or is moribund*, decrease the dose for the next animal. If the animal survives and appears well increase the dose. When feasible, use a dose multiplier of 1.3. After reversal of initial outcome, i.e. the point where an increasing dose pattern is required to be decreased by a death or a decreasing dose pattern is required to be increased by a survival, dose an additional 4 animals and then stop. In each case, the next dose will be increased or decreased, depending upon the fate of the previous animal.

If 10 animals have been dosed with no deaths within 24 hours but delayed deaths are observed in 3 or more animals, stop the procedure. A delayed death is defined as an animal which did not die or appear moribund within about 24 hours but died later during the observation period. Report that an LD₅₀ could not be determined using this procedure.

Immediately after dosing, return the animal to ad libitum feeding.

*(such as shallow labored or irregular respiration, muscular weakness or tremors, absence of voluntary responses to external environmental stimuli, cyanosis and coma)

Observations:

Observe all animals for mortality and pharmacotoxic symptoms at frequent intervals during the first 4 hours after dosing (at least once during the first 30 minutes) and daily thereafter for the next 7 days. Record all pharmacotoxic symptoms and time of death. On all animals that die, perform a gross necropsy following the Test Facility's Standard Operating Procedures. Seven days after dosing weigh and perform a gross necropsy on the surviving animals. Record all findings. Discard animals following the Test Facility's Standard Operating Procedures.

[] Option A

No follow-up in males.

PROTOCOL C1BUP AND DOWN PROCEDURE FOR ESTIMATING
ACUTE ORAL TOXICITY (LD₅₀) IN RATS

Issue Date: May 1, 1984

Observations
(Cont'd): Option B

Run concurrently in both sexes, using males of the same strain and body weight range as specified on page 2 for females.

 Option C

Follow-up in males using the same strain and body weight as females: Dose 6 males at LD₅₀ dose estimated from females.

1. If the number of animals dying is 0, report that with 95% confidence the LD₅₀ value for males exceeds the administered dose.
2. If 1-2 animals die, report that the estimated LD₅₀ value for males exceeds the administered dose.
3. If 3 animals die, report that the estimated LD₅₀ value for males equals the administered dose.
4. If 4-6 animals die, report that the estimated LD₅₀ value for males is less than the administered dose.

 Option D

Follow-up in males: Same as Option C except if 6 of 6 die, execute the up-and-down procedure described in this protocol using males.

Report:

Report dates of study initiation and termination. Report individual dose levels, body weights, mortality, pharmacotoxic signs, gross necropsy results, etc., where appropriate. Calculate the LD₅₀ using the maximum likelihood method.* This may be done with the computer program MAXLIK, the NLIN procedure of SAS or BMDP program 3R. A historical estimate of sigma will be required; the value 0.12 should be used. Program output is an estimate of the logarithm of the LD₅₀ and its standard error. The LD₅₀ should be calculated as $LD_{50} = 10^{10^{\log LD_{50}}}$. An approximate 95% confidence interval (based upon historical data) should be calculated by substituting $\log LD_{50} \pm 1.96$ (std. error of $\log LD_{50}$) in the above equation. Report the LD₅₀ and its approximate 95% confidence interval as gm/kg based on test substance. The method of calculation used should be specified in the final report.

* D.J. Finney, Probit Analysis, 3rd Ed., Cambridge Univ. Press 1971, pp.50-80.

PROTOCOL C1B

UP AND DOWN PROCEDURE FOR ESTIMATING
ACUTE ORAL TOXICITY (LD₅₀) IN RATS

Issue Date: May 1, 1984

Report (Cont'd):

This report shall conform to all requirements outlined in Section 58.185, Subpart J, Good Laboratory Practices Regulations.

Sponsor: Caroline Cardin
Divisional Toxicologist

Date Approved by Sponsor's Divisional Toxicologist 1/16/85

Proposed Starting Date: Week of 1/28/85)

Defined as First Compound Administration)

Proposed Completion Date: Week of 3/04/85)

Defined as Submission of final report)To be completed
by the Test
Facility

Study Director: Wayne A. Madison)

Date: 1/25/85)

Study Cost: \$840.00)

BEAUTY CARE DIVISION
TEST SUBSTANCE CHARACTERIZATION REPORT*
 (TSCR)

For Your Office
 Use Only:
 BRD # BK0372
 TSTR # C4506.61

1. Test Article Name (should agree with BRD): B65 EC-3b Normal/Dry formula with 0.3% Octopirox
2. Making Notebook Ref. (with Plant Production Code if applicable): QC-0106-53A
3. Date Made: 1/9/85 Made by: S. K. McQueary Lab: 1B20
4. Physical Form: Viscous Liquid Color: Aqua-Blue Density: 0.99g/cc
5. Water Solubility: >50 % (wt/wt)
 For SENS test only - Ethanol Solubility: >50 % (wt/wt)
 Acetone Solubility: >50 % (wt/wt)
6. Sample Expiration Date: 1/9/86 Stability Testing is: [] Completed [x] In Progress
7. Hazards: None Storage Conditions: Ambient (50-90°F)
8. D.O.T. Classification (see Regulatory Personnel): Not Hazardous
9. Microbial Susceptibility Classification Approval: David Brainin DBS 1-15-85
 (Name) 1/10/85 (Date) (Signature)
10. Making Data: List ingredients in descending order of predominance. ---
 (For drug products list active ingredient(s) first.)

#	RAW MATERIAL NAME	NOMINAL %	ACTUAL %	RMS # -LOT
1	OCTOPIROX	0.3000	0.3007	BX-288-1
2	DND WATER	90.7270	90.7124	BX-158-2
3	STEDBAC	1.6000	1.6002	45595-3
4	DETAC	1.6000	1.6007	45570-6
5	CETYL ALCOHOL	1.3500	1.3505	48026-2
6	STEARYL ALCOHOL	1.3500	1.3505	48048-7
7	CETETH-2	0.8000	0.8001	45455-10
8	STEARETH-21	0.6000	0.6007	BX-076-2
9	PROTEIN D	0.5000	0.5007	48040-8
10	SMS	0.5000	0.5004	45601-37
11	STEARETH-2	0.4000	0.4004	BX-241-2
12	FLORIEM PLUS PERFUME	0.1000	0.0997	KF-305-3
13	CITRIC ACID	0.0800	0.0900	45076-14
14	FD&C BLUE #1 SOL'N	0.0600	0.0600	56510-10
15	KATHON CB	0.0330	0.0327	45572-4
TOTALS		100.0000	100.0000	

Comments on Making Data:

Packed in 16 oz. Cylinder Round Bottles (pn-008-9)
 Caps (pn-088-8)

Comments on Making Data: _____

*Submit typed original with BRD. Include copy of making records.

Issue Date 3/84

**TEST SUBSTANCE CHARACTERIZATION REPORT
(TSCR)**

For Test Office
Use Only:
DSD # 01-100-10
TSCN # 0100-01

11. Characterization, Microbial and Properties Information:

	Date Submitted	Submitter Code (if exists) or Lab Notebook #	Component or Property	(✓)	Measured Value	Units	Testing Lab or Data Source
1	1/9/85	JM 101	act	✓	Pass 24/25K	Must Pass	
2	1/9/85	OC-0106-31A	X Octopirox		.32	0.25-0.25	1821
3	1/10/85	B306-0366	quat		.43	0.37 - 0.43	Anal.
4	1/9/85	OC-0106-51A	ph		2.60	2.2-2.8	1821
5							
6							
7							
8							
9							
10							
11							
12							
13							
14							
15							

12. Approvals:

The test substance as made and characterized is a representative example of the intended formulation. Making records for plant-made product should be obtained and evaluated by Products Research.

a. Process Development: ADM. ADM. 1/13/85 (Signature) DW McLEOD (Name) 1/13/85 (Date)

b. Products Research: [Signature] (Signature) T.J. Reynolds (Name) 1/13/85 (Date)

finished product samples will be retained by Quality Assurance.
samples

c. QP-Quality Assur.: [Signature] (Signature) (Name) 1/13/85 (Date)

13. The characterization tests requested are appropriate and the test substance is acceptable for: acute animal test; subchronic animal test; chronic animal test; human safety test; in vitro test; environmental safety test.

Cassie Rardin (Toxicologist's Signature) CASSIE RARDIN (Name) 1/15/85 (Date)

TSCR Distribution: Original - Test Office; Copies - Toxicologist, QP/QA, Products Research and Process Dev.

TO Operations Section - MVL RETENTION (LIMIT) NON-REGULATORY
SUBJECT NONCLINICAL STUDY - REGULATORY ATTENTION
STATUS

Notifications pertaining to:

IND # BY12072
TSIN 60506.01

1. Studies requested on the above document:
 - are expected to be submitted to the following regulatory agencies as a GLP regulated study: FDA
 - are expected to be submitted to the following regulatory agencies but is not a GLP regulated study: _____
 - Metabolism, Pharmacological Screen, Other: _____
 - are not expected to be submitted to a regulatory agency. (Boxes #3 and #4 below need not be checked).
2. - The test substance has been characterized and results are shown on the test substance characterization report which accompanies the IND.
3. - The method of synthesis fabrication or derivation of the test related substances has been documented. (Required for regulated studies).
4. - Stability testing has been done or will be done on the test substance. (Required for regulated studies).

Sponsor's Divisional Toxicologist: Cassius Rardin

Date: 1/10/85

By: NEQUAZ