

Test No.: 933718
Test substance : CGA 329351

Report on the acute toxicity test
of CGA 329351 techn. (Enantiomer of CGA 48988)
to Rainbow Trout (*Oncorhynchus mykiss*)

Study Director : Dr. 5.1.2.e Woo
Testing Facility : CIBA-GEIGY Ltd.
Product Safety
Ecotoxicology
CH-4002 Basel / Switzerland
Test Guideline : OECD - Guideline No.: 203, Paris 17/07/92
Limit test, static system
Study completed : 01/12/94
(day/month/year)
Sponsor : CIBA-GEIGY Ltd
PP - Division
CH-4002 Basel / Switzerland
represented by : Dr. 5.1.2.e Woo
Project No. of Sponsor : 933718

This report contains 17 pages.

European Registration Dossier
Dossier File N°: 8.2.1/6
Ciba File N°: 329351/25

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Test No.: 933718
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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 this page of this report, 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 : Dr. 5.1.2.e Woo

Signature :

5.1.2.e Woo

Date:

29.11.94

Statement of Compliance with Good Laboratory Practices

This study has been performed in compliance with Good Laboratory Practice (GLP) in Switzerland, Procedures and Principles, March 1986 (Verfahren und Grundsätze der Guten Laborpraxis (GLP) in der Schweiz), 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. 5.1.2.e Woo

Signature :

Date: 22/11/94...

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Reserved for flagging statements

Test No.:
Test substance :

938718
CGA 329351

Quality Assurance Statement
 Ciba-Geigy Ltd., Toxicology Services, Quality Assurance (GLP), 4002 Basel

Project 933718
 Test Substance CGA 329351
 Study Title Acute toxicity test of CGA 329351 techn. (Enantiomer of CGA 48988) to Rainbow Trout (*Oncorhynchus mykiss*)
 Study Director Dr. 5.1.2.e Woo
 QA-Inspector 5.1.2.e Woo

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

Activity	Performed	Reported
Facility Inspection	March 07, 1994	April 14, 1994
Facility Inspection	May 05, 1994	May 09, 1994
Protocol Audit	May 30, 1994	May 31, 1994
Study Related Inspection	June 10, 1994	June 10, 1994
Final Report Audit	November 29, 1994	December 01, 1994

.....
 Date December 08, 1994
 Form: QSSTAT12

5.1.2.e Woo

Inspector Quality Assurance

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Test No.: 933718
 Test substance : CGA 329351

Table of contents

	Page
Proprietary information	2
Statement of compliance with GLP	3
Reserved page for Flagging Statement	4
Quality Assurance Statement	5
1. Summary	7
2. Introduction	8
2.1. Purpose	8
2.2. Guideline	8
2.3. Deviations	8
2.4. Testing facility	8
2.5. Archives	8
2.6. Personnel	9
2.7. Dates	9
2.8. Distribution	9
3. Materials and Methods	10
3.1. Test substance	10
3.2. Test system / species	10
3.3. Design and procedure	11
3.4. Stock solution	11
3.5. Test concentrations	11
3.6. Observations	12
3.7. Measurements	12
3.8. Calculations / statistical analysis	12
4. Results	13
4.1. Values calculated	13
4.2. Values graphically determined	13
4.3. Values observed	13
4.4. Controls	13
4.5. Time / Toxicity curve	13
4.6. Conclusion	13
5. Tables	14 - 15
Appendix:	
Analysis report on test no 933718, CGA 329351	16 - 17

Test No.: 933718
 Test substance : CGA 329351

1. Summary

Study : Determination of LC 50 (96 h) :
 Concentration at which 50% of the fish population died.

Test system : Rainbow Trout (*Oncorhynchus mykiss*)

Duration : 96 hours

Guideline : OECD - Guideline No.: 203, Paris 17/07/92
 Limit test, static system

Deviations : Mean length of fish: 59 mm (55-61 mm) due to season.

Test substance: Identification Code : CGA 329351
 Batch No.: KGL 4634/6
 Purity : 97.3 %

Design :

Test concentration nominal : 100 mg test substance/l (limit test)

After the preparation of the test concentration and an equilibration time of 5 hours, 7 fish were exposed in each concentration and control (3 and 4 fish per 20 l glass aquaria containing 15 l of test solution). The temperature was maintained constant at 15°C and the oxygen content between 87 and 100% of saturation value. The pH was 7.7-8.2.

Results :

Measured test concentrations at the beginning and the end of the exposure period ranged from 94 to 94% of the nominal concentration. Values are therefore based on nominal concentrations. The test substance appeared homogeneously distributed in the test vessel at all test times.

LC 50 (96 h)	:	>100 mg/l
Confidence limits	:	none
NOEC (96 h)	:	100 mg/l
LC 0 (96 h)	:	100 mg/l
LC 100 (96 h)	:	>100 mg/l

No mortality occurred at the concentration tested and no sublethal effects were observed.

Conclusion :

With reference to the 7th Amendment to Directive 67/548/EEC, i.e. Directive 92/32/EEC, the ecotoxicological classification of CGA 329351 is "not toxic to fish".

Test No.: 933718
 Test substance : CGA 329351

2. Introduction

- 2.1. Purpose :** At the request of the sponsor an acute toxicity study was conducted. This report describes the experimental techniques and the results obtained in this study to determine the acute toxicity of the test substance on fish. Results from pretests for this study or studies not fulfilling the validity criteria are not reported but documented in the raw data.
- 2.2. Guideline :** OECD - Guideline No.: 203, Paris 17/07/92
 Limit test, static system
- 2.3. Deviations :**
 - Guideline : Mean length of fish: 59 mm (55-61 mm) due to season.
- 2.4. Testing Facility :** CIBA-GEIGY Ltd.
 Product Safety
 Ecotoxicology
 R-1066.P.
 CH-4002 Basel / Switzerland
- 2.5. Archives :** CIBA-GEIGY Ltd.
 R-1066.1.42
 CH-4002 Basel

Test No.: 933718
 Test substance : CGA 329351

2.6. Personnel

• Study director : ... 5.1.2.e Woo Date : 21/12/94
 Dr. Voorts kan op dit document op grond van een wettelijke verplichting tot openbaarmaking.

• Analytical scientist contributing to this report :
 Dr. 5.1.2.e Woo Date : 2 Dec. 1994

• Test Facility Management :
 Dr. 5.1.2.e Woo Date : 5-12-94

Technical personnel : 5.1.2.e Woo (principal coworker)
 5.1.2.e Woo

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

2.7. Dates :
 (d/m/y) Begin of test (Study plan) : 27/05/94
 Experimental start : 30/05/94
 Experimental end : 25/11/94
 Study completed : see page 1

2.8. Distribution : Sponsor
 Archives

Test No.: 933718
Test substance : CGA 329351

3. Materials and Methods

3.1. Test substance

Identification Code : CGA 329351
Generic/Trade name :
Batch No.: KGL 4634/6
Appearance : yellow liquid
Purity : 97.3 %
Solubility (in water):
Received : 28/02/94
Storage : room temperature
Stability : /02/98

3.2. Test system / species

Fish : Rainbow Trout (*Oncorhynchus mykiss*)
Supplier : XXXXXXXXXX / CH-4314 Zeiningen
Number of fish : 7 per concentration and control.
3 / 4 per aquarium.
Length (mean) : 59 mm (55 - 61 mm) based on 7 fish
Weight (mean) : 1.70 g (1.41 - 1.94 g) based on 7 fish
Loading : 0.40 g/l
Feeding : None
Adaptation : 24 hours / no food 24 hours prior to exposure
Acclimatization : 33 days
Treatment : None

Test No.: 933718
Test substance : CGA 329351

3.3 Design and procedure

Vessels : Glass aquaria of 20 liters filled with 15 liters (36/22/25 cm).
Procedure : Limit test, static system
Water : Dechlorinated tap water (carbon filter)
Hardness : 182 mg CaCO₃/l
Temperature : 15 °C
Aeration : Gentle aeration during exposure
Lighting : Fluorescent light, 16 hours daily
Duration : 96 hours

3.4 Stock solution

3.01 g test substance were mixed with and made up to 1000 ml with water.

3.5. Test concentrations

Nominal : 100 mg test substance/l (limit test)
Controls :
Blank : Dechlorinated tap water
Remarks : Calculated amounts of the stock solution to produce the desired test concentrations were given into the water and were homogeneously distributed. After an equilibration time of 5 hours the fish were transferred into the aquaria (begin of exposure).

The test substance appeared homogeneously distributed in the test vessels at all test times.

Test No.: 933718
Test substance : CGA 329351

Sampling
for analysis : Composite samples of each test concentration were drawn by mixing identical volumes of the test solutions taken from the approximate center of the test vessels. They were taken immediately before the exposure and after 96 hours exposure and kept at -18°C to -22°C until analysis.

3.6. Observations

Mortality was recorded after 2-4, 24, 48, 72 and 96 hours exposure and is given on table 1.

The fish were examined daily for the symptoms listed on table 2.

3.7. Measurements

The oxygen content, pH and temperature were measured at 0, 24, 48, 72 and 96 hours. For the values see table 3.

Description of analytical determination of test substance concentration in Appendix.

3.8. Calculations / Statistical Analysis

None

Test No.: 933718
 Test substance : CGA 329351

4. Results

Measured test concentrations at the beginning and the end of the exposure period ranged from 94 to 94% of the nominal concentration (see Appendix). Values are therefore based on nominal concentrations. The test substance appeared homogeneously distributed in the test vessel at all test times.

4.1. Values

LC 50 (96 h)	: >100 mg/l
Conf. limits	: none
LC 50 (72 h)	: >100 mg/l
Conf. limits	: none
LC 50 (48 h)	: >100 mg/l
Conf. limits	: none
LC 50 (24 h)	: >100 mg/l
Conf. limits	: none

4.2. Values graphically determined

LC 50 (96 h)	: not determined
--------------	------------------

4.3. Values observed

NOEC (96 h)	: 100 mg/l
LC 0 (96 h)	: 100 mg/l
LC 100 (96 h)	: >100 mg/l

No mortality occurred at the concentration tested and no sublethal effects were observed.

4.4. Controls

Mortalities in blank: 0 %

4.5. Time / Toxicity curve

Due to the results obtained, no time / toxicity curve is available.

4.6 Conclusion

With reference to the 7th Amendment to Directive 67/548/EEC, i.e. Directive 92/32/EEC, the ecotoxicological classification of CGA 329351 is "not toxic to fish".

Test No.: 933718
 Test substance : CGA 329351

5. Tables

Table 1 Mortalities (Initial number of fish: 7 per test concentration)

Conc. nominal mg/l	Mortality Number of dead fish				
	2-4 h	24 h	48 h	72 h	96 h
Blank	0	0	0	0	0
100	0	0	0	0	0

Table 2 Symptoms observed

Conc. nominal mg/l	Swimming behaviour					Loss of equilibrium					Respiratory function					Exophthalmus					Pigmentation				
	2-4	24	48	72	96	2-4	24	48	72	96	2-4	24	48	72	96	2-4	24	48	72	96	2-4	24	48	72	96 h
Blank	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
100	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

- 1: light symptoms
 2: moderate symptoms
 3: severe symptoms

Test No.: 933718
 Test substance : CGA 329351

Table 3 Measurements

Conc. nominal mg/l	0 h			24 h			48 h			72 h			96 h		
	T °C	pH	O2 %	T °C	pH	O2 %	T °C	pH	O2 %	T °C	pH	O2 %	T °C	pH	O2 %
Blank	15	7.7	99	15	7.9	87	15	8.1	97	15	8.2	96	15	8.1	100
100	15	7.7	97	15	8.0	95	15	8.2	95	15	8.2	96	15	8.2	100

T: Temperature

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Test No.: 933718
 Test substance : CGA 329351

Appendix:

Ciba Crop Protection/Residue Analysis Basel/Switzerland

ANALYSIS REPORT ON TEST NO. 933718 (PROJECT NO. OF SPONSOR: 933718)
 CGA 329351 WATER

DETERMINATION OF CGA 329351 IN WATER SPECIMENS FROM ACUTE TOXICITY TEST TO RAINBOW TROUT

1. DESCRIPTION OF SPECIMENS

Refer to protocol of project.
 Arrival of specimens: 20 Jun 1994.
 Storage: at -20°C until analysis.
 Analysis: 29 Sep 1994.

2. ANALYTICAL METHOD

General Analytical Method for "Test Substances Used for Ecotoxicity Studies", Residue Analysis,
 8 Feb. 1988.
 Calculations according to General Calculation Method REM 119.04.

Abstract of the method:

HPLC with UV detection: the injected specimen is preconcentrated and precleaned on a short column (C₁₈, 5 µm), and then transferred onto the analytical HPLC column (C₁₈). The substance is eluted with water-acetonitrile (65 vol. + 35 vol.) and detected at 240 nm.

Details of the method:

The HPLC system is equipped with a short column (1 cm length, 4 mm i.d., packed with Nucleosil 100 C₁₈, 5 µm), a switching valve and an analytical column (12 cm length, 4 mm i.d., packed with Nucleosil 100 C₁₈, 5 µm). 1 mL of the water specimen (appropriately diluted with water if necessary) is injected and transferred onto the short column, where it is preconcentrated and precleaned by washing with water. By means of the switching valve and water-acetonitrile (65 vol. + 35 vol.) as the mobile phase the substance is eluted from the short column and transferred onto the analytical column, from where it is eluted by the mobile phase and detected with an UV detector at 240 nm. CGA 329351 is used as the reference substance.

Quantitation: by alternate injections of water specimens and of reference substance solutions. Interpolation by method of weighted least squares of peak heights, regression of 1st order. From the measured contents of CGA 329351 the corresponding values of the test product were calculated (the product contains 97.3% CGA 329351).

The procedure was checked with recovery experiments at two spike levels. 4.5 ml of the control specimen was spiked with 0.5 ml of an appropriate standard solution of CGA 329351 in water.

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Test No.: 933718
 Test substance : CGA 329351

Appendix continued:

Ciba
 Test No. 933718

Crop Protection/Residue Analysis

Basel/Switzerland
 page 2 of 2

3. RESULTS

specimen description		nominal conc. CGA 329351 techn. [mg/L]	conc. found CGA 329351 [mg/L]	conc. found (corr.) CGA 329351 techn. [mg/L]	conc. found (corr.) relative to conc. nominal [%]
06 Jun 94	0 h	100	94.3	93.6	94
10 Jun 94	96 h	100	94.5	93.8	94
06 Jun 94	0 h	control	<1.00	<0.99	-
10 Jun 94	96 h	control	<1.00	<0.99	-

Remarks:

- conc. found (corr.): these results are corrected for an average recovery of 103.5 %.

Recoveries:

Spike level 2.0 mg/L CGA 329351 (2.1 mg/L CGA 329351 techn.): 103%
 Spike level 8.0 mg/L CGA 329351 (8.2 mg/L CGA 329351 techn.): 104 %

Analyst: P. Forzy

25 NOV 1994

date

5.1.2.9 NCG
 (principal investigator for analytics)

Distribution: Dr. [redacted] (study director)

Original report and raw data in archives of Residue Analysis, PP 2.53.

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