03

100 INDEPENDENCE MALL WEST, PHILADELPHIA, PA 19106-2399 USA
TELEPHONE (215) 592-3000 CENTRAL FAX (215) 592-3377

8EHQ-0501-14902

Contain NO CBI

CBI

MR 47870

RECEIVED
OPPT CBIC

May 8, 2001

2001 MAY 15 AM 7:05

ROHM HAAS

Document Processing Center (TS-790)
Attention: Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

8EHQ-01-14902

Ref.: Letter, March 27, 2001, describing the voluntary review of certain categories of health and environmental studies recently acquired by Rohm and Haas Company.

Dear Coordinator:

Rohm and Haas Company submits this notice in accordance with Section 8(e) of the Toxic Substances Control Act.

This letter transmits results of a 23-day range- finding toxicity test with albino rats exposed to monomethyltin trisisooctylthioglycolate (CAS No. = 54849-38-6) at dietary levels of 0, 3, 10, 30, and 100 ppm.

In the two highest dose groups, decreased feed intake, weight loss, neurotoxic effects (tremors and ataxia), and deaths were seen. These animals either died or were killed within a two week period.

In the 100 ppm group, two male and female rats were killed in moribund condition. Hispathological findings in the brain (necrotic pyramidal neurons in the hypocampus and necrotic purkinje cells), spleen (atrophy of white pulp), stomach (hyperkeratosis and haemorrhagic erosion), pancreas (loss of zymogen granules), and testis (degenerative changes) were observed in the 10 ppm group..

In the 10 ppm group, kidney weights were increased. At necropsy, degeneration of tubular cells in the kidneys were observed in males and females.

No treatment related effects were observed in the 3 ppm group.

Rohm and Haas Company does not consider the exact identity of this chemical to be Confidential Business Information (CBI)

If you have any questions concerning this submittal, my telephone number is (215) 592-2986.

Sincerely,

George J. Powell
TSCA Manager
EHS Corporate Center

RECEIVED
OPPT NCIC
2001 MAY 21 AM 9:59

89010000181

A 04

74RM-10

CENTRAAL INSTITUUT VOOR VOEDINGSONDERZOEK TNO

Utrechtseweg 48
Zeist

CENTRAL INSTITUTE FOR NUTRITION AND FOOD RESEARCH
INSTITUT CENTRAL DE LA NUTRITION ET DE L'ALIMENTATION
ZENTRALINSTITUT FÜR ERNÄHRUNGSFORSCHUNG

CAS# = 54849-38-6

RAPPORT NR. R 4392

Title: Range-finding (28-day) toxicity study with trimethyltin isooctylthioglycolate in albino rats

Authors: Dr. H.P. Til, M.Th. Spanjers and Mrs. Drs. Harriet C. Dreef-van der Meulen

At the request of: Cincinnati Milacron Chemicals Inc., New Brunswick, N

Approved by: Dr. A.P. de Groot

Date: June 1974

Gehele of gedeeltelijke publikatie van dit rapport is zonder schriftelijke toestemming verboden.
Total or partial publication of this report without written assent is not allowed.

23-15.000-1073

SUMMARY

1. The toxicity of trimethyltin isooctylthioglycolate was studied in a range-finding (28-day) toxicity test with albino rats fed the test substance at dietary levels of 0, 3, 10, 30 and 100 ppm.

2. Tremors, ataxy, deaths, weight loss and decrease of food intake occurred at the two highest feeding levels. General appearance, growth and food intake were not distinctly affected at the 3 and 10 ppm level.

3. No distinct differences in haemoglobin content were observed between the 3 and 10 ppm group and the controls.

4. The water content of the brain was not increased.

5. The weights of the kidneys were distinctly increased and those of the thymus were decreased at 10 ppm. Thymus weight was also relatively low in the 3 ppm group.

6. At microscopic examination degeneration of tubular cells in the kidneys were noticed in males and females of the 10 ppm group. In addition histopathological changes in the brain, spleen, stomach, pancreas and testis were observed in the highest dosage group.

Range-finding (28-day) toxicity study with trimethyltin isooctylthioglycolate in albino rats

1. INTRODUCTION

At the request of Cincinnati Milacron, the toxicity of a trimethyltin compound was studied in a range-finding test by feeding the material at various dietary levels to albino rats during a four-week period.

Growth, food intake, haemoglobin content, water content of the brain, weights of the liver, kidneys, thymus and brain and microscopic examination of these organs were used as criteria for disclosing possible harmful effects.

2. MATERIAL AND METHODS

The test compound was stated to be trimethyltin isooctylthioglycolate. Four 50 ml samples of the same batch (No. 1084 - 45) were received from Cincinnati Milacron on February 2nd, 1974. The product was a clear, colourless liquid.

Twenty five male and 25 female weanling rats from the CIVO-colony (Wistar derived) were divided according to body weight into five groups of five males and five females each and fed on stock diet with the tin compound added at levels of 0, 3, 10, 30 and 1 ppm.

Body weights and food consumption were recorded at weekly intervals. Haemoglobin content was determined terminally in all surviving rats.

At the end of week 4 all surviving animals were killed by decapitation and examined grossly. The brain, liver, kidneys and thymus were weighed and samples of these organs were collected for histological examination.

After weighing of the brain, appropriate samples of this organ were taken for determinations of the water content by drying at 105°C till constant weight (24 hours).

3. RESULTS

3.1 General appearance, growth and food intake

After the fourth day all rats of the highest dosage group showed slight tremors. Thereafter, the severity of this phenomenon increased gradually. The animals looked sick and showed decrease

activity, ataxy and emaciation. All animals died or were killed in extremis within two weeks. Similar signs of intoxication were noticed in the 30 ppm group after the first week. All rats in th group died in the second and third week.

No mortality or abnormalities in appearance and behaviour occurred in the other groups.

Mean body weights and food intake were markedly decreased i the two highest dosage groups (tables 1 and 2). These effects we not noticed in the lower dietary level groups. Food efficiency figures (table 2) of the 3 and 10 ppm groups were comparable to those of the controls.

Table 1. Average body weights

group no.	ppm trimethyltin in the diet	mean body weights (in g) at end of wee				
		0	1	2	3	4
		groups of five males				
7226	0	58.8	83	113	139	15
7227	3	60.4	87	117	147	17
7228	10	59.0	88	123	144	1
7229	30	59.4	75	59**	-[1])	
7230	100	59.0	43*	-	-	
		groups of five females				
7226	0	53.8	75	100	115	12
7227	3	53.8	75	98	112	12
7228	10	53.8	77	102	113	11
7229	30	55.2	68	55*	-	
7230	100	55.2	39*	-	-	

*P < 0.05; **P < 0.01.

[1]) = all rats dead.

Table 2. Average food intake (in g/rat/day) and food efficiency

ppm trimethyltin in the diet	food intake in week				food efficiency during week 1-4		
	1	2	3	4	gain	food	gain/food
	groups of five males						
0	8.7	11.5	13.1	12.7	100	322	0.31
3	8.9	11.7	13.6	13.1	111	331	0.34
10	9.9	13.4	13.5	13.7	108	354	0.31
30	9.0	5.5	-[1]	-	-	-	-
100	3.6	-	-	-	-	-	-
	groups of five females						
0	8.1	10.5	11.3	10.1	73	280	0.26
3	7.7	9.5	10.5	10.1	70	265	0.26
10	8.1	10.6	10.3	10.1	65	274	0.24
30	8.1	5.2	-	-	-	-	-
100	3.4	-	-	-	-	-	-

[1]- = all rats dead.

3.2 Haematology

Haemoglobin content was not affected at the dietary levels of 3 and 10 ppm (table 3).

Table 3. Average haemoglobin content, recorded at day 27

ppm trimethyltin in the diet	haemoglobin content (g/100 ml)	
	males	females
	groups of five rats	
0	15.2	16.1
3	14.7	15.7
10	15.6	16.8

3.3 Water content of the brain

The average water content of the brain was slightly decreased at the 10 ppm level in males (table 4), which is in contrast to the increased water content of the brain induced by certain other organotin compounds.

Table 4. Terminal water content of the brain

ppm trimethyltin in the diet	% water in the brain	
	males	females
groups of five rats		
0	80.2	77.7
3	79.1	78.0
10	78.6**	76.8

**P < 0.01.

3.5 Organ weights

Average absolute and relative organ weights are shown in table 5.

Both the absolute and relative weight of the kidneys were distinctly increased and those of the thymus were decreased at 10 ppm. Thymus weight was also relatively low at the 3 ppm level, although the differences with the controls were not statistically significant.

Table 5. Mean absolute and relative organ weight recorded at week 4

ppm trimethyltin in the diet	liver		kidneys		thymus		brain	
	g	g/100	g	g/100	g	g/100	g	g/100
groups of five males								
0	7.49	4.73	1.38	0.87	0.439	0.279	1.60	0.94
3	7.78	4.53	1.60	0.93	0.380	0.223	1.50	0.88
10	7.75	4.65	1.64	0.98*	0.335	0.212**	1.55	0.94
groups of five females								
0	5.56	4.37	1.09	0.86	0.354	0.279	1.35	1.07
3	5.14	4.16	1.07	0.87	0.298	0.241	1.43	1.16
10	4.78	4.00*	1.24	1.04**	0.263*	0.220**	1.42	1.19*

*P < 0.05; **P < 0.01.

3.6 Pathology

At autopsy after four weeks, no gross changes were observed in the 3 and 10 ppm group that could be ascribed to the ingestion of the test substance.

At microscopic examination, degenerative kidney changes were observed, consisting of swollen tubular cells with large pale nuclei in the inner cortex layer of males and females fed 10 ppm.

No treatment-related changes could be observed in the 3 ppm group.

In order to obtain some information about the histopathology of the rats in the highest dosage group two male and two female rats of the 100 ppm group were autopsied when moribund in the second week and a wide range of organs was collected for histological examination. Treatment-related histological changes consisted of pathological changes in the brain (necrotic pyramidal neurons in the hypocampus and necrotic purkinje cells), atrophy of the white pulp in the spleen, degeneration of cortical tubules in the kidneys, hyperkeratosis and haemorrhagic erosions in the stomach, loss of zymogen granules in the pancreas and degenerative changes (multinucleated giant cells) in the testis.