Propiconazole/Fenpropidin

Propiconazole/Fenpropidin EC (A9050B) - Acute Oral Toxicity Study in the Rat (Up and Down Procedure)

Final Report

DATA REQUIREMENT(S): OECD Test Guideline 425 (2008)
EPA OPPTS 870.1100 (2002)

AUTHOR(S): Judit Tavaszi, M.Sc.

STUDY COMPLETION DATE: 03 May 2011

PERFORMING LABORATORY: LAB Research Ltd.
H-8200 Veszprém, Szabadságpuszta,
Hungary

LABORATORY PROJECT ID: Report Number: 10/290-001P
Study Number: 10/290-001P
Task Number: TK0037022

SPONSOR(S): 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 accordance with the Principles of Good Laboratory Practice (Hungarian GLP Regulations: 9/2001. (III. 30.) EüM-FVM joint decree of the Minister of Health and the Minister of Agriculture and Regional Development which corresponds to the OECD GLP, ENV/MC/CHEM (98) 17.).

This study was conducted in accordance with a written Study Plan, authorized by the Sponsor and LAB Research Ltd. management, and followed applicable Standard Operating Procedures.

Signature: _____ Date: 03 May 2011

Judit Tavaszi, M.Sc.
Study Director

Performing Laboratory: LAB Research Ltd.
H-8200 Veszprém, Szabadságpuszta,
Hungary

FLAGGING STATEMENT

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QUALITY ASSURANCE STATEMENT

Study Number: 10/290-001P

Study Title: Propiconazole/Fenpropidin EC (A9050B) – Acute Oral Toxicity Study in the Rat (Up and Down Procedure)

Test Item: Propiconazole/Fenpropidin EC (A9050B)

This study has been inspected, and this report audited by the Quality Assurance Unit in compliance with the Principles of Good Laboratory Practice. As far as it can be reasonably established the methods described and the results incorporated in this report accurately reflect the raw data produced during this study.

All inspections, data reviews and the report audit were reported in written form to the study director and to management. The dates of such inspections and of the report audit are given below:

Date of Inspection	Phase(s) Inspected/Audited	Date of report to	
		Management	Study Director
12 January 2011	Study Plan	12 January 2011	12 January 2011
25 January 2011	Body weight measurement	25 January 2011	30 January 2011
01 April 2011	Draft Report	01 April 2011	01 April 2011
03 May 2011	Final Report	03 May 2011	03 May 2011

Signature: _____ Date: 03 May 2011

Istvánné Kiss, M.Sc.
QA Inspector

MANAGEMENT STATEMENT

According to the conditions of the research and development agreement between Syngenta Ltd. (as Sponsor) and LAB Research Ltd. (Test facility), the study titled "Propiconazole/Fenpropidin EC (A9050B) - Acute Oral Toxicity Study in the Rat (Up and Down Procedure)" was performed, in compliance with OECD 425 (October 2008), OPPTS 870.1100 (EPA 712-C-02-190, December 2002) and applicable SOP's of LAB Research Ltd.

Signature: _____ Date: 03 May 2011

Christopher Banks, DABT
Managing Director

GENERAL INFORMATION

Contributors

The following contributed to this report in the capacities indicated:

Name	Function
Judit Tavaszi, M.Sc.	Study Director
Viktória Zelenák, M.Sc.	Assistant scientist
Istvánné Kiss, M.Sc.	Quality Assurance Unit
István Pásztor, DVM	Veterinary control
Peter Maslej, DVM, PhD	Head of Pathology Unit
Tamás Mészáros, PhD	Head of Central Dispensary
Eric Yau	Syngenta Study Manager

Study dates

Experimental Starting Date	18 January 2011
Experimental Completion Date	17 February 2011
Reception of Animals	13 January 2011
Acclimatization	At least 5 days

Treatment	18 January 2011 (female no. 3997) 20 January 2011 (female no. 3998) 25 January 2011 (female no. 3999) 27 January 2011 (female no. 4000) 01 February 2011 (female no. 4001) 03 February 2011 (female no. 4002)
Observation	18 - 20 January 2011 (female no. 3997) 20 January – 03 February 2011 (female no. 3998) 25 – 27 January 2011 (female no. 3999) 27 January – 10 February 2011 (female no. 4000) 01 – 02 February 2011 (female no. 4001) 03 – 17 February 2011 (female no. 4002)

Deviations from the study plan

The Draft Report was sent later than indicated in the Study Plan.

This deviation has no impact on the outcome of the study and interpretation of the results.

Performing laboratory test substance reference number

10/238K/1 101004

Other

The study documents:
- study plan,
- all raw data,
- sample of the test item,
- original final study report and any amendments,
- correspondence

will be archived according to the Hungarian GLP and to applicable SOP's in the archives of LAB Research Ltd. 8200 Veszprém, Szabadságpuszta, Hungary.

After the retention time of 15 years has elapsed all the archived materials listed above will be returned to the Sponsor or retained for a further period if agreed by a contract. Otherwise the materials will be discarded.

TABLE OF CONTENTS

1.0 EXECUTIVE SUMMARY

1.1 Study Design

A single oral (gavage) dose was administered followed by a 14 day observation period. The animals were fasted overnight prior to treatment. Animals were weighed before dosing and food was returned 3 hours after dosing.

Single animals were dosed sequentially at no less than approximately 48 hour intervals. The time intervals between dosing were determined by the onset, duration and severity of toxic signs.

A limit test was started at a dose level of 5000 mg/kg bw. Due to the mortality of the first animal, the limit test was terminated and a main test was conducted with the starting dose level of 1750 mg/kg bw as requested by the Sponsor.

Surviving animals were observed individually after dosing at 30 minutes, 1, 2, 3, 4 and 6 hours post treatment and once each day for 14 days thereafter. Body weight was measured on Day -1 and just before treatment and weekly after. All surviving animals were examined macroscopically at the end of the study.

1.2 Results

Propiconazole/Fenpropidin EC (A9050B) caused mortalities at 5000 mg/kg bw (3/3). No deaths occurred in any animals treated at 1750 mg/kg bw.

Clinical signs were observed in animals treated at 5000 mg/kg bw and 1750 mg/kg bw. Two animals treated at 5000 mg/kg bw were observed with decreased activity, hunched back and piloerection, one of them displayed incoordination. Additionally, one animal dosed at 1750 mg/kg bw presented with hunched back and piloerection.

Body weight and body weight changes of the surviving animals during the study showed no indication of a treatment-related effect.

During necropsy, beige mucoid material found in the digestive content of the esophagus, stomach and small intestines were observed in 1/3 rats treated at 5000 mg/kg bw. No treatment related macroscopic finding were observed in any other animal treated.

1.3 Conclusion

Under the conditions of this study, the estimated acute oral median lethal dose (LD_{50}) of Propiconazole/Fenpropidin EC (A9050B) was calculated to be 2958 mg/kg bw in female RjHan:WI rats.

2.0 INTRODUCTION

2.1 Purpose

The purpose of the study was to assess the oral toxicity of the test item Propiconazole/Fenpropidin EC (A9050B) when administered as a single dose to rats. The results of the study allow the test item to be ranked according to most classification systems currently in use.

2.2 Guidelines

The study was performed according to the following guidelines:

OECD guideline reference 425 (2008): 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-02-190, December 2002.

2.3 Test Facility

This study was performed in an AAALAC-accredited laboratory. The Institutional Animal Care and Use Committee (IACUC) of LAB Research Ltd. reviewed the study plan and authorized the conduct of the study.

3.0 MATERIALS AND METHODS

3.1 Test Substance

Data as supplied by the Sponsor.

Name:	Propiconazole/Fenpropidin EC (A9050B)
Batch number:	SMO0G120
Purity:	
	- Propiconazole – 129 g/L corresponding to 13.6 % w/w
	- Fenpropidin – 278 g/L corresponding to 29.2 % w/w
Product code:	A9050B
Appearance:	Brown, liquid
Density:	952 kg/m^3
Reanalysis date:	End of September 2015
Storage conditions:	Room temperature (<30 ^oC)
Supplier:	Syngenta Crop Protection AG Postfach CH-4002 Basel, Switzerland
Safety Precautions:	Routine safety precautions (lab coat, safety glasses, gloves, face mask) for unknown materials were applied to assure personnel health and safety

The certificate of analysis is attached in Appendix 2.

3.1.1 Identification, receipt

The test item of a suitable chemical purity together with all precautions required in the handling and disposal of the test item were supplied by the Sponsor. The identification of test item was made in the Central Dispensary Unit of LAB Research Ltd. on the basis of the information provided by Sponsor.

3.1.2 Formulation

Propiconazole/Fenpropidin EC (A9050B) was administered undiluted.

3.1.3 Details of material used for euthanasia

Name:	Euthasol® 40%
Lot No.:	10C25 7
Expiry Date:	02 2013
Produced by:	AST Beheer B.V. Oudewater Netherlands

3.2 Experimental Animals

Species and strain:	RjHan:WI rats
Source:	Laboratoire Elevage Janvier, B.P. 4105, Route des Chênes Secs, 53940 Le Genest-St-Isle CEDEX FRANCE
Hygienic level at arrival:	SPF
Hygienic level during the study:	Standard housing conditions
Justification of strain:	Recognized by international guidelines as a recommended test system.
Number of animals:	1 animal/step
Sex:	Female rats, nulliparous and non-pregnant.
Age when treated:	Young adult rats, 8-10 weeks old.
Body weight (at dosing):	201 - 234 g
Randomization:	Selected by hand at time of delivery.
Acclimatization time:	At least 5 days under laboratory conditions, after health examination. Only animals without any visible signs of illness were used for the study.

3.2.1 Husbandry

Animal health:	Only healthy animals were used for the test. The health status was certified by the veterinarian.
Room number:	522/5

Housing:	Individual caging
Cage type:	Type II. polypropylene/polycarbonate
Bedding:	Lignocel Bedding for Laboratory Animals was available to animals during the study.
Light:	12 hours daily, from 6.00 a.m. to 6.00 p.m.
Temperature:	22 ± 3 °C
Relative humidity:	30 - 70%
Ventilation:	15-20 air exchanges/hour
Enrichment:	Rodents were housed with deep wood sawdust bedding to allow digging and other normal rodent activities.

The temperature and relative humidity was recorded twice daily during the study and the acclimation period.

3.2.2 Food and water supply

Animals received ssniff® SM R/M-Z+H "Autoclavable complete feed for rats and mice – breeding and maintenance" produced by ssniff Spezialdiäten GmbH, D-59494 Soest Germany (batch: 802 4830, exp. date: 05/2011) *ad libitum*, and tap water from municipal supply, as for human consumption from 500 mL bottle *ad libitum*. The food was considered not to contain any contaminants that could reasonably be expected to affect the purpose or integrity of the study. Details of the diet are archived with the raw data.

Water quality control analysis is performed once every three months and microbiological assessment is performed monthly, by Veszprém County Institute of State Public Health and Medical Officer Service (ÁNTSZ, H-8201 Veszprém, József A.u.36., Hungary). The quality control results are retained in the archive at LAB Research Ltd.

3.2.3 Identification

Animals were individually identified by numbers written on the tail with a permanent marker pen. The numbers were given on the basis of the LAB Research Ltd. master file, for each animal allocated to the study.

The boxes were identified by cards holding information on the study code, the sex of animals, the dose group, the cage number and the individual animal number.

3.3 Experimental Design

3.3.1 Dosages

Justification of the doses:

The limit dose (5000 mg/kg bw) was selected by the Sponsor. Due to mortality, the limit test was terminated. The study then proceeded as a main test, in accordance with OECD 425 (2008) and OOPTS 870.1100 (2002) guidelines. The starting dose level of the main test was 1750 mg/kg bw.

The test substance was administered undiluted

Animal Number	Dosage [mg/kg body weight]	Volume [mL/kg body weight]
3997	5000	5.25
3998	1750	1.84
3999	5000	5.25
4000	1750	1.84
4001	5000	5.25
4002	1750	1.84

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

3.3.2 Procedure

A single oral (gavage) administration was followed by a 14 day observation period. The day before treatment the animals were fasted. Food, but not water, was withheld overnight. Animals were weighed before dosing and food was returned 3 hours after the treatment.

Single animals were dosed sequentially following an interval of no less than approximately 48 hours with the exception of mortality. The time intervals between dosing were determined by the onset, duration and severity of toxic signs. Treatment of an animal at the next dose was performed when no significant clinical signs were noted in the previous animal or the animal produced mortality.

3.4 Observations

3.4.1 Clinical observations

Surviving animals were observed individually after dosing at 30 minutes, 1, 2, 3, 4, and 6 hours after dosing and once each day for 14 days thereafter. Individual observations were performed on the skin and fur, eyes and mucous membranes and also respiratory, circulatory, autonomic and central nervous system, somatomotor activity and behaviour pattern. Particular attention was directed to observation of tremors, convulsions, salivation, diarrhoea, lethargy, sleep and coma.

3.4.2 Body weight measurement

The body weights were recorded on Day -1 and Days 0 (beginning of the experiment) 7 and 14 (surviving animals).

3.5 Necropsy

All animals were subjected to macroscopic examination. Surviving animals were exsanguinated under pentobarbital anaesthesia. After examination of the external appearance, the cranial, thoracic and abdominal cavities were opened and the appearance of the tissues and organs were observed. All gross pathological changes were recorded for each animal on the post mortem record sheets.

3.6 Data Evaluation

The LD_{50} was calculated using the AOT425StatPgm program. This program was prepared for the US Environmental Protection Agency by Westat, May 2001 and updated by the US EPA June 2003. This programme was constructed using the most appropriate method to of estimate the LD_{50}.

The type, severity and duration of clinical observations are described. Body weight and body weight changes are summarised in tabular form. Necropsy findings are described and summarised in tabular form.

4.0 RESULTS AND DISCUSSION

Individual clinical observations and mortality results are presented in Table 1. Individual body weights and necropsy results are presented in Tables 2 and 3, respectively.

4.1 Mortality

Propiconazole/Fenpropidin EC (A9050B) caused mortalities at 5000 mg/kg bw (3/3). No deaths occurred in any animals treated at 1750 mg/kg bw.

4.2 Body Weights

Body weight and body weight changes of the surviving animals during the study showed no indication of a treatment-related effect.

4.3 Clinical Signs

Clinical signs were observed in animals treated at 5000 mg/kg bw and 1750 mg/kg bw. Two animals treated at 5000 mg/kg bw were observed with decreased activity, hunched back and

piloerection, one of them displayed incoordination. Additionally, one animal dosed at 1750 mg/kg bw was observed with hunched back and piloerection.

4.4 Macroscopic Findings

During necropsy, beige mucoid material found in the digestive content of the esophagus, stomach and small intestines were observed in 1/3 rat treated at 5000 mg/kg.

Dark/red discoloration of the non-collapsed lungs and/or thymus were observed in animals dose at 5000 mg/kg bw and 1750 mg/kg bw. These findings are considered to be agonal changes and are not treatment related.

5.0 CONCLUSIONS

Under the conditions of this study, the estimated acute oral median lethal dose (LD_{50}) of Propiconazole/Fenpropidin EC (A9050B) was calculated to be 2958 mg/kg bw in female RjHan:WI rats.

TABLES SECTION

TABLE 1 Individual Findings – Clinical Signs

DOSE LEVEL: 1750 mg/kg bw **SEX: FEMALE**

Cage No.	Animal Number	Observations	Observation days																			Freq
			0						1	2	3	4	5	6	7	8	9	10	11	12	11-14	
			30'	1h	2h	3h	4h	6h														
2	3998	Symptom Free	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	19/20
		Hunched back	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	1/20
		Piloerection	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	1/20
4	4000	Symptom Free	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	20/20
6	4002	Symptom Free	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	20/20

TABLE 1 Individual Findings – Clinical Signs (Continued)

DOSE LEVEL: 5000 mg/kg bw **SEX: FEMALE**

Cage No.	Animal Number	Observations	Observation days																	Freq
			0						1	2	3	4	5	6	7	8	9	10	11	12	13-14	
			30'	1h	2h	3h	4h	6h														
1	3997 #	Symptom Free	+	+	-	-	-	-	-	Found dead												2/7
		Activity decreased	-	-	-	-	-	1	1													2/7
		Hunched back	-	-	+	+	+	-	+													4/7
		Incoordinaiton	-	-	-	-	-	+1	-													1/7
		Piloerection	-	-	-	-	-	+	+													2/7
		Found dead	-	-	-	-	-	-	-	+												-
3	3999 #	Symptom Free	+	+	-	-	-	-	-	Found dead												2/7
		Activity decreased	-	-	1	1	1	2	2													5/7
		Hunched back	-	-	-	-	+	+	+													3/7
		Piloerection	-	-	-	-	+	+	+													3/7
		Found dead	-	-	-	-	-	-	-	+												-
5	4001 #	Symptom Free	+	+	+	+	+	+	Found dead													6/6
		Found dead	-	-	-	-	-	-	+													-

Remarks:

+: present # = Found dead

-: absent Treatment day= Day 0

h=hour (s)

Freq: Frequency of observation = number of occurence of observation / total number of observations

TABLE 2 Body Weight and Body Weight Gain

DOSE LEVEL: 1750 mg/kg bw **SEX: FEMALE**

Cage No.	Animal No.	Body Weight (g) Days				Body Weight Gain (g)			
		-1	0	7	14	-1-0	0-7	7- 14	-1 - 14
2	3998	230	207	234	249	-23	27	15	19
4	4000	256	233	270	292	-23	37	22	36
6	4002	240	228	253	263	-12	25	10	23
Mean:		242.0	222.7	252.3	268.0	-19.3	29.7	15.7	26.0
Standard deviation:		13.1	13.8	18.0	21.9	6.4	6.4	6.0	8.9

DOSE LEVEL: 5000 mg/kg bw **SEX: FEMALE**

Cage No.	Animal No.	Body Weight (g) Days				Body Weight Gain (g)			
		-1	0	7	14	-1-0	0-7	7- 14	-1 - 14
1	3997 #	229	201	-	-	-28	-	-	-
3	3999 #	238	227	-	-	-11	-	-	-
5	4001 #	257	234	-	-	-23	-	-	-
Mean:		241.3	220.7	-	-	-20.7	-	-	-
Standard deviation:		14.3	17.4	-	-	8.7	-	-	-

Remarks: -: No data
Treatment day= Day 0 # = Found dead

TABLE 3 Macroscopic Findings

DOSE LEVEL: 1750 mg/kg bw **SEX: FEMALE**

Cage No.	Animal ID	Necropsy Date	External Observations	Internal Observations	Organ/Tissue
2	3998	03 February 2011	No external observations recorded	Mottled, brown, all lobes	Lungs
4	4000	10 February 2011	No external observations recorded	No internal observations recorded	Not applicable
6	4002	17 February 2011	No external observations recorded	No internal observations recorded	Not applicable

DOSE LEVEL: 5000 mg/kg bw **SEX: FEMALE**

Cage No.	Animal ID	Necropsy Date	External Observations	Internal Observations	Organ/Tissue
1	3997 #	20 January 2011	No external observations recorded	Non collapsed	Lungs
				Dark discoloration, red, diffuse, all lobes	
				Digestive content; mucoid material, beige, opaque	Esophagus, stomach, small intestine; ileum, duodenum, jejunum
3	3999 #	27 January 2011	No external observations recorded	Dark discoloration, red, diffuse	Thymus
				Dark discoloration, red, diffuse, all lobes	Lungs
				Non collapsed	
5	4001 #	02 February 2011	No external observations recorded	Non collapsed	Lungs
				Dark discoloration, red, diffuse, all lobes	

Remark: # = Found dead

APPENDICES SECTION

APPENDIX 1 Pathology Report

LAB Study code. 10/290-001P

PATHOLOGY REPORT

INTRODUCTION

The objective of the study was to assess the acute oral toxicity of Propiconazole/ Fenpropidin EC (A9050B) when administered in a single dose to female rats at one or more defined doses. The results of the study allows the calculation of the estimated oral LD_{50} of the test item and permits the test item to be ranked according to most classification systems currently in use.

RESULTS AND DISCUSSION

Surviving animals were euthanized upon completion of the treatment period on Day 14. Rats were anesthetized with pentobarbital, followed by exsanguination. Gross pathology consisted of an external examination, including identification of all clinically-recorded lesions, as well as a detailed internal examination. Histopathological examination was not performed.

MORTALITY

Three animals were found dead on Days 1 or 2. Necropsy was performed on 3/3 rats dosed at 5000 mg/kg bw.

FOUND DEAD

Macroscopic Findings

Beige mucoid material found in the digestive content of the esophagus, stomach and small intestines in 1/3 rat was considered to be test item-related.

Other changes including dark/red discoloration of the non-collapsed lungs and/or thymus were likely agonal.

TERMINAL (DAY 14)

Macroscopic Findings

There was no evidence of the test item-related macroscopic observations at a dose level of 1750 mg/kg bw.

Brown mottling of the lungs in 1/3 female was probably associated with terminal procedure.

CONCLUSION

A single oral gavage of Propiconazole/Fenpropidin EC (A9050B) to the RjHan:WI female rat at a dose level of 5000 mg/kg bw led to the death of three animals on Day 1 or 2. Beige mucoid material found in the digestive content of the esophagus, stomach and small intestines in 1/3 rat was regarded as test item-related.

In animals receiving 1750 mg/kg bw of Propiconazole/ Fenpropidin EC (A9050B) and subjected to the necropsy on Day 14, no test item-related gross findings were seen.

Peter Maslej, D.V.M., Ph.D.
Head, Pathology Department

03 Feb 2011
Date

APPENDIX 2 Certificate of Analysis

GLP Testing Facility WMU
Analytical Development &
Product Chemistry GS2131

Syngenta Crop Protection Münchwilen AG
Breitenloh 5
CH-4333 Münchwilen

Certificate of Analysis

A9050B
propiconazole / fenpropidin EC (125/275)
SMO0G120

Batch Identification	**SMO0G120**
Product Code	**A9050B**
Other Product Code(s)	CGA64250/CGA114900 EC (125/275)

Chemical Analysis
(Active Ingredient Content)

– **Identity of the Active Ingredient(s)***	**confirmed**
– **Content of propiconazole ***	**13.6 % w/w corresponding to 129 g/l**
– **Content of fenpropidin ***	**29.2 % w/w corresponding to 278 g/l**

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

Methodology used for Characterization / Recertification: GC,

Physical Analysis

– **Appearance**	**brown, liquid**
– **Density ***	**952 kg/m^3**

Stability:

– **Storage Temperature**	**< 30°C**
– **Recertification Date**	**End of September 2015**

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: 121786

Study number(s) of batch recertification:

Authorisation: October 12, 2010

Dr. A.M. Dos Santos Alves
Analytical Development & Product Chemistry

APPENDIX 3 GLP Certificate

ORSZÁGOS GYÓGYSZERÉSZETI INTÉZET
National Institute of Pharmacy

FŐIGAZGATÓ
1051 Budapest, Zrínyi u. 3.
tel: (1) 8869-320
fax: (1) 8869-480
e-mail: szepezdi.zsuzsanna@ogyi.hu

Ref. no: OGYI/8242-11/2010
Admin.: Urbin Magdolna Zita
Date: 16 December, 2010

GOOD LABORATORY PRACTICE (GLP) CERTIFICATE

It is hereby certified that the test facility

LAB Research Kft.

(Base facility: H-8201 Veszprém, Szabadságpuszta, Hungary)

is able to carry out

physico-chemical testing, toxicity studies, mutagenicity studies, environmental toxicity studies on aquatic or terrestrial organisms, studies on behaviour in water, soil and air;bio-accumulation , safety pharmacology testing, reproduction toxicology, inhalation toxicology, analytical chemistry and contract archiving

in compliance with the Principles of GLP (Good Laboratory Practice) and also complies with the corresponding OECD/European Community requirements.

Date of the inspection: **4-8 October, 2010.**

Zsuzsanna Szepezdi, Ph. D.
Director-General