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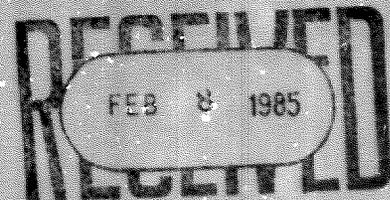
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**Great Lakes**  
Chemical Corporation

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January 31, 1985

Mr. John Harris  
TS-778  
Room 425, ET  
U.S. EPA, Test Rules Development Branch  
401 M St. SW  
Washington, D.C. 204060



Dear Mr. Harris:

As required under TSCA 8(d) enclosed are copies of toxicology studies performed with pentabromoethylbenzene for Great Lakes Chemical Corporation. The studies are:

1. Acute toxicity studies in rats and rabbits.
2. Mutagenicity evaluation of pentabromoethylbenzene.
3. Twenty-eight day toxicity study in rats.

Sincerely,

GREAT LAKES CHEMICAL CORPORATION

*Dennis L. McFadden*  
Dennis L. McFadden  
Product Safety Coordinator

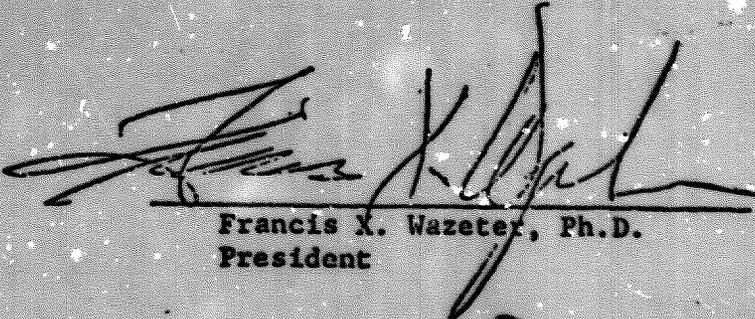
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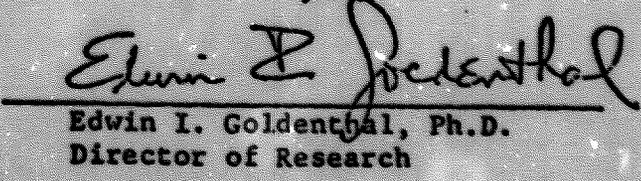
*International Research and Development Corporation*

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**SPONSOR:** Great Lakes Chemical Corporation  
**COMPOUND:** Pentabromoethylbenzene  
**SUBJECT:** Acute Toxicity Studies in Rats  
and Rabbits.

RECEIVED  
FEB 8 1985

  
Francis X. Wazeter, Ph.D.  
President

  
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Director of Research

Collaborator:  
W. P. Dean

Date: April 6, 1973

# International Research and Development Corporation

## TABLE OF CONTENTS

	<u>Page</u>
I. Synopsis . . . . .	1
II. Compound . . . . .	2
III. Eye Irritation in Albino Rabbits . . . . .	3
A. Method . . . . .	3
B. Results . . . . .	3
IV. Primary Skin Irritation in Albino Rabbits . . . . .	7
A. Method . . . . .	7
B. Results . . . . .	7
V. Acute Dermal Toxicity in the Albino Rabbit . . . . .	11
A. Method . . . . .	11
B. Results . . . . .	11
VI. Acute Inhalation Toxicity in the Male Albino Rat . . . . .	12
A. Method . . . . .	12
1. General Procedure . . . . .	12
2. Compound Administration . . . . .	12
B. Results . . . . .	13
1. 2 mg/L . . . . .	13
2. 200 mg/L . . . . .	13
3. Acute Inhalation Toxicity . . . . .	14
VII. Acute Oral Toxicity in the Albino Rat . . . . .	15
A. Method . . . . .	15
B. Results . . . . .	15

### Table No.

1. Eye Irritation in the Albino Rabbit, Observations . . . . .	5
2. Eye Irritation Scores . . . . .	6
3. Summation of Primary Skin Observations . . . . .	9
4. Primary Irritation Score . . . . .	10

**I. SYNOPSIS**

The test compound was examined for acute toxicity in rats and rabbits. The following tests were conducted in accordance with the requirements of the Federal Hazardous Substances Act:

**Eye Irritation Test in Albino Rabbits:**

A possible slight eye irritant.

**Primary Skin Irritation in the Albino Rabbit:**

Not a primary skin irritant.

**Acute Dermal Toxicity in the Albino Rabbit:**

Not a toxic substance by the dermal route of administration.

**Acute Inhalation Toxicity in Albino Rats:**

Not a toxic substance by the inhalation route of administration.

**Acute Oral Toxicity in Albino Rats:**

Not a toxic substance by the oral route of administration.

In addition to the above, based upon the results obtained, Pentabromoethylbenzene would not be considered a poisonous article under the regulations of the Interstate Commerce Commission.

II. COMPOUND

The test compound was received from the Great Lakes Chemical Corporation, West Lafayette, Indiana, on January 29, 1973.

It was identified as "Pentabromoethylbenzene, Ref. No. 6327, Date 1/16/73" and was received as an off-white grainy powder.

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III. EYE IRRITATION IN ALBINO RABBITS (Unwashed Technique)

A. METHOD:

Three male and 3 female New Zealand White rabbits were used in this study. The rabbits weighed from 2539 to 3292 grams at the beginning of the study. Food and water were available ad libitum.

Prior to compound administration, the eyes of each rabbit were examined with ultraviolet light after instillation of one drop of a 2.0 percent sodium fluorescein solution. Rabbits exhibiting corneal lesions were discarded.

100 milligrams of the test material were instilled into the cupped conjunctival sac of the right eye of each rabbit.

Examinations were made for ocular irritation at 24, 48, and 72 hours and at 7 days. At the 72 hour examination, sodium fluorescein and ultraviolet light were used again to aid in revealing possible corneal injury.

The scale for scoring ocular irritation appears on the following page.

B. RESULTS:

Examination at 72 hours with sodium fluorescein and ultraviolet light did not reveal corneal damage in any of the rabbits tested.

Table 1 presents a summary of the results obtained at each examination period. The average scores for each examination period are presented in Table 2.

Based upon the results obtained, Pentabromoethylbenzene would be considered a possible slight eye irritant.

Cornea

(A) Opacity-degree of density (area most dense taken for reading)	
No opacity . . . . .	0
Scattered or diffuse area, details of iris clearly visible . . . . .	1
Easily discernible translucent areas, details of iris slightly obscured. . . . .	2
Opalescent areas, no details of iris visible, size of pupil barely discernible. . . . .	3
Opaque, iris invisible . . . . .	4
(B) Area of cornea involved	
One quarter (or less) but not zero . . . . .	1
Greater than one quarter, but less than half . . . . .	2
Greater than half, but less than three quarters. . . . .	3
Greater than three quarters, up to whole area. . . . .	4
Score equals A x 5	Total maximum = 20

Iris

(A) Values	
Normal . . . . .	0
Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof) iris still reacting to light (sluggish reaction is positive) . . . . .	1
No reaction to light, hemorrhage, gross destruction (any or all of these) . . . . .	2
Score equals A x 5	Total maximum = 10

Conjunctivae

(A) Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris)	
Vessels normal . . . . .	0
Vessels definitely injected above normal . . . . .	1
More diffuse, deeper crimson red, individual vessels not easily discernible . . . . .	2
Diffuse beefy red. . . . .	3
(B) Chemosis	
No swelling. . . . .	0
Any swelling above normal (includes nictitating membrane). . . . .	1
Obvious swelling with partial eversion of lids . . . . .	2
Swelling with lids about half closed . . . . .	3
Swelling with lids about half closed to completely closed. . . . .	4
(C) Discharge	
No discharge . . . . .	0
Any amount different from normal (does not include small amounts observed in inner canthus of normal animals). . . . .	1
Discharge with moistening of the lids and hairs just adjacent to the lids . . . . .	2
Discharge with moistening of the lids and hairs, and considerable area around the eye . . . . .	3
Score equals (A + B + C) x 2	Total maximum = 20

The maximum total score is the sum of all scores obtained for the cornea, and conjunctivae. Total maximum score possible = 50

ize, J. H., Appraisal of the Safety of Chemicals in Foods, Drugs, andmetics, Assoc. Food and Drug Officials of the U. S., Austin, Texas, 1959, p. 51,ified according to revision in 1964. Edited by A. J. Lehman.

Pentabromo-  
ethylbenzene:

## Eye Irritation in the Albino Rabbit.

TABLE 1.

## Observations.

Observation	Examination Interval (No. Positive/No. Dosed)				
	Hours			Days	
	24	48	72	7	
<u>Cornea:</u>	Dulling normal corneal luster	0/6	0/6	0/6	0/6
	Corneal opacity: very slight				
	slight				
	moderate				
	marked				
<u>Iris:</u>	Iridal Irritation	0/6	0/6	0/6	0/6
<u>Conjunctivae:</u>	Redness:				
	very slight			3/6	2/6
	slight	2/6	3/6	2/6	3/6
	moderate	3/6	1/6		1/6
	marked				
	Chemosis:				
	very slight	1/6	1/6	0/6	0/6
	slight				
	moderate				
	marked				
	Discharge:				
	very slight	0/6	0/6	0/6	0/6
	slight				
	moderate				
	marked				
	Purulent Discharge	0/6	0/6	0/6	0/6

Pentabromo-  
ethylbenzene:

## Eye Irritation in the Albino Rabbit.

TABLE 2.

## Eye Irritation Scores.

Ocular Area		Average Scores (Range)			
		Observation Period			
		24 Hrs.	48 Hrs.	72 Hrs.	7 Days
Cornea	A	0	0	0	0
	B	0	0	0	0
Cornea Score		0	0	0	0
Iris	A	0	0	0	0
Iris Score		0	0	0	0
Conjunctivae	A	1.3 (1.0-2.0)	0.8 (1.0-2.0)	0.6 (0.5-1.0)	0.9 (0.5-1.5)
	B	0.2 (0 -1.0)	0.2 (0 -1.0)	0	0
	C	0	0	0	0
Conjunctivae Score		3.0	1.0	1.2	1.8
Total Score		3.0	2.0	1.2	1.8

IV. PRIMARY SKIN IRRITATION IN ALBINO RABBITS

A. METHOD:

Three male and 3 female New Zealand White rabbits were used. The rabbits weighed from 2361 to 2995 grams at the beginning of the study.

The hair was removed from the back of each rabbit with an electric clipper. The skin of 3 of the rabbits was abraded with a scalpel blade. Food and water were available ad libitum.

500 milligrams of the test material were applied to the back of each rabbit. The area of application was then occluded and wrapped with a gauze bandage. Twenty-four hours later the bandages were removed and the area was washed with tepid tap water and examined for skin irritation in accordance with the scale on the following page. These examinations were repeated at 72 hours.

B. RESULTS:

Table 3 presents a summation of the observations obtained. Table 4 presents the calculated primary irritation score of 0.2.

Based upon the results obtained, Pentabromoethylbenzene would not be considered a primary skin irritant.

Erythema and Eschar Formation:

	<u>Value*</u>
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 1.0 mm)	3
Severe edema (raised more than 1.0 mm extending beyond the area of exposure)	4

\*The "Value" recorded for each reading is the average value of six or more animals subjected to the test.

The values for erythema and eschar formation at 24 hours and at 72 hours for the intact animals' skin were added to similar values obtained for the abraded skin animals (a total of 4 values).

Similarly, the values for edema formation at 24 and 72 hours for intact and abraded skin animals were added together (a total of 4 values). The primary irritant score is the sum of the 8 values divided by 4. As scored by this method, a primary irritant is a substance which is not corrosive, but which results in a score of 5 or more. (Section 191.1 (g) (2) of the regulations of the Federal Hazardous Substances Act.)

Pentabromo-ethylbenzene: Primary Skin Irritation in the Albino Rabbit.

TABLE 3. Summation of Primary Skin Observations.

Observation	Examination Interval (No. Reacting/No. Dosed)			
	Intact Sites		Abraded Sites	
	24 hrs	72 hrs	24 hrs	72 hrs
<b>Erythema and Eschar Formation</b>				
No erythema	2/3	3/3	2/3	3/3
Very slight erythema	1/3		1/3	
Well defined erythema				
Moderate to severe erythema				
Severe erythema				
<b>Edema Formation</b>				
No edema	3/3	3/3	3/3	3/3
Very slight edema				
Slight edema				
Moderate edema				
Severe edema				

Pentabromo-  
ethylbenzene:

## Primary Skin Irritation in the Albino Rabbit.

TABLE 4.

## Primary Irritation Score.

Permal Irritation	Observation Time	"Value"
<b>Erythema and eschar formation:</b>		
	<b>Hours</b>	
Intact skin	24	0.3
	72	0
Abraded skin	24	0.3
	72	<u>0</u>
Subtotal		0.6
<b>Edema formation:</b>		
Intact skin	24	0
	72	0
Abraded skin	24	0
	72	<u>0</u>
Subtotal		<u>0</u>
<b>Total</b>		<u><u>0.6</u></u>

Primary irritation score is  $0.6 \div 4 = 0.2$

V. ACUTE DERMAL TOXICITY IN THE ALBINO RABBIT

A. METHOD:

Four New Zealand White rabbits (2 male and 2 female) were used at each of two dosage levels. The rabbits weighed from 2383 to 3083 grams at the start of the study period. Food and water were available ad libitum. Body weights were measured initially and at 14 days after compound application.

The hair was removed from the back of each rabbit with an electric clipper.

The compound was applied once only to the back of each rabbit. Four rabbits received 200 mg/kg and four rabbits received 2000 mg/kg of the test material. The area of application was then occluded and wrapped with a gauze bandage. Twenty-four hours later the bandages were removed and the backs were washed with tepid tap water. The rabbits were observed for mortality for a period of 14 days.

B. RESULTS:

None of the rabbits at either dosage level died during the 14 day period of observation. Three of four rabbits at each dosage level exhibited body weight gains during the observation period. One of four rabbits receiving 200 mg/kg of the test compound showed a 314 gram loss in body weight and one of four rabbits at the 2000 mg/kg level a 612 gram loss during the 14 day observation period. The loss of body weight observed for each of these rabbits was attributed to injuries sustained while in the stocks and was not considered related to compound.

Based upon the results obtained, Pentabromoethylbenzene would not be considered a toxic material by the dermal route of administration.

VI. ACUTE INHALATION TOXICITY IN THE MALE ALBINO RAT

A. METHOD:

1. General Procedure:

Twenty male rats of the Carworth CFE strain, weighing from 225 to 264 grams, were used in this test. The rats were housed in groups of 5 in metal cages elevated above the droppings and maintained in temperature and humidity controlled quarters throughout the pre-exposure and post-exposure periods. Purina Laboratory Chow and water were available ad libitum. The rats were divided into 2 groups of 10 rats each. One group received the test material at an atmospheric concentration of 2 mg/L., the second group at a concentration of 200 mg/L.

During the 1 hour exposure to the test compound, the rats were observed continuously for changes in behavior and/or appearance. Immediately following the exposure and for a period of 14 days thereafter, the rats were examined closely for pharmacodynamic and/or toxic signs.

2. Compound Administration:

Each group of 10 rats was placed in a sealed 59.1 liter glass chamber and exposed for 1 hour to a dynamic atmosphere containing the dust of the test material. In order to prevent "piling up" during the exposure, the rats were separated into 4 units of 2 or 3 rats each.

Addition of the test compound to the test chamber atmosphere was controlled by a Wright Dust Feeder. Two Wright Dust Feeders were used at the 200 mg/L. dosage level. One feeder was used at the 2 mg/L. dosage level. Dried and filtered air was passed through the

mechanism and directly into the exposure chamber. Airflow was regulated by means of a flowmeter<sup>1</sup>.

The calculated atmospheric concentrations administered were approximately 2 and 200 mg/L. of the test compound.

B. RESULTS:

1. 2 mg/L.:

All of the rats exposed to the 2 mg/L. atmospheric concentration survived through the 14-day observation period.

Signs seen during the exposure period included eye squint, increased followed by decreased respiratory rates, prostration, salivation, lacrimation, erythema, and decreased motor activity. At 24 hours all rats were essentially normal and remained so for the balance of the observation period.

All rats at this concentration exhibited normal body weight gains during the observation period.

2. 200 mg/L.:

All of the rats exposed to the 200 mg/L. atmospheric concentration survived through the 14-day observation period.

Signs seen during the exposure period included eye squint, increased followed by decreased respiratory rates, dyspnea, prostration, salivation, lacrimation, erythema, and decreased motor activity. From 24 hours to the ninth day following compound exposure several rats exhibited corneal opacity, chemosis and drying of the corneal surface. Also during this period, rats showed a slight decrease in motor activity. On the 10th and 11th day, 1 rat exhibited corneal

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<sup>1</sup>Gelman Instrument Company, Ann Arbor, Michigan, Model No. 8221.

opacity. On days 12 and 13 all 10 rats appeared normal. On the 14th day following compound exposure 1 rat exhibited corneal opacity with the remainder of the rats appearing normal.

All rats at this concentration exhibited normal body weight gains during the observation period.

3. Acute Inhalation Toxicity:

Based on the results obtained, Pentabromoethylbenzene would not be considered a toxic substance by the inhalation route of administration.

VII. ACUTE ORAL TOXICITY IN THE ALBINO RAT

A. METHOD:

Five male albino rats of the Carworth CFE strain were used at each of three dosage levels. The rats weighed from 200 to 209 grams at the initiation of the study period. The animals were maintained in temperature and humidity controlled quarters throughout the study. The rats had food and water available ad libitum except for an overnight period preceding compound administration during which food, but not water was withheld.

The test material was administered to 5 rats each at dosage levels of 50, 500 and 5000 mg/kg. The test compound was suspended in corn oil at concentrations enabling the administration of 10 ml/kg at each dosage level. All rats were observed for mortality for a period of 14 days. Body weights were measured initially and at 14 days.

B. RESULTS:

None of the rats at any of the dosage levels died during the 14 day observation period. All rats exhibited normal body weight gains.

Based upon the results obtained, Pentabromoethylbenzene would not be considered a toxic material by the oral route of administration.