European Registration Dossier
Dossier File N°: 5.2.2 / 01
Ciba File N°: 329351/3

Acute Dermal Toxicity in the Rat

Test No. 943027

CGA 329351 tech.

Report

Study director: Dr. med. vet. 5.1.2.e Woo

Testing facility: Short-term Toxicology
CIBA-GEIGY Limited
4332 Stein / Switzerland

Test Guideline: OECD 402; 92/69/EEC, B.3.

Study completed: May 5, 1994

Sponsor: CIBA-GEIGY Limited
Plant Protection
4002 Basel / Switzerland

This report contains: 15 pages

Certification of GLP and verification of the report

(Certification of Good Laboratory Practice and verification of a complete and unaltered copy of the report by the sponsor)

The Statement of Compliance with Good Laboratory Practice found on page 4, and signed by the Study Director is truthful and accurate. This report as provided by the testing facility is complete and unaltered.

For the Sponsor:

Signature: .... Date: ....

Statement of compliance with Good Laboratory Practice

This study has been performed in compliance with Good Laboratory Practice (GLP) in Switzerland (Verfahren und Grundsaetze der Guten Laborpraxis (GLP) in der Schweiz), Procedures and Principles, March 1986, issued by the Swiss Federal Department of the Interior and the Intercantonal Office for the Control of Medicaments. These procedures are in essence consistent with:

- OECD Principles of Good Laboratory Practice (Council Decision 81/30, adopted on May 12, 1981, and the OECD Recommendation 83/95 concerning the 'Mutual Recognition of Compliance with Good Laboratory Practice', adopted on July 26, 1983).
- United States Environmental Protection Agency, Title 40 Code of Federal Regulations Part 160 (FIFRA); Federal Register, August 17, 1989.
- United States Environmental Protection Agency, Title 40 Code of Federal Regulations Part 792 (TSCA); Federal Register, August 17, 1989.
- Japan Ministry of Agriculture, Forestry and Fisheries, NohSan, Notification No. 3850, Agricultural Production Bureau, August 10, 1984.

Study director: Dr. med. vet. 5.1.2.e Woo

Signature: ... Date: May 5, 1994

Reserved page for flagging statements

Quality assurance statement

Test Article: **CGA 329351 tech.**

Study Title: **Acute Dermal Toxicity in the Rat**

Test Number: **943027**

Study Director: **Dr. med. vet.** 5.1.2.e Woo

I hereby certify that the following Quality Assurance activities were performed:

QA-Activity	Date performed	Date reported
Facility Inspection	March 23, 1994	April 08, 1994
Protocol Audit	March 25, 1994	March 25, 1994
Study Inspection	March 29, 1994	April 05, 1994
Final Report Audit	May 04, 1994	May 05, 1994

Quality Assurance Inspector: 5.1.2.e Woo (for 5.1.2.e Woo)

Signature: 5.1.2.e Woo Date: May 10, 1994

1. SUMMARY AND CONCLUSIONS

Upon an acute dermal administration and a 14 day post-treatment observation period, the following LD50 was determined for CGA 329351 tech.

LD50 in male rats: greater than 2000 mg/kg body weight

LD50 in female rats: greater than 2000 mg/kg body weight

LD50 in rats of both sexes: greater than 2000 mg/kg body weight

Observations

No symptoms were observed in this study.

At autopsy, no deviations from normal morphology were found.

2. INTRODUCTION

2.1. Purpose

At the request of the Plant Protection of CIBA-GEIGY Limited, Test No. 943027, was conducted to determine the acute dermal toxicity of CGA 329351 tech. in albino rats.

2.2. Basis

The study design followed the OECD Guideline 402, "Acute Dermal Toxicity", adopted February 24, 1987 and the study protocol.

As requested by the sponsor, the whole study was subjected to quality assurance.

2.3. Testing facility

All the work was done in the testing facility:
CIBA-GEIGY Limited
Short-term Toxicology
4332 Stein / Switzerland

Technical assistant: Mr. [illegible]

Archives are located at:
CIBA-GEIGY Limited
Werk Stein
4332 Stein / Switzerland
Raw data, protocol and report will be stored at this location.

The job descriptions and the summaries of training and professional experience for all personnel participating in this study are archived in the test facility.

2.4. Dates

Date of protocol: March 22, 1994

Date of administration: March 29, 1994
April 6, 1994

Experimental completion date: April 20, 1994

2.5. Distribution

Sponsor (1)
Archives

3. MATERIALS AND METHODS

3.1. Test Article

Test article:	CGA 329351 tech.
Batch No.:	KGL 4634/6
Purity/Contents:	97.30%
Physical properties:	viscous
Storage conditions:	room temperature
Date of reanalysis:	February, 1998
Safety precautions:	gloves and face masks
Test material received:	March 16, 1994

3.2. Animals

3.2.1. Choice of species

The rat has been selected for this test as being a standard species for the determination of the acute dermal toxicity.

Young adult albino rats of both sexes (Tif: RAI f (SPF), bred and raised on the premises, were used in the experiment.

Source:	CIBA-GEIGY Limited Animal Production 4332 Stein / Switzerland
Initial body weight range:	200 to 268 g

3.2.2. Husbandry and Diet

The rats were kept in an animal room under conventional laboratory conditions on a 12 hour/day light cycle. The air conditioning system (approximately 15 air changes per hour) maintained a temperature of 22 ± 2 °C and a relative humidity of 55 ± 10 %. The rats were individually housed in Macrolon cages type 3, with standardized soft wood bedding (Societe Parisienne des Sciures, Pantin, France). They were acclimatized for at least 5 days before exposure.

Rat diet (NAFAG 890 Tox, NAFAG, Gossau/SG, Switzerland) and water were provided ad libitum.

3.2.3. Group size and identification

The dose group consisted of 10 rats (5 males and 5 females). During and after exposure, the animals were placed in their cages, which were marked with a cage card containing the date of administration and the characteristics of the experiment and dose group.

3.3. Design and Procedure

Pretreatment:	Approximately 24 hours before treatment an area on the back of the rat of at least 10% of the body surface was shaved with an electric clipper.
Application:	The test article was evenly dispersed on the skin. It was covered with a gauze-lined semiocclusive dressing fastened around the trunk with an adhesive elastic bandage. After 24 hours the dressing was removed and the skin was cleaned with lukewarm water. Thereafter the skin reaction was appraised repeatedly.
Frequency of application:	One single dose.
Dose level:	2000 mg/kg body weight
Total number of animals:	10
Vehicle:	liquid substance, used undiluted
Volume (ml/kg body weight) applied:	2
Observation period:	14 days

3.4. Observations and records

Mortality:	daily; a.m. and p.m. on working days, a.m. on weekend days
Signs and symptoms:	daily for 14 days

Body weight:	immediately before application and on days 7 and 14
Necropsies:	The animals were submitted to a gross necropsy at the end of the observation period.

4. RESULTS

4.1. In-life observations

No symptoms were observed in this study.

4.2. Body weight changes

Individual body weight, their group means and standard deviations are shown in table 1.

4.3. Mortalities

No mortalities occurred in this study.

4.4. Necropsies

At necropsy, no deviations from normal morphology were found.

TABLE 1

Body weight and necropsy findings

Animal Number	Body Weights (g) d 0	d 7	d 14	*	Gross Necropsy Findings
2000 mg/kg, males					
1	268	311	349	TS	NOA
2	255	297	349	TS	NOA
3	245	269	300	TS	NOA
4	245	292	339	TS	NOA
5	241	283	320	TS	NOA
mean	251	290	331		
SD	10.9	15.7	21.2		
2000 mg/kg, females					
1	203	229	249	TS	NOA
2	200	219	242	TS	NOA
3	224	209	243	TS	NOA
4	208	223	231	TS	NOA
5	217	214	230	TS	NOA
mean	210	219	239		
SD	10.0	7.8	8.2		

* TS terminal sacrifice
NOA no observable abnormalities

TABLE OF CONTENTS

Page

24

CIBA-GEIGY Limited
Short-term Toxicology
Stein / Switzerland

May 5, 1995

Report Addendum to Test No 943027

(Acute Dermal Toxicity in the Rat with CGA 329351 tech.)

The above mentioned study started on March 29, 1994 according to the protocol signed on March 22, 1994.

The procedure for the application of the test article followed the SOP No. 2.1.12 edition 4: July 10, 1987.

The test article was evenly dispersed on the skin. It was covered with gauze (4 layers, 4 x 6 cm, Rhena, IVF, 8212 Neuhausen, Switzerland) and fastened around the trunk with an adhesive but non-irritating elastic bandage (Isocomfort, Isoplast AG, 5200 Brugg, Switzerland). After 24 hours the dressing was removed and the skin was cleaned with lukewarm water. Thereafter the skin reaction was appraised repeatedly.

(For)

Study director: Dr. med. vet. [redacted] (absent)

Signature: [redacted] Date: May 5, 1995

Im Wasser ungenuegend loesliche Praeparate werden mit CMCPS80 oder, in Spezialfaellen, mit OL zu Suspensionen oder Emulsionen verarbeitet, (mittels hochtourigem Homogenisator oder durch Anruehren in Reibschale).

Das Anwaermen der Suspension im Wasserbad darf nur auf Anweisung des Sponsors oder des Versuchsleiters erfolgen.

6. Vorgehen

Die 200 bis 300 g schweren Ratten werden randomisiert in Einzelhaltung gesetzt.

Am Tag vor der Applikation werden die Ruecken- und Flankenpartien auf einer Flaeche von etwa 60 cm^2 mit Hilfe der elektrischen Haarschneidemaschine geschoren. Die geschorenen Hautpartien werden sorgfaeltig auf Verletzungen kontrolliert.

Die Versuchstiere werden gewogen und die Versuchsprotokolle ausgefuellt.

Die individuellen Applikationsmengen pro Tier werden berechnet, auf die geschorene Hautflaeche aufgetragen und mit einem Spachtel verstrichen, so dass eine moeglichst duenne Praeparatschicht entsteht. Fluessige Praeparate werden unverduennt (langsam) auf die Haut aufgetragen.

Die aufgetragene Substanz wird mit Gaze abgedeckt und mit hautfreundlichem Pflaster und Klebestreifen fixiert.

Die Applikationsdauer betraegt 24 Stunden. Danach wird das Pflaster entfernt und allfaellige Substanzreste mit lauwarmem Wasser von der Rueckenhaut schonend abgewaschen.

7. Praeparatresten

Nach der Applikation anfallende Praeparatreste werden waehrend des Versuchs in einem bezeichneten Behaelter zur spaeteren Vernichtung gesammelt.

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