REVIEWER

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Pyridate Herbicide - Review of Additional data on Dermal Sensitization Studies with Pyridate " Pure" and Pyridate "Standard"

Tox Chem No.: 716A
HED Project No.: 9-0874
Record No. 239467

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Registrant: Agrolinz, Inc.

In response to EPA,s request, Agrolinz, Inc. has submitted additional information concerning the purity of Pyridate (CL 11.334) used in two different delayed contact hypersensitivity studies, in guinea pigs. In the first study, "Delayed Contact Hypersensitivity with CL 11.344 Pure Active Ingredient in the Albino Guinea Pig" (see attached DER) the registrant reported that the purity of Pyridate used was 98.2 percent (analytical grade). In the second study, titled "Delayed Contact Hypersensitivity with CL 11.344 (Standard) in the Albino Guinea Pig" (see attached DER) the registrant reported that the purity of pyridate used was 90.3 percent (technical grade.)

Toxicology Branch II, considers this deficiency (the only deficiency identified in each of the two studies) resolved. Thus, both aforementioned studies are upgraded from a Core Supplementary to core-Minimum classification.

Attachments

Subject: Delayed Contact Hypersensitivity in the Albino Guinea Pig with CL-11344 (Standard)

Test Material: Pyridate (CL-11344 - Standard)

Accession Number: 072340

Sponsor: Chemie Linz, A.G., Austria

Testing Facility: Huntingdon Research Centre, Huntingdon, England

Study Number: 6498/D13/76

Report Submitted to the Sponsor: September 15, 1976

Methods and Materials:

Ten male albino guinea pigs of the Hartley/Dunkin strain (obtained from Redfern Animal Breeders Limited, Brenchley, Kent) were used for assessing the sensitizing potential of CL-11344 (Standard). The animals were housed in a suspended cage with wire mesh and had free access to food (Vitamin C enriched pelleted diet) and tap water. Animals received cabbage and hay once weekly.

For detections of delayed contact hypersensitivity the guinea pig maximization test described by Magnusson and Kligman (1970) was employed. Preliminary investigations indicated that the maximum concentration of CL-11344 (Standard) suitable for intradermal injection was found to be 1 percent v/v in liquid paraffin and for topical application to be undiluted CL-11344.

The procedure used was carried out in two steps:

1. Induction. (a) Intradermal Injections: Animals were prepared for treatment by clipping free of hair a 4 x 6 cm area of the dorsal skin from the scapular region. Three pairs of injections were made simultaneously into the prepared area as shown in figure 1. The composition of each injection (1, 2, or 3) is also shown in figure 1.

   (b) Topical Applications: Seven days after the intradermal injections, a 0.4 mL volume of undiluted CL-11344 (Standard) was spread over a 3 x 6 cm patch of Whatman paper and placed on the skin (same area used for intradermal injections). The patch was held in place with impermeable adhesive tape secured by an elastic adhesive bandage around the torso of the animal. The dressing was left in place for 48 hours.

2. Challenge: The animals were challenged topically 2 weeks after the induction period using CL-11344 (Standard) 50 percent v/v in liquid paraffin. The test material (0.1 mL) was applied on 2 x 2 cm patch of Whatman paper

and placed on the skin for 24 hours (an area of 5 x 5 cm on the left flank was clipped free of hair) in a similar fashion to that used for the topical induction application.

The challenge site was evaluated at 24, 48, and 72 hours after removal of the patch. Observation of the sites was aided by clipping away the hair 3 hours before evaluation.

Reactions were scored according to the following arbitrary scale:

Erythema and eschar formation:

No erythema	0
Slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4

Oedema formation:

No oedema	0
Slight oedema (barely perceptible)	1
Well-defined oedema (edges of area well-defined by definite raising)	2
Moderate oedema (raised approximately 1 millimeter)	3
Severe oedema (raised more than 1 millimeter and extending beyond the area of exposure)	4

Results:

Induction: No dermal irritation was observed following intradermal injections with CL-11344 (Standard) 1 percent v/v alone. Injections of Freund's complete adjuvant alone or mixed with CL-11344 (Standard) elicited dermal response (note: the intensity of the irritation was not reported by the authors). Topically applied undiluted CL-11344 (Standard) elicited slight to well-defined dermal reactions in all animals.

Challenge: The numerical scores awarded to the dermal reactions elicited by the challenge application (CL-11344 50 percent v/v in liquid paraffin) are presented in table 1. Slight to moderate erythema and edema were observed in all guinea pigs at the 24-hour reading. Progressively more pronounced reaction was seen in most animals at 48 hours after application. At the 72-hour reading, 5 out of 10 animals showed severe erythema and edema while the rest of the animals had slight to moderate reaction to the test article. Thus, all animals exhibited persistent dermal reaction to CL-11344 (Standard), ranging from slight to severe.

Conclusion:

Results reported here indicate that CL-11344 (Standard) is a positive delayed contact sensitizing agent in guinea pigs.

Classification:

The present study is classified as Core-Supplementary mainly because the test article was not clearly identified, i.e., the composition of CL-11344 Standard was not specified.

The attached analytical data for Pyridate Technical (standard) should be traslated to English.

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TABLE 1

Dermal reactions elicited by the challenge application CL 11.344 (standard) 50% v/v in liquid paraffin.

Guinea-pig Number	E = Erythema O = Oedema	Score			Results Positive (+) Negative (-)
		24 hours	48 hours	72 hours	
1	E	2	2*	4*	+
	O	2	3	4	
2	E	2	3	3	+
	O	1	3	3	
3	E	2	3	4	+
	O	2	3	4	
4	E	1	1*	1*	+
	O	1	1	2	
5	E	1	2	3	+
	O	1	3	3	
6	E	3	4	4	+
	O	2	4	4	
7	E	3	4	4	+
	O	3	3	4	
8	E	3	4	4	+
	O	3	4	4	
9	E	2	2*	2*	+
	O	1	1	1	
10	E	2	2*	2*	+
	O	1	1	3	

* = Dryness and sloughing of the epidermis