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Submitting Organization		
CIBA GEIGY CORP		
Contractor		
Document Title		
<p>REPORT ON SKIN SENSITIZING EFFECT IN GUINEA PIGS OF TK 10 637/1 WITH COVER LETTER DATED 060589</p>		
Chemical Category		
TOLYL TRIAZOLE (29385-43-1)		

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CIBA-GEIGY



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June 5, 1989

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

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

Re : February 28, 1989 Federal Register at p. 8484; 8(d)
Reporting of Certain Pesticide Inert Ingredients

Dear Sir or Madam:

This letter and the attached health and safety studies contain no Confidential Business Information.

In compliance with the subject 8(d) reporting rule, we enclosed copies of health and safety studies for two of the pesticide inert ingredients. The specific chemicals and enclosed studies are enumerated below.

A. CAS No. 29385-43-1; Toly1 Triazole or 1 H-Benzotriazole, methyl- (aka TK 10 637/1 - 97.8% Purity)

1. Salmonella/Mammalian - Microsome Mutagenicity Test with TK 10 637/1; May 27, 1982.
- ✓ 2. Report on Skin Sensitizing (Contact Allergenic) Effect in Guinea Pigs of TK 10 637/1, Reomet TTA, Lot 1179/1186; June 17, 1982.
3. Report on Biodegradation of TK 10637/1, Modified OECD Screening Test No. 301 E; September 9, 1982.

B. CAS No. 102-71-6; Triethanolamine or Ethanol, 2,2',2" -
nitrilotris

1. Report on Biodegradation of TK 12965, Modified OECD
Screening Test No. 301 E; April 11, 1983. (Test
material TK 12965 contains 25% free triethanolamine,
50% of a triethanolamine salt of another substance and
25% water).

Please contact the undersigned if you have any questions.

Sincerely,

Anthony Di Battista

Anthony Di Battista
Manager, Regulatory Affairs & Toxic Substances Compliance
Toxicology, Regulatory Auditing & Compliance

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Attachments

EPA-OTS



000657104N

86-890000273

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CIBA-GEIGY AG
CH - 4002 BASEL (SWITZERLAND)

Test No.: 820331

Toxicology GU 2.5

Tolyl triazole; CASRN 29385-43-1

~~REOMET TTA Lot 1179/1186.~~ (CONTACT ALLERGENIC) EFFECT IN
GUinea-pig SKIN TEST 10'637/1 REOMET TTA Lot 1179/1186.

Sponsor: Plastics and Additives Division
Testing facility: Toxicology GU 2.5, Ciba-Geigy AG, BASEL
Study director: Dr. Th. Maurer
Technical assistant: Mrs. M. Rink
Test material received: 09.03.1982
Validity: 12/82
Study initiated: 19.04.1982
Study completed: 09.06.1982

Summary and conclusion

Under the experimental conditions employed, no differences between the test group and the vehicle-treated controls were seen, after either intradermal or epidermal challenge application of TK 10'637/1.

TK 10'637/1 was found to be devoid of skin-sensitizing (contact allergenic) potency in albino guinea-pig.

Study director:

Th. Maurer
Dr. phil. Th. Maurer

Approved by:

R. Hess
Prof. Dr. med. R. Hess
(Head of Toxicology)

Reported:

June 17, 1982

Archive of raw data and final report: R 1062.3.07

Toxicology GU 2.5

Test No.: 820331

1. Material

Test material: TK 10'637/1
 Identification: Lot 1179/1186
 Concentrations: 0.1% for intradermal application
 10% for epidermal application

Vehicles: intradermal, physiological saline
 epidermal, Vaseline PHH VI

2. Method

The optimization test¹⁾ was used, an intracutaneous sensitization procedure exceeding the sensitivity of the method recommended in the "Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics" (1959), the US Association of Food and Drug Officials (AFDO).

a) Animals

The test was performed on 10 male and 10 female guinea pigs of the Pirbright white strain, bred on our premises and weighing between 221 to 431 grams (~ 10 weeks old).

Animals received: 07.04.1982
 Acclimatisation period: 12 days

The animals were housed individually in Macrolon cages type 3, assigned to the different groups by means of random numbers generated by the random number generator incorporated in the Hewlett-Packard desk computer, identified with individual ear tags, kept at a constant room temperature of 20 ± 1° C, at a relative humidity of 50 ± 10% and on a 14 hours light cycle day. The animals received ad libitum standard guinea pig pellets - NAFAG No. 830, Gossau SG - and water, supplemented with fresh carrots. The animals were acclimatized for 12 days.

1) Maurer th., Thomann P., Weirich E.G., Hess R.
 The optimization test in the guinea pig.
 Agents & Actions 5(2), 174-179, 1975.
 Predictive evaluation in animals of the contact allergenic potential of medically important substances.
 Contact Dermatitis 4, 321-333, 1978.
 Contact Dermatitis 5, 1-10, 1979.
 The optimization test in the guinea pig in relation to other predictive sensitization methods. Toxicology 15, 163-171, 1980.

b) Testing procedure

During the induction period the animals received one injection every second day (except weekends) to a total of 10 intracutaneous injections of a freshly prepared 0.1% solution of TK 10'637/1 in physiological saline. One control group was treated with the vehicle alone ("negative control").

On the first day, injections of 0.1 ml were administered into the shaved skin of the right flank and the back, while on the following days a single intracutaneous injection was given into the back.

During the second and third week of the induction period the test material was incorporated in a mixture of the normal vehicle with complete Bacto Adjuvant²⁾ (vehicle : adjuvant = 1 : 1).

Fourteen days after the last sensitizing injection, a challenge injection of 0.1 ml of a freshly prepared 0.1% solution of TK 10'637/1 in physiological saline was administered into the skin of the left flank.

Twenty-four hours after each injection during the first week of the induction period and 24 hours after the challenge injection the reactions were recorded.

The two largest perpendicular diameters (in mm) and the increase in the skin-fold thickness (in mm) were measured and by multiplication of these values a "reaction volume" was obtained (in μ l) for each reading from each animal. The mean volume plus one standard deviation of the induction reactions observed in the individual animal in the first week was taken as representing the

2) Bacto Adjuvant, complet Freund (Difco, Michigan, USA).

skin irritation "threshold" for each animal. Any challenge reaction greater than this threshold value in the induction period was graded as an allergic reaction and the animal termed "positive". The number of "positive" animals in the test group was compared with the number of animals in the control group (treated with the vehicle alone) that showed a non-specific reaction of at least the same magnitude ("negative control").

Ten days after the intracutaneous challenge injection a subirritant dose of the test compound (10% TK 10'637/1 in vaseline) was applied epicutaneously under occlusive dressings which were left in place for 24 hours. The reactions were evaluated 24 hours after removing of the bandages according the Draize scoring scale.

3. Results

Intradermal injections of the vehicle alone failed to induce sensitization.

Table 1 summarize the incidence of positive reactors after intradermal and epidermal challenge application.

Tables 2 and 3 show the reaction volumes for individual animals of the control and test group.

3) The exact Fisher test for comparison of the basic probability of two binomial distributions, L. Sachs, Statistische Auswertungsmethoden, Thieme Verlag, Stuttgart, 1971. A probability of $P \leq 0.01$ was considered to indicate a significant difference.

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Table 2 Reaction volumes (μl) after intradermal injection of physiological saline

Animal identification number	INDUCTION				mean (\bar{x})	standard deviation (s)	$(\bar{x} + s)$	after skin sensitization	+ = positive reactor
	Application No.								
	1	2	3	4					
241 ♂	0	0	0	0	0	0	0	0	-
242	0	0	0	0	0	0	0	0	-
243	0	0	0	0	0	0	0	0	-
244	0	0	0	0	0	0	0	0	-
245	0	0	0	0	0	0	0	0	-
246	0	0	0	0	0	0	0	0	-
247	0	0	0	0	0	0	0	0	-
248	0	0	0	0	0	0	0	0	-
249	0	0	0	0	0	0	0	0	-
250	0	0	0	0	0	0	0	0	-
251 ♀	0	0	0	0	0	0	0	0	-
252	0	0	0	0	0	0	0	0	-
253	0	0	0	0	0	0	0	0	-
254	0	0	0	0	0	0	0	0	-
255	0	0	0	0	0	0	0	0	-
256	0	0	0	0	0	0	0	0	-
257	0	0	0	0	0	0	0	0	-
258	0	0	0	0	0	0	0	0	-
259	0	0	0	0	0	0	0	0	-
260	0	0	0	0	0	0	0	0	-
Group-mean	0	0	0	0				0	0/20

Toxicology GU 2.5

Test No.: 820331

Table 3 Reaction volumes (μ l) after intradermal injection of TK 10'637/1

Animal identification number	INDUCTION				mean (\bar{x})	standard deviation (s)	$(\bar{x} + s)$	after skin sensitization	+ = positiv reactor
	Application No.								
	1	2	3	4					
241 ♂	0	0	0	0	0	0	0	0	-
242	0	0	0	0	0	0	0	0	-
243	0	0	0	0	0	0	0	0	-
244	0	0	0	0	0	0	0	0	-
245	0	0	0	0	0	0	0	0	-
246	0	0	0	0	0	0	0	0	-
247	0	0	0	0	0	0	0	0	-
248	0	0	0	0	0	0	0	0	-
249	0	0	0	0	0	0	0	0	-
250	0	0	0	0	0	0	0	0	-
251 ♀	0	0	0	0	0	0	0	0	-
252	0	0	0	0	0	0	0	0	-
253	0	0	0	0	0	0	0	0	-
254	0	0	0	0	0	0	0	0	-
255	0	0	0	0	0	0	0	0	-
256	0	0	0	0	0	0	0	0	-
257	0	0	0	0	0	0	0	0	-
258	0	0	0	0	0	0	0	0	-
259	0	0	0	0	0	0	0	0	-
260	0	0	0	0	0	0	0	0	-
Group-mean	0	0	0	0				0	0/20

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