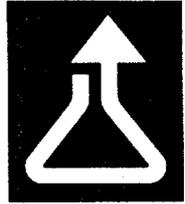


Contains NO CBI

1992 SEP -8 PM 1:29

August 12, 1992  
S CBI

(A)



**ROHM  
AND  
HAAS  
COMPANY**

Document Processing Center (TS-790)  
Office of Toxic Substances  
Attn: Section 8(e) Coordinator (CAP Agreement)  
Environmental Protection Agency  
401 M Street, S.W.  
Washington, DC 20460

889200 10309  
8EHQ-92-12071  
IHI

Dear Sir or Madam:

Re: 8(e) CAP-0103; Data Submission

The enclosed document is submitted pursuant to the TSCA Section 8(e) Compliance Audit Program and the CAP Agreement between Rohm and Haas Company and the Environmental Protection Agency. This document does not contain confidential business information.

The following is a summary of the contents of the submission under Unit II.C.3 of the CAP Agreement:

Tested Chemical:	Benzoic acid, 2-benzoyl-1-(1,1-dimethyl ethyl) hydrazide
CASRN:	112225-87-3
Title of Report or Study:	RH-5849: Oral (Gavage) Developmental Toxicity Screen in Rats (Report No. 85R-251)
Reportable Effect:	Fetotoxicity in the oral teratology study at 100 mg/kg in rats.

If additional information is required, please contact the undersigned at (215) 592-3139.  
Thank you.

Sincerely,

Ronald L. Keener, Ph.D.  
Regulatory Affairs Director  
Product Integrity Department

RLK:fs  
Enclosure

mm  
2/15/95

2

**RH-5849: Oral (Gavage) Developmental  
Toxicity Screen in Rats  
Protocol No. 85P-482 Report No. 85R-251**

**Data Summary**

RH-5849, also known as RH-65,849, (Lot No. WDW 57:58A, Toxicology Department Sample Number (TD No.) 85-284), containing 90% of the following active ingredient: 1-t-butyl-1,2-dibenzoyl hydrazine, was suspended in 0.5% aqueous methylcellulose and administered orally by gavage to four groups (10 rats/group) of presumed pregnant rats (CrI:CD®BR) at dosages of 0 (control), 30, 100 or 300 mg/kg on Days 6-15 of gestation (G). All doses were administered at a constant volume of 10 ml/kg. Clinical signs were taken at least once daily between Days 0-20 G. The dams were weighed on Days 0, 6-10, 13, 16, and 20 G. On Day 20 G the dams were killed and the thoracic and abdominal cavities were examined for gross changes. The gravid and empty uterus were weighed and corpora lutea, implantation sites and resorptions were counted. The number of fetuses per litter were counted and their location within the uterus recorded. Fetuses were then weighed and examined for external, visceral and skeletal alterations.

No dams died in the control or 30 mg/kg groups. Maternal mortality occurred at 100 mg/kg (4/10 dams) and 300 mg/kg (10/10 dams). No significant differences were noted between the control and 30 mg/kg group in the type or incidence of adverse clinical signs. At 100 and 300 mg/kg, significant increases were observed in the incidence of scant feces and passiveness. A significant increase in the number of dams in a hunched position occurred at 100 mg/kg. Presumably, hunched position was not seen among dams at 300 mg/kg since they all died by the second day of treatment.

A loss in maternal body weight occurred between Days 6-10 G at 100 mg/kg. This loss contributed to the significant decrease in mean maternal body weight gain during the treatment period (Days 6-15 G). At 30 mg/kg, maternal body weight gain was significantly reduced between Days 6-10 G. The decrease was transient since body weight gain during the treatment period (Days 6-15) was similar among dams in the control and 30 mg/kg groups.

The type and incidence of maternal gross lesions were not significantly different between the control and treated groups.

(2)

**RH-5849: Oral (Gavage) Developmental  
Toxicity Screen in Rats  
Protocol No. 85P-482 Report No. 85R-251**

There were no significant differences between the control and 30 mg/kg group in the number of litters produced, or in the mean number per litter of corpora lutea, implantations, resorptions and live fetuses. At 100 and 300 mg/kg, a significant decrease was noted in the number of litters. This decrease was due to the excessive mortality in these groups.

Mean fetal body weight was similar between the control and 30 mg/kg groups. Mean fetal body weight was significantly lower at 100 mg/kg.

There were no treatment-related increases in the type or incidence of malformed fetuses in the 30 or 100 mg/kg groups when compared to the control value. One malformed fetus was detected at 30 mg/kg. In this fetus, the 12th pair of ribs was absent.

The type and incidence of individual developmental variations and individual variations due to retarded development were similar between the control and 30 mg/kg groups. At 100 mg/kg, increases in the incidence of beaded ribs (0 out of 10 control litters vs. 2 out of 6 litters at 100 mg/kg) and wavy ribs (0 out of 10 control litters vs. 2 out of 6 litters at 100 mg/kg) were considered to be treatment related even though they were not statistically significant. These alterations occurred at a dose level that was maternally lethal (4 of 10 deaths). There were no significant differences between the control, 30 or 100 mg/kg groups in the total number of fetuses per litter with developmental variations or variations due to retarded development or in the total number of fetuses per litter with any type of variation (sum of both types of variations).

#### **CONCLUSION**

RH-5849 administered to pregnant rats orally by gavage on Days 6-15 of gestation at dosages up to and including 300 mg/kg has a no-observable effect level (NOEL) of 30 mg/kg for the fetus. A no-observable effect level was not demonstrated for the dam. The test material was maternally lethal at 100 mg/kg and greater. Fetal toxicity was noted at 100 mg/kg by the decrease in mean fetal body weight and by the increase in minor skeletal variations.

RH-5849: Oral (Gavage) Developmental  
 Toxicity Screen In Rats  
 Protocol No. 85P-482 Report No. 85R-251

Table 1  
Pregnancy and Mortality Rates

<u>Females</u>	Daily Dose (mg/kg)			
	<u>0</u>	<u>30</u>	<u>100</u>	<u>300</u>
No. Mated	10	10	10	10
No. Pregnant	10	10	10	9
Spontaneous Deaths #	0	0	4*	10*
Killed Moribund	0	0	0	0
Total No. Dead #	0	0	4*	10*

\* Significantly different from control value,  $p \leq 0.05$ .

# Significant treatment-related response,  $p \leq 0.05$ .

RH-5849: Oral (Gavage) Developmental  
 Toxicity Screen In Rats  
 Protocol No. 85P-482      Report No. 85R-251

Table 2

Incidence of Clinical Observations

<u>Days of Gestation</u>	<u>Observation</u>	Daily Dose	0	30	100	300
		(mg/kg): Number <u>Examined:</u>	<u>10</u>	<u>10</u>	<u>10</u>	<u>10</u>
0 - 6	Alopecia		0(0)	0(0)	0(0)	1(1)a
7 - 16	Alopecia		0(0)	1(3)	1(2)	1(1)
	Ataxia		0(0)	0(0)	2(2)	0(0)
	Eye, red stain		0(0)	0(0)	0(0)	2(2)
	Feces, no.		0(0)	0(0)	1(1)	0(0)
	Feces, scant #		0(0)	1(1)	10(51)*	9(13)*
	Hunched		0(0)	0(0)	4(6)*	0(0)
	Mouth, red stain		0(0)	0(0)	3(3)	0(0)
	Nose, red stain		0(0)	0(0)	0(0)	3(4)
	Passive #		0(0)	0(0)	6(9)*	7(9)*
	Perineum, yellow stain		0(0)	0(0)	1(1)	0(0)
17 - 20	Alopecia		0(0)	2(5)	0(0)	0(0)
	Feces, scant		0(0)	0(0)	2(2)	0(0)
	Hunched		0(0)	0(0)	2(3)	0(0)
	Passive		0(0)	0(0)	2(2)	0(0)

a Number of animals that exhibited the given sign  
 (Total No. of Occurrences).

\* Significantly different from control value,  $p < 0.05$

# Significant treatment-related response,  $p < 0.05$ .

RH-5849: Oral (Gavage) Developmental  
Toxicity Screen In Rats  
Protocol No. 85P-482      Report No. 85R-251

Table 3 a,b  
Mean Maternal Body Weight Changes

Daily Dose mg/kg	N	Day of Gestation					
		0-6	6-10 #	10-13	13-16	6-16 #	16-20
0	10	33 (1.9) <sup>c</sup>	16 (1.3)	16 (1.2)	24 (0.7)	57 (1.7)	67 (3.3)
30	10	32 (2.2)	8* (1.9)	17 (2.2)	26 (1.7)	51 (2.7)	64 (3.0)
100	6	35 (2.5)	-2* (3.7)	10 (3.7)	26 (4.8)	34* (3.7)	69 (5.1)
300	0	<sup>d</sup> ---	---	---	---	---	---

- a Data were excluded from females that were not pregnant or that died.  
b Grams/rat/day.  
c SEM (Standard Error)  
d All females died at this dose level.  
\* Significantly different from control value,  $p \leq 0.05$ .  
# Significant treatment-related response,  $p \leq 0.05$ .

RH-5849: Oral (Gavage) Developmental  
 Toxicity Screen In Rats  
 Protocol No. 85P-482      Report No. 85R-251

Table 4

Summary of Necropsy Observations

Observations	0.0 mg/kg	30 mg/kg	100 mg/kg	300 mg/kg
Number Examined	10	10	10	10
Lungs	<sup>a</sup>			
Black foci	---	---	2	---
Liver				
Tan areas	---	---	1	---
Kidneys				
Dilatation renal pelvis, Rt	---	1	1	---
Granular, clear-fluid filled	---	1	---	---
Clear-fluid filled	---	---	1	---
Pale	---	---	1	---
Spleen				
Enlarged (2x)	---	---	1	---
Stomach				
Gas filled	---	---	1	---
Intestines				
Gas filled	---	---	1	---
Yellow tinged #	---	---	---	4*
Colon				
Dark	---	---	---	1
Multiple pinpoint foci	---	---	---	1
Lt. Ovary				
Cyst	---	1	---	---
Uterine Horns				
Multiple dark foci	---	---	---	1

a --- indicate zero incidence.

\* Significantly different from control value,  $p \leq 0.05$ .

# Significant treatment-related response,  $p \leq 0.05$ .

RH-5849: Oral (Gavage) Developmental  
 Toxicity Screen In Rats  
 Protocol No. 85P-482      Report No. 85R-251

Table 5

Summary of Reproductive Outcome

<u>Females</u>	<u>Daily Level (mg/kg)</u>			
	<u>0.0</u>	<u>30</u>	<u>100</u>	<u>300</u>
No. mated	10	10	10	10
No. pregnant	10	10	10	9
No. non-pregnant	0	0	0	1
No. litters #	10	10	6*	0*
Mean No. Corpora Lutea	17.3	17.3	19.3	---a
Mean No. Implantations	15.1	14.7	15.5	---
 <u>Fetuses</u>				
No. dead	0	0	0	---
No. resorptions	1	3	3	---
Mean No. Resorptions	0.1	0.3	0.5	---
No. Live	150	145	90	---
Mean No. Live	15.0	14.5	15.0	---
Mean No. Males	8.8	7.5	7.7	---
Mean No. Females	6.2	7.0	7.3	---
No. stunted	0	0	1	---
Mean Weight #	3.55	3.58	3.19*	---

a --- indicate no applicable data.

\* Significantly different from control value,  $p \leq 0.05$ .

# Significant treatment-related response,  $p \leq 0.05$ .

RH-5849: Oral (Gavage) Developmental  
Toxicity Screen In Rats  
Protocol No. 85P-482      Report No. 85R-251

Table 6  
Fetal Developmental Variations

<u>Developmental Variations</u>	<u>Daily Dose (mg/kg)</u>			
	<u>0</u>	<u>30</u>	<u>100</u>	<u>300</u>
<b>External</b>				
No. Examined	150(10)a	144(10)	90(6)	---b
No. Affected	0(0)	0(0)	0(0)	---
<b>Visceral</b>				
No. Examined	76(10)	69(10)	44(6)	---
No. Affected	1(1)	2(2)	3(1)	---
Kidney - small papilla	0(0)	1(1)	3(1)	---
Pulmonary Artery				
- Common Trunk	1(1)	0(0)	0(0)	---
- Displaced Ventrally	0(0)	1(1)	0(0)	---
Ureter				
- Distended	0(0)	1(1)	1(1)	---
- Sinuous	0(0)	1(1)	1(1)	---
<b>Head</b>				
No. Examined	76(10)	69(10)	44(6)	---
No. Affected	0(0)	0(0)	0(0)	---
<b>Skeletal</b>				
No. Examined	150(10)	144(10)	90(6)	---
No. Affected	13(6)	13(7)	12(5)	---
Centrum				
- Bipartite	6(2)	0(0)	2(2)	---
- Dumbelled	9(5)	12(6)	6(2)	---
Rib				
- Beaded #	0(0)	0(0)	4(2)	---
- Rudimentary (14th rib)	2(1)	1(1)	0(0)	---
<b>Total with Developmental Variations</b>				
	14(7)	15(7)	15(5)	---
<b>Mean % Affected/Litter (SEM)</b>				
	9.5 (2.76)	11.8 (5.22)	16.6 (4.49)	---

a Fetuses (Litters).

b --- indicate no applicable data.

# Significant treatment-related response, P < 0.05.

RH-5849: Oral (Gavage) Developmental  
Toxicity Screen In Rats  
Protocol No. 85P-482      Report No. 85R-251

Table 7

Fetal Variations Due To Retarded Development

Variations Due to Retarded Development	Daily Dose (mg/kg)			
	0	30	100	300
<b>External</b>				
No. Examined	150(10) a	144(10)	90(6)	---b
No. Affected	0(0)	0(0)	0(0)	---
<b>Visceral</b>				
No. Examined	76(10)	69(10)	44(6)	---
No. Affected	0(0)	0(0)	0(0)	---
<b>Head</b>				
No. Examined	76(10)	69(10)	44(6)	---
No. Affected	0(0)	0(0)	0(0)	---
<b>Skeletal</b>				
No. Examined	150(10)	144(10)	90(6)	---
No. Affected	11(7)	18(8)	11(5)	---
<b>Centrum</b>				
- Partially ossified	0(0)	1(1)	1(1)	---
- Unilateral ossification	0(0)	0(0)	1(1)	---
<b>Hyoid</b>				
- Unossified	4(4)	10(4)	0(0)	---
<b>Pubis</b>				
- Partial ossified	0(0)	1(1)	0(0)	---
<b>Ribs</b>				
- Reduced (13th rib)	4(4)	5(3)	4(2)	---
- Partial or no ossification	1(1)	1(1)	1(1)	---
- Wavy #	0(0)	0(0)	2(2)	---
<b>Sternebrae</b>				
- partially or no ossification	3(2)	1(1)	3(3)	---

a Fetuses (Litters).

b --- indicate no applicable data.

# Significant treatment-related response,  $P \leq 0.05$ .

RH-5849: Oral (Gavage) Developmental  
 Toxicity Screen In Rats  
 Protocol No. 85P-482 Report No. 85R-251

Table 7 (Continued)  
Fetal Variations Due To Retarded Development

Variations Due to Retarded Development	Daily Dose (mg/kg)			
	0	30	100	300
Total with Variations Due to Retarded Development	11(7)a	18(8)	11(5)	---b
Mean % Affected/Litter (SEM)	7.3 (1.98)	12.4 (3.78)	12.2 (3.51)	--- ---

a Fetuses (Litters).

b --- indicate no applicable data.

RH-5849: Oral (Gavage) Developmental  
 Toxicity Screen In Rats  
 Protocol No. 85P-482 Report No. 85R-251

Table 8  
Total Fetal Variations

Variations	Daily Dose (mg/kg)			
	0	30	100	300
Total with Developmental Variations	14(7) <sup>a</sup>	15(7)	15(5)	--- <sup>b</sup>
Mean % Affected/Litter (SEM)	9.5 (2.76)	11.8 (5.22)	16.6 (4.49)	--- ---
Total with Variations Due to Retarded Development	11(7) <sup>a</sup>	18(8)	11(5)	---
Mean % Affected/Litter (SEM)	7.3 (1.98)	12.4 (3.78)	12.2 (3.51)	--- ---
Total with Variations	25(9)	31(8)	25(6)	---
Mean % Affected/Litter (SEM)	16.9 (4.22)	22.8 (6.53)	27.7 (6.27)	--- ---

a Fetuses (Litters).

b --- indicate no applicable data.



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

Ronald L. Keener, Ph.D.  
Regulatory Affairs Director, Product Integrity Department  
Rohm and Haas Company  
Independence Mall West  
Philadelphia, Pennsylvania 19105

OFFICE OF  
PREVENTION, PESTICIDES AND  
TOXIC SUBSTANCES

APR 18 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and refer to the reverse side of this page for "EPA Information Requests".

All TSCA 8(e) submissions are placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA §8(e) policy statement (43 FR 11110, March 16, 1978). Confidential submissions received pursuant to the TSCA §8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims. This information is required and should be submitted if not done so previously. To substantiate claims, submit responses to the questions in the enclosure "Support Information for Confidentiality Claims". This same enclosure is used to support confidentiality claims for non-CAP submissions.

Please address any further correspondence with the Agency related to this TSCA 8(e) submission to:

Document Processing Center (7407)  
Attn: TSCA Section 8(e) Coordinator  
Office of Pollution Prevention and Toxics  
U.S. Environmental Protection Agency  
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

*Terry R. O'Bryan*  
Terry R. O'Bryan  
Risk Analysis Branch

Enclosure

12071A



Recycled/Recyclable  
Printed with Soy/Canola Ink on paper that  
contains at least 50% recycled fiber

Triage of 8(e) Submissions

Date sent to triage: APR 20 1995

NON-CAP

CAP

Submission number: 12071A

TSCA Inventory:

Y

N

D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO

AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX

SBTOX

SEN

w/NEUR

Group 3 - Elizabeth Margosches (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; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY**

For Contractor Use Only

entire document: 0 1 2 pages 1

pages 123

Notes:

Contractor reviewer: *PR*

Date: 4/3/95

CECATS DATA: Submission # BEHO 0992-12071 SEQ. # 4

TYPE: INT SUPP FLWP

SUBMITTER NAME: Behm and Haas Company

INFORMATION REQUESTED: FLWP DATE: \_\_\_\_\_  
 0501 NO INFO REQUESTED  
 0502 INFO REQUESTED (TECH)  
 0503 INFO REQUESTED (VOL ACTIONS)  
 0504 INFO REQUESTED (REPORTING RATIONALE)  
 DISPOSITION:  
 REFER TO CHEMICAL SCREENING  
 CAP NOTICE

OPTIONARY ACTIONS:  
 NO ACTION REPUTED  
 0402 STUDIES PLANNED/INITIATED  
 0403 NOTIFICATION OF WORKING STATUS  
 0404 LABEL/MSDS (TRANGLIS)  
 0405 PROCESS/ANALYSIS (TRANGLIS)  
 0406 APP USE DISCONTINUED  
 0407 PRODUCTION DISCONTINUED  
 0408 COPY IDENTICAL

SUB DATE: 08/12/92 OTS DATE: 09/08/92 CSRAD DATE: 02/15/95

CHEMICAL NAME: Benzoic acid, 2-benzoyl-1-(1,1-dimethylethyl) hydrazide  
 CAS# 12225-87-3

INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C
0201 ONCO (HUMAN)	01 02 04	0216 EPI/CLIN	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 CHEM/PHYS 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 <u>0207</u> REPRO/TERATO (HUMAN)	01 02 04	0221 ENV. OCCURREL/FATE	01 02 04	0246 CLASTO (HUMAN)	01 02 04
0208 REPRO/TERATO (ANIMAL)	01 02 04	0222 EMER INCI OF ENV CONTAM	01 02 04	0247 DNA DAM/REPAIR	01 02 04
0209 NEURO (HUMAN)	01 02 04	0223 RESPONSE REQUEST DELAY	01 02 04	0248 PROD/USE/PROC	01 02 04
0210 ACUTE TOX (HUMAN)	01 02 04	0224 PROD/COMP/CHEM ID	01 02 04	0251 MSDS	01 02 04
0211 CHR. TOX (HUMAN)	01 02 04	0225 REPORTING RATIONALE	01 02 04	OTHER	01 02 04
0212 ACUTE TOX (ANIMAL)	01 02 04	0226 CONFIDENTIAL	01 02 04		
0213 SUB ACUTE TOX (ANIMAL)	01 02 04	0227 ALLERG (HUMAN)	01 02 04		
0214 SUB CHRONIC TOX (ANIMAL)	01 02 04	0228 ALLERG (ANIMAL)	01 02 04		
0215 CHRONIC TOX (ANIMAL)	01 02 04	0229 METAB/PHARMACO (HUMAN)	01 02 04		

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

CAS SR NO: (M) 114111 YES (DROP/PREFER): NO (CONTINUE): REF-R

*garage, levels*  
 300 mg/kg - 100% mortality by 2nd week treatment  
 100 mg/kg - 10% mortality by 2nd week treatment  
 30 mg/kg - red BW gain during treatment  
 NONE for developmental test  
 not established for maternal toxicity