Pinoxaden/Cloquintocet-Mexyl

Pinoxaden/Cloquintocet-Mexyl EC (A13617AV) - Primary Skin Irritation Study in Rabbits (4 Hour Semi-Occlusive Application)

Final Report

DATA REQUIREMENT(S): OECD 404 (2002)
EC No 440/2008, B.4 (2008)

AUTHOR(S): Dr. M. Mallaun

STUDY COMPLETION DATE: 18-Oct-2010

PERFORMING LABORATORY: Harlan Laboratories Ltd.
Wölferstrasse 4
4414 Füllinsdorf / Switzerland

LABORATORY PROJECT ID: Report Number: C97204
Study Number: C97204
Task Number: TK0028293

SPONSOR(S): Syngenta Ltd.
Jealott's Hill, International Research Centre
Bracknell, Berkshire, RG42 6EY / United Kingdom

STATEMENT OF DATA CONFIDENTIALITY CLAIMS

This page intentionally left blank.

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

The pH measurement of the test item was performed before the study initiation date. This procedure is therefore excluded from this statement.

This study has been performed in compliance with the Swiss Ordinance relating to Good Laboratory Practice, adopted May 18, 2005 [SR 813.112.1]. This Ordinance is based on the OECD Principles of Good Laboratory Practice, as revised in 1997 and adopted November 26, 1997 by decision of the OECD Council [C(97)186/Final].

There were no circumstances that may have affected the quality or integrity of the data.

Dr. M. Mallaun
Study Director
Acute Toxicology

18-Oct-2010
Date

Performing Laboratory:

Harlan Laboratories Ltd.,
Wölferstrasse 4
4414 Füllinsdorf / Switzerland

FLAGGING STATEMENT

This page intentionally left blank.

QUALITY ASSURANCE STATEMENT

Harlan Laboratories Ltd., Zelgliweg 1, 4452 Itingen / Switzerland

Harlan Laboratories Study:	C97204
Syngenta Task No:	TK0028293
Test Item:	Pinoxaden/Cloquintocet-Mexyl EC (A13617AV)
Study Director:	Dr. M. Mallaun
Study Title:	Pinoxaden/Cloquintocet-Mexyl EC (A13617AV) - Primary Skin Irritation Study in Rabbits (4-Hour Semi-Occlusive Application)

The general facilities and activities are inspected at least once a year and the results are reported to the responsible person and the management.

Study procedures were periodically audited. The study plan and this report were audited by the Quality Assurance. The dates are given below.

Dates and Types of QA Inspections		**Dates of Reports to the Study Director and Test Facility Management**
06-Aug-2010	Study Plan	06-Aug-2010
03-Aug-2010	Process based (Test System)	03-Aug-2010
28/30-Sep-2010	Report	30-Sep-2010

This statement also confirms that this final report reflects the raw data.

Quality Assurance: for K. Bezares

.....

Date: 18-Oct-2010

GENERAL INFORMATION

Contributors
The following contributed to this report in the capacities indicated:

Name	Function
Dr. M. Mallaun	Study Director
G. Arcelin	Deputy Study Director
T. Fink	Manager Quality Assurance
E. Yau	Syngenta Study Manager

Study dates

Experimental starting date:	11-Aug-2010
Experimental completion date:	07-Sep-2010
Acclimatization:	11-Aug-2010 to 15-Aug-2010 (female no. 66) 11-Aug-2010 to 16-Aug-2010 (females no. 65, 67)
Treatment:	16-Aug-2010 (female no. 66) 17-Aug-2010 (females no. 65, 67)
Observation of local dermal signs:	16-Aug-2010 to 06-Sep-2010 (female no. 66) 17-Aug-2010 to 07-Sep-2010 (females no. 65, 67)
Termination:	07-Sep-2010

Deviations from the guidelines
None

Retention of samples
See other below

Performing laboratory test substance reference number
234351/A

Other
Harlan Laboratories Ltd. (4452 Itingen / Switzerland) will retain the study plan, raw data, a sample of the test item and the original final report of the present study for at least ten years. No data will be discarded without the Sponsor’s written consent.

TABLE OF CONTENTS

1.0 EXECUTIVE SUMMARY

1.1 Study Design

The primary skin irritation potential of Pinoxaden/Cloquintocet-Mexyl EC (A13617AV) was investigated according to OECD test guideline no. 404. The test item was applied by topical semi-occlusive application of 0.5 mL to the intact left flank of each of 3 young adult New Zealand White rabbits. The duration of treatment was four hours. The scoring of skin reactions was performed 1, 24, 48 and 72 hours as well as 7, 10, 14, 17 and 21 days after removal of the dressing.

1.2 Results

The primary irritation index was calculated by totalling the mean cumulative scores at 24, 48 and 72 hours and then dividing by the number of data points. The primary irritation index was 2.56 (max. 8.0).

The application of Pinoxaden/Cloquintocet-Mexyl EC (A13617AV) to rabbit skin resulted in mild to moderate signs of irritation. All animals exhibited very slight to well-defined erythema and very slight oedema from 1 hour after application. Erythema completely reversed in all animals by test day 10 (1/3 animals) or test day 14 (2/3 animals). Furthermore, scaling was observed in all 3 animals during the declining phase of the skin reaction, which reversed in 2/3 animals by test day 21. No corrosive effects were noted on the treated skin of any animal at any of the measuring intervals and no clinical signs were recorded.

Thus, the test item did not induce significant or irreversible damage to the skin.

1.3 Conclusion

According to Draize classification criteria Pinoxaden/Cloquintocet-Mexyl EC (A13617AV) is considered to be a “moderate irritant” to rabbit skin (P.I.I. = 2.56).

2.0 INTRODUCTION

2.1 Purpose

The purpose of this primary skin irritation study was to assess the possible irritation potential when a single dose of Pinoxaden/Cloquintocet-Mexyl EC (A13617AV) was placed on the skin of rabbits for approximately 4 hours.

This study should provide a rational basis for hazard assessment in man as skin contact is one of the possible routes of human exposure.

The test item was administered at 0.5 mL/animal, the dose specified in the test guidelines for a liquid test item.

2.2 Guidelines

The study was done according to the following guidelines:

OECD Guidelines for Testing of Chemicals, Section 4, number 404 “Acute Dermal Irritation / Corrosion”, adopted April 24, 2002.

Commission Regulation (EC) No 440/2008 of 30 May 2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), B.4 Acute Toxicity: Dermal Irritation/Corrosion (Official Journal No L 142, 31/05/2008 p. 0182-0190.

2.3 Test Facility

This study was performed in an AAALAC-accredited laboratory in accordance with the Swiss Animal Protection Law under license no. 56.

3.0 MATERIALS AND METHODS

3.1 Test Substance

The following information was provided by the Sponsor:

Identification:		Pinoxaden/Cloquintocet-Mexyl EC (A13617AV)
Description:		Light yellow liquid
Batch Number:		SMU0EP001
Purity:	Content of pinoxaden:	5.14 % w/w corresponding to 49.7 g/L
	Content of cloquintocet-mexyl:	1.34 % w/w corresponding to 13.0 g/L
	Content of water:	0.24 % w/w
Stability of Test Item:		Stable under specified storage conditions.
Reanalysis Date:		30-Nov-2012
Storage Conditions:		At a temperature < 30°C (as specified by the Sponsor) At room temperature of 20±5°C (as handled by Harlan Laboratories Ltd.), light protected.
Safety Precautions:		Routine hygienic procedures were used to ensure the health and safety of the personnel.

The certificate of analysis as attached in Appendix 1.

3.2 Experimental Design

0.5 mL (per animal) of Pinoxaden/Cloquintocet-Mexyl EC (A13617AV) was used as delivered by the Sponsor.

The pH of the test item was determined before the study initiation date. By using pH strips, a pH of 5 was measured from an aliquot of the test item.

According to Commission Regulation (EC) No 440/2008, B.4. and OECD Guidelines 404, a test item is not required to be tested if the pH-value is less than 2 or greater than 11.5, owing to its predictable corrosive properties.

Four days before treatment, the left flank was clipped with an electric clipper, exposing an area of approximately 100 cm^2 (10 cm x 10 cm). The skin of the animals was examined 1 day before treatment, and any regrown fur observed was clipped again.

On the day of treatment, 0.5 mL of Pinoxaden/Cloquintocet-Mexyl EC (A13617AV) was placed on a surgical gauze patch (ca. 2.5 cm x 2.5 cm). This gauze patch was applied to the intact skin of the clipped area. The patch was covered with a semi-occlusive dressing. The dressing was wrapped around the abdomen and anchored with tape.

The duration of treatment was 4 hours. Then the dressing was removed and the skin was flushed with lukewarm tap water to clean the application site.

A single animal was treated first. As neither a corrosive effect nor a severe irritant effect was observed after the 4-hour exposure, the test was completed using the 2 remaining animals for an exposure period of four hours.

Viability/mortality was recorded daily from acclimatization of the animals to the termination of the test.

Clinical signs were recorded daily from acclimatization of the animals to the termination of test.

Body weights were recorded at start of acclimatization, on the day of application and at termination of observation.

3.2.1 Animals

Animal Species and Strain:	Young Adult New Zealand White Rabbit, SPF
Rationale:	Recognized by international guidelines as a recommended test system.
Breeder:	Charles River Stolzenseeweg 32-36 88353 Kisslegg / Germany
Number of Animals:	3 females
Age (when treated):	12 – 16 weeks
Body Weights (when treated):	2990 – 3070 g
Identification:	By unique cage number and corresponding ear number.
Acclimatization:	Under laboratory conditions after health examination and at least for 5 days. Only animals without any visual signs of illness were used for the study.
Randomization:	Selected by hand at time of delivery. No computer generated randomization program.
Allocation:	Nos. 65 – 67

3.2.2 Husbandry

Room Number:	0501 / Harlan Laboratories Ltd., Füllinsdorf
Conditions:	Standard Laboratory Conditions

	Air-conditioned with a room temperature of 17-23°C, a relative humidity between 30-70% and approximately 10-15 air changes per hour. Room temperature and humidity were monitored continuously; these data are not reported but are retained at Harlan Laboratories Ltd. The animals were provided with an automatically controlled light cycle of 12 hours light and 12 hours dark. Music was played during the daytime light period.
Accommodation:	Individually in stainless steel cages equipped with feed hoppers and drinking water bowls.
Diet:	Pelleted standard Teklad Global High Fiber Rabbit Diet 2031C (batch no. 25/10, provided by Provimi Kliba AG, 4303 Kaiseraugst / Switzerland) available *ad libitum*. Results of analyses for contaminants are archived at Harlan Laboratories Ltd.
	A piece of wood (batch no. 102240, imported by Indulab AG, Gams / Switzerland from ABEDD® - LAB & VET GmbH, 1160 Vienna / Austria) and a haystick 4642 (batch no. 54/09, provided by Provimi Kliba AG, 4303 Kaiseraugst / Switzerland) were also provided for environmental enrichment.
Water:	Community tap water from Füllinsdorf, *ad libitum*. Results of bacteriological, chemical and contaminant analyses are archived at Harlan Laboratories Ltd.

3.3 *Post Mortem* Investigations

All rabbits were killed by an intravenous injection of 1.0 mL/kg of at least 162 mg/mL sodium pentobarbitone (but no more than 200 mg/mL sodium pentobarbitone) into the ear vein and discarded. No necropsy was performed.

3.4 Data Evaluation

The skin reaction was assessed according to the numerical scoring system listed in the Commission Regulation (EC) No 440/2008 of 30 May 2008, which was based on the Draize score system.

The skin reaction was assessed at approximately 1, 24, 48 and 72 hours after exposure (removal of the dressing, gauze patch and test item).

Data were summarized in tabular form, showing for each animal the irritation scores for erythema and oedema at all measurement intervals. Any lesions were described, including

the degree and nature of irritation, corrosion or any other toxic effects observed, and their reversibility.

The mean score was calculated across 3 scoring times (24, 48 and 72 hours after patch removal) for each animal for erythema/eschar grades and for oedema grades, separately.

The Cumulative Scores for the Skin Irritation Scores were calculated and represent the sum of all numerical scores for each animal at each time point. The resulting Mean Cumulative Skin Irritation Score was calculated for all animals at each time point.

The Primary Irritation Index (P.I.I.) was calculated by totalling the mean cumulative scores at 24, 48 and 72 hours and then dividing by the number of available figures.

The irritation was classified according to the following criteria:

P.I.I. = 0	Not Irritant
$0 < P.I.I. \leq 2$	Mild Irritant
$2 < P.I.I. \leq 5$	Moderate Irritant
$5 < P.I.I.$	Severe Irritant

Viability/mortality, clinical signs and local dermal signs were recorded on data sheets and transcribed for compilation and analysis.

Body weights were recorded on-line.

No statistical analysis was performed.

The RCC Tox Computer System (RCC-Tox-Lims) has been validated with respect to data collection, storage and retrievability.

4.0 RESULTS AND DISCUSSION

The mean score was calculated across 3 scoring times (24, 48 and 72 hours after patch removal) for each animal for erythema/eschar grades and for oedema grades, separately. The mean erythema/eschar scores of the 3 animals were 2.00, 2.00 and 1.00 and the mean oedema scores were 1.00, 1.00 and 0.67.

The primary irritation index was calculated by totalling the mean cumulative scores at 24, 48 and 72 hours and then dividing by the number of data points. The primary irritation index was 2.56 (max. 8.0).

The application of Pinoxaden/Cloquintocet-Mexyl EC (A13617AV) to rabbit skin resulted in mild to moderate signs of irritation. All animals exhibited very slight to well-defined erythema and very slight oedema from 1 hour after application. Erythema completely reversed in all animals by test day 10 (1/3 animals) or test day 14 (2/3 animals). Furthermore, scaling was observed in all 3 animals during the declining phase of the skin reaction, which reversed in 2/3 animals by test day 21. No corrosive effects were noted on the treated skin of any animal at any of the measuring intervals and no clinical signs were recorded.

No system clinical signs or any intercurrent mortality was observed in this study.

The body weights of all rabbits were considered to be within the normal range for this strain and age.

5.0 CONCLUSION

According to Draize classification criteria Pinoxaden/Cloquintocet-Mexyl EC (A13617AV) is considered to be a “moderate irritant” to rabbit skin (P.I.I. = 2.56).

6.0 REFERENCES

Literature references listed are available upon request.

External references

Draize, J.H. (1959): Dermal Toxicity. In Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics, pp. 46-49. Austin, Texas: Association of Food and Drug Officials of the United States.

Draize, J.H., Woodward, G. & Calvery, H.O. (1944): Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. J. Pharmacol. Exper. Therap. 83: 377-390.

TABLES SECTION

GLOSSARY FOR TABLE 1

Grading of Skin Reactions

Erythema and Eschar Formation

No erythema	0
Very slight erythema	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beef redness) or eschar formation (injuries in depth preventing erythema) reading	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 (edges raised approximately 1 mm)	3
Severe oedema (raised more than 1 mm and extending beyond the area of exposure)	4

Primary Irritation Index (P.I.I.)

The irritation was classified according to the following criteria:

P.I.I. = 0	Not Irritant
$0 < P.I.I. \leq 2$	Mild Irritant
$2 < P.I.I. \leq 5$	Moderate Irritant
$5 < P.I.I.$	Severe Irritant

TABLE 1 Skin Irritation Scores - Individual Values

Animal Number	Sex	Evaluation Interval*	Erythema	Oedema	Cumulative Score	Cumulative Mean	Scaling
65	F		1	0	1.00		
66	F	**1 hour**	1	0	1.00	1.00	
67	F		1	0	1.00		
65	F		2	1	3.00		
66	F	**24 hours**	2	1	3.00	2.33	
67	F		1	0	1.00		
65	F		2	1	3.00		
66	F	**48 hours**	2	1	3.00	2.67	
67	F		1	1	2.00		
65	F		2	1	3.00		
66	F	**72 hours**	2	1	3.00	2.67	
67	F		1	1	2.00		
65	F		1	0	1.00		x
66	F	**7 days**	2	1	3.00	1.33	x
67	F		0	0	0.00		x
65	F		1	0	1.00		x
66	F	**10 days**	1	0	1.00	0.67	x
67	F		0	0	0.00		x
65	F		0	0	0.00		x
66	F	**14 days**	0	0	0.00	0.00	x
67	F		0	0	0.00		x
65	F		0	0	0.00		x
66	F	**17 days**	0	0	0.00	0.00	x
67	F		0	0	0.00		x
65	F		0	0	0.00		
66	F	**21 days**	0	0	0.00	0.00	x
67	F		0	0	0.00		

* Examinations were performed at the specified times after removal of the dressing.
x = scaling

TABLE 2 Skin Irritation Scores - Mean Values after 24, 48 and 72 Hours

Animal Number	Sex	Erythema	N	Oedema	N	Primary Skin Irritation Index
65	F	2.00	3	1.00	3	
66	F	2.00	3	1.00	3	**2.56**
67	F	1.00	3	0.67	3	
Mean score		1.67		0.89		

N = number of available data points

TABLE 3 Body Weights

Animal No.	Sex	Body Weight (g)		
		First Day of Acclimatization	Day of Treatment	Last Day of Observation
65	F	2813	3070	3572
66	F	2981	2990	3367
67	F	2706	3042	3969

APPENDICES SECTION

APPENDIX 1 Certificate of Analysis

syngenta

GLP Testing Facility WMU
Analytical Development &
Product Chemistry GS2131

Syngenta Crop Protection
Münchwilen AG
Breitenloh 5
CH-4333 Münchwilen

Certificate of Analysis

A13617AV
pinoxaden/cloquintocet-mexyl
EC (050/012.5)
SMU0EP001

Batch Identification	**SMU0EP001**
Product Code	**A13617AV**
Other Product Code(s)	pinoxaden/cloquintocet-mexyl EC (050/012.5)

Chemical Analysis (Active Ingredient Content)

– **Identity of the Active Ingredient(s)***	**confirmed**
– **Content of pinoxaden***	**5.14 % w/w corresponding to 49.7 g/l**
– **Content of cloquintocet-mexyl***	**1.34 % w/w corresponding to 13.0 g/l**
– **Content of water***	**0.24 % w/w**

The Active Ingredient(s) content is within the FAO limits.

Methodology used for Characterization	HPLC, Karl Fischer Titration

Physical Analysis

– **Appearance**	**light yellow liquid**
– **Density ***	**967 kg/m^3**

Stability:

– **Storage Temperature**	**< 30°C**
– **Recertification Date**	**End of November 2012**

If stored under the conditions given above, this test substance can be considered stable until the recertification date is reached.

This Certificate of Analysis summarizes data which originates either from a single study or from several individual studies. Tests marked with an asterisk (*) have been conducted in compliance with GLP. Raw data, documentation, study plans, any amendments to study plans and reports pertaining to this/these study/studies are stored under the study number(s) referenced below within the archives of the GLP Testing Facility WMU at Syngenta Crop Protection Muenchwilen AG.

Study number of batch characterization: 121383
Study number(s) of batch recertification:

Authorisation: Jul 21, 2010

S. De Benedictis
Analytical Development & Product Chemistry

APPENDIX 2 Individual Local Findings

Animal No. 65, Female

After 1 hour:	Erythema:	Slightly reddened
	Oedema:	No Abnormal Findings Noted
	Scaling:	No Abnormal Findings Noted
	Staining:	No Staining Present
After 24 hours:	Erythema:	Moderately reddened
	Oedema:	Slight swelling
	Scaling:	No Abnormal Findings Noted
	Staining:	No Staining Present
After 48 hours:	Erythema:	Moderately reddened
	Oedema:	Slight swelling
	Scaling:	No Abnormal Findings Noted
	Staining:	No Staining Present
After 72 hours:	Erythema:	Moderately reddened
	Oedema:	Slight swelling
	Scaling:	No Abnormal Findings Noted
	Staining:	No Staining Present
After 7 days:	Erythema:	Slightly reddened
	Oedema:	Slight swelling
	Scaling:	present
	Staining:	No Staining Present
After 10 days:	Erythema:	Slightly reddened
	Oedema:	No Abnormal Findings Noted
	Scaling:	present
	Staining:	No Staining Present

APPENDIX 2 Individual Local Findings (Continued)

Animal No. 65, Female

After 14 days:	Erythema:	No Abnormal Findings Noted
	Oedema:	No Abnormal Findings Noted
	Scaling:	present
	Staining:	No Staining Present
After 17 days:	Erythema:	No Abnormal Findings Noted
	Oedema:	No Abnormal Findings Noted
	Scaling:	present
	Staining:	No Staining Present
After 21 days:	Erythema:	No Abnormal Findings Noted
	Oedema:	No Abnormal Findings Noted
	Scaling:	No Abnormal Findings Noted
	Staining:	No Staining Present

APPENDIX 2 Individual Local Findings (Continued)

Animal No. 66, Female

After 1 hour:	Erythema:	Slightly reddened
	Oedema:	No Abnormal Findings Noted
	Scaling:	No Abnormal Findings Noted
	Staining:	No Staining Present
After 24 hours:	Erythema:	Moderately reddened
	Oedema:	Slight swelling
	Scaling:	No Abnormal Findings Noted
	Staining:	No Staining Present
After 48 hours:	Erythema:	Moderately reddened
	Oedema:	Slight swelling
	Scaling:	No Abnormal Findings Noted
	Staining:	No Staining Present
After 72 hours:	Erythema:	Moderately reddened
	Oedema:	Slight swelling
	Scaling:	No Abnormal Findings Noted
	Staining:	No Staining Present
After 7 days:	Erythema:	Moderately reddened
	Oedema:	Slight swelling
	Scaling:	present
	Staining:	No Staining Present
After 10 days:	Erythema:	Slightly reddened
	Oedema:	No Abnormal Findings Noted
	Scaling:	present
	Staining:	No Staining Present

APPENDIX 2 Individual Local Findings (Continued)

Animal No. 66, Female

After 14 days:	Erythema:	No Abnormal Findings Noted
	Oedema:	No Abnormal Findings Noted
	Scaling:	present
	Staining:	No Staining Present
After 17 days:	Erythema:	No Abnormal Findings Noted
	Oedema:	No Abnormal Findings Noted
	Scaling:	present
	Staining:	No Staining Present
After 21 days:	Erythema:	No Abnormal Findings Noted
	Oedema:	No Abnormal Findings Noted
	Scaling:	present
	Staining:	No Staining Present

APPENDIX 2 Individual Local Findings (Continued)

Animal No. 67, Female

After 1 hour:	Erythema:	Slightly reddened
	Oedema:	No Abnormal Findings Noted
	Scaling:	No Abnormal Findings Noted
	Staining:	No Staining Present
After 24 hours:	Erythema:	Slightly reddened
	Oedema:	No Abnormal Findings Noted
	Scaling:	No Abnormal Findings Noted
	Staining:	No Staining Present
After 48 hours:	Erythema:	Slightly reddened
	Oedema:	Slight swelling
	Scaling:	No Abnormal Findings Noted
	Staining:	No Staining Present
After 72 hours:	Erythema:	Slightly reddened
	Oedema:	Slight swelling
	Scaling:	No Abnormal Findings Noted
	Staining:	No Staining Present
After 7 days:	Erythema:	No Abnormal Findings Noted
	Oedema:	No Abnormal Findings Noted
	Scaling:	present
	Staining:	No Staining Present
After 10 days:	Erythema:	No Abnormal Findings Noted
	Oedema:	No Abnormal Findings Noted
	Scaling:	present
	Staining:	No Staining Present

APPENDIX 2 Individual Local Findings (Continued)

Animal No. 67, Female

After 14 days:	Erythema:	No Abnormal Findings Noted
	Oedema:	No Abnormal Findings Noted
	Scaling:	present
	Staining:	No Staining Present
After 17 days:	Erythema:	No Abnormal Findings Noted
	Oedema:	No Abnormal Findings Noted
	Scaling:	present
	Staining:	No Staining Present
After 21 days:	Erythema:	No Abnormal Findings Noted
	Oedema:	No Abnormal Findings Noted
	Scaling:	No Abnormal Findings Noted
	Staining:	No Staining Present

APPENDIX 3 GLP Certificate

The Swiss GLP Monitoring Authorities

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Swiss Confederation

Federal Department of Home Affairs DHA
Federal Office of Public Health FOPH

Federal Department of the Environment, Transport, Energy and Communications DETEC
Federal Office for the Environment FOEN

swissmedic
Swiss Agency for Therapeutic Products

Statement of GLP Compliance

According to Article 14 paragraph 3 Ordinance on Good Laboratory Practice [OGLP, SR 813.112.1]

The notification authority for chemicals confirms that the following test facility was inspected with respect to the compliance with the Swiss Ordinance on Good Laboratory Practice, adopted on 18th May 2005 [OGLP, SR 813.112.1]. This Ordinance is based on the OECD Principles of Good Laboratory Practice, as revised in 1997 and adopted on 26th November 1997 by decision of the OECD Council [C(97)186/Final].

Unequivocal name and address of the test facility:	Areas of expertise according to article 3 paragraph 1 letter d OGLP:
Harlan Laboratories Ltd. Zelgliweg 1 4452 Itingen, Switzerland.	1./ Physical-chemical testing, 2./ Toxicity studies, 4./ Environmental toxicity studies on aquatic and terrestrial organisms, 5./ Studies on behaviour in water, soil and air; bioaccumulation, 6./ Residue studies, 7./ Studies on effects on mesocosms and natural ecosystems, 8./ Analytical and clinical chemistry testing, 9./ Other studies (safety pharmacology and animal metabolism).

Inspection authority: Federal Office for the Environment (FOEN) / Federal Office of Public Health (FOPH) / Swiss Agency for Therapeutic Products (Swissmedic)

Date of inspection: 05th to 09th and 26th to 30th November 2007

Date of decision: 30th April 2008

Based on the above mentioned decision it can be confirmed that the above mentioned test facility is able to conduct studies according to the aforementioned areas of expertise in compliance with the principles of GLP. The above mentioned test facility is listed in the register and GLP list according to the Article 14 OGLP and is inspected on a regular basis according to Article 6 paragraph 2 OGLP.

Swiss Federal Office of Public Health
Consumer protection directorate
Notification authority for chemicals
CH-3003 Bern

Dag Kappes

FEDERAL OFFICE OF PUBLIC HEALTH

Bern, 12th November 2008, The Head, Dr. Dag Kappes.

The notification authority for chemicals is the coordination and decision authority for the good laboratory practice (GLP) for the FOEN, the FOPH and Swissmedic.
Swiss Federal Office of Public Health, Consumer protection directorate, Notification authority for chemicals, CH-3003 Bern.
www.glp.admin.ch, Phone: +41 (0)31 322 73 05, Fax: +41 (0)31 323 54 86