

**A 01**

CODING FORMS FOR SRC INDEXING

Microfiche No.		OTS0559856			
New Doc ID	88000000049	Old Doc ID	8EHQ-1299-14609		
Date Produced	03/01/78	Date Received	12/10/99	TSCA Section	8E
Submitting Organization		CYTEC INDUSTRIES INC			
Contractor		SHELL RESEARCH LTD, LONDON			
Document Title		INITIAL SUBMISSION: TOXICOLOGY OF MINING CHEMICALS - ACUTE TOXICITY, SKIN AND EYE IRRITANCY AND SKIN SENSITIZATION POTENTIAL OF SODIUM ISOPROPYL XANTHATE, W/CVR LTR DATED 120299			
Chemical Category		SODIUM ISOPROPYL XANTHATE			

**B 01**

**INITIAL  
SUB-  
MISSION**

A 03

8EHQ-1299-14609

# CYTEC

Cytec Industries Inc.  
5 Garret Mountain Plaza  
West Paterson, NJ 07424

RECEIVED  
OPPT CBIC

1999 DEC 10 AM 11:29

FEDERAL EXPRESS WITH TRACER

December 2, 1999



8EHQ-99-14609

*MR 29722*

OPPT Document Processing Center (TS-700)  
ATTN: SECTION 8(E) COORDINATOR  
Office of Pollution Prevention and Toxics (OPPT)  
U.S. Environmental Protection Agency  
401 M Street, S.W.  
Washington, DC 20460

Dear Sir/Madam:

The purpose of this letter is to inform you under Section 8(e) of TSCA of the results obtained from a study entitled "Toxicology of Mining Chemicals: Acute Toxicity, Skin and Eye Irritancy and Skin Sensitization Potential Of Sodium Isopropyl Xanthate".

The study indicates that this product is a moderate skin sensitizer.

This study was conducted with a product Cytec recently acquired from another company. The acquired company provided us their toxicology data in November and we just completed our extensive review.

In addition, this report also indicates that the test material is severely irritating to rabbit eyes. However, due to the pH of the product, ~9 in aqueous solution - this result is an expected outcome.

Please direct all communications on this subject to Patricia Ann Vernon, Product Regulatory Compliance Manager, Asia-Pacific at the address above or call her at (973) 357-3375.

Sincerely,

*Suzanne Sherman*  
Suzanne Sherman, M.D.  
Corporate Medical Director

*FA Wadsworth*

Cc: R.Deskin  
T. Mesevage  
F. Cappuccitti - CG

CONTAINS NO CBI



88000000049

RECEIVED  
OPPT NCIC  
99 DEC 23 PM 2:08

B 03

A 04

RECEIVED  
OPPT CBIC

1999 DEC 10 AM 11:29



A 05

**PUBLIC COPY  
DOES NOT CONTAIN  
CONFIDENTIAL BUSINESS INFORMATION**

GROUP RESEARCH REPORT  
TLGR.0047.78  
TOXICOLOGY OF MINING CHEMICALS: ACUTE  
TOXICITY, SKIN AND EYE IRRITANCY AND  
SKIN SENSITIZATION POTENTIAL OF  
SODIUM ISOPROPYL XANTHATE  
SICC/CIMS Budget Ref. 50070612

Contain NO CBI

**CONFIDENTIAL**

The copyright of this CONFIDENTIAL document is owned by Shell Research Limited, London which is responsible for the distribution listed within. Any further distribution must be authorised by the sponsoring Company/Function indicated on the title page. Before issue to non-Group Companies or organisations, the sponsoring Company/Function must obtain the agreement of the copyright owner. All recipients must use its contents with discretion.

**SHELL RESEARCH LIMITED, LONDON**

SITTINGBOURNE RESEARCH CENTRE  
SHELL TOXICOLOGY LABORATORY (TUNSTALL)



A 05

SHELL TOXICOLOGY LABORATORY (TUNSTALL)

Group Research Report TLGR.0047.78

**Title:** Toxicology of Mining Chemicals: Acute toxicity, skin and eye irritancy and skin sensitizing potential of Sodium Isopropyl Xanthate.

**Authors:** S. L. Cassidy and D. G. Clark.

**Reviewed by:** V. K. E. Brown.

**Work done by:** Experimental Toxicology Division of Shell Toxicology Laboratory (Tunstall).

**Object:** To determine the acute oral and percutaneous toxicity, skin and eye irritation and skin sensitizing potential of the test material.

**Summary:**

1. The acute oral LD<sub>50</sub> of the test material in rats was approximately 800 mg/kg.
2. The acute (24 h) percutaneous LD<sub>50</sub> of the test material in rats was greater than 1000 mg/kg.
3. A single 24 h application of the test material to occluded rabbit skin was slightly irritating.
4. The test material was severely irritating to rabbit eyes.
5. The test material was a moderate skin sensitizer in guinea-pigs.

*E. Thorpe*

E. THORPE, B.V.M.S., D.V.M., Ph.D., M.R.C.V.S., M.R.C.Path.  
Director, Shell Toxicology Laboratory (Tunstall).

Date: March, 1978.

**PUBLIC COPY  
DOES NOT CONTAIN  
CONFIDENTIAL BUSINESS INFORMATION**

Throughout this document the words 'Shell' and 'Group' are used collectively in relation to companies associated together under the name of the Royal Dutch/Shell Group of Companies

B 05

INTRODUCTION

Sodium isopropyl xanthate is destined for use as a collector (promoter) in froth flotation concentration of sulphide ores of copper, zinc and lead in the mining industry.

The toxicological work reported here was undertaken to determine the acute handling hazards associated with use of the chemical.

**PUBLIC COPY  
DOES NOT CONTAIN  
CONFIDENTIAL BUSINESS INFORMATION**

PUBLIC COPY  
REG. 0047:78

**MATERIALS AND METHODS**  
**DOES NOT CONTAIN**  
**CONFIDENTIAL BUSINESS INFORMATION**

Sample

A sample of the chemical was received from Shell-Flot, Chile (reference No. SF 113).

Animals

Species	Strain/Breed	Source
Rat	Wistar	Shell Toxicology Laboratory (Tunstall), Breeding Unit.
Guinea-pig	'p' Strain	
Rabbit	New Zealand White	Ranch Rabbit, Crawley, Sussex.

Acute oral toxicity

Male and female rats aged approximately 12 weeks, were used at each dose level. Four animals of one sex were housed in each cage. The animals were weighed, fasted overnight and the calculated dose of material administered by intraoesophageal intubation using a ball point needle fitted to a syringe. After dosing food and water were freely available throughout a 9 day observation period.

Acute percutaneous toxicity

The method of Noakes and Sanderson (Appendix I) was used to determine the acute (24 h) LD50 in groups of male and female rats. Observation was continued for 9 days.

Primary skin irritation

The occlusive patch test of Draize (Appendix II) was used to assess the skin irritation to intact and abraded rabbit skin.

Eye irritation

The method of Draize as described in the Federal Register (Appendix III) was used to assess the eye irritation in groups of three rabbits.

Skin sensitization

The skin sensitizing potential of the material was assessed using groups of 10 male and female guinea-pigs in the Magnusson and Kligman maximization test (Appendix IV) following preliminary range finding tests to determine suitable concentrations for intradermal induction and topical induction and challenge.

PUBLIC COPY  
 DOES NOT CONTAIN  
 TLGR.0047.78

**CONFIDENTIAL BUSINESS INFORMATION**

Acute oral toxicity

Dosing groups of 4 male and 4 female rats with a 50% w/v solution in water resulted in the following mortalities:

Dose (mg/kg)	Daily mortality (days 1-9)								Cumulative mortality (9 days)		
	Day 1		Day 2		Day 3		Day 9		M	F	Total
	M	F	M	F	M	F	M	F			
200			1								
400									1/4	0/4	1/8
800		1	2	1			1		0/4	0/4	0/8
1600	4	3		1					2/4	3/4	5/8
									4/4	4/4	8/8

Using these figures the acute oral LD<sub>50</sub> was estimated to be approximately 800 mg/kg.

Rats showed signs of lethargy and died following a period of coma.

Acute percutaneous toxicity

The application of a 50% w/v solution in water for 24 hours to groups of 4 male and 4 female rats resulted in the following mortalities:

Dose (mg/kg)	Daily mortality (days 1-9)								Cumulative mortality (9 days)		
	Day 1		Day 2		Day 3		Day 9		M	F	Total
	M	F	M	F	M	F	M	F			
1000				1					0/4	1/4	1/8

On the basis of these figures the acute percutaneous LD<sub>50</sub> was estimated to be greater than 1000 mg/kg - the maximum that could be applied to the skin.

Rats showed no signs of toxic reaction.

Primary skin irritation

The erythema and oedema resulting from the application of powdered chemical to rabbit skin were scored at 24 hours, 72 hours and 7 days using standard scales ranging from 0 to 4. The results are tabulated below:

Rabbit number and sex	Response											
	Abraded skin						Non abraded skin					
	24 hours		72 hours		7 days		24 hours		72 hours		7 days	
	E	O	E	O	E	O	E	O	E	O	E	O
1 M	1	0	0-1	0	0	0	0-1	0	0-1	0	0	0
2 M	0-1	0	0	0	0	0	0-1	0	0	0	0	0
3 M	1	0	0-1	0	0	0	0-1	0	0	0	0	0
Mean	0.8	0	0.3	0	0	0	0.7	0	0.3	0	0	0

Using these figures the material would be classified as slightly irritating to rabbit skin.

Eye irritation

The conjunctival redness chemosis and discharge, corneal opacity and damage to the iris following the instillation of 100-200 mg of powder into the conjunctival sac of three rabbit eyes was scored using standard scales. The results are tabulated below:

	Mean response				
	1-2 hours	1 day	2 days	3 days	7 days
Conjunctiva					
Redness	2	2	2	1.7	1.3
Chemosis	1	1	1	0.7	0
Discharge	1	0	0.3	0	0
Cornea					
Opacity	2	2	2	2	2
Area	4	4	4	4	4
Iris	2	2	2	2	1.3

On the basis of these scores the material would be classified as severely irritating to rabbit eyes.

Immediately on instillation into the rabbit eyes a moderate pain reaction was observed.

**PUBLIC COPY**  
**DOES NOT CONTAIN**  
**CONFIDENTIAL BUSINESS INFORMATION**

Skin sensitization

Following initial range finding tests the following concentrations were used in the method of Magnusson and Kligman.

- Intradermal induction: 1% w/v in H<sub>2</sub>O
- Topical induction: 10% w/v in H<sub>2</sub>O
- Topical challenge: 5% w/v in H<sub>2</sub>O

The erythema resulting from the topical challenge was scored on a four point scale (- ve; trace; + ve; ++ ve) immediately on removal of the challenge patch and 24 and 48 hours later. The results are tabulated below:

Animal number	Response					
	Immediate		24 hours		48 hours	
	Male	Female	Male	Female	Male	Female
Test						
1	-	tr	+	+	+	+
2	tr	tr	+	tr	tr	-
3	-	tr	-	+	-	tr
4	tr	tr	+	+	tr	tr
5	-	tr	-	-	-	-
6	tr	+	+	+	+	+
7	tr	-	tr	tr	-	-
8	-	+	-	+	-	tr
9	+	+	+	+	tr	tr
10	-	-	tr	-	-	-
Control						
1	-	-	-	-	-	-
2	-	-	-	-	-	-
3	-	-	-	-	-	-
4	-	-	-	-	-	-
5	-	-	-	-	-	-

PUBLIC COPY  
 DOES NOT CONTAIN  
 CONFIDENTIAL BUSINESS INFORMATION

A 1

CC

A 1

TLGR.0047.78

Based on the number of animals showing a response, the degree of intensity of the response and its persistence, the material is considered to be a moderate skin sensitizer in guinea-pigs.

Archives

The data on which this report is based is filed under Experiment number 1385.

*S. L. Cassidy*

S. L. Cassidy, B.Sc.

*D. G. Clark*

D. G. Clark, B.Sc., Ph.D., M.I. Biol.

**PUBLIC COPY  
DOES NOT CONTAIN  
CONFIDENTIAL BUSINESS INFORMATION**

APPENDIX IACUTE PERCUTANEOUS TOXICITY

The method of Noakes and Sanderson\* was used.

Groups of rats of each sex, aged 12-13 weeks, were used at each dose level. The test material was placed onto the shorn dorso-lumbar skin and bandaged into contact with the skin using an impermeable dressing of aluminium foil and water proof plaster. The rats were housed individually over the 24 hours exposure period during which time they were deprived of food but allowed water ad libitum.

After 24 hours the dressings were removed and the exposed area was washed with a tepid dilute detergent solution. The rats were then housed in cages of four of one sex and observed for signs of toxicity during the following 9 days.

PUBLIC COPY  
DOES NOT CONTAIN  
CONFIDENTIAL BUSINESS INFORMATION

\*Noakes, D. N. and Sanderson, D. M., (1969).  
A method for determining toxicity of pesticides.  
Br. J. industr. Med., 26, 59-64.

PUBLIC COPY

DO NOT DESTROY

APPENDIX II

CONFIDENTIAL BUSINESS INFORMATION

PRIMARY IRRITATION OF THE SKIN

The method of Draize\* was used.

Primary irritation of the abraded and intact skin of each of three male rabbits was measured. The dorsal hair between the shoulders, and the hindquarters was closely shorn by means of electric clippers. A 2 x 2 cm area of the shorn skin was abraded using a fine hypodermic needle, the injuries being deep enough to disturb the stratum corneum but not sufficiently deep to cause bleeding. Lint patches (2 x 2 cm) were applied to the abraded and intact skin and 0.5 ml test material was applied to each. The patches were covered by an occlusive polyethylene film which was secured in position by means of an elastic adhesive bandage (3" Poroplast). The patches were left in place for 24 hour.

Following removal of the patches the skin reactions were assessed visually for the degree of erythema and oedema using the 0-4 scale tabulated below at 24 and 72 hours. Seven days after the application of the test material a final visual assessment was made.

No erythema	=	0	No oedema	=	0
Pale pink	=	1	Soft skin	=	1
Redness	=	2	Oedema	=	2
Severe redness	=	3	More definite oedema	=	3
Best redness	=	4	Severe oedema	=	4

\* Draize, J. H., (1969). 'Dermal Toxicity' in "Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics. Association of Food and Drug Officials of the United States of America.

PUBLIC COPY  
DOES NOT CONTAIN  
CONFIDENTIAL BUSINESS INFORMATION

APPENDIX III

The method of Draize as described in the U.S. Federal Register\* was used.

The test compound was instilled into the conjunctival sac of one eye of each of three rabbits; the untreated eyes served as controls. A visual assessment of irritancy was made 1 to 2 hours after instillation and again at 1, 2, 3 and 7 days, thence every 4 days until eye irritancy was no longer observed using the standard scales detailed below:

CORNEA

- No ulceration or opacity . . . . 0
- Scattered or diffuse areas of opacity (other than slight dulling or normal lustre), details of iris clearly visible . . . . . 1
- Easily discernible translucent areas, details of iris slightly obscured . . . . . 2
- Nacreous areas, no details of iris visible, size of pupil barely discernible . . . . . 3
- Complete corneal opacity, iris not discernible . . . . . 4

IRIS

- Normal . . . . . 0
- Markedly deepened folds, congestion, swelling, moderate circumcorneal injection (any of these or combination thereof), iris still reacting to light (sluggish reaction is positive) . . . . . 1
- No reaction to light, haemorrhage, gross destruction (any or all of these) . . . . . 2

CONJUNCTIVAE

- Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris)
- Vessels normal . . . . . 0
- Some vessels definitely injected . . . 1
- Diffuse, crimson red, individual vessels not easily discernible . . . . 2
- Diffuse beefy red . . . . . 3

CHEMOSIS

- No swelling . . . . . 0
- Any swelling above normal (includes nictitating membrane) . . . . . 1
- Obvious swelling with partial eversion of lids . . . . . 2
- Swelling with lids about half closed . . . . . 3
- Swelling with lids more than half closed . . . . . 4

DISCHARGE

- No discharge . . . . . 0
- Any amount different from normal (does not include small amounts observed in inner canthus of normal animals) . . . . . 1
- Discharge with moistening of lids and hairs just adjacent to lids . . . 2
- Discharge with moistening of lids and hairs and considerable area around the eye . . . . . 3

\*Federal Register, 28 (110), 6.6.1963. para. 191.12  
Test for eye irritants.

APPENDIX IVSKIN SENSITIZATION

The guinea-pig maximization procedure of Magnusson and Kligman\* was used to assess the skin sensitizing potential of the test material.

A preliminary screen was carried out using groups of two male and two female guinea-pigs to determine the concentrations of test material to be used for intradermal induction, topical induction and topical challenge.

In the test itself groups of ten male and ten female guinea-pigs were used with a further five males and five females as controls.

Induction

Induction was accomplished in two stages:

(i) Intradermal injection

Two rows of three injections were made: one on each side of the midline in the shorn skin of the shoulder region as follows:

<u>Test animals</u>	<u>Controls</u>
2 x 0.1 ml Freund's complete adjuvant	FCA
2 x 0.1 ml Test material in solvent	Solvent
2 x 0.1 ml Test material in 50:50 FCA/solvent	50:50 FCA/solvent

The injection sites were just within the boundary of a 4 x 4 cm shaved area.

(ii) Topical application

One week after the intradermal injections the same area was clipped free from hair. A 4 x 4 cm patch of Whatman No. 3 mm filter paper was soaked in a solution of the test material, placed over the injection sites of the experimental animals and covered by overlapping plastic adhesive tape (1½" Blenderm). This in turn was firmly secured by an elastic adhesive bandage (3" Poroplast). The dressing was left in place for 48 hours.

**PUBLIC COPY  
DOES NOT CONTAIN  
CONFIDENTIAL BUSINESS INFORMATION**

B 02

B 03

TLGR.0047.78

APPENDIX IV (continued)

Challenge

The challenge procedure was carried out 2 weeks after topical induction. Challenge was accomplished by topical application of the challenge solution of the test material to the flank of both test and control groups of animals.

Hair was removed from a 3 x 3 cm area on the flank by clipping and then shaving with an electric razor. A 2½ x 2½ cm patch of Whatman No. 3 mm filter paper was soaked in the challenge solution and placed over the shaved area. This was then covered by overlapping adhesive tape (1½" Blenderm) which was in turn firmly secured by an elastic adhesive bandage (3" Poroplast). The patch was left in place for 24 hours and examination of the challenge site was immediately, 24 and 48 hours after removal of the dressing. Three hours before the 24 hour reading the treated skin was closely shaved by means of an electric razor.

**PUBLIC COPY  
DOES NOT CONTAIN  
CONFIDENTIAL BUSINESS INFORMATION**

\*Magnusson, B. and Kligman, A. M., (1969).  
The identification of contact allergens by animal assay.  
The guinea-pig maximization test.  
J. Invest. Derm., 52, 268-276.

B.03

TLGR.0047.78

TOXICOLOGY OF MINING CHEMICALS: ACUTE TOXICITY, SKIN AND EYE IRRITANCY  
AND SKIN SENSITIZING POTENTIAL OF SODIUM ISOPROPYL XANTHATE

DISTRIBUTION

Central Offices, The Hague

SICM (CMF/04)  
TOX

18  
1

Central Offices, London

Shell U.K. Limited (UASC/3153)  
SIPC (TOX/3)  
RSRL/54  
MDL  
SICC (CIMS/7)

3  
2  
1  
1  
10

**PUBLIC COPY  
DOES NOT CONTAIN  
CONFIDENTIAL BUSINESS INFORMATION**

**CERTIFICATE OF AUTHENTICITY**

THIS IS TO CERTIFY that the microimages appearing on this microfiche are accurate and complete reproductions of the records of U.S. Environmental Protection Agency documents as delivered in the regular course of business for microfilming.

Date produced 10 18 00 Mary Furbuck  
(Month) (Day) (Year) Camera Operator

Place Syracuse New York  
(City) (State)



**B 05**

**END**