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<b>Document Title</b> TOXICOLOGICAL INVESTIGATION OF CYCLOHEXYL ISOCYANATE WITH COVER LETTER DATED 121090		
<b>Chemical Category</b> CYCLOHEXYL ISOCYANATE (3173-53-3)		

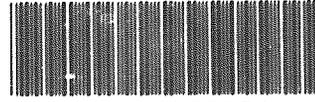
A Bayer USA INC COMPANY

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December 10, 1990

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Attention: 8(d) Health and Safety Reporting Rule  
(Notification/Reporting)

Gentlemen:

Enclosed is a copy of Health and Safety Studies, submitted on behalf of Mobay Corporation, Mobay Road, Pittsburgh, Pennsylvania 15205. We are filing these Health and Safety Studies to comply with the regulations codified at 40 CFR, Part 716.

The information required at 40 CFR 716.35 is given below.

Chemical Name: Cyclohexane, isocyanato-

CAS No: 3173-53-3

Name of Study: Toxicological Investigation of: Cyclohexylisocyanate

Submitting Official: Francis J. Rattay  
Title: Manager, Regulatory Compliance  
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Pittsburgh, Pa 15205

Telephone No.: (412) 777-7471

Sincerely,



Francis J. Rattay  
Manager, Regulatory Compliance

Attachment

cc: J. R. Bankston  
8(d) File

Certified Mail No.: P 520 613 276

# YOUNGER LABORATORIES INCORPORATED

Consulting and Analytical Services

CHEMICAL . . . MICROBIOLOGICAL . . . BIOLOGICAL

123 CLIFF CAVE ROAD  
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PHONE: (314) 487-6661

October 31st, 1974

## Certificate of Analysis

SUBJECT -

Toxicological Investigation Of: CYCLOHEXYLISOCYANATE

STUDY CONDUCTED FOR -

MOBAY CHEMICAL COMPANY, New Martinsville, West Virginia

DATE SUBMITTED: September 30th, 1974

Y.L. RESEARCH NUMBER: 9495YLR74

SUMMARY -

- C  
O  
P  
Y
- A) Single Oral Dose LD<sub>50</sub> (Albino Rats)  
The Single Oral Dose LD<sub>50</sub> for male and female per kilogram with lower and upper limits of 490 and 1100 milligrams per kilogram. The compound was classed as mildly toxic by oral dose in male and female rats.
- B) Acute Skin Absorption Minimal Lethal Dose (Albino Rabbits) - 24-hours exposure  
The Acute Skin Absorption Minimal Lethal Dose for male and female rabbits was found to be greater than 2,000 milligrams per kilogram and less than 3,160 milligrams per kilogram. The compound was classed as slightly toxic by skin absorption in male and female rabbits.
- C) Skin Irritation (Albino Rabbits) - F.H.S.A.\* - 24-Hours Exposure  
The compound was classed as a severe skin irritant under the grading system as outlined in the Federal Hazardous Substances Act.  
Primary Irritation Score: 3.8
- D) Eye Irritation (Albino Rabbits) - F.H.S.A.\* - 24-Hours Exposure  
The compound was classed as a severe eye irritant under the grading system as outlined in the Federal Hazardous Substances Act.  
\*Tests conducted in accordance with the Federal Hazardous Substances Act
- E) Vapor Inhalation (Male Rats) - Ambient Temperature  
All six animals succumbed within two and one-half hours after start of exposure. It was concluded that the vapors were highly toxic under conditions of the test. Average concentration of vapors in chamber: 7.16 Grams / M<sup>3</sup>
- Cyclohexyl  
150  
F. 203*

YOUNGER LABORATORIES, INC.

BY: MELVIN D. BIRCH

EXPERIMENTAL PROCEDURE -

A) Single Oral Dose LD<sub>50</sub> (Albino Rats)

The undiluted compound was fed by stomach tube to Sprague-Dawley strain albino male and female rats.

After the approximate Minimal Lethal Dose was determined, groups of male and female rats were fed in increasing doses at increments of 0.1 fractional log intervals at four levels designed to blanket the toxicity range thereby supplying data for calculation of the LD<sub>50</sub> which was done according to the method of E. J. de Beer. Observations were made for toxic signs and the viscera of the test animals were examined macroscopically.

The data are shown in Table I.

B) Acute Skin Absorption Minimal Lethal Dose (Albino Rabbits) - 24-Hours Exposure

The undiluted compound was applied in increasing doses at increments of 0.2 fractional log intervals to the closely clipped, intact skin of New Zealand albino male and female rabbits.

The treated areas were covered with plastic strips and the animals held in wooden stocks for periods up to twenty-four hours, after which time they were assigned to individual cages.

Observations were made for toxic signs and the viscera of the test animals were examined macroscopically.

The data are shown in Table II.

C) Skin Irritation (Albino Rabbits) - F.H.S.A.\* - 24-Hours Exposure

0.5 Milliliter of undiluted sample was applied to the clipped, intact, and abraded skin of six albino male and female rabbits under a one inch by one inch square patch, two single layers thick. The patches were held in place with adhesive tape. The trunk of each animal was wrapped with plastic strips, to retard evaporation and avoid contamination, for the twenty-four hour exposure period.

Observations were made over a period of fourteen days.

The data, scored according to the method of Draize, Woodard, and Calvery (Journal of Pharm. and Exp. Therapeutics, Volume 82, December, 1944) are shown in Table III.

D) Eye Irritation (Albino Rabbits) - F.H.S.A.\* - 24-Hours Exposure

0.1 Milliliter of undiluted sample was placed in the conjunctival sac of the right eye of each of six albino male and female rabbits and observations made over a period of seven days for inflammation.

The treated eyes were washed with sodium chloride solution USP after the twenty-four hour reading. The left eye served as a control.

The data, scored according to the method of Draize, et al, are shown in Table IV.

\*Tests conducted in accordance with the Federal Hazardous Substances Act

E) Vapor Inhalation (Male Rats) - Ambient Temperature

Six mature male rats were placed in a stainless steel chamber of 35-liters capacity and exposed for six hours to a concentrated atmosphere of vapors produced by passing a stream of air through 42.4 grams of the compound contained in a 500-milliliter erlenmeyer flask.

Vapors from the flask passed into a one liter bottle to remove droplets and then into the chamber. Air flow through the sample was 4.0 liters per minute as measured by a calibrated rotameter. No supplementary air was introduced inasmuch as the above supply was ample for the animals' oxygen requirements.

The animals were observed for behavior during exposure until all succumbed. The viscera of the test animals were examined macroscopically.

The data are shown in Table V.

T A B L E I  
THE SINGLE ORAL DOSE LD<sub>50</sub> OF  
CYCLOHEXYLISOCYANATE FOR RATS

Sample Fed Undiluted

<u>Animal No. - Sex</u>	<u>Weight Gm.</u>	<u>Dose Mg. / Kg.</u>	<u>Fate</u>
1 - Female	240	398	Survived
2 - Male	280	398	Died
3 - Female	230	398	Survived
4 - Male	210	398	Survived
5 - Female	235	398	Survived
6 - Male	205	501	Died
7 - Female	250	501	Survived
8 - Male	250	501	Survived
9 - Female	240	501	Survived
10 - Male	205	501	Died
11 - Female	205	631	Survived
12 - Male	210	631	Died
13 - Female	270	631	Died
14 - Male	260	631	Died
15 - Female	225	631	Survived
16 - Male	220	794	Died
17 - Female	230	794	Survived
18 - Male	205	794	Died
19 - Female	260	794	Died
20 - Male	255	794	Died

DISCUSSION -

The Single Oral Dose LD<sub>50</sub> for male and female rats was placed at 560 milligrams per kilogram with lower and upper limits of 490 to 630 milligrams per kilogram.

The compound was classed as mildly toxic by oral ingestion in male and female rats.

Survival time was several hours to two days with most deaths occurring within one day.

Toxic signs included reduced appetite and activity (one to three days in survivors), increasing weakness, collapse, and death.

At autopsy there was lung and liver hyperemia, and acute gastrointestinal inflammation.

Surviving animals were sacrificed fourteen days after dosing. The viscera appeared normal by macroscopic examination.

T A B L E II

THE ACUTE SKIN ABSORPTION MINIMAL LETHAL DOSE OF  
CYCLOHEXYLISOCYANATE  
FOR RABBITS

Sample Applied Undiluted - 24-Hours Exposure

<u>Animal No. - Sex</u>	<u>Weight Kg.</u>	<u>Dose Mg. / Kg.</u>	<u>Weight Change 5 Days Later Kg.</u>	<u>Fate</u>
1 - Female	2.5	794	+ 0.1	Survived
2 - Male	2.5	1,260	0.0	Survived
3 - Female	2.5	2,000	- 0.3	Survived
4 - Male	2.6	3,160	---	Died - One Day
5 - Female	2.4	5,010	---	Died - One Day

DISCUSSION -

The Acute Skin Absorption Minimal Lethal Dose for male and female rabbits was found to be greater than 2,000 milligrams per kilogram and less than 3,160 milligrams per kilogram.

The compound was classed as slightly toxic by skin absorption in male and female rabbits.

Survival time was less than twenty-four hours.

Toxic signs included reduced appetite and activity (two to four days in survivors), increasing weakness, collapse, and death.

At autopsy there was hemorrhagic lungs, slight liver discoloration, and gastrointestinal inflammation.

Surviving animals were sacrificed fourteen days after dosing. The viscera appeared normal by macroscopic examination.

T A B L E III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF  
 CYCLOHEXYLISOCYANATE

Test Conducted In Accordance With The Federal Hazardous Substances Act  
 Sample (0.5 Gram) Applied Undiluted

<u>Animal No.-Sex</u>	<u>Numerical Evaluation At The End Of</u>					
	<u>1 Hour</u>	<u>24 Hours</u>	<u>48 Hours</u>	<u>72 Hours</u>	<u>120 Hours</u>	<u>168 Hours</u>
<b>INTACT SKIN --</b>						
1 - Female	0	6	5	3	0	0
2 - Male	0	7	4	2	0	0
3 - Female	0	6	3	1	0	0
4 - Male	0	6	4	1	0	0
5 - Female	0	6	2	2	0	0
6 - Male	0	6	2	2	0	0
Average (Intact)	0.0	6.1	3.3	1.8	0.0	0.0
<b>ABRADED --</b>						
1 - Female	0	6	4	2	0	0
2 - Male	0	7	4	2	0	0
3 - Female	0	6	3	1	0	0
4 - Male	0	6	4	1	0	0
5 - Female	0	6	2	2	0	0
6 - Male	0	6	2	2	0	0
Average (Abraded)	0.0	6.1	3.1	1.6	0.0	0.0
<b>PRIMARY IRRITATION SCORE --</b>				<b>Exposure Time</b>	<b>Exposure Unit</b>	
				<b>Hours</b>	<b>Value</b>	
<b>Erythema and Eschar Formation:</b>						
Intact Skin .....				24	2.1	
Do .....				72	1.1	
Abraded Skin .....				24	2.1	
Do .....				72	1.0	
Sub-Total .....					6.3	
<b>Edema Formation:</b>						
Intact Skin .....				24	4.0	
Do .....				72	0.6	
Abraded Skin .....				24	4.0	
Do .....				72	0.6	
Sub-Total .....					9.2	
TOTAL .....					15.5	

PRIMARY IRRITATION SCORE  $(15.5 \div 4) = 3.8$

Continued .....

DISCUSSION -- TABLE III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF CYCLOHEXYLISOCYANATE

Intact and Abraded Skin

Cyclohexylisocyanate WAS NOT classed as a Primary Skin Irritant under the grading system as outlined in the Federal Hazardous Substances Act.\*

The Primary Irritation Score was 3.8.

\*The term 'primary irritant' is given to a substance which produces an empirical score (Primary Irritation Score) of five (5) or more when tested by the method described.

Observations Following Application -- Intact Skin

1-Hour:	No erythema or edema.
24-Hours:	Slight to moderate erythema, severe edema
48 - 72-Hours:	Gradual improvement
120-Hours:	All scored zero

Note: Defatting effect - skin sloughed off in ten to fourteen days.  
There was no injury in depth.

Observations Following Application -- Abraded Skin

1-Hour:	No erythema or edema
24-Hours:	Slight to moderate erythema, severe edema
48 - 72-Hours:	Gradual improvement
120-Hours:	All scored zero

T A B L E IV  
 EYE IRRITATION IN RABBITS AFTER APPLICATION OF  
 CYCLOHEXYLISOCYANATE

Test Conducted In Accordance With The Federal Hazardous Substances Act  
 Sample (0.1 Milliliter) Applied Undiluted

Animal No. - Sex	Numerical Evaluation At The End Of					
	1 Hour	24 Hours	48 Hours	72 Hours	120 Hours	168 Hours
1 - Male	20	90	61	61	66	70
2 - Female	20	75	70	70	70	66
3 - Male	18	55	73	58	51	47
4 - Female	20	90	90	73	79	59
5 - Male	18	65	68	73	71	49
6 - Female	18	65	73	73	56	59
AVERAGE ...	19.0	73.3	72.5	68.0	65.5	58.3

DISCUSSION --

Cyclohexylisocyanate WAS classed as an Eye Irritant under the grading system as outlined in the Federal Hazardous Substances Act.\*

\*An animal shall be considered as exhibiting a positive reaction if the test substance produces any of the readings:

- (i) ulceration of the cornea (other than a fine stippling) or
- (ii) opacity of the cornea (other than a slight dulling of the normal luster) or
- (iii) inflammation of the iris (other than a slight deepening of the folds (or rugae) or a slight circumcorneal injection of the blood vessels) or
- (iv) if such substances produce in the conjunctivae (excluding the cornea and iris) an obvious swelling with partial eversion of the lids or a diffuse crimson-red with individual vessels not easily discernible.

Observations Following Application --

10-Minutes: Slight erythema, very slight edema, copious discharge  
 1-Hour: Moderate to severe erythema, severe edema, copious discharge  
 24-Hours: Areas of slight to moderate corneal cloudiness, iris showed little or no reaction to light, severe erythema, severe edema, copious discharge containing whitish exudate  
 48 - 168-Hours: Varying degrees of corneal cloudiness, iris showed little or no reaction to light, moderate to severe erythema, very slight to slight edema, moderate to copious discharge  
 14-Days: Opaque areas of corneal cloudiness in three animals, slight ulceration (lower cornea) in two animals, one animal scored zero

T A B L E V  
 INHALATION OF  
 CYCLOHEXYLISOCYANATE  
 VAPORS BY RATS  
 (AMBIENT TEMPERATURE)

Average Temperature Inside Chamber .....	80° F.
Average Relative Humidity Inside Chamber .....	70 %
Amount of Sample -- To Start .....	42.4 Grams
Recovered .....	38.1 Grams
Total Vaporized .....	4.3 Grams (10.1 %)
Recovered from condenser .....	0.0 Gram (0.0 %)
Weight of Vapors Entering Chamber .....	4.3 Grams (10.1 %)
Average Concentration of Vapors in Chamber .....	7.16 Grams / M <sup>3</sup>

Animal No. - Sex	Fate	Observations During Exposure
1 - Male	Died	0 - 1 Hr.: Ocular discharge, labored breathing, slight lethargy
2 - Male	Died	
3 - Male	Died	1 - 2.5 Hrs.: Increasing weakness, collapse, and death
4 - Male	Died	
5 - Male	Died	
6 - Male	Died	

DISCUSSION --

All six animals succumbed within two and one-half hours after start of exposure. It was concluded that the vapors were highly toxic under conditions of the test.

Observations Following Exposure -

Gross autopsy was performed.

Decedents: Hemorrhagic lungs.

## CERTIFICATE OF AUTHENTICITY

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