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86/PTC015/682

190M

RC9927 :
ACUTE DERMAL IRRITATION/CORROSION
TEST IN THE RABBIT

To:
Pennwalt Corporation
900, 1st Avenue
P.O. Box C
King of Prussia
Pennsylvania 19406-00181

From:
Life Science Research Limited
Eye
Suffolk IP23 7PX
England

RC9927 :
ACUTE DERMAL IRRITATION/CORROSION
TEST IN THE RABBIT

LSR Report No: 86/PTC015/682

We the undersigned hereby declare that the report following constitutes a true and faithful account of the procedures adopted and the results obtained in the performance of this study. The aspects of the study conducted by Life Science Research were performed essentially in accordance with current OECD Good Laboratory Practice Principles and current EPA (TSCA) Good Laboratory Practice Standards relating to non-clinical studies.

In line with normal practice in this type of study, no analysis of the test material was received from the Sponsor.

The Study Director fulfilled the responsibilities required by these regulations.

K. D. Smith, B.Sc.
Study Director

.....K. D. Smith.....
...21...January 1987

H. A. Cummins, B.Sc.
Head, Sub-Department of
Short-Term Toxicology

.....HAC.....
..21...January 1987

RC9927 :
ACUTE DERMAL IRRITATION/CORROSION
TEST IN THE RABBIT

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QUALITY ASSURANCE INSPECTIONS

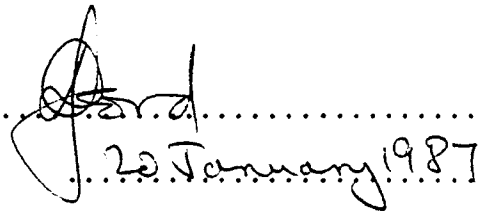
	Dates (Day/Month/Year)		
	Inspection	Report to Study Director	Report to Management
PROTOCOL			
Inspection of protocol was made in accordance with LSR Standard Operating Procedure QAU/020. Dates for inspection of protocol amendments in accordance with this S.O.P. are not quoted	24.9.86	26.9.86	26.9.86
DATA			
Inspection of data generated on this type of study was made in accordance with LSR Standard Operating Procedure QAU/050	13.10.86		14.10.86
PROCEDURES			
Inspection of procedures on this type of study was made in accordance with LSR Standard Operating Procedure QAU/040	23.9.86 23.9.86 16.10.86 4.11.86		23.9.86 23.9.86 23.10.86 27.11.86

Other routine procedures used in this type of study, and facilities were inspected regularly and reports made in accordance with LSR Standard Operating Procedure QAU/040.

This report has been reviewed by the LSR Quality Assurance Unit employing methods laid down in LSR Standard Operating Procedure QAU/060. The reported methods and procedures were found to describe those used and the results to constitute an accurate representation of the data recorded.

This review was completed on: 19 January 1987

D. J. Ford, B.Sc., Ph.D.
(Head of Quality Assurance Unit)



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PENNWALT CORPORATION
CHEMICALS ▪ EQUIPMENT ▪ HEALTH PRODUCTS
900 First Avenue, P.O. Box C, King of Prussia, Pennsylvania 19406-0018 ● (215) 337-6500

SAFETY, HEALTH AND ENVIRONMENTAL AFFAIRS

SUMMARY OF TOXICOLOGY STUDY

PERFORMED FOR THE VENTURE GROUP

Test Material:	FR-45B
Product Code:	RC 9927
Study Type:	Primary Dermal Irritation
Testing Laboratory:	Life Science Research Elm Farm Eye, Suffolk IP23 7PX, England
Summary of Results:	Slight erythema noted in three rabbits 1 hour after patch removal. This recovered by 24 hours in 2 of 3 and by 48 hours in the other.
Storage:	The report is filed in the Technical Records Center at King of Prussia under Master No. 22227.
Information for MSDS:	Slight, rapidly reversible irritation in 3 of 6 rabbits after 4-hour occluded contact.

Signatures

J. F. Jadlocki — 3-11-87

Joseph F. Jadlocki, Jr.
Manager, Product Safety

Date

Joel A. Seckar — 3/11/87

Joel A. Seckar, Ph.D.
Manager, Toxicology

Date

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1. SUMMARY

1.1 The potential of RC9927 to cause inflammatory or corrosive changes upon first contact with skin was assessed by semi-occluded application of 0.5 ml of the test material to the closely-clipped dorsa of six New Zealand White rabbits for four hours. Dermal reactions were assessed 1, 24, 48 and 72 hours after removal of the dressings.

1.2 Very slight erythema was observed at three test sites one hour after removal of the dressings, and in one animal only at the 24-hour examination. No other changes were apparent.

All dermal irritation responses had resolved by the 48-hour examination.

1.3 Under the conditions of this test, RC9927 was 'very slightly irritating' to skin.

2. INTRODUCTION

The objective of this Acute Dermal Irritation/Corrosion Test was to assess the potential for inflammatory or corrosive activity of the test material upon first contact with skin.

This study was designed to conform with Section 4, sub-section 404 of the O.E.C.D. Guidelines for Testing of Chemicals (1981) and the EPA Toxic Substances Control Act Test Guidelines (1985).

The experimental work was carried out at the Elm Farm Laboratories of Life Science Research during the period :

24 September - 27 September 1986

3. MATERIAL

A consignment of 502 g (stated nett) RC9927, a slightly viscous, light yellow liquid, was received at the Elm Farm Laboratories on 1 September 1986. It was further identified by the Code No. 6159-199-3.

The material was kept at ambient temperature, in the original container.

The identity, strength and purity of the test material received, and its stability under the storage conditions above, were the responsibility of the Sponsor.

4. METHODS

4.1 Animals and husbandry

Young albino rabbits of an outbred New Zealand White strain, supplied by Ranch Rabbits, Crawley Down, Sussex, England, were two and half to three months of age on arrival and within the bodyweight range 1.86 - 2.74 kg. They were individually housed in suspended stainless steel cages in batteries manufactured by Cope and Cope Limited. The cages measured 0.6 x 0.6 x 0.4 m high and were fitted with mesh floors and automatic watering. A sledge running the length of the battery removed waste matter as required. Animals had free access to a commercially available standard pelleted rabbit diet (SQC Rabbit Diet, Special Diet Services Limited, Witham, Essex, England). The manufacturer supplied analytical data with each batch of diet. This included the concentrations of nutritional components, aflatoxins and selected heavy metals, pesticides and micro-organisms. The diet contained no added antibiotic or other chemotherapeutic or prophylactic treatment. The rabbits had free access to tap water supplied to each cage by an automatic piped system. The water was derived from a protected subterranean source and met the World Health Organisation European Standard. Reports from the local Water Authority recorded the chemical and bacteriological quality of the water. There was no information indicating that normal levels of common contaminants would influence the outcome of the study.

4.2 Environmental control

The animals were housed in a lagomorph room within a limited-access building. The room was kept at slight positive pressure relative to the outside and had its own filtered air supply giving approximately 12 complete air changes per hour without re-circulation.

The maximum and minimum temperatures of the previous 24-hour period and relative humidity were recorded at the beginning of each working day. Environmental control equipment was set to achieve target values of 18°C (range 15°-23°C) and 55% R.H. (range 40%-70% R.H.), respectively. Electric time-switches operated a lighting cycle of 12 hours of artificial light per day. An emergency generator was available to maintain the electricity supply in the event of a power failure.

All personnel entering the building changed into clean protective clothing and wore an additional gown, plastic over-shoes, gloves and a face mask to service the rabbit-holding areas.

4.3 Pre-exposure period

Each animal was inspected on arrival and unsuitable individuals were rejected. Individual bodyweight was recorded on the day of arrival and at regular intervals thereafter. All animals were identified by a uniquely numbered ear-tag within 24 hours of arrival. An acclimatisation period of at least six days was allowed between arrival at the laboratory and administration of the test material.

Daily checks of the general condition of each animal were made and the record was consulted before the final selection of each animal.

Twenty-four hours before dosing, the dorsum between the limb girdles was clipped (chemical depilatories were not used). Any animal displaying abnormality or irritation of the dermal test site was replaced by another acclimatised animal.

Home Office requirements were satisfied by the labelling of each cage with details of the schedule number, ear-tag number, sex, route of administration, treatment level, licensee and day of dosing of the cage occupant.

Bodyweight on the day of dosing was within the range 2.08 - 3.14 kg. The rabbits were approximately three months old at this time.

4.4 Constitution of treatment groups

Six acclimatised rabbits (three males and three females) were allocated to this study.

4.5 Preparation of test material

An appropriate quantity of the test material as supplied by the Sponsor was dispensed on the morning of Day 1.

4.6 Administration of test material

The rabbit was securely restrained by a technician. Two test sites (6 x 6 cm) were marked on either side of the clipped area of dorsum. A single dose (0.5 ml) was impregnated onto an unmedicated gauze patch (3 x 2 cm) and was held in place on the left test site by strips of Blenderm (3-M Company). The right test site, acting as a control, was covered by a similar semi-occlusive dressing but otherwise remained untreated. Pads of cotton wool and elasticated bandage were used to protect the patches and ensure good contact between the skin and the test material during the four-hour exposure period.

4.7 Observation period

The dressings were removed after four hours exposure. Where necessary, the treatment sites were gently washed with warm water and dried with paper towels to remove excessive amounts of test material adhering to the skin.

Assessment of skin irritation responses at the control and treated test sites were made one hour, 24, 48 and 72 hours after removal of the dressings. Reactions of the test sites were assessed according to the criteria of Draize (section 4.8).

4.8 Criteria for assessment of skin irritation responses

Erythema and eschar formation	Value
No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injury in depth)	4
Oedema formation	
No oedema	0
Very slight oedema (barely perceptible)	1
Slight oedema (edges of area well-defined by definite raising)	2
Moderate oedema (raised approximately 1mm)	3
Severe oedema (raised more than 1 mm and extending beyond the area of exposure)	4

4.9 Name and address of facilities

Life Science Research Limited
Eye, Suffolk, IP23 7PX
England

A full list of apparatus, diets, etc., and names and addresses of the suppliers concerned is maintained by the Chief Animal Technician, Department of Animal Management, Life Science Research, Eye, Suffolk.

Original data pertaining to this study are held in the archives of Life Science Research.

5. RESULTS (Tables 1 and 2)

Very slight erythema was observed at three test sites one hour after removal of the dressings, and in one animal only at the 24-hour examination. No other changes were apparent.

All dermal irritation responses had resolved by the 48-hour examination.

The control sites did not show any response to the control procedure.

6. CONCLUSION

Under the conditions of this test, RC9927 was 'very slightly irritating' to skin.

TABLE 1

Mean values for erythema and oedema recorded one hour, 24, 48 and 72 hours after treatment+

Type of response		Time after removal of dressings			
		1 hour	24 hours	48 hours	72 hours
Erythema	Test	0.5	0.2	0.0	0.0
	Control	0.0	0.0	0.0	0.0
Oedema	Test	0.0	0.0	0.0	0.0
	Control	0.0	0.0	0.0	0.0

+ The mean values were calculated using the individual scores for all rabbits on each occasion of examination.

TABLE 2

Scoring of irritance responses+ elicited by single dermal application of 0.5 ml RC9927 to the dorsa of New Zealand White rabbits under a semi-occlusive dressing

Animal number	Type of Response	Score 1 hour after removal of dressing		Score 24 hours after removal of dressing		Score 48 hours after removal of dressing		Score 72 hours after removal of dressing	
		Test Skin	Control Skin	Test Skin	Control Skin	Test Skin	Control Skin	Test Skin	Control Skin
12TX	Erythema	0	0	0	0	0	0	0	0
857	Oedema	0	0	0	0	0	0	0	0
12TX	Erythema	1	0	0	0	0	0	0	0
858	Oedema	0	0	0	0	0	0	0	0
12TX	Erythema	0	0	0	0	0	0	0	0
845	Oedema	0	0	0	0	0	0	0	0

+ Criteria documented in Section 4.8

TABLE 2 - continued

Scoring of irritance responses+ elicited by single dermal application of 0.5 ml RC9927 to the dorsa of New Zealand White rabbits under a semi-occlusive dressing

Animal number	Type of Response	Score 1 hour after removal of dressing		Score 24 hours after removal of dressing		Score 48 hours after removal of dressing		Score 72 hours after removal of dressing	
		Test Skin	Control Skin	Test Skin	Control Skin	Test Skin	Control Skin	Test Skin	Control Skin
12TX	Erythema	0	0	0	0	0	0	0	0
866	Oedema	0	0	0	0	0	0	0	0
12TX	Erythema	1	0	1	0	0	0	0	0
859	Oedema	0	0	0	0	0	0	0	0
12TX	Erythema	1	0	0	0	0	0	0	0
868	Oedema	0	0	0	0	0	0	0	0

+ Criteria documented in Section 4.8