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August 5, 1992



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Office of Toxic Substances
Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

Attention: Section 8(e) Coordinator (CAP Agreement)

This submission is pursuant to the TSCA Section 8(e) Compliance Audit Program and CAP Agreement #8ECAP-0036.

The information included herein is characterized as follows:

Chemical Identity - MIXTURE OF 5 ISOMERS OF TETRAMETHYL CYCLOHEXANE

Chemical CAS No. - NOT FOUND

Information/Study Type - II,B,2,b/Acute Toxicity/Irritation Study

Information/Study Identification - Acute Oral Toxicity Study with an Equitoxic Mixture of Five Isomers in Female Albino Rats
BT-73-080

Identification of Reportable Endpoint: SIGNS OF NEUROTOXICITY

NOTE: While several compounds were tested, the reported endpoint is only for the chemical identified in this letter.

Previous TSCA 8(e) or PMN submissions, if any, for the reference chemical can be found in Appendix A.

It should be noted that this summary is not all inclusive. Therefore, it may not highlight all adverse effects that EPA may judge to meet TSCA 8(e) reportability. This submission/report does not contain confidential business information.

Sincerely,

J. R. Condray
Director, Regulatory Management
(314) 694-8883

0003

PROJECT NO.
REPORT FILE

~~BTL-73-56, 73-57, 73-58, 73-59, 73-60, 73-61, 73-62, 73-63, 73-64, 73-65, 73-66, 73-67, 73-68, 73-69, 73-70, 73-71, 73-72, 73-73, 73-74, 73-75, 73-76, 73-77, 73-78, 73-79, 73-80, 73-81, 73-82, 73-83, 73-84, 73-85, 73-86, 73-87, 73-88, 73-89~~
BTL-73-89

707

Industrial **BIO-TEST** *Laboratories, Inc.*
1810 FRONTAGE ROAD
NORTHBROOK, ILLINOIS 60062

REPORT TO

MONSANTO COMPANY

ACUTE ORAL TOXICITY STUDY WITH
AN EQUITOXIC MIXTURE OF FIVE ISOMERS
IN FEMALE ALBINO RATS

BTL NOS. 73-60, 73-56, 73-57, 73-58, 74-8

BTL 73-89

MAY 29, 1974

IBT NO. 601-04538

0 0 0 4

478

Industrial BIO-TEST Laboratories, Inc.
1810 FRONTAGE ROAD
NORTHBROOK, ILLINOIS 60062

May 29, 1974

Dr. Paul L. Wright
Manager of Toxicology
The Monsanto Company
800 North Lindbergh Boulevard
St. Louis, Missouri 63166

Dear Dr. Wright:

Re: IBT No. 601-04538 - Acute Oral Toxicity Study
with an Equitoxic Mixture of Five Isomers in
Female Albino Rats - BTL Nos. 73-60, 73-56,
73-58 and 74-8

We are submitting herewith our laboratory report dated
May 29, 1974, prepared in connection with the above study.

Very truly yours,



J. C. Calandra
President

JCC:bp

the product and maybe given to responsible sales contacts, but it is not to be used by them in advertising copy. The source of this material is not to be divulged until it appears in formal publications. No exceptions to the established rule may be made without the approval of the Medical Department in St. Louis. Customers' inquiries regarding matters of toxicity are to be referred as before to the Medical Department in St. Louis for reply.

—Monsanto Company

REPORT TO

MONSANTO COMPANY

ACUTE ORAL TOXICITY STUDY WITH
AN EQUITOXIC MIXTURE OF FIVE ISOMERS
IN FEMALE ALBINO RATS

BTL NOS. 73-60, 73-56, 73-57, 73-58, 74-8

MAY 29, 1974

IBT NO. 601-04538

I. Introduction

At the request of Monsanto Company, an acute oral toxicity study was conducted in order to determine if an equitoxic mixture of five isomers enhances or inhibits the acute oral toxicity of the individual compounds. The acute oral LD₅₀ of each material was previously determined and reported under IBT Nos. 601-04535 and 601-04537. The isomers were identified as:

1. trans-1,1,3,5-Tetramethylcyclohexane, BTL-73-60 FE 99266
2. cis, trans-1,2,3,4-Tetramethylcyclohexane, BTL-73-56 FA 99266
3. cis, trans-1,2,3,5-Tetramethylcyclohexane, BTL-73-57 FB 99266
4. cis, trans-1,2,4,5-Tetramethylcyclohexane, BTL-73-58 FC 99266
5. cis, trans-1,1,2,3-Tetramethylcyclohexane, BTL-74-8 FF 99266

II. Summary

The results of the acute oral toxicity study in albino rats are summarized below.

These data indicate that the mixture has no significant effect on the acute oral LD₅₀'s of the individual compounds.

<u>Test Material</u>	<u>Results</u>
<u>trans</u> -1,1,3,5-Tetramethylcyclohexane	Relatively Harmless LD ₅₀ > 15,380 mg/kg*
<u>cis, trans</u> -1,2,3,4-Tetramethylcyclohexane	Relatively Harmless LD ₅₀ > 15,380 mg/kg*
<u>cis, trans</u> -1,2,3,5-Tetramethylcyclohexane	Relatively Harmless LD ₅₀ > 15,380 mg/kg*
<u>cis, trans</u> -1,2,4,5-Tetramethylcyclohexane	Relatively Harmless LD ₅₀ > 15,380 mg/kg*
<u>cis, trans</u> -1,1,2,3-Tetramethylcyclohexane	Relatively Harmless LD ₅₀ > 15,380 mg/kg*
Equitoxic Mixture of Five Isomers	Relatively Harmless LD ₅₀ > 15,380 mg/kg

* LD₅₀ was previously determined and reported under IBT Nos. 601-04535 and 601-04537.

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

Report prepared by:

Carol F. Hintz

Carol Hintz
Senior Technician
Acute Toxicity

Report approved by:

C. W. Mastri

C. W. Mastri, B.S.
Section Head, Acute Toxicity

M. L. Keplinger

M. L. Keplinger, Ph.D.
Manager, Toxicology

III. Investigational Procedure

The detailed investigational procedure employed in this study is presented in the appendix.

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IV. Results

A. Mortality and Body Weights

Individual mortality and body weight data are presented in

Table I.

TABLE I

Acute Oral Toxicity Study - Female Albino Rats

Mortality and Body Weight Data

Test Material: Equitoxic Mixture of Five Isomers
Form Administered: Undiluted*
Acute Oral LD₅₀ > 15,380 mg/kg

Strain: Charles River
IBT No.: 601-04538
Classification: Relatively
Harmless

Dose Level (mg/kg)	Animal Number	Individual Body Weights (grams)		Number Dead / Number Tested	Percent Dead
		Test Day 0	Test Day 14		
15 380	1	162	193	0/2	0
	2	152	207		

* The test material was prepared using equal weights of each isomer. Due to the paucity of test material, only two rats were dosed.

B. Reactions

The untoward reactions exhibited by the rats following dosing are presented in Table II.

Necropsy examination of all animals at sacrifice revealed no gross pathologic alterations.

TABLE II
Acute Oral Toxicity Study - Female Albino Rats

Summary of Reactions

Test Material: Equitoxic Mixture of Five Isomers
Concentration: Undiluted
IBT No.: 601-04536

Dose Level (mg/kg)	Reaction	Time of Onset	Duration	Time of Death
		Following Dose Administration	of Reaction	Following Dose Administration
15,380	Hypoactivity	1 minute	3 days	-
	Ruffed fur	1 minute	3 days	
	Chewing motions	1 minute	6-22 hours	
	Labored breathing	1 minute	6-22 hours	
	Muscle incoordination of forepaws and neck	1 minute	9 minutes	
	Diarrhea	30 minutes	6-22 hours	
	High stance	30 minutes	6-22 hours	
	Muscular weakness	2 hours	6-22 hours	
	Diuresis	6-22 hours	2 days	

IV. Appendix

The detailed investigational procedure employed in this study is presented in the following pages.

ACUTE ORAL TOXICITY STUDY - ALBINO RATS

Young albino rats derived from Sprague-Dawley stock were used as test animals. All animals were kept under observation for five days prior to experimental use, during which period they were checked for general health and suitability as test animals. The animals were housed in stock cages and were permitted a standard laboratory diet plus water ad libitum, except during the 16-hour period immediately prior to oral intubation when food was withheld.

Initial screening was conducted in order to determine the general level of toxicity of the test material. Selected groups of albino rats were administered the test material at several dose levels. All doses were administered directly into the stomach of the rats using a hypodermic syringe equipped with a ball-tipped intubating needle.

After oral administration of the test material, the rats were housed individually in suspended, wire-mesh cages and observed for the following 14 days. Initial and final body weights, mortalities, and reactions were recorded. A necropsy examination was conducted on all animals.

At the end of the observation period, the acute oral median lethal dose (LD₅₀) of the test material was calculated, if possible, using the techniques of Litchfield and Wilcoxon*. The test material was then assigned a classification in accordance with Harold C. Hodge**. The classification system is presented in the following Table.

* Litchfield, J. T. Jr., and Wilcoxon, F., "A Simplified Method of Evaluating Dose-Effect Experiments," J. Pharm. & Exp. Ther. 96, 99 (1949).

** Hodge, Harold C., "The LD₅₀ and its value", American Perfumer and Cosmetics 80, 57 (1965).

TABLE

Acute Oral Toxicity Study - Albino Rats

Classification of Test Materials
Based on Acute Oral LD₅₀

Acute Oral LD ₅₀ (Range of Values)	Classification	Probable lethal dose for a 70 kg man in commonly used measures
Less than 5 mg/kg	Extremely toxic	a taste (less than 7 drops)
5 - 50 mg/kg	Highly toxic	between 7 drops and 1 teaspoonful
50 - 500 mg/kg	Moderately toxic	between 1 teaspoonful and 1 ounce
500 - 5,000 mg/kg	Slightly toxic	between 1 ounce and 1 pint or 1 pound
5,000 - 15,000 mg/kg	Practically non-toxic	between 1 pint and 1 quart
Greater than 15,000 mg/kg	Relatively harmless	more than 1 quart