



PPG Industries, Inc.  
One PPG Place  
Pittsburgh, PA 15272 USA

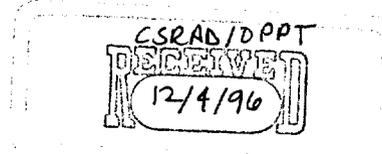
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96 OCT 17 AM 8:10

R. Kenneth Lee  
Manager, Product Safety  
Environment, Health & Safety  
Chemicals  
(412) 434-2604  
FAX: (412) 434-2137



8EHQ-96-13765



October 15, 1996

Certified Mail

Document Processing Office  
(TS-790)

8EHQ-1096-13765

US EPA  
401 M Street, SW  
Washington, DC 20460  
Attention: Section 8e Coordinator

(A)

Dear Sir,

PPG Industries is submitting the following new information on pentabutylguanidine (CAS No. 114591-53-6) pursuant to TSCA Section 8(e). This information comes from an acute dermal toxicity study conducted with rabbits (attached). Dose levels of 25, 50 and 100 mg/kg were selected for testing. This testing was done in accordance with GLP standards as defined by EPA and OECD except the verification of the test material. Based upon the test results the single dose acute dermal defined LD-50 of the test substance is 52 mg/kg of bodyweight when applied as received. The test material is not on the TSCA inventory. Please find attached the test report from Product Safety Labs. There are no Confidential claims.

Please also find attached an acute oral and skin corrosion study, as well as the current Experimental Product Data Sheet.

Should you require additional information, please contact my office or Dr. Heather Burleigh-Flayer at 412-434-2245.

Yours very truly,

R. Kenneth Lee



8897000015

Attachments

96 OCT 23 PM 12:05

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10/23/96



# product safety labs

725 Cranbury Road • East Brunswick, New Jersey 08816-3206 • 908-254-9200 • 800-425-0002 • Fax-908-254-6736

October 2, 1996

TO: Heather Burleigh-Flayer, Ph.D.  
**PPG**  
One PPG Place  
Pittsburgh, PA 15272

FROM: Leslie R. Kohn  
Administrative Assistant

RE: **INVOICE & REPORT**

Enclosed please find the following:

STUDY NO.	INVOICE NO.	PRICE	PSL NO.	TEST	PRODUCT ID
4615	14662	\$4,050	E60722-1R	Acute Dermal Tox LD <sub>50</sub>	Pentabutylguanidine Lot 737-210
"	"	\$ 45	"	Sample Return	"

If you have any questions, please call Gary Wnorowski, our Study Director.

\_\_\_\_\_  
LRK



## ACUTE DERMAL TOXICITY DEFINED LD<sub>50</sub>

**PROTOCOL NO.:** P322

**AGENCY:** EPA (TSCA) & OECD

**STUDY NUMBER:** 4615

**SPONSOR:** PPG INDUSTRIES, INC.  
One PPG Place  
Pittsburgh, PA 15272

**PRODUCT IDENTIFICATION:** Pentabutylguanidine, Lot #737-210

**PRODUCT DESCRIPTION:** Amber liquid

**DATE RECEIVED:** July 22, 1996

**PSL REFERENCE NO.:** E60722-1R

**DATE OF PROTOCOL APPROVAL:** July 22, 1996

**DATES OF ADMINISTRATION:** August 2, 19 and 29, 1996

**TERMINATION OF IN-LIFE PHASE:** September 3, 1996

**STUDY COMPLETION DATE:** September 30, 1996

**NOTEBOOK NO.:** 96-35: pages 72-124

### 1. PURPOSE:

To determine the Acute Dermal Defined LD<sub>50</sub> of Pentabutylguanidine, Lot #737-210. Data from this study may be used as a basis for classification and labeling.

### 2. SUMMARY:

An Acute Dermal Toxicity test was conducted with rabbits to determine the potential for Pentabutylguanidine, Lot #737-210 to produce toxicity after topical application. Based on the results of this study, the single dose Acute Dermal Defined LD<sub>50</sub> of the test substance is 52 mg/kg of bodyweight when applied as received.

After acclimation to the laboratory, 30 healthy rabbits were selected for test and equally distributed into three dose groups of five males and five females each. Dose levels of 25, 50 and 100 mg/kg were selected for testing. For each test group, the test substance was applied to the skin for 24 hours. The test animals were observed for signs of gross toxicity and

behavioral changes at least once daily for 14 days or until mortality. Bodyweights were recorded prior to application and again on days 7 and 14 or after death. Necropsies were performed on all animals.

The incidence of mortality at each dose level is summarized below:

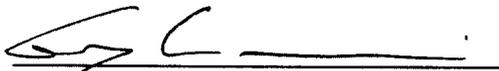
Dose Level mg/kg	Mortality		
	Males	Females	Total
25	1/5	0/5	1/10
50	3/5	1/5	4/10
100	5/5	5/5	10/10

Following application, animals from all dose levels exhibited one or more of the following clinical signs: abnormal posture, hypoactivity, irregular respiration and/or ano-genital staining. Dermal irritation (erythema, edema and eschar) was also noted at all dose sites between days 1 and 14. Apart from soft feces and reduced fecal volume evident in one female from the 50 mg/kg dose level on days 8 and 9, all surviving animals recovered from the above symptoms by day 2. Although this female also lost bodyweight through day 7, all surviving animals gained weight over the entire 14-day observation period. Gross necropsy of the decedents revealed discoloration of the lungs, liver, spleen and intestines and/or edema of the lungs. Pink or clear fluid in the thoracic cavity and light yellow fluid in the abdominal cavity were also present in several decedents from the 25 and 50 mg/kg dose groups. Gross necropsy findings at terminal sacrifice were unremarkable.

## Pentabutylguanidine, Lot #737-210

ACUTE DERMAL TOXICITY DEFINED LD<sub>50</sub>

This study meets the requirements of Good Laboratory Practice Standards as defined by EPA (TSCA)-40 CFR Part 792 and OECD-C(81) 30 (Final) Annex 2 with the following exception: The stability, characterization, identity and verification of the test substance concentration as received and tested are the responsibility of the study sponsor.



Gary Wnorowski, B.A.  
Study Director

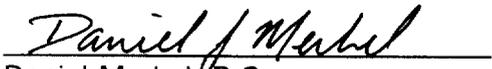
Sep 30, 1996  
Date

We the undersigned declare that the methods, results and data contained in this report faithfully reflect the procedures and raw data used or collected during the study.



Jacek Ochalski, D.V.M.  
Principal Toxicology Technician

Sep. 30. 1996  
Date



Daniel Merkel, B.S.  
Assistant Toxicology Technician

September 30, 1996  
Date

**3. MATERIALS:****A. Test Substance:**

The test substance identified as Pentabutylguanidine, Lot #737-210 was received on July 22, 1996 and was further identified with PSL Code Number E60722-1R. The test substance was an amber liquid and was stored at room temperature. The sample was applied as received. Documentation of the methods of synthesis, fabrication, or derivation of the test substance is retained at PPG Chemicals Technical Center, Monroeville, PA.

Characterization of the test substance as provided to Product Safety Labs by the sponsor was:

**Composition:** Pentabutylguanidine - 96.3%  
Tetrabutylurea - 3.1%

**pH:** 11.0

**Solubility:** Soluble in methanol, ethanol, acetone and mineral oil

**Stability:** Stable

**Expiration Date:** None

**B. Animals:**

**3.B.1 Number of Animals:** 30

**3.B.2 Sex:** 15 males and 15 females

**3.B.3 Number of Animals/Dose Level:** 5 males and 5 females/dose level

**3.B.4 Species/Strain:** Rabbit/New Zealand albino

**3.B.5 Age/Bodyweight:** Young adult/males 2.3-2.7 kilograms and females 2.4-2.8 kilograms at initiation

**3.B.6 Source:** Received from Davidson's Mill Farm, South Brunswick, NJ on July 26, August 9 and 19, 1996

**4. METHODS:****A. Husbandry:**

**4.A.1 Housing:** The animals were singly housed in suspended stainless steel caging with mesh floors which conform to the size recommendations in the Guide for the Care and Use of Laboratory Animals DHEW (NIH) No. 86.23. Litter paper was placed beneath the cage and was changed at least three times per week.

**4.A.2 Animal Room Temperature Range:** 66-71 °F

**4.A.3 Photoperiod:** 12 hour light/dark cycle

**4.A.4 Acclimation Period:** 7 or 10 days

**4.A.5 Food:** Pelleted Purina Rabbit Chow #5326

**4.A.6 Water:** Filtered tap water was supplied *ad libitum* by automatic water dispensing system.

**4.A.7 Contaminants:** There were no known contaminants reasonably expected to be found in the food or water at levels which would have interfered with the results of this study. Analyses of the food and water are conducted at least once a year and the records are kept on file at Product Safety Labs. The dates of the most recent analyses are presented in Appendix A.

**B. Identification:**

**4.B.1 Cage:** Each cage was identified with a cage card indicating at least the study number and identification and sex of the animals.

**4.B.2 Animal:** A number was allocated to each rabbit on receipt and a stainless steel ear tag bearing this number was attached to the animal. This number, together with a sequential animal number assigned to study 4615, constituted unique identification.

**5. PROCEDURE:**

**A. Selection of Animals:**

On the day before dosing, each group of animals was prepared by clipping the dorsal area and the trunk. After clipping and prior to application, the animals were examined for health, weighed (initial) and the skin checked for any abnormalities. Ten (five male and five female) healthy rabbits were selected for each test.

**B. Dose Calculations:**

Individual doses were calculated based on the initial bodyweights, taking into account the specific gravity (determined by PSL) of the test substance.

**C. Application of Test Substance:**

The appropriate amount of the test substance (25, 50 or 100 mg/kg) was applied evenly over a dose area ranging from approximately 1 (25 mg/kg) to 6 (100 mg/kg) square inches and covered with a 4x8", 6-ply gauze pad. The gauze and entire trunk of each animal were then wrapped with 3" Durapore tape to avoid dislocation of the pad and to minimize evaporation of the test substance. Elizabethan collars were placed on each rabbit and they were returned to their designated cages.

After 24 hours of exposure to the test substance, the pads and collars were removed and the test sites gently wiped with 95% ethanol then water, using a clean towel to remove any residual test substance.

**D. Bodyweights:**

Individual bodyweights of the animals were recorded prior to test substance application (initial) and again on days 7 and 14 or after death (See Tables 2, 5 and 8).

**E. Cage-Side Observations:**

The animals were observed for signs of gross toxicity and behavioral changes at least once daily for 14 days or until mortality. Observations included gross evaluation of skin and fur, eyes and mucous membranes, respiratory, circulatory, autonomic and central nervous systems, somatomotor activity and behavior pattern. Particular attention was directed to observation of tremors, convulsions, salivation, diarrhea and coma (See Table 3, 6 and 9).

**F. Necropsy:**

Surviving rabbits were euthanized via sodium pentobarbital injection on day 14. A gross necropsy was performed on all decedents and euthanized animals. Tissues and organs of the thoracic and abdominal cavities were examined (See Tables 4, 7 and 10).

**6. STUDY CONDUCT:**

This study was conducted at Product Safety Labs, 725 Cranbury Road, East Brunswick, NJ 08816, to comply with good laboratory practices as defined in 40 CFR 792: U.S. EPA Good Laboratory Practice Standards: Toxic Substances Control Act (TSCA) and OECD Principles of Good Laboratory Practice C(81)30 (Final) Annex 2.

The procedures employed were based on Health Effects Testing Guidelines, Subpart B: Acute Dermal Toxicity, 40 CFR 798.1100 and OECD Guidelines for Testing of Chemicals, Procedure 402.

**7. QUALITY ASSURANCE:**

The final report was audited for agreement with the raw data records and for compliance with the protocol, Product Safety Labs Standard Operating Procedures and appropriate Good Laboratory Practice Standards. Dates of inspections and audits performed during the study, and the dates of reporting of the inspection and audit findings to the Study Director and Facility Management are presented in the Quality Assurance Statement.

**8. DEVIATIONS FROM FINAL PROTOCOL: None**

**9. RECORDS TO BE MAINTAINED:**

A copy of this signed report, together with the protocol and all raw data generated at Product Safety Labs, is retained in the Product Safety Labs Archives.

**10. RESULTS:****25 mg/kg**

One male died within 13 days of test substance application. Irregular respiration was observed prior to death. Several surviving rabbits also exhibited irregular respiration. Apart from dermal irritation (erythema, edema and eschar) noted at all dose sites between days 1 and 14, the affected animals recovered by day 2 and gained weight over the 14-day observation period. Gross necropsy of the decedent revealed discoloration of the lungs, liver and intestines, edema of the lungs, light yellow fluid present in the abdominal cavity and pink fluid present in the thoracic cavity. Gross necropsy findings at terminal sacrifice were unremarkable. All tissues and organs appeared normal.

**50 mg/kg**

Three males and one female died within 23 hours of test substance application. Toxic signs prior to death included hypoactivity and/or irregular respiration. The surviving rabbits exhibited hunched posture, irregular respiration and/or ano-genital staining. Dermal irritation (erythema, edema and eschar) was also noted at all dose sites between days 1 and 14. Apart from soft feces and reduced fecal volume evident in one female on days 8 and 9, all animals recovered from the above symptoms by day 2. Although this female also lost bodyweight through day 7, all surviving rabbits gained weight over the entire 14-day observations period. Gross necropsy of the decedents revealed discoloration of the lungs, liver, spleen and/or intestines. A small amount of clear fluid was also present in the thoracic cavity of one female decedent. Gross necropsy findings at terminal sacrifice were unremarkable. All tissues and organs appeared normal.

**100 mg/kg**

All animals died within 3 hours of test substance application. Toxic signs prior to death included hypoactivity, irregular respiration and/or a prone posture. Gross necropsy of the decedents revealed discoloration of the lungs and intestines and/or edema of the lungs.

- A. **Summary of Mortality Data:** See Table 1
- B. **Individual Bodyweight, Dosage and Mortality:** See Tables 2, 5 and 8
- C. **Individual Cage-Side Observations:** See Tables 3, 6 and 9
- D. **Individual Necropsy Observations:** See Tables 4, 7 and 10

**11. CONCLUSION:**

Based on the findings summarized above, the Acute Dermal Defined LD<sub>50</sub> of Pentabutylguanidine, Lot #737-210 calculated by Probit Analysis was 52 milligrams of the test substance per kilogram of bodyweight (when applied as received) with 95% Confidence Limits of 75 mg/kg (upper) and 36 mg/kg (lower). Calculated separately, the LD<sub>50</sub> for each sex was 42 mg/kg with 95% Confidence Limits of 71 mg/kg (upper) and 25 mg/kg (lower) for the males and 56 mg/kg with 95% Confidence Limits of 70 mg/kg (upper) and 45 mg/kg (lower) for the females.

TABLE - 1

SUMMARY OF MORTALITY DATA

Dose Level	Mortality		
mg/kg	Males	Females	Total
25	1/5	0/5	1/10
50	3/5	1/5	4/10
100	5/5	5/5	10/10
	Males <sup>1</sup>	Females <sup>1</sup>	Total <sup>1</sup>
LD <sub>50</sub>	42	56	52
	95% Confidence Limits		
Upper:	71	70	75
Lower:	25	45	36

<sup>1</sup> LD<sub>50</sub> calculated by the Litchfield-Wilcoxon Method of Probit Analysis; Litchfield, J.T., F.W. Wilcoxon. J. Pharmacology and Experimental Therapeutics 96:99-115 (1949).

TABLE - 2

INDIVIDUAL BODYWEIGHT, DOSAGE AND MORTALITY

DOSE LEVEL: 25 mg/kg

Animal No.	Sex	Bodyweight (kg)			Actual Dose <sup>1</sup>		Mortality	
		Initial	Day 7	Day 14	mg/kg	mL	Day	Weight
0333	M	2.3	2.5	2.6	25	0.069	E	-
0334	M	2.6	2.7	2.9	25	0.078	E	-
0335	M	2.5	2.6	-	25	0.075	13	2.6
0336	M	2.6	2.7	2.8	25	0.078	E	-
0337	M	2.5	2.5	2.7	25	0.075	E	-
0338	F	2.4	2.5	2.6	25	0.072	E	-
0339	F	2.5	2.5	2.7	25	0.075	E	-
0340	F	2.4	2.5	2.6	25	0.072	E	-
0341	F	2.4	2.5	2.6	25	0.072	E	-
0342	F	2.5	2.5	2.6	25	0.075	E	-

E - Euthanized via sodium pentobarbital injection after weighing on day 14

<sup>1</sup> Applied as received. Specific Gravity - 0.846 g/mL.

TABLE - 3

INDIVIDUAL CAGE-SIDE OBSERVATIONS

DOSE LEVEL: 25 mg/kg

<u>Animal Number</u>	<u>Finding</u>	<u>Day of Occurrence</u>
<u>MALES</u>		
0333, 0334, 0337	Active and healthy Erythema/Edema present at dose site Eschar present at dose site	0(1 hr)-14 1 2-14
0335	Active and healthy Irregular respiration Erythema/Edema present at dose site Eschar present at dose site Dead	0(1 hr), 1-12 0(4 hr) 1 2-12 13
0336	Irregular respiration Erythema/Edema present at dose site Active and healthy Eschar present at dose site	0(1 hr)-1 1 2-14 2-14
<u>FEMALES</u>		
0338, 0341	Active and healthy Erythema/Edema present at dose site Eschar present at dose site	0(1 hr)-14 1 2-14
0339, 0340, 0342	Active and healthy Irregular respiration Erythema/Edema present at dose site Eschar present at dose site	0(1 hr), 1-14 0(4 hr) 1 2-14

TABLE - 4INDIVIDUAL NECROPSY OBSERVATIONSDOSE LEVEL: 25 mg/kg

<u>Animal Number</u>	<u>Tissue</u>	<u>Findings</u>
<u>MALES</u>		
0333, 0334, 0336, 0337	All tissues/organs	Appeared normal
0335	Lungs Liver Intestines Abdominal cavity Thoracic cavity	Slightly red, moderate edema Discolored Slightly red Light yellow fluid present Pink fluid present
<u>FEMALES</u>		
0338-0342	All tissues/organs	Appeared normal

TABLE - 5

INDIVIDUAL BODYWEIGHT, DOSAGE AND MORTALITY

DOSE LEVEL: 50 mg/kg

Animal No.	Sex	Bodyweight (kg)			Actual Dose <sup>1</sup>		Mortality	
		Initial	Day 7	Day 14	mg/kg	mL	Day	Weight
0241	M	2.5	2.6	2.7	51	0.15	E	-
0242	M	2.4	-	-	49	0.14	O	2.4
0243	M	2.6	2.7	2.9	52	0.16	E	-
0244	M	2.6	-	-	52	0.16	O	2.5
0245	M	2.6	-	-	52	0.16	O	2.6
0246	F	2.5	2.6	2.8	51	0.15	E	-
0247	F	2.5	2.6	2.8	51	0.15	E	-
0248	F	2.5	2.6	2.7	51	0.15	E	-
0249	F	2.5	-	-	51	0.15	O	2.5
0250	F	2.5	2.3	2.6	51	0.15	E	-

E - Euthanized via sodium pentobarbital injection after weighing on day 14

<sup>1</sup> Applied as received. Specific Gravity - 0.846 g/mL.

TABLE - 6

INDIVIDUAL CAGE-SIDE OBSERVATIONSDOSE LEVEL: 50 mg/kg

<u>Animal Number</u>	<u>Finding</u>	<u>Day of Occurrence</u>
<u>MALES</u>		
0241, 0243	Active and healthy Irregular respiration Erythema/Edema present at dose site Eschar present at dose site	0(1-3 hr), 2-14 0(4 hr)-1 1-14 6-14
0242	Irregular respiration Dead	0(1-3 hr) 0(4 hr)
0244, 0245	Irregular respiration Hypoactive Dead	0(1-4 hr) 0(4 hr) 0(23 hr)
<u>FEMALES</u>		
0246	Irregular respiration Erythema/Edema present at dose site Active and healthy Eschar present at dose site	0(1 hr)-1 1-14 2-14 6-14
0247	Irregular respiration Hunched posture Erythema/Edema present at dose site Active and healthy Eschar present at dose site	0(1 hr)-1 0(23 hr)-1 1-14 2-14 6-14
0248	Active and healthy Irregular respiration Erythema/Edema present at dose site Eschar present at dose site	0(1 hr), 2-14 0(3 hr)-1 1-14 6-14
0249	Irregular respiration Hypoactive Dead	0(1-4 hr) 0(4 hr) 0(23 hr)
0250	Irregular respiration Ano-genital staining Erythema/Edema present at dose site Active and healthy Eschar present at dose site Soft feces Reduced fecal volume	0(1 hr)-1 1 1-14 2-7, 10-14 6-14 8-9 9

TABLE - 7

INDIVIDUAL NECROPSY OBSERVATIONS

DOSE LEVEL: 50 mg/kg

<u>Animal Number</u>	<u>Tissue</u>	<u>Findings</u>
<u>MALES</u>		
0241, 0243	All tissues/organs	Appeared normal
0242	Lungs Liver Intestines	Mottled red Discolored Pink/red
0244	Lungs Liver	Mottled red Discolored
0245	Lungs Liver Spleen Intestines	Mottled red Discolored Black spots on edges Red
<u>FEMALES</u>		
0246, 0247, 0248, 0250	All tissues/organs	Appeared normal
0249	Lungs Thoracic cavity  Liver Intestines	Mottled red Small amount of clear fluid present Discolored Pink/red

TABLE - 8

INDIVIDUAL BODYWEIGHT, DOSAGE AND MORTALITY

DOSE LEVEL: 100 mg/kg

Animal No.	Sex	Bodyweight (kg)			Actual Dose <sup>1</sup>		Mortality	
		Initial	Day 7	Day 14	mg/kg	mL	Day	Weight
0400	M	2.7	-	-	100	0.32	0	2.7
0401	M	2.6	-	-	101	0.31	0	2.6
0402	M	2.7	-	-	100	0.32	0	2.7
0403	M	2.6	-	-	101	0.31	0	2.6
0404	M	2.7	-	-	100	0.32	0	2.7
0405	F	2.6	-	-	101	0.31	0	2.5
0406	F	2.6	-	-	101	0.31	0	2.6
0407	F	2.6	-	-	101	0.31	0	2.6
0408	F	2.5	-	-	102	0.30	0	2.4
0409	F	2.8	-	-	103	0.34	0	2.8

<sup>1</sup> Applied as received. Specific Gravity - 0.846 g/mL.

TABLE - 9

INDIVIDUAL CAGE-SIDE OBSERVATIONSDOSE LEVEL: 100 mg/kg

<u>Animal Number</u>	<u>Finding</u>	<u>Day of Occurrence</u>
<u>MALES</u>		
0400, 0401, 0403	Irregular respiration Dead	0(1 hr) 0(3 hr)
0402, 0404	Dead	0(1 hr)
<u>FEMALES</u>		
0405, 0407, 0409	Irregular respiration Dead	0(1 hr) 0(3 hr)
0406	Irregular respiration, hypoactive Dead	0(1 hr) 0(3 hr)
0408	Irregular respiration, hypoactive, prone Dead	0(1 hr) 0(3 hr)

TABLE - 10

INDIVIDUAL NECROPSY OBSERVATIONS

DOSE LEVEL: 100 mg/kg

<u>Animal Number</u>	<u>Tissue</u>	<u>Findings</u>
<u>MALES</u>		
0400, 0403	Lungs	Mottled red
0401	Lungs Intestines	Mottled red Red
0402	Lungs	Moderately red, slight edema
0404	Lungs	Moderately red
<u>FEMALES</u>		
0405, 0406, 0407, 0409	Lungs	Mottled red
0408	Lungs Intestines	Moderately red Red

APPENDIX A

Animal feed analysis independently performed on October 10, 1995 for the presence of the following contaminants:

Aldrin	Ethyl Parathion
BHC	Heptachlor
Chlordane	Heptachlor Epoxide
DDD	Hexachlorobenzene - HCB
DDE	Lindane
DDT	Malathion
Diazinon	Methoxychlor
Dieldrin	Methyl Parathion
Endosulfan I & II	Mirex
Endosulfan Sulfate	Parathion
Endrin	PCB
Endrin aldehyde	Toxaphene
Ethion	

LABORATORY: WOODSON-TENENT LABORATORIES  
345 Adams Avenue  
P.O. Box 2135  
Memphis, TN 38101

Water analysis performed on November 15, 1995 for NJDEPE Safe Drinking Water Act parameters.

LABORATORY: NEW JERSEY LABORATORIES  
NJDEPE LAB I.D. #12034  
A.A. Labs Division  
222 Easton Avenue  
New Brunswick, NJ 08901

SAMPLE ID: 30981-1

Results of feed and water analysis for possible contaminants: Acceptable; none detected or within regulatory standards.

QUALITY ASSURANCE INSPECTIONS

Intervals for QA inspections are randomly selected prior to study initiation by the Quality Assurance Unit. Records of the findings of these inspections are kept on file. The summary below provides verification of statements made in the final report section which addresses Quality Assurance audits.

Inspections were made of:

<u>DATE</u>	<u>PROCEDURE INSPECTED</u>
8/2/96	Test substance dispensing records (50 mg/kg)
8/2/96	Initial bodyweights (50 mg/kg)
8/22/96	Test substance dispensing records (25 mg/kg)
8/29/96	Initial bodyweights (100 mg/kg)
9/26/96	Raw data
9/26/96	Draft report
<u>9/27/96</u>	Final report

Findings reported to: Study Director 8/2, 9/13, 9/26/96

Management 8/5, 9/24, 9/27/96

  
Frank Fielder, B.S.  
Quality Assurance Supervisor

# Experimental Product Data Sheet

\*\* 24-HOUR EMERGENCY ASSISTANCE: 304-843-1300 \*\*



PPG INDUSTRIES, INC.  
One PPG Place  
Pittsburgh, PA 15272

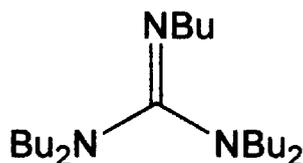
10/11/96

**Name:** 1,1,3,3,4-Pentabutylguanidine  
**Synonyms:** Pentabutylguanidine; PBG;  
N,N,N',N',N''-pentabutylguanidine

**CAS Registry No:** [114591-53-6]

**Formula:** C<sub>21</sub>H<sub>45</sub>N<sub>3</sub>

**Structure:**



**Appearance:** Lt. yellow oil

**Boiling Point:** 130-135 at 0.2 mm Hg

**Solubility at 25°C:** Soluble in common organic solvents. Insoluble in water.

**Fire Extinguishing Data:** Water spray, carbon dioxide, dry chemical powder or appropriate foam.

**Signal Word:** DANGER!

**Emergency Overview:** Corrosive - Causes severe burns to skin and eyes. Do not swallow. Do not breathe vapors. Use appropriate respiratory protection. Use only with adequate ventilation.

## **Toxicity Data:**

**Acute Dermal:** Dose levels of 25, 50, and 100 mg/kg were applied to rabbits for 24-hours. Test results indicated a single dose acute dermal defined LD<sub>50</sub> of 52 mg/kg. Pentabutylguanidine would be classified as corrosive, class 8 and Packing Group 1 by DOT.

**Acute Oral:** An acute oral toxicity defined LD<sub>50</sub> study was performed with dose levels of 50, 250, 500, and 5,000 mg/kg of animal body weight. All animals from the 500 and 5000 mg/kg dose level died within 2 hours of dosing. At 250 mg/kg, all of the female rats and 2/5 male rats died following dosing. No mortality was noted for animals dosed at 50 mg/kg. Clinical signs noted following dosing at 50 and 250 mg/kg included hunched posture, hypoactivity, piloerection, irregular respiration, ano-genital staining, and/or soft feces. Thus, **the single dose oral LD<sub>50</sub> is 190 mg/kg.**

**Storage:** Store in a cool dry place. Store only in closed, properly labeled containers. Keep container closed when not in use.

**DOT:** Corrosive Liquid, Toxic, NOS, (1,1,3,3,4-Pentabutylguanidine), 8 (6.1), UN2922, PGI

**TSCA:** This chemical is not listed on the TSCA Inventory - This chemical can only be used in R&D (by a technically qualified individual only) and FDA regulated applications.

**EINECS:** This material is not listed on the EINECS - This product can only be used in R&D applications.



## ACUTE ORAL TOXICITY DEFINED LD<sub>50</sub>

**PROTOCOL NO.:** P320

**AGENCY:** EPA (TSCA) & OECD

**STUDY NUMBER:** 4270

**SPONSOR:** PPG INDUSTRIES, INC.  
One PPG Place  
Pittsburgh, PA 15272

**TEST SUBSTANCE IDENTIFICATION:** Pentabutylguanidine, Lot #737-207

**TEST SUBSTANCE DESCRIPTION:** Amber (oil) liquid

**DATE RECEIVED:** February 20, 1996

**PSL REFERENCE NO.:** E60220-2R

**DATE OF PROTOCOL APPROVAL:** February 26, 1996

**DATES OF ADMINISTRATION:** February 27, March 7, 12 and 19, 1996

**TERMINATION OF IN-LIFE PHASE:** April 2, 1996

**STUDY COMPLETION DATE:** May 3, 1996

**NOTEBOOK NO.:** 96-12; pages 111-176C

### 1. PURPOSE:

To determine the Acute Oral Defined LD<sub>50</sub> of Pentabutylguanidine, Lot #737-207. Data from this study may be used as a basis for classification and labeling.

### 2. SUMMARY:

An Acute Oral Toxicity test was conducted with rats to determine the potential for Pentabutylguanidine, Lot #737-207 to produce toxicity via the oral route. Based on the results of this study, the Acute Oral Defined LD<sub>50</sub> of the test substance is 190 mg/kg as a 10% w/w solution in corn oil (See Table 1).

After acclimation to the laboratory, 40 healthy rats were selected for test and equally distributed into four dose groups of five males and five females each. Dose levels of 50, 250, 500 and 5,000 mg/kg were selected for testing. The test substance was administered as

received for the 500 and 5,000 mg/kg dose levels and was diluted to a 10% w/w solution in corn oil for the 50 and 250 mg/kg dose levels. Following administration, all test groups were observed for signs of gross toxicity and behavioral changes at least once daily for 14 days or until mortality. Bodyweights were recorded prior to administration and again on days 7 and 14 or after death. Necropsies were performed on all animals.

The incidence of mortality at each dose level is summarized below:

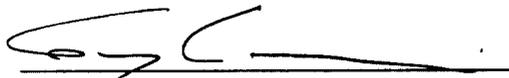
Dose Level	Mortality		
	Males	Females	Total
mg/kg			
50	0/5	0/5	0/10
250	2/5	5/5	7/10
500	5/5	5/5	10/10
5,000	5/5	5/5	10/10

All animals from the 500 and 5,000 mg/kg dose levels died within 2 hours of dosing. Prior to death, several animals from the 500 mg/kg dose group exhibited hunched posture, hypoactivity, piloerection and irregular respiration. Following administration animals from the 50 and 250 mg/kg dose levels developed one or more of the following clinical signs: hunched posture, hypoactivity, piloerection, irregular respiration, ano-genital staining and/or soft feces. Prior to death, two animals from the 250 mg/kg dose level also exhibited facial staining or diarrhea. Surviving rats from the two lower dose levels recovered from the above symptoms by day 9 and gained bodyweight over the 14-day observation period. Gross necropsy of the decedents from all levels revealed discoloration of the lungs, liver and gastrointestinal tract, distention of the gastrointestinal tract, edema of the lungs and/or rigor mortis. Gross necropsy findings at terminal sacrifice of the survivors were generally unremarkable.

Pentabutylguanidine, Lot #737-207

ACUTE ORAL TOXICITY DEFINED LD<sub>50</sub>

This study meets the requirements of Good Laboratory Practices as defined by EPA (TSCA)-40 CFR Part 792 and OECD C(81)30 (Final) Annex 2 with the following exception: The stability, characterization, identity and verification of the test substance concentration as received and tested are the responsibility of the study sponsor.



Gary Wnorowski, B.A.  
Study Director

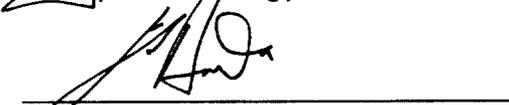
May 3, 1996  
Date

We the undersigned declare that the methods, results and data contained in this report faithfully reflect the procedures and raw data used or collected during the study.



Jacek Ochalski, D.V.M.  
Principal Toxicology Technician

May 3 1996  
Date



Jasbir Bawa, B.S.  
Assistant Toxicology Technician

May 3, 1996  
Date

**3. MATERIALS:****A. Test Substance:**

The test substance identified as Pentabutylguanidine, Lot #737-207 was received on February 20, 1996 and was further identified with PSL Code Number E60220-2R. The test substance was an amber (oil) liquid and was stored at room temperature. The sample was administered as received for the 5,000 and 500 mg/kg dose levels. Due to the low dose volumes that would be required for the 50 and 250 mg/kg dose groups if the undiluted test substance was administered, these animals received a 10% w/w solution of the test substance in corn oil. Documentation of the methods of synthesis, fabrication, or derivation of the test substance is retained by PPG Chemicals Technical Center, Monroeville, PA.

Characterization of the test substance as provided to Product Safety Labs by the sponsor was:

**Composition:** Pentabutylguanidine - 99.4%  
Tetrabutylurea - 0.21%  
Toluene - 0.19%  
Tetrabutylguanidine - 0.19%

**pH:** 11.0

**Solubility:** Soluble in acetone, mineral oil, ethanol, methanol and corn oil

**Stability:** Stable

**Expiration Date:** None

**B. Animals:**

**3.B.1 Number of Animals:** 40

**3.B.2 Sex:** 20 males and 20 females

**3.B.3 Number of Animals/Dose Level:** 5 males and 5 females/dose level

**3.B.4 Species/Strain:** Rat/Sprague-Dawley derived, albino

**3.B.5 Age/Bodyweight:** Young adult/males 184-240 grams and females 189-228 grams at initiation

**3.B.6 Source:** Received from Hilltop Lab Animals, Scottdale, PA on February 14, 28 and March 6, 1996

**4. METHODS:****A. Husbandry:**

**4.A.1 Housing:** The animals were singly housed in suspended stainless steel caging with mesh floors which conform to the size recommendations in the Guide for the Care and Use of Laboratory Animals DHEW (NIH) No. 86.23. Litter paper was placed beneath the cage and was changed at least three times per week.

**4.A.2 Animal Room Temperature Range:** 67-71 °F

**4.A.3 Photoperiod:** 12 hour light/dark cycle

**4.A.4 Acclimation Period:** 8 or 13 days

**4.A.5 Food:** Purina Rodent Chow #5012

**4.A.6 Water:** Filtered tap water was supplied *ad libitum* by automatic water dispensing system.

**4.A.7 Contaminants:** There were no known contaminants reasonably expected to be found in the food or water which interfered with the results of this study. Results of the analysis of the food and water are kept on file at Product Safety Labs. The dates of the most recent analyses are presented in Appendix A.

**B. Identification:**

**4.B.1 Cage:** Each cage was identified with a cage card indicating at least the study number and identification and sex of the animals.

**4.B.2 Animal:** A number was allocated to each rat on receipt and a stainless steel ear tag bearing this number was attached to the rat. This number, together with a sequential animal number assigned to study 4270, constituted unique identification.

**5. PROCEDURE:****A. Selection of Animals:**

Prior to dosing, each group of animals was fasted for approximately 17-20 hours by removing feed from their cages. During the fasting period, the rats were examined for health and weighed (initial). Ten (five male and five female) healthy rats were selected for each dose level.

**B. Dose Calculations:**

Individual doses were calculated based on the initial bodyweights, taking into account the specific gravity and concentration (as appropriate) of the test solution.

**C. Dosing:**

Each animal received the appropriate amount of the test substance (50, 250, 500 or 5,000 mg/kg) by intubation using a stainless steel ball-tipped gavage needle attached to an appropriate syringe. The test substance was administered as received (5,000 & 500 mg/kg dose groups) or as a 10% w/w solution in corn oil (50 & 250 mg/kg dose groups). After administration, each animal was returned to its designated cage. Feed was replaced approximately 3 hours after dosing.

**D. Bodyweights:**

Individual bodyweights of the animals were recorded prior to test substance administration (initial) and again on days 7 and 14 or after death (See Tables 2, 5, 8 and 11).

**E. Cage-Side Observations:**

The animals were observed for signs of gross toxicity and behavioral changes at least once daily for 14 days or until mortality. Observations included gross evaluation of skin and fur, eyes and mucous membranes, respiratory, circulatory, autonomic and central nervous systems, somatomotor activity and behavior pattern. Particular attention was directed to observation of tremors, convulsions, salivation, diarrhea and coma (See Tables 3, 6, 9 and 12).

**F. Necropsy:**

Surviving rats were euthanized via CO<sub>2</sub> inhalation on day 14. A gross necropsy was performed on all decedents and euthanized animals. Tissues and organs of the thoracic and abdominal cavities were examined (See Tables 4, 7, 10 and 13).

**6. STUDY CONDUCT:**

This study was conducted at Product Safety Labs, 725 Cranbury Road, East Brunswick, NJ 08816, to comply with the Good Laboratory Practices as defined in 40 CFR 792: U.S. EPA Good Laboratory Practice Standards: Toxic Substances Control Act (TSCA) and OECD Principles of Good Laboratory Practice C(81)30 (Final) Annex 2.

The procedure employed were based on Health Effects Testing Guidelines, Subpart B: Acute Oral Toxicity, 40 CFR 798.1175 and OECD Guidelines for Testing of Chemicals, Procedure 401.

**7. QUALITY ASSURANCE:**

The final report was audited for agreement with the raw data records and for compliance with the protocol, Product Safety Labs Standard Operating Procedures and appropriate Good Laboratory Practice Standards. Dates of inspections and audits performed during the study, and the dates of reporting of the inspection and audit findings to the Study Director and Facility Management are presented in the Quality Assurance Statement.

**8. DEVIATIONS FROM FINAL PROTOCOL: None****9. RECORDS TO BE MAINTAINED:**

A copy of this signed report, together with the protocol and all raw data generated at Product Safety Labs, is retained in the Product Safety Labs Archives.

**10. RESULTS:****50 mg/kg**

All animals survived and gained weight during the study. Following test substance administration, all rats exhibited hunched posture, hypoactivity, piloerection, irregular respiration, ano-genital staining and/or soft feces. All animals recovered from the above symptoms by day 3 and remained active and healthy for the remainder of the 14-day observation period. Gross necropsy findings at terminal sacrifice were generally unremarkable. Apart from red lung discoloration consistent with euthanasia by CO<sub>2</sub> inhalation, all other tissues and organs appeared normal.

**250 mg/kg**

Two males and all five females died within twenty-three hours of test substance administration. Toxic signs prior to death included hunched posture, hypoactivity, piloerection, irregular respiration, facial staining, ano-genital staining and/or diarrhea. The survivors, all males, exhibited similar clinical signs with the exception of facial staining and diarrhea. However, soft feces was evident in one of these animals. All survivors recovered from the above conditions by day 9 and gained bodyweight over the 14 day observation period. Gross necropsy of the decedents revealed discoloration of the lungs, liver and gastrointestinal tract, distention of the gastrointestinal tract, edema of the lungs and/or rigor mortis. Gross necropsy findings at terminal sacrifice of the survivors were generally unremarkable. Apart from red lung discoloration consistent with euthanasia by CO<sub>2</sub> inhalation, all other tissues and organs appeared normal.

**500 mg/kg**

All animals died within two hours of test substance administration. Prior to death, several animals exhibited hunched posture, hypoactivity, piloerection and/or irregular respiration. Gross necropsy of the decedents revealed discoloration of the lungs and gastrointestinal tract and edema of the lungs.

**5,000 mg/kg**

All animals died within one hour of test substance administration. There were no observed toxic signs prior to death. Gross necropsy of the decedents revealed discoloration of the lungs and gastrointestinal tract.

- A. **Summary of Mortality Data:** See Table 1
- B. **Individual Bodyweight, Dosage and Mortality:** See Tables 2, 5, 8 and 11
- C. **Individual Cage-Side Observations:** See Tables 3, 6, 9 and 12
- D. **Individual Necropsy Observations:** See Tables 4, 7, 10 and 13

**11. CONCLUSION:**

Based on the findings summarized above, the Acute Oral Defined LD<sub>50</sub> of Pentabutylguanidine, Lot #737-207 calculated by Probit Analysis was 190 milligrams of the test substance per kilogram of bodyweight (when administered as received or as a 10% w/w solution in corn oil) with 95% Confidence Limits of 249 mg/kg (upper) and 145 mg/kg (lower). The LD<sub>50</sub> for males was 245 mg/kg with 95% Confidence Limits of 351 mg/kg (upper) and 171 mg/kg (lower). The data does not permit calculation of the LD<sub>50</sub> for females by Probit Analysis. Graphically, the LD<sub>50</sub> for females was estimated to be 112 mg/kg.

TABLE - 1

SUMMARY OF MORTALITY DATA

Dose Level	Mortality		
mg/kg	Males	Females	Total
50	0/5	0/5	0/10
250	2/5	5/5	7/10
500	5/10	5/10	10/10
5,000	5/10	5/10	10/10
	Males <sup>1</sup>	Females <sup>2</sup>	Total <sup>1</sup>
LD <sub>50</sub>	245	112	190
	95% Confidence Limits		
Upper:	351	-	249
Lower:	171	-	145

<sup>1</sup> LD<sub>50</sub> calculated by the Litchfield-Wilcoxon Method of Probit Analysis; Litchfield, J.T. and Wilcoxon, F.W. *J. Pharmacol. Exper. Ther.* 1949;96:99-115.

<sup>2</sup> LD<sub>50</sub> estimated graphically. Data does not permit calculation by Probit Analysis.

TABLE - 2

INDIVIDUAL BODYWEIGHT, DOSAGE AND MORTALITY

DOSE LEVEL: 50 mg/kg

Animal No.	Sex	Bodyweight (g)			Actual Dose <sup>1</sup>	
		Initial	Day 7	Day 14	mg/kg	mL
0824	M	221	289	346	49	0.12
0825	M	240	279	307	49	0.13
0826	M	235	307	364	50	0.13
0827	M	219	265	310	49	0.12
0828	M	220	278	328	49	0.12
0829	F	224	240	267	52	0.13
0830	F	208	231	255	52	0.12
0831	F	210	255	270	51	0.12
0832	F	218	238	269	49	0.12
0833	F	228	252	265	51	0.13

<sup>1</sup> Administered as a 10% w/w solution in corn oil. Specific Gravity - 0.896 g/mL.

TABLE - 3

INDIVIDUAL CAGE-SIDE OBSERVATIONS

DOSE LEVEL: 50 mg/kg

<u>Animal Number</u>	<u>Finding</u>	<u>Day of Occurrence</u>
<u>MALES</u>		
0824	Active and healthy Hunched posture Piloerection	0(1 hr), 2-14 0(3-6 hr) 0(3 hr)-1
0825	Active and healthy Piloerection Ano-genital staining	0(1 hr), 3-14 0(3 hr)-2 1
0826	Active and healthy Ano-genital staining	0(1-6 hr), 3-14 1-2
0827	Piloerection, hunched posture Hypoactive Irregular respiration Ano-genital staining Active and healthy	0(1 hr)-2 0(3 hr)-1 1 1-2 3-14
0828	Active and healthy Hunched posture Piloerection	0(1 hr), 2-14 0(3-6 hr) 0(3 hr)-1

TABLE - 3 (cont.)

INDIVIDUAL CAGE-SIDE OBSERVATIONSDOSE LEVEL: 50 mg/kg

<u>Animal Number</u>	<u>Finding</u>	<u>Day of Occurrence</u>
<u>FEMALES</u>		
0829	Active and healthy Piloerection, hunched posture	0(1 hr), 1-14 0(3-6 hr)
0830	Active and healthy Hunched posture Piloerection	0(1 hr), 2-14 0(3-6 hr) 0(3 hr)-1
0831	Piloerection Hunched posture Soft feces Active and healthy	0(1 hr)-1 0(1 hr)-2 1 3-14
0832	Active and healthy Ano-genital staining, soft feces	0(1-6 hr), 2-14 1
0833	Active and healthy Hunched posture	0(1 hr), 1-14 0(3-6 hr)

TABLE - 4

INDIVIDUAL NECROPSY OBSERVATIONS

DOSE LEVEL: 50 mg/kg

<u>Animal Number</u>	<u>Tissue</u>	<u>Findings</u>
<u>MALES</u>		
0824-0828	Lungs	Moderately red <sup>1</sup>
<u>FEMALES</u>		
0829-0833	Lungs	Moderately red <sup>1</sup>

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<sup>1</sup> Customarily seen with CO<sub>2</sub> inhalation, euthanasia procedure.

TABLE - 5

INDIVIDUAL BODYWEIGHT, DOSAGE AND MORTALITY

DOSE LEVEL: 250 mg/kg

Animal No.	Sex	Bodyweight (g)			Actual Dose <sup>1</sup>		Mortality	
		Initial	Day 7	Day 14	mg/kg	mL	Day	Weight
0914	M	228	-	-	252	0.64	0	209
0915	M	218	-	-	251	0.61	0	205
0916	M	218	270	314	251	0.61	E	-
0917	M	208	265	300	250	0.58	E	-
0918	M	230	251	330	249	0.64	E	-
0919	F	214	-	-	251	0.60	0	202
0920	F	224	-	-	248	0.62	0	208
0921	F	217	-	-	252	0.61	0	203
0922	F	213	-	-	248	0.59	0	197
0923	F	210	-	-	252	0.59	0	195

E - Euthanized on day 14 via CO<sub>2</sub> inhalation after weighing

<sup>1</sup> Administered as a 10% w/w solution in corn oil. Specific Gravity - 0.896 g/mL.

TABLE - 6

INDIVIDUAL CAGE-SIDE OBSERVATIONS

DOSE LEVEL: 250 mg/kg

<u>Animal Number</u>	<u>Finding</u>	<u>Day of Occurrence</u>
<u>MALES</u>		
0914	Facial staining, piloerection, hunched posture, hypoactive Irregular respiration Dead	0(1-3 hr) 0(3 hr) 0(22.5 hr)
0915	Piloerection Hunched posture Dead	0(1-3 hr) 0(3 hr) 0(22.5 hr)
0916	Active and healthy Piloerection Hypoactive Hunched posture Ano-genital staining Soft feces	0(1 hr), 6-14 0(3 hr)-2 0(22.5 hr)-1 0(22.5 hr)-3 2-5 3
0917	Piloerection Hypoactive Hunched posture Ano-genital staining Active and healthy	0(1 hr)-3 0(3 hr)-1 0(3 hr)-2 0(22.5 hr)-6 7-14
0918	Active and healthy Piloerection Hypoactive Hunched posture Ano-genital staining	0(1 hr), 9-14 0(3 hr)-6 0(22.5 hr)-4 0(22.5 hr)-5 0(22.5 hr)-8

TABLE - 6 (cont.)

INDIVIDUAL CAGE-SIDE OBSERVATIONS

DOSE LEVEL: 250 mg/kg

<u>Animal Number</u>	<u>Finding</u>	<u>Day of Occurrence</u>
<u>FEMALES</u>		
0919	Active and healthy	0(1 hr)
	Ano-genital staining, hunched posture, hypoactive, diarrhea	0(3 hr)
	Dead	0(6 hr)
0920	Active and healthy	0(1 hr)
	Piloerection, hunched posture, hypoactive	0(3 hr)
	Dead	0(5 hr)
0921	Hunched posture	0(1-3 hr)
	Dead	0(7 hr)
0922	Active and healthy	0(1 hr)
	Hunched posture, hypoactive	0(3 hr)
	Dead	0(6 hr)
0923	Active and healthy	0(1-3 hr)
	Dead	0(22.5 hr)

TABLE - 7INDIVIDUAL NECROPSY OBSERVATIONSDOSE LEVEL: 250 mg/kg

<u>Animal Number</u>	<u>Tissue</u>	<u>Findings</u>
<u>MALES</u>		
0914, 0915	Lungs Gastrointestinal tract	Moderately red, slight edema Yellow, slight gaseous distention
0916-0918	Lungs	Moderately red <sup>1</sup>
<u>FEMALES</u>		
0919	Lungs Gastrointestinal tract	Moderately red, moderate edema Red, gaseous distention
0920	Lungs Intestines	Moderately red Pink/red, moderate gaseous distention
0921	Lungs Stomach Intestines Liver General appearance	Moderately red Distended Distended Black spots, shriveled Rigor mortis
0922	Lungs Stomach Intestines	Slightly red, moderate edema Red, gaseous distention Red, gaseous distention
0923	Lungs Gastrointestinal tract	Moderately red, slight edema Yellow, slight gaseous distention

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<sup>1</sup> Customarily seen with CO<sub>2</sub> inhalation, euthanasia procedure.

TABLE - 8

INDIVIDUAL BODYWEIGHT, DOSAGE AND MORTALITY

DOSE LEVEL: 500 mg/kg

Animal No.	Sex	Bodyweight (g)			Actual Dose <sup>1</sup>		Mortality	
		Initial	Day 7	Day 14	mg/kg	mL	Day	Weight
0784	M	187	-	-	495	0.11	0	182
0785	M	188	-	-	492	0.11	0	180
0786	M	197	-	-	512	0.12	0	192
0787	M	184	-	-	503	0.11	0	180
0788	M	194	-	-	477	0.11	0	189
0789	F	198	-	-	510	0.12	0	189
0790	F	202	-	-	500	0.12	0	198
0791	F	189	-	-	489	0.11	0	181
0792	F	204	-	-	495	0.12	0	194
0793	F	202	-	-	500	0.12	0	195

<sup>1</sup> Administered as received. Specific Gravity - 0.841 g/mL.

TABLE - 9INDIVIDUAL CAGE-SIDE OBSERVATIONSDOSE LEVEL: 500 mg/kg

<u>Animal Number</u>	<u>Finding</u>	<u>Day of Occurrence</u>
<u>MALES</u>		
0784, 0787, 0788	Dead	0(1 hr)
0785	Piloerection, hunched posture, hypoactive Dead	0(1 hr) 0(2 hr)
0786	Piloerection, irregular respiration, hunched posture, hypoactive Dead	0(1 hr) 0(2 hr)
<u>FEMALES</u>		
0789, 0791, 0792, 0793	Dead	0(1 hr)
0790	Piloerection, irregular respiration, hunched posture, hypoactive Dead	0(1 hr) 0(2 hr)

TABLE - 10

INDIVIDUAL NECROPSY OBSERVATIONS

DOSE LEVEL: 500 mg/kg

<u>Animal Number</u>	<u>Tissue</u>	<u>Findings</u>
<u>MALES</u>		
0784	Lungs Intestines	Extremely red Red
0785, 0786	Lungs Stomach Intestines	Extremely red, moderate edema Extremely red Red
0787	Lungs Stomach Intestines	Extremely red, slight edema Extremely red Red
0788	Lungs Stomach	Moderately red, moderate edema Extremely red
<u>FEMALES</u>		
0789, 0791, 0792	Lungs Stomach	Moderately red, moderate edema Extremely red
0790	Lungs Stomach Intestines	Extremely red, moderate edema Extremely red Red
0793	Lungs Stomach Intestines	Extremely red, moderate edema Extremely red Red

TABLE - 11

INDIVIDUAL BODYWEIGHT, DOSAGE AND MORTALITY

DOSE LEVEL: 5,000 mg/kg

Animal No.	Sex	Bodyweight (g)			Actual Dose <sup>1</sup>		Mortality	
		Initial	Day 7	Day 14	mg/kg	mL	Day	Weight
0694	M	208	-	-	4,852	1.2	0	204
0695	M	195	-	-	5,175	1.2	0	189
0696	M	205	-	-	4,923	1.2	0	199
0697	M	211	-	-	5,182	1.3	0	200
0698	M	204	-	-	4,947	1.2	0	200
0699	F	194	-	-	5,202	1.2	0	190
0700	F	199	-	-	5,071	1.2	0	196
0701	F	204	-	-	4,947	1.2	0	201
0702	F	190	-	-	4,869	1.1	0	187
0703	F	194	-	-	5,202	1.2	0	191

<sup>1</sup> Administered as received. Specific Gravity - 0.841 g/mL.

TABLE - 12

INDIVIDUAL CAGE-SIDE OBSERVATIONS

DOSE LEVEL: 5,000 mg/kg

<u>Animal Number</u>	<u>Finding</u>	<u>Day of Occurrence</u>
<u>MALES</u>		
0694-0698	Dead	0(1 hr)
<u>FEMALES</u>		
0699-0703	Dead	0(1 hr)

TABLE - 13

INDIVIDUAL NECROPSY OBSERVATIONS

DOSE LEVEL: 5,000 mg/kg

<u>Animal Number</u>	<u>Tissue</u>	<u>Findings</u>
<u>MALES</u>		
0694, 0696, 0697, 0698	Lungs Intestines	Extremely red Extremely red
0695	Lungs Stomach	Extremely red Extremely red
<u>FEMALES</u>		
0699, 0700, 0703	Lungs Stomach	Extremely red Extremely red
0701, 0702	Lungs Intestines	Extremely red Extremely red

APPENDIX A

Animal feed analysis independently performed on October 10, 1995 for the presence of the following contaminants:

Aldrin	Ethyl Parathion
BHC	Heptachlor
Chlordane	Heptachlor Epoxide
DDD	Hexachlorobenzene - HCB
DDE	Lindane
DDT	Malathion
Diazinon	Methoxychlor
Dieldrin	Methyl Parathion
Endosulfan I & II	Mirex
Endosulfan Sulfate	Parathion
Endrin	PCB
Endrin aldehyde	Toxaphene
Ethion	

LABORATORY: WOODSON-TENENT LABORATORIES  
345 Adams Avenue  
P.O. Box 2135  
Memphis, TN 38101

Water analysis performed on May 7, 1995 for NJDEPE Safe Drinking Water Act parameters and percent fluoride content.

LABORATORY: NEW JERSEY LABORATORIES  
DEPE #12660  
A.A. Labs Division  
222 Easton Avenue  
New Brunswick, NJ 08901

SAMPLE ID: 26849

Results of feed and water analysis for possible contaminants: Acceptable; none detected or within regulatory standards

QUALITY ASSURANCE INSPECTIONS

Intervals for QA inspections are randomly selected prior to study initiation by the Quality Assurance Unit. Records of the findings of these inspections are kept on file. The summary below provides verification of statements made in the final report section which addresses Quality Assurance audits.

Inspections were made of:

<u>DATE</u>	<u>PROCEDURE INSPECTED</u>
2/27/96	Decedent bodyweights (5,000 mg/kg)
2/27/96	Decedent gross necropsy (5,000 mg/kg)
3/7/96	Initial bodyweights (500 mg/kg)
3/12/96	Initiation of dosing (50 mg/kg)
3/19/96	Initiation of dosing (250 mg/kg)
3/26/96	Terminal gross necropsy (50 mg/kg)
4/2/96	Terminal bodyweights (250 mg/kg)
4/25/96	Raw data
4/25/96	Draft report *
<u>5/3/96</u>	Final report

Findings reported to: Study Director 4/5, 4/25/96

Management 4/16, 5/3/96

  
 \_\_\_\_\_  
 Frank Fielder, B.S.  
 Quality Assurance Supervisor



## DOT SKIN CORROSION

**PROTOCOL NO.:** P214.GLP, Class 8

**AGENCY:** EPA (TSCA), OECD & DOT

**STUDY NUMBER:** 4271

**SPONSOR:** PPG INDUSTRIES, INC.  
One PPG Place  
Pittsburgh, PA 15272

**PRODUCT IDENTIFICATION:** Pentabutylguanidine, Lot #737-207

**PRODUCT DESCRIPTION:** Amber oil

**DATE RECEIVED:** February 20, 1996

**PSL REFERENCE NO.:** E60220-2H

**DATE OF PROTOCOL APPROVAL:** March 25, 1996

**DATE OF TEST:** March 29, 1996

**STUDY COMPLETION DATE:** April 25, 1996

**NOTEBOOK NO.:** 96-10; pages 242-246

### 1. PURPOSE:

To determine the corrosive effects of a 3 minute, 1 hour and 4 hour exposure of the test material by the dermal route on the intact skin. Data from this study may be used as a basis for classification and labeling.

### 2. SUMMARY:

A skin corrosion test was conducted with rabbits to determine the potential for Pentabutylguanidine, Lot #737-207 to produce irritation and/or corrosion after topical application.

Five-tenths of a milliliter of the test substance was placed directly onto the skin of three rabbits 3 minute and 1 hour exposure periods (See Section 8). Following exposure, all test

sites were evaluated for corrosion and dermal irritation by the method of Draize *et al*<sup>1</sup> (See Table 3).

Visible necrosis of the skin tissue was observed at one test site after 3 minutes of exposure and at all test sites after 1 hour of exposure. In addition, one test animal was found dead at the 1 hour interval. Subsequently, the "4 hour" patches were removed at 1 hour and the sponsor authorized termination of the study and euthanasia of the remaining two animals due to the irreversible nature of the irritation (See Table 1).

**Pentabutylguanidine, Lot #737-207**

**DOT SKIN CORROSION TEST**

This study meets the requirements of Good Laboratory Practices as defined by EPA (TSCA)-40 CFR Part 792, OECD-C(81) 30 (Final) Annex 2 with the following exception: The stability, characterization, identity and verification of the test substance concentration as received and tested are the responsibility of the study sponsor.

  
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Gary Wnоровski, B.A.  
Study Director

April 25, 1996  
Date

We the undersigned declare that the methods, results and data contained in this report faithfully reflect the procedures and raw data used or collected during the study.

  
\_\_\_\_\_  
Andrew Becker, B.A.  
Principal Toxicology Technician

April 25, 1996  
Date

  
\_\_\_\_\_  
John Zyracki, M.S.  
Assistant Toxicology Technician

April 25, 1996  
Date

<sup>1</sup> Draize, J.H., Woodward, G. and Calvery, H.O. Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. *J. Pharmacol. Exp. Ther.* 1944; 82:377-390.

**3. MATERIALS:****A. Test Substance:**

The test substance identified as Pentabutylguanidine, Lot #737-207 was received on February 20, 1996 and was further identified with PSL Code Number E60220-2H. The test substance was an amber oil and was stored at room temperature. The sample was applied as received. Documentation of the methods of synthesis, fabrication, or derivation of the test substance is retained by the sponsor.

Characterization of the test substance as provided to Product Safety Labs by the sponsor was:

**Composition:** Pentabutylguanidine - 99.4%  
Tetrabutylurea - 0.21%  
Toluene - 0.19%  
Tetrabutylguanidine - 0.19%

**pH:** 11.0

**Solubility:** Soluble in acetone, mineral oil, ethanol and methanol

**Stability:** Stable

**Expiration Date:** None

**B. Animals:**

**3.B.1 Number of Animals:** 3

**3.B.2 Sex:** 2 males and 1 female

**3.B.3 Species/Strain:** Rabbit/New Zealand albino

**3.B.4 Age:** Adult

**3.B.5 Source:** Received from Davidson's Mill Farm, South Brunswick, NJ on March 22, 1996

**4. METHODS:****A. Husbandry:**

**4.A.1 Housing:** The animals were singly housed in suspended stainless steel caging with mesh floors which conform to the size recommendations in the Guide for the Care and Use of Laboratory Animals DHEW (NIH) No. 86.23. Litter paper was placed beneath the cage and was changed at least three times per week.

**4.A.2 Animal Room Temperature Range:** 69°F

**4.A.3 Photoperiod:** 12 hour light/dark cycle

**4.A.4 Acclimation Period:** 7 days

**4.A.5 Food:** Pelleted Purina Rabbit Chow #5326

**4.A.6 Water:** Filtered tap water was supplied *ad libitum* by automatic water dispensing system.

**4.A.7 Contaminants:** There were no known contaminants reasonably expected to be found in the food or water which interfered with the results of this study. Results of the analysis of the food and water are kept on file at Product Safety Labs. The dates of the most recent analyses are presented in Appendix A.

**B. Identification:**

**4.B.1 Cage:** Each cage was identified with a cage card indicating at least the study number and identification and sex of the animals.

**4.B.2 Animal:** A number was allocated to each rabbit on receipt and a stainless steel ear tag bearing this number was attached to the animal. This number, together with a sequential animal number assigned to study 4271, constituted unique identification.

**5. PROCEDURE:**

**A. Preparation and Selection of Animals:**

On the day before application, a group of animals was prepared by clipping (Oster model #A2-small) the dorsal area of the trunks free of hair. Three test sites, each approximately 2.5 cm<sup>2</sup>, were delineated on each animal. After clipping and prior to application, the animals were examined for health and the skin checked for any abnormalities. Only healthy animals without pre-existing dermal irritation were selected for test.

**B. Application of Test Substance:**

Five-tenths of a milliliter of the test substance was placed directly onto each dose site and covered with a 1x1 inch 4-ply gauze pad. The 3 minute, 1 and 4 hour patches were then wrapped with 3" semi-occlusive Micropore tape to avoid dislocation of the patches. Elizabethan collars were placed on each rabbit and they were returned to their designated cages.

Following exposure, the patches were removed from the appropriate dose sites at the 3 minute and 1 hour intervals. The "4 hour" patches were also removed at 1 hour due

to the severity of irritation noted (See Section 8). The sites were then gently wiped with ethanol, then water and a clean towel to remove any residual test material. In addition, one animal was found dead at the 1 hour interval. Subsequently, the sponsor was contacted and authorized termination of the study and euthanasia of the remaining two animals.

**C. Evaluation of Test Sites:**

All test sites were evaluated for corrosion within 1 hour after patch removal. Corrosion was considered to have resulted if the test substance caused full-thickness necrosis (or ulceration) at the test site in at least one test animal. Full-thickness necrosis is defined as moderate to severe tissue destruction with well-defined dark brown or black discoloration and/or stiffened texture, covering a substantial area. Epidermal sloughing, erythema, edema or fissuring were not considered tissue destruction.

The test sites were also evaluated for skin irritation according to the Draize<sup>1</sup> scoring system (See Table 3) at the same intervals mentioned above.

**D. Cage-Side Observations:**

The animals were observed for signs of gross toxicity and behavioral changes at least once daily during the test period. Observations included gross evaluation of skin and fur, eyes and mucous membranes, respiratory, circulatory, autonomic and central nervous systems, somatomotor activity and behavior pattern. Particular attention was directed to observation of tremors, convulsions, salivation, diarrhea and coma.

**6. STUDY CONDUCT:**

This study was conducted at Product Safety Labs, 725 Cranbury Road, East Brunswick, New Jersey 08816 in compliance with Good Laboratory Practices as defined in 40 CFR 792: U.S. EPA Good Laboratory Practice Standards: Toxic Substances Control Act (TSCA) and OECD Principles of Good Laboratory Practice C(81)30 (Final) Annex 2.

The procedures employed were based on Health Effects Testing Guidelines, Subpart E: Primary Dermal Irritation, 40 CFR 798.4470 and OECD Guidelines for Testing of Chemicals, Procedure 404.

**7. QUALITY ASSURANCE:**

The final report was audited for agreement with the raw data records and for compliance with the protocol, Product Safety Labs Standard Operating Procedures and appropriate Good Laboratory Practice Standards. Dates of inspections and audits performed during the study,

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<sup>1</sup> Draize, J.H., Woodward, G. and Calvery, H.O. Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. *J. Pharmacol. Exp. Ther.* 1944; 82:377-390.

and the dates of reporting of the inspection and audit findings to the Study Director and Facility Management are presented in the Quality Assurance Statement.

**8. DEVIATIONS FROM FINAL PROTOCOL:**

The protocol specifies that skin irritation and corrosion should be evaluated after a 3 minute, 1 hour and 4 hour exposure to the test substance. Due to the severity of irritation noted at the 3 minute and 1 hour dose sites, and the death of one test animal at the 1 hour interval, The "4 hour" patch was also removed at 1 hour and the sponsor was contacted and authorized termination of the study and euthanasia of the remaining two animals.

**9. RECORDS TO BE MAINTAINED:**

A copy of this signed report, together with the protocol and all raw data generated at Product Safety Labs, is retained in the Product Safety Labs Archives.

**10. RESULTS:**

One animal was found dead at the 1 hour interval. The remaining two animals exhibited clinical signs including irregular respiration, prone posture, ano-genital staining and lethargy.

Visible necrosis of the skin tissue was observed at one test site after 3 minutes of exposure and at all test sites after 1 hour of exposure.

- A. Individual Skin Corrosion Scores: See Table 1
- B. Individual Primary Skin Irritation Scores: See Table 2
- C. Primary Skin Irritation Scoring System: See Table 3

**11. CONCLUSION:**

Skin corrosion was noted at one test site within 1 hour of removal of the 3 minute patch. These results place Pentabutylguanidine, Lot #737-207 into Class 8, Packing Group 1.

TABLE - 1  
INDIVIDUAL SKIN CORROSION SCORES<sup>1</sup>

3 MINUTE EXPOSURE

Animal No.	Sex	1 Hour After Patch Removal
9465	M	P
9466	F	N
9467	M	N

1 HOUR EXPOSURE

Animal No.	Sex	Within 30 min. of Patch Removal
9465	M	P
9466	F	P
9467	M	P

4<sup>2</sup> HOUR EXPOSURE

Animal No.	Sex	Within 30 min. of Patch Removal
9464	M	P
9466	F	P
9467	M	P

N = Negative P = Positive

<sup>1</sup> Corrosion - defined as full-thickness necrosis of the dose site.

<sup>2</sup> The "4 hour" patches were removed concurrently with the "1 hour" patches due to severity of irritation noted.

**TABLE - 2**  
**PRIMARY SKIN IRRITATION SCORES**  
**ERYTHEMA AND ESCHAR/EDEMA**

**3 MINUTE EXPOSURE**

Animal No.	Sex	1 Hour After Patch Removal
9465	M	3/2 <sup>1</sup>
9466	F	3/2
9467	M	3/2
<b>Total</b>		9/6
<b>Mean</b>		3.0/2.0

**1 HOUR EXPOSURE**

Animal No.	Sex	Within 30 min. of Patch Removal
9465	M	4/2 <sup>2</sup>
9466	F	4/2 <sup>2</sup>
9467	M	4/2 <sup>2</sup>
<b>Total</b>		12/6
<b>Mean</b>		4.0/2.0

**4<sup>3</sup> HOUR EXPOSURE**

Animal No.	Sex	Within 30 min. of Patch Removal
9465	M	4/2 <sup>2</sup>
9466	F	4/2 <sup>2</sup>
9467	M	4/2 <sup>2</sup>
<b>Total</b>		12/6
<b>Mean</b>		4.0/2.0

<sup>1</sup> Slight black discoloration of the dose site.

<sup>2</sup> Green/grey discoloration of the dose site.

<sup>3</sup> The "4 hour" patches were removed concurrently with the "1 hour" patches due to severity of irritation noted.

TABLE - 3

PRIMARY SKIN IRRITATION SCORING SYSTEM<sup>1</sup>

<u>Evaluation of Skin Reactions</u>	<u>Value</u>
Erythema and eschar formation:	
No erythema . . . . .	0
Very slight erythema (barely perceptible) . . . . .	1
Well-defined erythema . . . . .	2
Moderate to severe erythema . . . . .	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth) . . . . .	4
Edema formation:	
No edema . . . . .	0
Very slight edema (barely perceptible) . . . . .	1
Slight edema (edges of area well defined by definite raising) . . . . .	2
Moderate edema (raised approximately 1 millimeter) . . . . .	3
Severe edema (raised more than 1 millimeter and extending beyond the area of exposure) . . . . .	4
Corrosion: Irreversible alteration of the tissue	
Desquamation: Dry flaky area, diffuse or defined	
Hyperkeratosis: Thickening of the skin	

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<sup>1</sup> 16 CFR 1500.41

QUALITY ASSURANCE INSPECTIONS

Intervals for QA inspections are randomly selected prior to study initiation by the Quality Assurance Unit. Records of the findings of these inspections are kept on file. The summary below provides verification of statements made in the final report section which addresses Quality Assurance audits.

Inspections were made of:

<u>DATE</u>	<u>PROCEDURE INSPECTED</u>
4/5/96	Test substance dispensing records
4/19/96	Raw data
4/19/96	Draft report
<u>4/25/96</u>	Final report

Findings reported to: Study Director 4/5, 4/19/96

Management 4/16, 4/25/96

  
Frank Fielder, B.S.  
Quality Assurance Supervisor

## Triage of 8(e) Submissions

Date sent to triage: 12/18/96

**NON-CAP**

**CAP**

Submission number: 13765 A

TSCA Inventory:

Y

**N**

D

Study type (circle appropriate):

Group 1 - Gordon Cash (1 copy total)

ECO

AQUATO

Group 2 - Ernie Falke (1 copy total)

**ATOX**

SBTOX

SEN

w/NEUR

Group 3 - HERD (1 copy each)

STOX

CTOX

EPI

RTOX

GTOX

STOX/ONCO

CTOX/ONCO

IMMUNO

CYTO

NEUR

Other (FATE, EXPO, MET, etc.): \_\_\_\_\_

Notes:

- This is the **original 8(e)** submission; refile after triage evaluation.
- This **original** submission has been **split**; rejoin after triage evaluation.
- Other:

### Photocopies Needed for Triage Evaluation

entire document: 0    1    2    3

front section and CECATS: 0    1    2    3

Initials: \_\_\_\_\_

Date: \_\_\_\_\_

CECATS DATA  
 Submission # BEHQ 1096-13765 SEQ A  
 TYPE:  INT SUPP FLWP  
 SUBMITTER NAME: PPG Industries, Inc.

INFORMATION REQUESTED, FLWP DATE:  
 0501 NO INFO REQUESTED  
 0502 INFO REQUESTED (TECI)  
 0503 INFO REQUESTED (VOL ACTIONS)  
 0504 INFO REQUESTED (REPORTING RATIONALE)  
 DISPOSITION:  
 0639 REFER TO CHEMICAL SCREENING  
 0678 CAP NOTICE

VOLUNTARY ACTIONS  
 0401 NO ACTION AT PRIORITY  
 0402 STUDIES PLANNED/IN PROGRESS  
 0403 NOTIFICATION OF WORK IN PROGRESS  
 0404 LABEL/ASSETS (TRANSFERS)  
 0405 PROFESSIONAL/IND. TRANSFERS  
 0406 APP USE DISCONTINUED  
 0407 PRODUCTION DISCONTINUED  
 0408 CONFIDENTIAL

SUB DATE: 10-15-96 OTS DATE: 10-17-96 CSRAD DATE: 12-4-96

CHEMICAL NAME: pentabutylguanidine CAS# 114591-53-6

INFORMATION TYPE	P F C	INFORMATION TYPE	P F C	INFORMATION TYPE	P F C
0201 ONCO (HUMAN)	01 02 04	0216 EPICLIN	01 02 04	0241 IMMUNO (ANIMAL)	01 02 04
0202 ONCO (ANIMAL)	01 02 04	0217 HUMAN EXPOS (PROD CONTAM)	01 02 04	0242 IMMUNO (HUMAN)	01 02 04
0203 CELL TRANS (IN VITRO)	01 02 04	0218 HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243 CHEMPHYS PROP	01 02 04
0204 MUTA (IN VITRO)	01 02 04	0219 HUMAN EXPOS (MONITORING)	01 02 04	0244 CLASTO (IN VITRO)	01 02 04
0205 MUTA (IN VIVO)	01 02 04	0220 ECO/AQUA TOX	01 02 04	0245 CLASTO (ANIMAL)	01 02 04
0206 REPRO/TERATO (HUMAN)	01 02 04	0221 ENV. OCCUR/EL/FATE	01 02 04	0246 CLASTO (HUMAN)	01 02 04
0207 REPRO/TERATO (ANIMAL)	01 02 04	0222 EMER INCI OF ENV CONTAM	01 02 04	0247 DNA DAM/REPAIR	01 02 04
0208 NEURO (HUMAN)	01 02 04	0223 RESPONSE REQEST DELAY	01 02 04	0248 PRODUSE/PROC	01 02 04
0209 NEURO (ANIMAL)	01 02 04	0224 PRODCOMP/CHEM ID	01 02 04	0251 MSDS	01 02 04
0210 ACUTE TOX. (HUMAN)	01 02 04	0225 REPORTING RATIONALE	01 02 04	OTHER	01 02 04
0211 CHR. TOX. (HUMAN)	01 02 04	0226 CONFIDENTIAL	01 02 04		
0212 ACUTE TOX. (ANIMAL)	01 02 04	0227 ALLERG (HUMAN)	01 02 04		
0213 SUB ACUTE TOX (ANIMAL)	01 02 04	0228 ALLERG (ANIMAL)	01 02 04		
0214 SUB CHRONIC TOX (ANIMAL)	01 02 04	0229 METAB/PHARMACO (ANIMAL)	01 02 04		
0215 CHRONIC TOX (ANIMAL)	01 02 04	0240 METAB/PHARMACO (HUMAN)	01 02 04		

TRIAGE DATA:  NON-CBI INVENTORY  ONGOING REVIEW  SPECIES  TOXICOLOGICAL CONCERN:  USE:  PRODUCTION:

CAS SR  YES  NO  YES (DROPPED)  NO (CONTINUE)  LOW  MED  HIGH

IM T/M/INI  REFTR  Rabbit fox

UNSUPP'D