Pinoxaden/Clodinafop-Propargyl/Cloquintocet-Mexyl

Pinoxaden/Clodinafop-Propargyl/Cloquintocet-Mexyl EC (A14298H) - Acute Oral Toxicity Study in the Rat (Up and Down Procedure)

Final Report

DATA REQUIREMENT(S): OECD [Test Guideline, Number 425]
EPA [OPPTS 870.1100]

AUTHOR(S): Dr. M. Mallaun

STUDY COMPLETION DATE: 08-Oct-2010

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

LABORATORY PROJECT ID: Report Number: C97057
Study Number: C97057
Task Number: TK0028274

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

STATEMENT OF DATA CONFIDENTIALITY CLAIMS

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GOOD LABORATORY PRACTICE COMPLIANCE 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].

These principles are compatible with Good Laboratory Practice regulations specified by regulatory authorities throughout the European Community, the United States (EPA and FDA), and Japan (MHLW, MAFF and METI).

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

Dr. M. Mallaun
Study Director
Acute Toxicology

08-Oct-2010
Date

Performing Laboratory:

Harlan Laboratories Ltd.,
Wölferstrasse 4
4414 Füllinsdorf / Switzerland

FLAGGING STATEMENT

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QUALITY ASSURANCE STATEMENT

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

Harlan Laboratories Study:	C97057
Syngenta Task Number:	TK0028274
Test Item:	Pinoxaden/Clodinafop-Propargyl/Cloquintocet-Mexyl EC (A14298H)
Study Director:	Dr. M. Mallaun
Study Title:	Pinoxaden/Clodinafop-Propargyl/Cloquintocet-Mexyl EC (A14298H) - Acute Oral Toxicity Study in the Rat (Up and Down Procedure)

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**
28-Jul-2010	Study Plan	28-Jul-2010
03-Aug-2010	Process based (Test Item, Dose Preparation, Test System, Treatment)	03-Aug-2010
29-Sep-2010	Report	29-Sep-2010

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

Quality Assurance: N. Engelke

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Date: 07-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
C. Elliott	Syngenta Study Manager

Study dates

Experimental starting date:	29 July 2010
Experimental completion date:	31 August 2010
Delivery of animals:	06 July 2010 (females no. 1-2) 03 August 2010 (females no. 3-5)
Acclimatization:	29 July 2010 to 02 August 2010 (female no. 1) 29 July 2010 to 04 August 2010 (female no. 2) 03 August 2010 to 09 August 2010 (female no. 3) 03 August 2010 to 11 August 2010 (female no. 4) 03 August 2010 to 16 August 2010 (female no. 5)
Treatment:	03 August 2010 (female no. 1) 05 August 2010 (female no. 2) 10 August 2010 (female no. 3) 12 August 2010 (female no. 4) 17 August 2010 (female no. 5)
Observation after Treatment:	03 August 2010 to 17 August 2010 (female no. 1) 05 August 2010 to 19 August 2010 (female no. 2) 10 August 2010 to 24 August 2010 (female no. 3) 12-August 2010 to 26 August 2010 (female no. 4) 17 August 2010 to 31 August 2010 (female no. 5)
Termination:	17 August 2010 (female no. 1) 19 August 2010 (female no. 2) 24 August 2010 (female no. 3) 26 August 2010 (female no. 4) 31 August 2010 (female no. 5)

Deviation from the Guidelines

OECD guideline 425 specifies that each animal should be between 8 and 12 weeks old at the commencement of its dosing. The first animal used in this study was 14 weeks old and therefore outside these limits. However, since this animal showed consistent experimental outcome like the other 4 animals, we have no reason to assume that this deviation had an impact on the outcome of this study. The other 4 animals used were between 10 – 11 weeks old.

Retention of samples

See below under Other.

Performing laboratory test substance reference number

234369/A

Other

Harlan Laboratories Ltd. (4452 Itingen / Switzerland) will retain the study plan, all raw data, a sample of the test item and the 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

A main test with 5 animals (female RccHan:WIST (SPF) rats) was conducted. These animals were treated with Pinoxaden/Clodinafop-Propargyl/Cloquintocet-Mexyl EC (A14298H) by gavage at a dose of 2000 mg/kg body weight. The test item was applied undiluted at a volume dosage of 2.061 mL/kg.

The animals were examined daily during the acclimatization period and mortality, viability and clinical signs were recorded. All animals were examined for clinical signs prior to treatment, once during the first 30 minutes and at approximately 1, 2, 3 and 5 hours after treatment on day 1 and once daily during test days 2 to 15. Mortality/viability was recorded prior to treatment once during the first 30 minutes and at approximately 1, 2, 3 and 5 hours after administration on test day 1 (with the clinical signs) and twice daily during days 2 to 15. Body weights were recorded on day -1 (prior to removal of food), day 1 (prior to administration) and on days 8 and 15. All animals were examined macroscopically immediately after the end of the respective observation period.

1.2 Results

All animals treated at 2000 mg/kg body survived until the end of the observation period.

Clinical signs were observed in only one animal (Animal No. 1). These included transiently ruffled fur and hunched posture during the first test day. No other clinical signs were observed throughout the entire observation period.

The body weights were within the range commonly recorded for this strain and age.

No macroscopic findings were recorded at necropsy.

1.3 Conclusion

The median lethal dose, LD_{50}, of Pinoxaden/Clodinafop-Propargyl/Cloquintocet-Mexyl EC (A14298H) after single oral administration to female rats, observed over a period of 14 days, is:

LD_{50} (female rat): greater than 2000 mg/kg body weight

2.0 INTRODUCTION

2.1 Purpose

The purpose of this study was to investigate the acute oral toxicity of the test item using the Modified Up-and-Down Procedure (ASTM, 1987).

2.2 Guidelines

The study was done according to the following guidelines:

OECD guideline reference 425 (2001): Acute Oral Toxicity - Up-and-Down Procedure.

United States Environmental Protection Agency, Health Effects Test Guidelines, OPPTS 870.1100 Acute Oral Toxicity EPA 712-C-03-190, December 2002.

2.3 Test Facility

This study was performed in an AAALAC-accredited laboratory in accordance with the Swiss Animal Protection Law under license no. 254.

3.0 MATERIALS AND METHODS

3.1 Test Substance

The following information was provided by the Sponsor:

Identification:	Pinoxaden/Clodinafop-Propargyl/Cloquintocet-Mexyl EC (A14298H)
Description:	Light yellow liquid
Batch Number:	SMU0EP001
Purity: Content of pinoxaden:	2.58 % w/w corresponding to 25.0 g/L
Content of clodinafop-propargyl:	2.66 % w/w corresponding to 25.8 g/L
Content of cloquintocet-mexyl:	0.66 % w/w corresponding to 6.40 g/L
Content of water:	0.23 % w/w
Density:	970 kg/m^3
Stability of Test Item:	stable under specified storage conditions
Recertification Date:	30-Nov-2012
Storage Conditions:	At a temperature < 30°C (as given by the Sponsor). At room temperature (range of 20 ± 5 °C), light protected (as handled by Harlan Laboratories Ltd.).
Safety Precautions:	Routine hygienic procedures were used to ensure the health and safety of the personnel.

The certificate of analysis is attached in Appendix 1.

3.2 Experimental Design

The animals received a single dose of the test item by oral gavage administration after being fasted for approximately 17 to 20 hours, but with free access to water. Food was presented approximately 3 to 4 hours after dosing.

The test item was applied undiluted as delivered by the Sponsor. No dose formulations were prepared.

Dosing started in one female at a dosage level of 2000 mg/kg. The application volume was 2.061 mL/kg body weight. Since this animal survived, the next animal was also treated at 2000 mg/kg. In total, 5 animals were treated at the limit dose of 2000 mg/kg and survived.

Application scheme:

Animal Number	Dosage [mg/kg body weight]	Volume [mL/kg body weight]	Viability / Mortality
1	2000	2.061	Survived
2	2000	2.061	Survived
3	2000	2.061	Survived
4	2000	2.061	Survived
5	2000	2.061	Survived

Rationale: Oral administration was considered to be an appropriate application method as it is a possible route of human exposure.

The animals were examined daily during the acclimatization period and mortality, viability and clinical signs were recorded. All animals were examined for clinical signs prior to treatment, once within the first 30 minutes and at approximately 1, 2, 3 and 5 hours after treatment on day 1 and once daily during test days 2-15. Mortality/viability was recorded prior to treatment, once within the first 30 minutes and at approximately 1, 2, 3 and 5 hours after administration on test day 1 (with the clinical signs) and twice daily during days 2-15. Body weights were recorded on day –1 (prior to removal of food), day 1 (prior to administration) and on days 8 and 15. All animals were examined macroscopically immediately after the end of the respective observation period.

3.2.1 Animals

Animal Species and Strain:	Rat, RccHan:WIST (SPF)
Rationale:	Recognized by international guidelines as a recommended test system.
Breeder/Supplier:	Harlan Laboratories B.V. Kreuzelweg 53 5961 NM Horst / The Netherlands
Number of Animals per Group:	One female
Total Number of Animals:	5 females
Age (when treated):	10 – 14 weeks
Body Weight Range (when treated):	182.6 g – 219.6 g
Identification:	Unique cage number and corresponding color-coded spots on the tail. The animals were marked at acclimatization start.
Randomization:	Randomly selected by hand at time of delivery. No computer generated randomization program.

Acclimatization:	Under laboratory conditions, after health examination for at least 5 days. Only animals without any visible signs of illness were used for the study.

3.2.2 Husbandry

Room Number:	0105 / Harlan Laboratories Ltd., Füllinsdorf
Conditions:	Standard Laboratory Conditions. Air-conditioned with 10-15 air changes per hour, and continuously monitored environment with a room temperature of 22 ± 3 °C and a relative humidity between 30-70%, automatically controlled light cycle of 12 hours light and 12 hours dark and music played during the daytime light period.
Accommodation:	During acclimatization in groups of three in Makrolon type-4 cages. During treatment and observation individually in Makrolon type-3 cages. Accommodation with standard softwood bedding (‘Lignocel’ J. Rettenmaier&Söhne GmbH&CoKG, 73494 Rosenberg / Germany, imported by Provimi Kliba AG, 4303 Kaiseraugst / Switzerland) and paper enrichment, batch no. -67 (Enviro-dri from Lillico, Biotechnology, Surrey, UK).
Diet:	Teklad Rat-Mouse Diet 2914C, irradiated, batch no. 30/10 (Provimi Kliba AG, 4303 Kaiseraugst / Switzerland) *ad libitum* (except for the overnight fasting period prior to oral gavage and approximately 3-4 hours post dose. Results of analyses for contaminants are archived at Harlan Laboratories Ltd.
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 animals were killed at the end of the observation period by carbon dioxide asphyxiation and discarded after macroscopic examinations were performed. An external examination and opening of the abdominal and thoracic cavities for examinations of major organs were performed. The appearance of any macroscopic abnormalities was recorded. No organs or tissues were retained.

3.4 Data Compilation

Viability/mortality was recorded on data sheets.

Body weights were recorded on-line by the ToxControl Computer System.

Clinical signs and macroscopic findings were compiled into the ToxControl Computer System during recording.

The ToxControl Computer System has been licensed for Harlan Laboratories and validated with respect to data acquisition, storage and retrievability.

Data were evaluated using the Acute Oral Toxicity (OECD Test Guidelines 425) Statistical Programme (AOT 425 Stat Pgm).

4.0 RESULTS AND DISCUSSION

Individual viability/mortality data, clinical observations, body weights and necropsy results are presented in Table 1, Table 2, Table 3 and Table 4, respectively.

4.1 Mortality

No deaths occurred during the course of the study.

4.2 Body Weights

The body weights were within the range commonly recorded for this strain and age.

4.3 Clinical Signs

Animal No. 1 (2000 mg/kg) showed a hunched posture and slightly ruffled fur from 2 to 3 hours after oral administration. Thereafter, the animal was free of clinical signs up to test day 15, the end of observation time.

For animals No. 2 – 5 (2000 mg/kg) no clinical signs were recorded throughout the entire observation period.

4.4 Macroscopic Findings

No macroscopic findings were recorded at necropsy.

5.0 CONCLUSIONS

The median lethal dose, LD_{50}, of Pinoxaden/Clodinafop-Propargyl/Cloquintocet-Mexyl EC (A14298H) after single oral administration to female rats, observed over a period of 14 days post treatment, is:

LD_{50} (female rat): greater than 2000 mg/kg body weight

6.0 REFERENCES

Literature references listed are available upon request.

External references

ASTM (1987). Standard Test Method for Estimating Acute Oral Toxicity in Rats. American Society for Testing and Materials, Philadelphia, PA, E 1163 - 1187.

Acute Oral Toxicity (OECD Test Guideline 425) Statistical Programme (AOT 425 Stat Pgm). Version: 1.0, 2001(http://www.epa.gov/oppfead1/harmonization).

TABLES SECTION

TABLE 1 Individual Findings - Mortality Data

MORTALITY DATA
ALL NECROPSIES
FEMALES

Group 1 (2000 mg/kg)

Acclimatization (Days 1 to 14)

No mortality data recorded

Treatment (Days 1 to 15)

ANIMAL	DEATH DATE	DAY	P	K	S	O	COMMENT
1	17-AUG-10	15	X				
		Total:	1	0	0	0	

P = PLANNED NECROPSY , K = KILLED IN EXTR. , S = SPONTAN. DEATH , O = OTHER

TABLE 1 Individual Findings - Mortality Data (Continued)

MORTALITY DATA
ALL NECROPSIES
FEMALES

Group 2 (2000 mg/kg)

Acclimatization (Days 1 to 14)

No mortality data recorded

Treatment (Days 1 to 15)

ANIMAL	DEATH DATE	DAY	P	K	S	O	COMMENT
2	19-AUG-10	15	X				
		Total:	1	0	0	0	

P = PLANNED NECROPSY , K = KILLED IN EXTR. , S = SPONTAN. DEATH , O = OTHER

TABLE 1 Individual Findings - Mortality Data (Continued)

MORTALITY DATA
ALL NECROPSIES
FEMALES

Group 3 (2000 mg/kg)

Acclimatization (Days 1 to 14)

No mortality data recorded

Treatment (Days 1 to 15)

ANIMAL	DEATH DATE	DAY	P	K	S	O	COMMENT
3	24-AUG-10	15	X				
		Total:	1	0	0	0	

P = PLANNED NECROPSY , K = KILLED IN EXTR. , S = SPONTAN. DEATH , O = OTHER

TABLE 1 Individual Findings - Mortality Data (Continued)

MORTALITY DATA
ALL NECROPSIES
FEMALES

Group 4 (2000 mg/kg)

Acclimatization (Days 1 to 14)

No mortality data recorded

Treatment (Days 1 to 15)

ANIMAL	DEATH DATE	DAY	P	K	S	O	COMMENT
4	26-AUG-10	15	X				
		Total:	1	0	0	0	

P = PLANNED NECROPSY , K = KILLED IN EXTR. , S = SPONTAN. DEATH , O = OTHER

TABLE 1 Individual Findings - Mortality Data (Continued)

MORTALITY DATA
ALL NECROPSIES
FEMALES

Group 5 (2000 mg/kg)

Acclimatization (Days 1 to 14)

No mortality data recorded

Treatment (Days 1 to 15)

ANIMAL	DEATH DATE	DAY	P	K	S	O	COMMENT
5	31-AUG-10	15	X				
		Total:	1	0	0	0	

P = PLANNED NECROPSY , K = KILLED IN EXTR. , S = SPONTAN. DEATH , O = OTHER

TABLE 2 Individual Findings – Clinical Signs

Clinical signs

Comments

Data excluded from Summary Report

Not Reported

Daily Observations

A	Clinical Signs
B	Within 30min After Appli
C	1h After Application
D	2h After Application
E	3h After Application
F	5h After Application

Incomplete Recordings

Selection of Findings

All findings reported

TABLE 2 Individual Findings – Clinical Signs (Continued)

Clinical signs
FEMALES

Acclimatization

	Weeks / Days / Daily Observations (A)
	1 2
	1 2 3 4 5 6 7 1 2 3 4 5 6 7
	A A A A A A A A A A A A A A

Group 1 (2000 mg/kg)

No abnormality recorded.

Group 2 (2000 mg/kg)

No abnormality recorded.

Group 3 (2000 mg/kg)

No abnormality recorded.

Group 4 (2000 mg/kg)

No abnormality recorded.

Group 5 (2000 mg/kg)

No abnormality recorded.

TABLE 2 Individual Findings – Clinical Signs (Continued)

Clinical signs
FEMALES

Treatment

	Weeks / Days / Daily Observations (A,B,C,D,E,F)						
	1						
	1	2	3	4	5	6	7
	ABCDEFA-----	A-----	A-----	A-----	A-----	A-----	A-----
Group 1 (2000 mg/kg)							
Animal 1							
APPEARANCE							
-HUNCHED POSTURE (1)	...11..	.	.	.	.	.	
-RUFFLED FUR (3)	...11..	.	.	.	.	.	

No further abnormality recorded.

Group 2 (2000 mg/kg)

No abnormality recorded.

Group 3 (2000 mg/kg)

No abnormality recorded.

Group 4 (2000 mg/kg)

No abnormality recorded.

Group 5 (2000 mg/kg)

No abnormality recorded.

TABLE 2 Individual Findings – Clinical Signs (Continued)

Clinical signs
FEMALES

Treatment

	Weeks / Days / Daily Observations (A,B,C,D,E,F)						
	2 1 A	2 A	3 A	4 A	5 A	6 A	7 A
Group 1 (2000 mg/kg)							
No abnormality recorded.							
Group 2 (2000 mg/kg)							
No abnormality recorded.							
Group 3 (2000 mg/kg)							
No abnormality recorded.							
Group 4 (2000 mg/kg)							
No abnormality recorded.							
Group 5 (2000 mg/kg)							
No abnormality recorded.							

TABLE 2 Individual Findings – Clinical Signs (Continued)

Clinical signs
FEMALES

Treatment

	Weeks / Days / Daily Observations (A,B,C,D,E,F)
	3
	1
	A-----

Group 1 (2000 mg/kg)

No abnormality recorded.

Group 2 (2000 mg/kg)

No abnormality recorded.

Group 3 (2000 mg/kg)

No abnormality recorded.

Group 4 (2000 mg/kg)

No abnormality recorded.

Group 5 (2000 mg/kg)

No abnormality recorded.

TABLE 3 Body Weights

BODY WEIGHTS (G)
FEMALES

Group 1 (2000 mg/kg)

Animal		1
Acclimatization		
Day	5	228.2

Animal		1
Treatment		
Day	1	219.6
	8	233.9
	15	242.6

TABLE 3 Body Weights (Continued)

BODY WEIGHTS (G)
FEMALES

Group 2 (2000 mg/kg)

Animal		2
Acclimatization		
Day	7	217.3

Animal		2
Treatment		
Day	1	218.1
	8	224.9
	15	224.0

TABLE 3 Body Weights (Continued)

BODY WEIGHTS (G)
FEMALES

Group 3 (2000 mg/kg)

Animal		3
Acclimatization		
Day	7	194.2

Animal		3
Treatment		
Day	1	191.7
	8	215.7
	15	229.5

TABLE 3 Body Weights (Continued)

BODY WEIGHTS (G)
FEMALES

Group 4 (2000 mg/kg)

Animal		4
Acclimatization		
Day	9	191.2

Animal		4
Treatment		
Day	1	182.6
	8	209.5
	15	220.4

TABLE 3 Body Weights (Continued)

BODY WEIGHTS (G)
FEMALES

Group 5 (2000 mg/kg)

Animal		5
Acclimatization		
Day	14	200.4

Animal		5
Treatment		
Day	1	195.4
	8	207.9
	15	217.1

TABLE 4 Macroscopic Findings

MACROSCOPICAL FINDINGS
Final necropsy
ALL NECROPSIES
FEMALES

Group 1 (2000 mg/kg)

Animal 1 PLANNED NECROPSY , 17-AUG-2010

NO FINDINGS NOTED

TABLE 4 Macroscopic Findings (Continued)

MACROSCOPICAL FINDINGS
Final necropsy
ALL NECROPSIES
FEMALES

Group 2 (2000 mg/kg)

Animal 2 PLANNED NECROPSY , 19-AUG-2010

NO FINDINGS NOTED

TABLE 4 Macroscopic Findings (Continued)

MACROSCOPICAL FINDINGS
Final necropsy
ALL NECROPSIES
FEMALES

Group 3 (2000 mg/kg)

Animal 3 PLANNED NECROPSY , 24-AUG-2010

NO FINDINGS NOTED

TABLE 4 Macroscopic Findings (Continued)

MACROSCOPICAL FINDINGS
Final necropsy
ALL NECROPSIES
FEMALES

Group 4 (2000 mg/kg)

Animal 4 PLANNED NECROPSY , 26-AUG-2010

NO FINDINGS NOTED

TABLE 4 Macroscopic Findings (Continued)

MACROSCOPICAL FINDINGS
Final necropsy
ALL NECROPSIES
FEMALES

Group 5 (2000 mg/kg)

Animal 5 PLANNED NECROPSY , 31-AUG-2010

NO FINDINGS NOTED

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

A14298H

pinoxaden/clodinafop-propargyl/ cloquintocet-mexyl

EC (025/025/006.25)

SMU0EP001

Batch Identification	**SMU0EP001**
Product Code	**A14298H**
Other Product Code(s)	pinoxaden/clodinafop-propargyl/cloquintocet-mexyl EC (025/025/006.25)
Chemical Analysis (Active Ingredient Content)	
– **Identity of the Active Ingredient(s)***	**confirmed**
– **Content of pinoxaden***	**2.58 % w/w corresponding to 25.0 g/l**
– **Content of clodinafop-propargyl***	**2.66 % w/w corresponding to 25.8 g/l**
– **Content of cloquintocet-mexyl***	**0.66 % w/w corresponding to 6.40 g/l**
– **Content of water***	**0.23 % 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 ***	**970 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: 121382

Study number(s) of batch recertification:

Authorisation: Jul 21, 2010

S. De Benedictis
Analytical Development & Product Chemistry

APPENDIX 2 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

FEDERAL OFFICE OF PUBLIC HEALTH

Dag Kappes

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