

# LEBERCO LABORATORIES

123 HAWTHORNE STREET — ROSELLE PARK, N. J. 07204

DIAL 201 245 1933

November 1, 1979

SUBMITTED TO:

COMPANY SANITIZED

CAS# 939-97-9  
para-t-Butyl  
benzaldehyde

ASSAY NUMBER:

DATE RECEIVED: October 3, 1979

TEST MATERIAL: 30 gm. Bu Benz

METHOD OF ASSAY:

Normal, healthy rats of the Charles River strain, weighing 200 to 300 grams were used in this study. The animals were fasted for eighteen hours prior to dosing.

The test material was administered orally, to groups of five rats. A rigid stomach tube was used for the dosing. Following the administration of each dose level the animals were observed for seven days for signs of toxicity.

Throughout the observation period the animals were housed in raised wire mesh cages, in air conditioned quarters and maintained on their regular diet of Lab Blox and water ad libitum. The animals were examined daily, mortality recorded, and if autolysis had not occurred an autopsy was performed.

2006 DEC 11 AM 6:05

RECEIVED  
OPPT/CBIC



MR 300752

## RESULTS:

<u>Ml. /Kilo Rat</u>	<u>No. Fed</u>	<u>No. Dead</u>
0.5	5	0
1.0	5	4
2.0	5	5
5.0	5	5

The LD<sub>50</sub> is less than 1 ml. per kilo rat. Just before the animals died they showed whole body tremors.

LEBERCO LABORATORIES



Irving Levenstein, Ph. D.  
Director

IL:mr



# LEBERCO LABORATORIES

123 HAWTHORNE STREET — ROSELLE PARK, N. J. 07204

DIAL 201 245 1933

January 7, 1980

SUBMITTED TO:

CAS# 939-97-9  
para-t-Butyl  
benzaldehyde

ASSAY NUMBER:

DATE RECEIVED: December 17, 1979

TEST MATERIAL: 1 sample Bu Benz

*p-t-Butyl benzaldehyde*

METHOD OF ASSAY:

Normal, healthy rats of the Charles River strain, weighing 200 to 300 grams were used in this study. The animals were fasted for eighteen hours prior to dosing.

The test material was administered orally, to groups of five rats. A rigid stomach tube was used for the dosing. Following the administration of each dose level the animals were observed for seven days for signs of toxicity.

Throughout the observation period the animals were housed in raised wire mesh cages, in air conditioned quarters and maintained on their regular diet of Lab Blox and water ad libitum. The animals were examined daily, mortality recorded, and if autolysis had not occurred an autopsy was performed.

## RESULTS:

<u>Mg. /Kilo Rat</u>	<u>No. Fed</u>	<u>No. Dead</u>
1000	5	3
800	5	1
650	5	0
500	5	0

The LD<sub>50</sub> of the test material is greater than 800 mg. per kilo rat.

LEBERCO LABORATORIES



Irving Levenstein, Ph. D.  
Director

IL:mr

Autoren

Datum 4.9.1981

Titel A 5-day oral toxicity study with  
in male rats.

13-0787 and

---

CAS# 939-97-9  
para-t-Butyl  
benzaldehyde

The test articles . . . . . p.-tert. butyl  
benzaldehyde 13-0787 and . . . . . were sus-  
pended in rape oil and administered orally to SPF-albino rats for 5 conse-  
cutive days. The study was carried out with 4 test groups each con-  
sisting of 7 male rats. The dose levels were 100 mg/kg for 13-0787  
as well . . . . . The control males only  
received vehicle. Mortality, general symptoms and body weights were re-  
corded. All male rats were autopsied. Liver, kidneys and testes of all  
animals were microscopically examined.

Premature losses did not occur. An initial loss of body weight was ob-  
served in treated animals but these male rats showed subsequent weight

gain at the end of the treatment period. Besides findings which were not compound related, red coloured testes were seen in 2 rats treated with ..... as a result of administration of the test articles there was a decrease in the testis weights observed at necropsy for all treated animals in comparison with the controls. Microscopic examination of the testes from the treated males revealed injuries in the seminiferous epithelium.

1. Introduction

The study was carried out to assess toxicological properties of  
para-tertiary butyl benzaldehyde (13-0787)  
and

The experimental work was performed during June 1981. The histological evaluation was made during August 1981.

2. Experimental procedures

2.1. Test articles

The test articles were supplied by the study sponsor:

as a clear liquid in a metal bottle labelled 13-0787 (about 100 ml) and

The control article was Rüböl DAB 6 (R. P. Scherer GmbH, D-6930 Eberbach).

2.2. Route of administration

The control article and test article preparations were administered by gavage using a metal stomach tube.

2.3. Dose levels

Four groups of 7 male rats were treated with control or test articles at the dose levels shown on the following scheme. These doses were based on the mortality results obtained from a dose range-finding study.

Substance	Dose level	Dose volume	Number of male rats
rape oil	control	10 ml/kg	7
13-0787	100 mg/kg	10 ml/kg	7

2.4. Frequency of administration

The control and test articles were administered once daily for 5 consecutive days.

## 2.5. Test animals and experimental conditions

Thirty six male Albino-SPF rats obtained from the . . . were acclimatised to the conditions of the animal room for 7 days. Twenty eight male rats which met the laboratory criteria for normal were selected for allocation to the 4 test groups. At commencement of treatment individual body weights were within the range 144 - 164 g. The animals were head and back marked to permit individual identification. The rats were caged single or in groups of 2. The animals were housed in a single air-conditioned room maintained at a mean temperature between 19 - 23 °C, mean relative humidity between 45 - 65 % and exposed to artificial light for 12 hours (darkness for 12 hours). The animals were allowed free access to food (NAFAG No. 850, pulverized) and to tap water.

## 2.6. Evaluation of effects

### 2.6.1. General observation

The rats were observed for overt signs of toxicity or behavioural change once daily during the treatment period and on the day after treatment. All observations were recorded.

### 2.6.2. Body weight

Individual body weights were recorded once daily during the treatment period and on the day after treatment.

### 2.6.3. Necropsy

All rats were euthanized by the use of CO<sub>2</sub> and exsanguinated by incision of the neck on the day after the 5th application. A gross necropsy examination was performed on all rats. Liver, kidneys and testicles were weighed (wet weight; paired organs = weight of both parts).

### 2.6.4. Histology

Samples of liver, kidneys and testicles were fixed in 4 % formol and embedded in PARAPLAST PLUS. The tissue sections were stained as indicated:  
testicles (Haematoxylin-Eosin),  
liver (Haematoxylin-Eosin, Berlin Blue Stain + Periodic Acid Schiff's reaction),  
kidneys (Haematoxylin-Eosin, Berlin Blue Stain + Periodic Acid Schiff's reaction).  
Sections of these organs were examined under the microscope.

3.1. General observation

Mortalities did not occur throughout the study.

all animals appeared normal throughout the test period. Lethargy was seen in male no. 92 on the 2nd test day and males no. 92, 93, 94 had shaggy fur on the 3rd test day.

3.2. Body weight (Table 1, page 5; Fig. 1, page 1)

Slight weight loss was apparent in treated male rats up to 3 days following treatment. A tendency to return to normal was noted at the end of treatment.

3.3. Necropsy and organ weights (Tables 2 - 4, pages 7 - 9)

During the dissection of all rats, an agenesis of the kidney and testis on the left in male no. 87 (treated with 13-0787) was observed.

There was a treatment related decrease in the weight of testes in comparison with the controls.

3.4. Histology (Tables 5 - 7, pages 10 - 12)

All abnormalities and variations from normal are described in the appended tables. The histological evaluation of liver and kidney sections of male rats that were treated for 5 days with 13-0787 (100 mg/kg) and revealed no sign of any compound related pathological alteration when compared to the control males. However, an acute hepatitis and acute interstitial nephritis occurred in male rats of all test groups. These histological findings commonly seen in our laboratory rats were possibly caused by parasitic infestation.

The effect of the above mentioned substances on the testes was very evident. The seminiferous epithelium of all treated rats was changed. Lesions seen in the epithelia are degeneration of spermatocytes and spermatids, reduction of spermatozoa as well appearance of giant cells. Sertoli cells and interstitial cells of Leydig were unaffected.

The intensity of the testicular damage showed the following sequence of effectiveness:

3. 100 mg/kg para-tertiary butyl benzaldehyde 13-0787).

#### 4. Summary

The test articles p.-tert. butyl benz-  
aldehyde 13-0787 and were suspended in  
rape oil and administered orally to SPF-albino rats for 5 consecutive days. The  
study was carried out with 4 test groups each consisting of 7 male rats. The  
dose levels were 100 mg/kg for 13-0787

The control males only received vehicle. Mortality, general symptoms  
and body weights were recorded. All male rats were autopsied. Liver, kidneys  
and testes of all animals were microscopically examined.

Premature losses did not occur. An initial loss of body weight was observed in  
the treated animals but these male rats showed subsequent weight gain at the end  
of the treatment period. Besides findings which were not compound related,

As a result of  
administration of the test articles there was a decrease in the testis weights  
observed at necropsy for all treated animals in comparison with the controls.  
Microscopic examination of the testes from the treated males revealed injuries  
in the seminiferous epithelium.

	Rat No.	Day					
		1	2	3	4	5	6
control	78	148	150	159	163	165	172
	79	160	162	174	179	179	189
	80	156	159	167	176	179	185
	81	160	166	176	183	189	200
	82	158	163	171	178	184	191
	83	144	148	157	161	165	172
	84	156	160	170	175	180	188
	mean	154,6	158,3	167,7	173,6	177,3	185,3

13-0787 100 mg/kg	85	148	151	147	153	155	161
	86	158	142	156	162	166	177
	87	161	149	150	160	165	175
	88	159	145	150	162	168	179
	89	157	147	147	160	166	170
	90	153	141	141	149	156	164
	91	153	142	142	145	154	163
	mean	155,6	145,3	147,6	155,9	161,4	169,9

Table: 1 A 5-day oral toxicity study with 13-0787 and  
in male rats, body weights (g)

bodyweight (g)

180

170

160

150

140

130

0

1

2

3

4

5

6

DAYS

\* — \* control  
● — ● 13-0787  
100 mg/Kg/Day

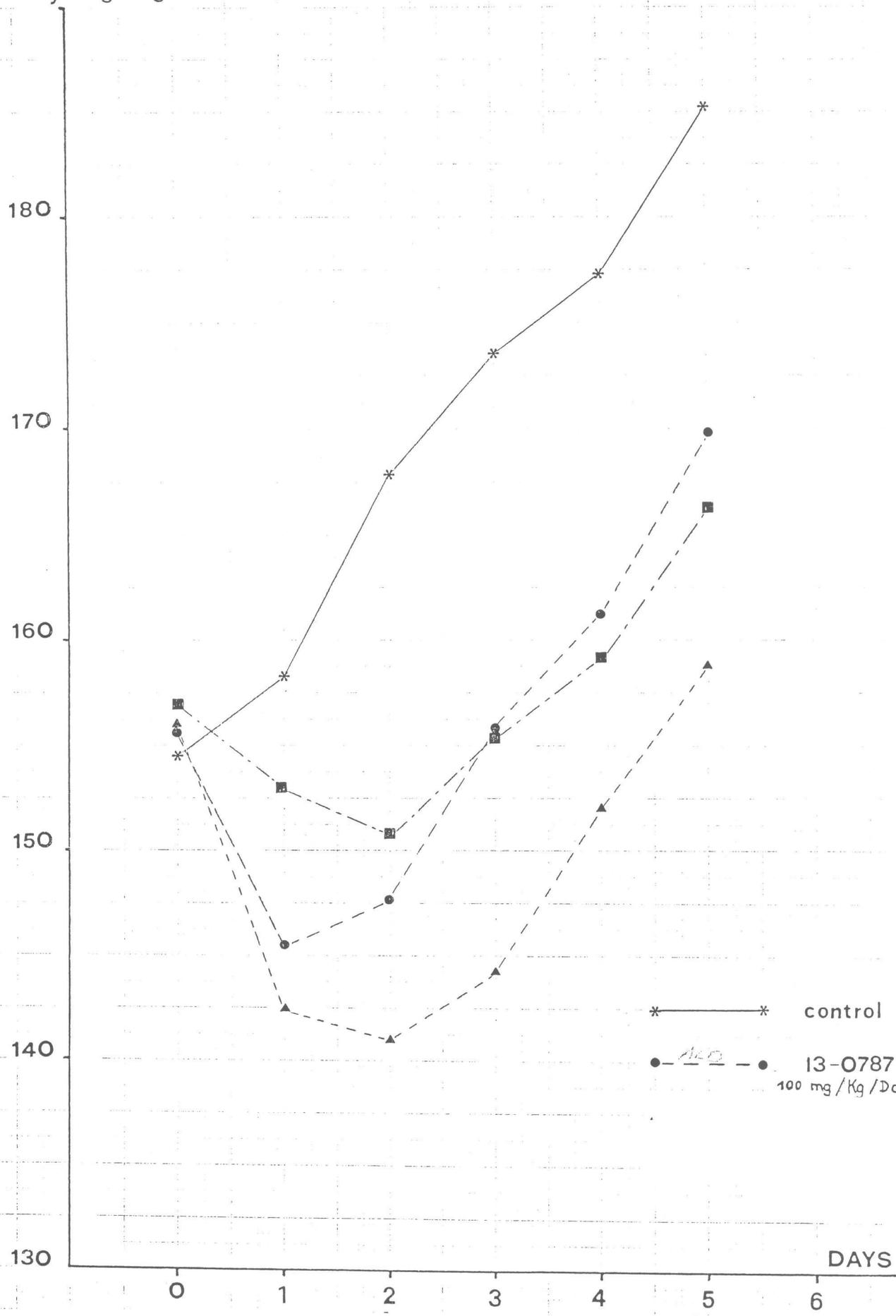


Fig.: 1 A 5-day oral toxicity study with in male rats

13-0787 and

17.06.61

TABLE 2

DOSE MG KG	ANIM NO	WEIGH G	LIVER G	KIDNE G	TESTI G
0	78	172.	9.29	1.72	2.09
	79	189.	11.41	1.88	2.17
	80	185.	9.00	1.80	2.06
	81	200.	11.72	1.91	2.15
	82	191.	11.93	2.14	1.98
	83	172.	9.00	1.63	2.02
MEAN ST.D		185.	10.52	1.86	2.07
		10.	1.19	0.17	0.07
100	85	161.	9.17	1.37	1.93
	86	177.	10.56	1.58	1.97
	87	175.	10.82	*1.57	*1.22
	88	179.	11.36	1.91	1.97
	89	170.	10.60	1.82	1.93
	91	164. 163.	11.44 9.94	1.82 1.62	1.69 1.54
MEAN ST.D		170.	10.56	1.67	1.75
		7.	0.80	0.19	0.29

\* agenesia of the kidney and testis on the left

TABLE 3 13-0787 P.O. RAT ORGAN WEIGHTS (G)  
MALES

17.06.81

17.06.81

TABLE 4

- 0 - no change
- 1 - minimal change
- 2 - moderate change
- 3 - severe change



- 0 - no change
- 1 - minimal change
- 2 - moderate change
- 3 - severe change



# LEBERCO LABORATORIES

123 HAWTHORNE STREET — ROSELLE PARK, N. J. 07204

DIAL 201 245 1933

October 15, 1979

SUBMITTED TO:

CAS# 939-97-9  
para-t-Butyl  
benzaldehyde

ASSAY NUMBER:

DATE RECEIVED: October 3, 1979

TEST MATERIAL: 50 gm. 0.5% Bu Benz in Propylene Glycol

*p-t-but. benzaldehyde*

SUBJECT OF ASSAY:

To determine if the test material produces any irritation when instilled into rabbits' eyes.

METHOD OF ASSAY:

Three normal, healthy, albino rabbits were used in this experiment. The method of procedure is that suggested by Dr. Draize and described in "Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics", published by the Association of Food and Drug Officials of the United States.

Each animal had 0.1 ml. of the test sample instilled into the right eye with no further treatment. The untreated left eye of each animal served as its own control.

Both the treated and control eyes were examined every twenty-four hours for four days and then again on the seventh day.

The scorings recorded were made according to the Draize scale for scoring ocular lesions.

Rabbit # 1

0.1 ml.

right eye

no wash

Days After Instillation

*Results*

I. Cornea

A. Opacity—Degree of Density (area which is most dense is taken for reading)

Scattered or diffuse area—details of iris clearly visible .....

Easily discernible translucent areas, details of iris slightly obscured .....

Opalescent areas, no details of iris visible, size of pupil barely discernible ..

Opaque, iris invisible .....

B. Area of Cornea Involved

One quarter (or less) but not zero .....

Greater than one quarter—less than one-half .....

Greater than one-half less than three quarters .....

Greater than three quarters up to whole area .....

Score equals A x B x 5 Total maximum = 80

	1	2	3	4	7
1	0	0	0	0	0
2					
3					
4					
1	0	0	0	0	0
2					
3					
4					
0x0x5 = 0					

II. Iris

A. Values

Folds above normal, congestion, swelling, circumcorneal injection (any one or all of these or combination of any thereof) iris still reacting to light (sluggish reaction if positive) .....

No reaction to light, hemorrhage; gross destruction (any one or all of these)

Score equals A x 5 Total possible maximum = 10

	1	2	3	4	5
1	0	0	0	0	0
2					
0 x 5 = 0					

III. Conjunctivae

A. Redness (refers to palpebral conjunctivae only)

Vessels definitely injected above normal .....

More diffuse, deeper crimson red, individual vessels not easily discernible ..

Diffuse beefy red .....

B. Chemosis

Any swelling above normal (includes nictitating membrane) .....

Obvious swelling with partial eversion of the lids .....

Swelling with lids about half closed .....

Swelling with lids about half closed to completely closed .....

C. Discharge

Any amount different from normal (does not include small amount observed in inner canthus of normal animals) .....

Discharge with moistening of the lids and hairs just adjacent to the lids ...

Discharge with moistening of the lids and considerable area around the eye

Score (A + B + C) x 2 Total maximum = 20

	1	2	3	4	5
1	0	0	0	0	0
2					
3					
1	0	0	0	0	0
2					
3					
(0+0+0)x2 = 0					

Rabbit # 2

0.1 ml.

right eye

no wash

Days After Instillation

Results

I. Cornea

A. Opacity—Degree of Density (area which is most dense is taken for reading)

- Scattered or diffuse area—details of iris clearly visible .....
- Easily discernible translucent areas, details of iris slightly obscured .....
- Opalescent areas, no details of iris visible, size of pupil barely discernible ..
- Opaque, iris invisible .....

	1	2	3	4	7
1	0	0	0	0	0
2	_____				
3	_____				
4	_____				

B. Area of Cornea Involved

- One quarter (or less) but not zero .....
- Greater than one quarter—less than one-half .....
- Greater than one-half less than three quarters .....
- Greater than three quarters up to whole area .....

1	0	0	0	0	0
2	_____				
3	_____				
4	_____				

Score equals A x B x 5 Total maximum = 80

0x0x5 = 0

II. Iris

A. Values

- Folds above normal, congestion, swelling, circumcorneal injection (any one or all of these or combination of any thereof) iris still reacting to light (sluggish reaction if positive) .....
- No reaction to light, hemorrhage; gross destruction (any one or all of these)

1	0	0	0	0	0
2	_____				

Score equals A x 5 Total possible maximum = 10

0x5 = 0

III. Conjunctivae

A. Redness (refers to palpebral conjunctivae only)

- Vessels definitely injected above normal .....
- More diffuse, deeper crimson red, individual vessels not easily discernible ..
- Diffuse beefy red .....

1	0	0	0	0	0
2	_____				
3	_____				

B. Chemosis

- Any swelling above normal (includes nictitating membrane) .....
- Obvious swelling with partial eversion of the lids .....
- Swelling with lids about half closed .....
- Swelling with lids about half closed to completely closed .....

1	0	0	0	0	0
2	_____				
3	_____				
4	_____				

C. Discharge

- Any amount different from normal (does not include small amount observed in inner canthus of normal animals) .....
- Discharge with moistening of the lids and hairs just adjacent to the lids ....
- Discharge with moistening of the lids and considerable area around the eye

1	0	0	0	0	0
2	_____				
3	_____				

Score (A + B + C) x 2 Total maximum = 20

(0+0+0)x2 = 0

Rabbit # 3

0.1 ml.

right eye

no wash

Days After Instillation

*Results*

I. Cornea

A. Opacity—Degree of Density (area which is most dense is taken for reading)

- Scattered or diffuse area—details of iris clearly visible .....
- Easily discernible translucent areas, details of iris slightly obscured .....
- Opalescent areas, no details of iris visible, size of pupil barely discernible ..
- Opaque, iris invisible .....

	1	2	3	4	7
1	0	0	0	0	0
2					
3					
4					

B. Area of Cornea Involved

- One quarter (or less) but not zero .....
- Greater than one quarter—less than one-half .....
- Greater than one-half less than three quarters .....
- Greater than three quarters up to whole area .....

1	0	0	0	0	0
2					
3					
4					

Score equals A x B x 5 Total maximum = 80

0x0x5 = 0

II. Iris

A. Values

- Folds above normal, congestion, swelling, circumcorneal injection (any one or all of these or combination of any thereof) iris still reacting to light (sluggish reaction if positive) .....
- No reaction to light, hemorrhage; gross destruction (any one or all of these)

1	0	0	0	0	0
2					

Score equals A x 5 Total possible maximum = 10

0x5 = 0

III. Conjunctivae

A. Redness (refers to palpebral conjunctivae only)

- Vessels definitely injected above normal .....
- More diffuse, deeper crimson red, individual vessels not easily discernible ..
- Diffuse beefy red .....

1	0	0	0	0	0
2					
3					

B. Chemosis

- Any swelling above normal (includes nictitating membrane) .....
- Obvious swelling with partial eversion of the lids .....
- Swelling with lids about half closed .....
- Swelling with lids about half closed to completely closed .....

1	0	0	0	0	0
2					
3					
4					

C. Discharge

- Any amount different from normal (does not include small amount observed in inner canthus of normal animals) .....
- Discharge with moistening of the lids and hairs just adjacent to the lids ...
- Discharge with moistening of the lids and considerable area around the eye

1	0	0	0	0	0
2					
3					

Score (A + B + C) x 2 Total maximum = 20

(0+0+0)x2 = 0

DISCUSSION: Instillation of 0.1 ml. of the test material into the right eye of each of three rabbits, in the manner described, did not produce any irritation.

LEBERCO LABORATORIES



Irving Levenstein, Ph. D.  
Director

IL:mr

---

from

to:

Dept. :

cc:

Date : August 8, 1980.

Theme :

Re. : p-t-Butylbenzaldehyde

CAS# 939-97-9  
para-t-Butyl  
benzaldehyde

(Letter

Date: August 8, 1980.

Re. : p-t-Butylbenzaldehyde

SKIN IRRITATION AND CAPACITY OF ALLERGENIC SENSITIZATION DETERMINED BY THE OPEN EPICUTANEOUS TEST (OET) ON GUINEA PIGS

---

MATERIAL AND METHOD

Animals: One to six experimental groups and one control group of 6 to 8 guinea pigs are used.

Test Material: is applied epicutaneously, uncovered, undiluted, and if possible and relevant, dissolved, suspended or emulsified in concentrations of 30, 10, 3 and 1% or lower in ethanol, acetone, H<sub>2</sub>O, vaseline, PEG and/or other suitable vehicles. Finished products are tested as such or diluted according to practical use (shampoos). Constant volumina of each concentration are applied with a pipette or syringe on standard areas of the clipped flank of each animal.

SKIN IRRITATION

One day before starting the induction procedure the THRESHOLD-TOXIC CONCENTRATION of the test material is estimated. A single application of 0.025 ml of each test concentration (e.g. 100, 30, 10 and 3%) is simultaneously performed on one of the areas measuring 2 cm<sup>2</sup> of the flank skin previously clipped and marked with a circular stamp.

The skin reactions are read 24 hours after the application of the test material. The minimal irritant and the maximal non-irritant concentrations are determined by an all-or-none criterion. The minimal irritant concentration is defined as the lowest one causing skin irritation. The maximal non-irritant concentration is defined as the highest one not causing macroscopic skin reactions in any of the animals. The estimation of the threshold concentration (minimal irritating and maximal non-irritating concentrations) is essential for the evaluation of the allergenic capacity of the test material based on the end point determination.

INDUCTION

Days 0-20 : On day "0" application of 0.1 ml of the test material, undiluted and if possible or necessary of its progressively diluted solutions or emulsions or suspensions, is performed to an area measuring 8 cm<sup>2</sup> on the clipped flank skin of 6 to 8 guinea pigs per concentration group, using 1 to 6 such groups for each test material.

The applications are repeated daily for 3 weeks or done 5-times weekly during 4 weeks, always using the same skin site. The application site is left uncovered and the reactions, if continuous daily applications are performed, can be read 24 hours after each application or at the end of each week. The maximal non-irritant and the minimal irritant concentrations after repeated applications are determined by the same all-or-none criterion as described above. When very strong skin reactions are provoked, the application site is changed.

LENGE

21 & 35: To determine whether or not contact sensitization was induced, all groups of guinea pigs previously treated for 21 days as described above, as well as 6 to 8 untreated or only with the vehicle pretreated controls are tested on days 21 and 35 on the contralateral flank with the test material at the minimal irritating and some lower concentrations. The minimal irritating concentration of each material is used in order to confirm the biological activity determined before starting the induction (day -1) and to exclude false results based on instability of test materials. These tests are performed by applying with a pipette 0.025 ml of each concentration to skin areas measuring 2 cm<sup>2</sup>, the reactions being read after 24, 48 and/or 72 hours. This procedure enables to determine the minimal sensitizing concentration necessary for inducing allergic contact hypersensitivity and the minimal eliciting concentration necessary to cause a positive reaction. The test material is considered allergenic at a concentration when at least one out of 8 animals of the concentration group concerned shows positive reactions with non-irritant concentrations used for challenge, i.e. its threshold concentration causing skin-reactions is shifted into the lower part of the concentration range used for challenge.

I. Skin irritation

a) after a single application

Solvent	Lowest irritant concentration	Highest non irritant concentration
Ethanol	30 %	10 %

b) after repeated applications over 21 successive days

Concentration %	Skin irritation after days		
	7	14	21
100	++ *	++ *	++
30	++ *	++ *	+
10	-	(+)	(+)
3	-	-	-

Degree of skin irritation: - = none  
 + = slight  
 ++ = moderate  
 +++ = strong

\*Because of moderate skin irritation at the end of one week's treatment the application sites were changed every other week.

II. Capacity to induce allergic sensitization

After daily applications over three weeks Concentration in %	Sensitization rate Number of animals Positive/Total	
	Day 21	Day 35
100	0/3	0/3
30	0/4	0/4
10	0/4	0/4
3	0/4	0/4

RESULTS:

After one application of p-t-Butylbenzaldehyde, 10% in alcohol no skin irritation occurs. After repeated applications only very slight ones can be found after the first week of the treatment.

p-t-Butylbenzaldehyde does not sensitize the guinea pig under conditions used in the OET.

Date: August 8, 1980.

Re. : p-t-Butylbenzaldehyde

CAS# 939-97-9  
para-t-Butyl  
benzaldehyde

CAPACITY FOR ALLERGIC SENSITIZATION DETERMINED BY THE INTRA-  
DERMAL TEST WITH FREUND'S COMPLETE ADJUVANT (FCAT) ON GUINEA PIGS

---

METHOD:

0,05 ml of the compound (undiluted, diluted or suspended) mixed with the same volume of FCA were injected intradermally into the neck on days 0, 2, 4, 7 and 9 (total dose approx. 250 mg). The experimental animals and controls, treated with 0.05 ml of FCA only, were tested epicutaneously on days 21 and 35. These tests were performed by applying 0,025 ml of each test-concentration to skin areas measuring 2 cm<sup>2</sup>. The reactions were read after 24, 48 and 72 hours.

<u>INDUCTION</u>	<u>CHALLENGE</u>	<u>SENSITIZATION RATE</u>				
		Day 21		Day 35		
5 intradermal injections of 0.1 ml of a 5% emulsion in FREUND'S COMPLETE ADJUVANT	Epicutaneously with primary non irritant solutions	Pos./Total				
		10%	3%	1%	0,3%	0,1%
		6/6	6/6	6/6	3/6	0/6

RESULTS: Under conditions used in the FCAT p-t-Butylbenzaldehyde shows sensitization properties. The preparation is one of the moderate intradermal sensitizer for the guinea pig.



FOOD AND DRUG  
*Research* LABORATORIES, INC.

60 Evergreen Place  
East Orange, New Jersey 07018  
(201) 677-9500

CAS# 939-97-9  
para-t-Butyl  
benzaldehyde

FINAL REPORT

CLINICAL SAFETY EVALUATION OF EIGHT PRODUCTS

2% t-Bu

10 Repeat Insult Patch Test

51 Subjects

Submitted to:

*Anastasia Koehler*  
Anastasia Koehler, MA  
Manager, Clinical Research

November 2, 1979

*Nathan Dorman, MD*  
Nathan Dorman, MD  
Dermatologist



CLINICAL SAFETY EVALUATION OF EIGHT PRODUCTS

PURPOSE

The purpose of this study was to determine whether the eight test are capable of producing dermal reactions indicative of irritation and/or sensitization in human subjects after repeated exposure under occlusion.

EXPERIMENTAL DESIGN

Panel Selection

Sixty subjects, 26 male and 34 female ranging in age from 16 to 72 years were selected for this test. The selection of the subjects was based on the following criteria:

- a. Willingness to participate in the study.
- b. Dependability and ability to read and understand instructions.
- c. Absence of any physical or dermatological condition which would preclude application of the test material.
- d. Reading, understanding and signing an informed consent contract (In the case of minors, parental consent was obtained).

Test Materials

The test materials used in this study were provided by They were received on August 8, 1979 and were as follows:

Product Code

Description

2% t-Bu

clear liquid

The samples had been prepared as solutions in dimethyl phthalate.



Method

10 Repeated Insult Patch Test

The 10 RIPT was conducted as follows:

Induction Phase:

Either the inner aspect of the arm or the back between scapulae and the waist, according to the the panelist's preference, was designated as the test material contact site.

About 0.2g of the test product was placed onto a 2 cm square of WebrilR (Kendall) affixed to Dermicel tape. This patch was applied to the contact site and was covered with strips of Blenderm (3M) tape to form an occlusive patch. This patch was left in place for 24 hours. At the end of this period, the subjects removed the patches. Twenty-four hour rest periods followed the Tuesday and Thursday removals and 48 hour rest periods followed the Saturday removal. The test site was scored just prior to the next patch application. This procedure was repeated until 10 applications of the test material had been made.

The choice of contact site for the second and subsequent applications depended on the condition of the previous site. Thus, if no irritation was observed at this time, the test material was reapplied to the same site. If, however, at least a 2+ reaction was observed, the test material was applied to a new site and the change in site was recorded. If a minimum of a 2+ reaction occurred in the new site, no new exposures were made. However, the subjects were challenged with the product.

Challenge

Ten to fourteen days after application of the last induction patch, the challenge patch was applied to the original contact site and to a fresh, adjacent site. The patches remained in place for 24 hours and the sites were scored 24 and 48 hours after application. The subjects were asked to report any delayed reactions which might have occurred after the last reading of the challenge to the laboratory.



RESULTS AND CONCLUSIONS

Individual test data are presented in the Tables.

Nine subject did not complete the test for personal reasons and not because of adverse reactions to the test products: Fifty one subjects completed the test.



RESULTS AND CONCLUSIONS

Sample 7 - 2% t-Bu (Table 7)

When tested as described, sample 2% t-Bu elicited no adverse dermal reactions from any of the subjects.

It appears, then, sample 2% t-Bu is not capable of eliciting irritation or of inducing sensitization under the conditions of this test.

Scale: 0 = no reaction

1+ = erythema

2+ = erythema and papules (mild edema)

3+ = erythema, papules (or mild edema) and vesicles

4+ = erythema, papules, marked edema and vesicles

\* = hours after exposure

c = change in patch site

- = no patch application

\*\* = reading taken at 72h

Scale: 0 = no reaction  
1+ = erythema  
2+ = erythema and papules (mild edema)  
3+ = erythema, papules (or mild edema) and vesicles  
4+ = erythema, papules, marked edema and vesicles

\* = hours after exposure  
c = change in patch site  
- = no patch application

Scale: 0 = no reaction  
1+ = erythema  
2+ = erythema and papules (mild edema)  
3+ = erythema, papules (or mild edema) and vesicles  
4+ = erythema, papules, marked edema and vesicles

\* = hours after exposure  
c = change in patch site  
- = no patch application  
\*\* = reading taken at 72h

Scale: 0 = no reaction  
1+ = erythema  
2+ = erythema and papules (mild edema)  
3+ = erythema, papules (or mild edema) and vesicles  
4+ = erythema, papules, marked edema and vesicles

\* = hours after exposure  
c = change in patch site  
- = no patch application

Scale: 0 = no reaction  
1+ = erythema  
2+ = erythema and papules (mild edema)  
3+ = erythema, papules (or mild edema) and vesicles  
4+ = erythema, papules, marked edema and vesicles

\* = hours after exposure  
c = change in patch site  
- = no patch application  
\*\* = reading taken at 72h

Scale: 0 = no reaction  
1+ = erythema  
2+ = erythema and papules (mild edema)  
3+ = erythema, papules (or mild edema) and vesicles  
4+ = erythema, papules, marked edema and vesicles

\* = hours after exposure  
c = change in patch site  
- = no patch application

TABLE 4

Scale: 0 = no reaction

1+ = erythema

2+ = erythema and papules (mild edema)

3+ = erythema, papules (or mild edema) and vesicles

4+ = erythema, papules, marked edema and vesicles

\* = hours after exposure

c = change in patch site

- = no patch application

\*\* = reading taken at 72h

Scale: 0 = no reaction  
1+ = erythema  
2+ = erythema and papules (mild edema)  
3+ = erythema, papules (or mild edema) and vesicles  
4+ = erythema, papules, marked edema and vesicles

\* = hours after exposure  
c = change in patch site  
- = no patch application

---

Scale: 0 = no reaction  
1+ = erythema  
2+ = erythema and papules (mild edema)  
3+ = erythema, papules (or mild edema) and vesicles  
4+ = erythema, papules, marked edema and vesicles

\* = hours after exposure  
c = change in patch site  
- = no patch application  
\*\* = reading taken at 72h

Scale: 0 = no reaction  
1+ = erythema  
2+ = erythema and papules (mild edema)  
3+ = erythema, papules (or mild edema) and vesicles  
4+ = erythema, papules, marked edema and vesicles

\* = hours after exposure  
c = change in patch site  
- = no patch application

Scale: 0 = no reaction  
1+ = erythema  
2+ = erythema and papules (mild edema)  
3+ = erythema, papules (or mild edema) and vesicles  
4+ = erythema, papules, marked edema and vesicles

\* = hours after exposure  
c = change in patch site  
- = no patch application  
\*\* = reading taken at 72h

Scale: 0 = no reaction  
1+ = erythema  
2+ = erythema and papules (mild edema)  
3+ = erythema, papules (or mild edema) and vesicles  
4+ = erythema, papules, marked edema and vesicles

\* = hours after exposure  
c = change in patch site  
- = no patch application

TABLE 7

Sample: 2% T-BuRepeat Insult Patch Test - Individual Scores

No.	Initial	Age	Sex	Exposure Number										Challenge				
				1	2	3	4	5	6	7	8	9	10	Original		Virgin		
														24*	48*	24*	48*	
1	JA	16	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	BFG	27	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	WH	27	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	MP	21	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	DR	22	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6	NF	68	M	0	0	0	0	0	0	0	0	0	0	-	-	0	0	0
7	PO	22	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8	MW	57	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9	BD	21	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10	DB	19	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11	MSH	18	M	Discontinued														
12	JM	69	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13	MSR	72	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14	MM	70	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15	VAM	21	F	Discontinued														
16	IR	18	F	Discontinued														
17	EW	20	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
18	JM	18	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
19	LB	21	F	0	0	0	0	0	0	0	0	0	0	0	0	0**	-	0**
20	TS	23	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
21	WS	21	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
22	VRO	21	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
23	JMcG	19	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
24	AGS	23	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
25	DF	20	M	0	0	0	0	0	0	0	0	0	0	0	-	0	-	0
26	EH	19	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
27	DP	21	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
28	KH	18	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
29	MD	20	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
30	MN	19	M	Discontinued														

Scale: 0 = no reaction

1+ = erythema

2+ = erythema and papules (mild edema)

3+ = erythema, papules (or mild edema) and vesicles

4+ = erythema, papules, marked edema and vesicles

\* = hours after exposure

c = change in patch site

- = no patch application

\*\* = reading taken at 72h

Sample: 2% T- BuRepeat Insult Patch Test - Individual Scores

No.	Initial	Age	Sex	Exposure Number										Challenge			
				1	2	3	4	5	6	7	8	9	10	Original		Virgin	
													24*	48*	24*	48*	
31	RW	20	M	Discontinued													
32	LH	21	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0
33	PG	20	M	Discontinued													
34	EK	21	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0
35	RS	21	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0
36	KK	20	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0
37	DF	20	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0
38	CD	31	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0
39	JDeM	19	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0
40	RB	20	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0
41	RC	21	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0
42	AF	19	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0
43	AG	21	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0
44	JC	20	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0
45	HY	18	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0
46	SH	18	F	Discontinued													
47	MJP	21	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0
48	JM	19	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0
49	RC	19	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50	LB	19	M														
51	VV	19	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0
52	MB	18	M	Discontinued													
53	KT	24	F	Discontinued													
54	AP	20	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0
55	JB	20	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0
56	LG	30	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0
57	CP	17	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0
58	JC	18	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0
59	PM	19	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0
60	ML	19	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Scale: 0 = no reaction

1+ = erythema

2+ = erythema and papules (mild edema)

3+ = erythema, papules (or mild edema) and vesicles

4+ = erythema, papules, marked edema and vesicles

\* = hours after exposure

c = change in patch site

- = no patch application

Scale: 0 = no reaction  
1+ = erythema  
2+ = erythema and papules (mild edema)  
3+ = erythema, papules (or mild edema) and vesicles  
4+ = erythema, papules, marked edema and vesicles

\* = hours after exposure  
c = change in patch site  
- = no patch application  
\*\* = reading taken at 72h

Scale: 0 = no reaction  
1+ = erythema  
2+ = erythema and papules (mild edema)  
3+ = erythema, papules (or mild edema) and vesicles  
4+ = erythema, papules, marked edema and vesicles

\* = hours after exposure  
c = change in patch site  
- = no patch application

KEY

FDRL PATCH TESTS (11/2/79)

CODE:

SECURITY INFORMATION (E) 15898  
DOES NOT CONTAIN  
Company Sanitized  
CONFIDENTIAL

t-Bu = p-t-Butylbenzaldehyde (Lot #9942-79)