Propiconazole/Pydiflumetofen

Propiconazole/Pydiflumetofen SE (A21573C) -
Acute Dermal Toxicity Study in Rats

Final Report Amendment 1

DATA REQUIREMENT(S): OECD 402 (1987)
EPA 870.1200 (1998)
EC 440/2008, B.3 (2008)

AUTHOR(S): Ádám Appl, M.Sc.

COMPLETION DATE: 04 May 2018

REPORT AMENDMENT 1 DATE: 19 June 2019

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

LABORATORY PROJECT ID: Report Number: 17/349-002P
Study Number: 17/349-002P
Task Number: TK0186806

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: 42/2014. (VIII. 19.) EMMI decree of the Ministry of Human Capacities which corresponds to the OECD GLP, ENV/MC/CHEM (98) 17.).

This study was conducted in accordance with a written Study Plan, authorised by the Sponsor and Citoxlab Hungary Ltd. Management, and followed applicable Standard Operating Procedures.

I, the undersigned, declare that this report constitutes a true record of the actions undertaken and the results obtained in the course of this study.

Ádám Appl, M.Sc.
Study Director

19 June 2019
Date

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

FLAGGING STATEMENT

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QUALITY ASSURANCE STATEMENT

Study Code: 17/349-002P

Study Title: Propiconazole/Pydiflumetofen SE (A21573C) – Acute Dermal Toxicity Study in Rats

Test Item: Propiconazole/Pydiflumetofen SE (A21573C)

This study has been inspected, and the report as well as the Final Report Amendment 1 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 and the Final Report Amendment 1 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
04 December 2017	Study Plan	04 December 2017	04 December 2017
05 December 2017	Observation	05 December 2017	05 December 2017
30 January 2018	Draft Report	30 January 2018	30 January 2018
04 May 2018	Final Report	04 May 2018	04 May 2018
19 June 2019	Final Report Amendment 1	19 June 2019	19 June 2019

Signature: _____ Date: 18 June 2019

Nikolett Németh, B.Sc.
On Behalf of QA

STATEMENT OF THE MANAGEMENT

According to the conditions of the research and development agreement between Syngenta Ltd. (as Sponsor) and Citoxlab Hungary Ltd. (as Test Facility) the study titled "Propiconazole/Pydiflumetofen SE (A21573C) – Acute Dermal Toxicity Study in Rats" was performed, in compliance with the Principles of Good Laboratory Practice.

Signature: _____ Date: 19 June 2019

Christopher Banks, DABT
Managing Director

GENERAL INFORMATION

Contributors

The following contributed to this report in the capacities indicated:

Name	Function
Ádám Appl, M.Sc.	Study Director
Zsolt Tarcai, M.Sc.	Assistant Scientist
Nikolett Németh, B.Sc.	Quality Assurance Unit
László Székelyhidi, D.V.M.	Veterinary Care
Peter Maslej, D.V.M., Ph.D.	Pathology
Tamás Mészáros, Ph.D.	Pharmacy
Monique Inforzato, B.Sc.	Syngenta Study Manager

Other trained, competent personnel worked on the study as required.

Study dates

Study initiation date:	04 December 2017
Experimental starting date:	05 December 2017
Acclimatization period:	30 November – 04 / 06 December 2017
Treatment date:	05 / 07 December 2017
Observation period:	05 / 07 December – 19 / 21 December 2017
Experimental completion date:	21 December 2017
Draft report:	01 February 2018

Deviations from the Study Plan

Due to technical reason, relative humidity value (minimum of 22%) outside the expected range of 30-70% was recorded one time (on 03 December 2017) during the study.

This deviation is considered to have no impact on the outcome of the study and interpretation of the results.

Performing laboratory test substance reference number

170356

Other

The study documents and samples:
- Study Plan,
- all raw data,
- sample of the test item,
- original Study Report and any amendments,
- correspondence

will be archived according to the Hungarian GLP regulations and to applicable SOPs in the archives of Citoxlab Hungary Ltd. 8200 Veszprém, Szabadságpuszta, Hungary. This is for a period of 15 years.

After the retention time 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

Five male and five female Crl:WI rats were treated with a single dermal application of propiconazole/pydiflumetofen SE (A21573C) at the limit dose of 5000 mg/kg body weight (bw). The application period was 24 hours, followed by a 14-day observation period.

Clinical observations along with a check of viability and mortality were performed on all animals at 1 and 5 hours after dosing and daily for 14 days thereafter. Body weight was measured on Day 0 (prior to dosing) and on Days 7 and 14 (before necropsy). All animals were examined macroscopically at necropsy at the end of the observation period.

1.2 Results

No mortality occurred during the study.

There were no adverse clinical signs noted in any animals throughout the study.

No local dermal signs were observed after treatment with the test item during the 14-day observation period.

There were no treatment related body weight changes. Body weights were within the range commonly recorded for this strain and age.

There was no evidence of the any macroscopic changes at a dose level of 5000 mg/kg bw at necropsy.

1.3 Conclusion

The median lethal dose (LD_{50}) of propiconazole/pydiflumetofen SE (A21573C) after a single 24-hour dermal administration was greater than 5000 mg/kg bw in male and female Crl:WI rats.

2.0 INTRODUCTION

2.1 Purpose

The purpose of the study was to assess the acute dermal toxicity of the test item propiconazole/pydiflumetofen SE (A21573C) when administered to Crl:WI male and female rats by a single 24-hour dermal application, followed by an observation period of 14 days.

This study was performed with vertebrate animals as no *in vitro* alternative is available. The study was designed such that the minimum numbers of animals were used.

This study should provide a rational basis for hazard assessment.

The Final Report (dated 04 May 2018) was reissued on 19 June 2019 by the Final Report Amendment 1 to amend test item details (Section 3.1. Test substance) in agreement with the Sponsor, to add the new GLP Certificate of the Test Facility to Appendix 3 and to update the responsible Test Facility member in the Management Statement.

2.2 Guidelines

The study was performed according to the following guidelines:

- OECD Guidelines for Testing of Chemicals, Section 4, Number 402 "Acute Dermal Toxicity", adopted February 24, 1987

- United States Environmental Protection Agency Health Effects Division Test Guidelines, OPPTS 870.1200 Acute Dermal Toxicity EPA 712-C-98-192, August 1998

- Commission Regulation (EC) No 440/2008, B.3 (L 142, 30 May 2008)

This study was being performed to meet safety assessment requirements outside the EU, hence the Commission regulation (EU) 2016/863 of 31 May 2016 restricting the performance of acute dermal toxicity studies was not apply.

2.3 Test Facility

This study was performed in an AAALAC-accredited laboratory. The Institutional Animal Care and Use Committee (IACUC) of Citoxlab Hungary Ltd. reviewed the Study Plan and authorised the conduct of the study.

3.0 MATERIALS AND METHODS

3.1 Test Substance

The following information was provided by the Sponsor.

Name:	Propiconazole/Pydiflumetofen SE (A21573C)
Batch number:	1007839
Active ingredient content:	Pydiflumetofen, 13.7 % w/w corresponding to 151 g/L Propiconazole, 11.6 % w/w corresponding to 128 g/L
Density:	1.100 g/cm^3
Appearance:	Beige liquid
Recertification date:	31 October 2020
Storage conditions:	Room temperature (<30°C)
Safety precautions:	Enhanced safety precautions were applied considering the supplied safety datasheet to assure personnel health and safety.

No correction for purity of the test item was applied.

The Certificate of Analysis is presented in Appendix 2.

3.1.1 Identification and receipt

The test item of a suitable chemical purity was provided by the Sponsor. All precautions required in the handling and disposal of the test item were outlined by the Sponsor. The test item was identified by the Pharmacy of Citoxlab Hungary Ltd. on the basis of the information supplied by the Sponsor.

3.1.2 Formulation

The test item was administered as supplied in a single dose.

3.2 Experimental Design

3.2.1 Animals

Species and strain:	Crl:WI Wistar rats
Source:	Charles River Laboratories, Research Models and Services, Germany GmbH, Sandhofer Weg 7, D-97633 Sulzfeld, Germany
Hygienic level:	SPF at arrival, standard housing condition during the study.
Justification of strain:	Recognized by international guidelines as a recommended test system.
Number of animals:	5 animals/sex
Sex:	Male and female, female rats were nulliparous and non-regnant.
Age of animals at dosing:	Young adult rats
Body weight at dosing:	Between 214 g and 262 g
Identification:	Animals were identified by numbers written on the tail with an indelible pen. The cages were marked with individual identity cards with information about study number, sex, cage number, dose group and individual animal number.
Randomization:	Selected by hand at time of delivery.
Acclimatisation time:	5 or 7 days

3.2.2 Husbandry

Animal health:	Only healthy animals were used for the study. The Veterinarian certified health status.
Room number:	242/8
Housing / Enrichment:	Animals were housed individually in Type II. polypropylene/polycarbonate cages. Rodents were housed with deep wood sawdust bedding to allow digging and other normal rodent activities.
Bedding / Nesting:	"Lignocel 3/4-S" Hygienic Animal Bedding and "Arbocel crinklets natural" nesting material (produced by J. Rettenmaier & Söhne GmbH + Co.KG, Germany) were available to animals during the study.
Light:	12 hours daily, from 6.00 a.m. to 6.00 p.m.
Temperature:	22.5 – 24.6 °C
Relative humidity:	22 – 62%
Ventilation:	15-20 air exchanges per hour

The temperature and relative humidity were recorded twice daily during the acclimatisation and experimental phases of the study.

3.2.3 Food and feeding

Animals received ssniff® SM R/M "Autoclavable complete diet for rats and mice – breeding and maintenance" produced by ssniff Spezialdiäten GmbH, D-59494, Soest, Germany (Lot number: 382 24962, Expiry date: 30 April 2018), *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. A detailed description of the contents of the lot used is archived with the raw data at Citoxlab Hungary Ltd.

3.2.4 Water supply and quality control

The animals received tap water, from the municipal supply, provided in 500 mL bottles, *ad libitum*. The tap water is suitable for human consumption and considered not to contain any contaminants that could reasonably be expected to affect the purpose or integrity of the study.

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 Attila utca 36., Hungary). The quality control results are retained in the archives at Citoxlab Hungary Ltd.

3.3 Experimental Design

3.3.1 Doses

A limit dose of 5000 mg/kg bw was chosen by the Study Director after discussion with the Sponsor.

3.3.2 Experimental design

Dose Group	Number of cages	Number of animals
Sentinel animal 5000 mg/kg bw male	Cage 1	1
5000 mg/kg bw males	Cages 2-5	4
Sentinel animal 5000 mg/kg bw female	Cage 6	1
5000 mg/kg bw females	Cages 7-10	4

A single administration was performed by the dermal route and was followed by a 14-day observation period.

One male and one female rats were dosed initially and the remaining four male and four female rats were dosed 48 hours later when it was clear there were no adverse effects.

3.3.3 Procedure

The back of the animal was shaved (approximately 10% area of the total body surface) approximately 24 hours prior to the treatment. Only those animals without injury or irritation on the skin were used in the test.
On Day 0, the test item was applied as a single dose of 5000 mg/kg bw, and distributed as uniformly as possible over the skin and remained on the skin throughout a 24-hour exposure period. Sterile gauze pads were placed on the skin of rats at the site of application. These gauze pads were kept in contact with the skin by a patch with adhesive hypoallergenic plaster. The entire trunk of the animal was then wrapped with semi occlusive plastic wrap for 24 hours. At the end of the exposure period, residual test item was removed, using body temperature water.

3.4 Observations

3.4.1 Clinical observations

A clinical examination was performed on the day of treatment, at 1 and 5 hours after the application of the test item, and once each day for 14 days thereafter.

Observations included the skin and fur, eyes and mucous membranes, and also respiratory, circulatory, autonomic and central nervous system, and somatomotor activity and behaviour pattern. Particular attention was directed to the observation of tremors, convulsions, salivation, diarrhoea, lethargy, sleep and coma.

3.4.2 Skin irritation

Adverse skin reactions at the site of application were recorded daily following the removal of the dressing.

3.4.3 Measurement of body weight

The body weight of all animals was recorded on Day 0 (day of treatment), and on Days 7 and 14 (before necropsy).

3.5 *Post Mortem* Investigations

All animals were subjected to gross macroscopic examination. All animals were anaesthetised with Euthanimal 40% (Pentobarbital sodium 400 mg/mL, details in 3.5.1.) and exsanguinated. After examination of the external appearance, the cranial, thoracic and abdominal cavities were opened and the appearance of the tissues and organs were observed. Any gross macroscopic findings were recorded.

3.5.1 Material used for euthanasia

Name:	Euthanimal 40% (Pentobarbital sodium)
Lot No.:	1609291-03
Expiry Date:	30 October 2019
Produced by:	Alfasan, Nederland BV., Kuipersweg 9, Woerden, The Netherlands

3.5.2 Data evaluation

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

4.0 RESULTS AND DISCUSSION

4.1 Mortality

No mortality occurred during the study.

4.2 Clinical Signs

There were no adverse clinical signs noted in any animals throughout the study. Individual clinical observations are presented in Table 1.

4.3 Local Dermal Signs

No local dermal signs were observed after treatment with the test item during the 14-day observation period. Individual local dermal signs are presented in Table 1.

4.4 Body Weight

There were no treatment related body weight changes. Body weights were within the range commonly recorded for this strain and age. Individual body weights are presented in Table 2.

4.5 Necropsy

No macroscopic changes were observed (Table 3). Pathology Report is presented in Appendix 1.

5.0 CONCLUSIONS

The median lethal dose (LD_{50}) of propiconazole/pydiflumetofen SE (A21573C) after a single 24-hour dermal administration was greater than 5000 mg/kg bw in male and female Crl:WI rats.

TABLES SECTION

TABLE 1 Clinical Observations

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

Cage No.	Animal No.	Observations	Observation days																Frequency
			0		1	2	3	4	5	6	7	8	9	10	11	12	13	14	
			1h	5h															
1	2100	Symptom Free	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	16/16
2	2101	Symptom Free	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	16/16
3	2102	Symptom Free	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	16/16
4	2103	Symptom Free	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	16/16
5	2104	Symptom Free	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	16/16

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

Cage No.	Animal No.	Observations	Observation days																Frequency
			0		1	2	3	4	5	6	7	8	9	10	11	12	13	14	
			1h	5h															
6	2105	Symptom Free	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	16/16
7	2106	Symptom Free	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	16/16
8	2107	Symptom Free	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	16/16
9	2108	Symptom Free	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	16/16
10	2109	Symptom Free	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	16/16

Remarks: + = present

h = hour (s) Treatment day = Day 0

Frequency of observation = number of occurrence of observation / total number of observations

TABLE 2 Body Weight and Body Weight Gain

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

Cage No.	Animal No.	Body weight (g) Days			Body Weight Gain (g)		
		0	7	14	0-7	7-14	0-14
1	2100	239	292	329	53	37	90
2	2101	257	301	338	44	37	81
3	2102	260	307	351	47	44	91
4	2103	259	308	351	49	43	92
5	2104	258	297	353	39	56	95
Mean:		254.6	301.0	344.4	46.4	43.4	89.8
Standard deviation:		8.8	6.7	10.5	5.3	7.8	5.3

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

Cage No.	Animal No.	Body weight (g) Days			Body Weight Gain (g)		
		0	7	14	0-7	7-14	0-14
6	2105	242	277	296	35	19	54
7	2106	214	220	226	6	6	12
8	2107	240	243	247	3	4	7
9	2108	227	231	237	4	6	10
10	2109	262	265	268	3	3	6
Mean:		237.0	247.2	254.8	10.2	7.6	17.8
Standard deviation:		17.9	23.6	27.7	13.9	6.5	20.4

TABLE 3 Macroscopic Findings

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

Cage No.	Animal No.	Necropsy Date/ Necropsy Day	External Observations	Internal Observations	Organ/ Tissue
1	2100	19 December 2017 Day 14	No external observations	No internal observations	Not applicable
2	2101	21 December 2017 Day 14	No external observations	No internal observations	Not applicable
3	2102	21 December 2017 Day 14	No external observations	No internal observations	Not applicable
4	2103	21 December 2017 Day 14	No external observations	No internal observations	Not applicable
5	2104	21 December 2017 Day 14	No external observations	No internal observations	Not applicable

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

Cage No.	Animal No.	Necropsy Date/ Necropsy Day	External Observations	Internal Observations	Organ/ Tissue
6	2105	19 December 2017 Day 14	No external observations	No internal observations	Not applicable
7	2106	21 December 2017 Day 14	No external observations	No internal observations	Not applicable
8	2107	21 December 2017 Day 14	No external observations	No internal observations	Not applicable
9	2108	21 December 2017 Day 14	No external observations	No internal observations	Not applicable
10	2109	21 December 2017 Day 14	No external observations	No internal observations	Not applicable

APPENDICES SECTION

APPENDIX 1 Pathology Report

Study code. 17/349-002P

PATHOLOGY REPORT

INTRODUCTION

The objective of the study was to assess the acute dermal toxicity of Propiconazole/Pydiflumetofen SE (A21573C) when administered in a single 24-hour dermal application to rats at a dose level of 5000 mg/kg bw followed by 14 days observation.

METHODS

All rats survived until the scheduled termination of the study.

All animals were euthanized upon completion of the treatment period on Day 14. Rats were anaesthetized 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.

TERMINAL (DAY 14)

Macroscopic Findings

There was no evidence of the any gross observations at a dose level of 5000 mg/kg bw.

CONCLUSION

A single 24-hour dermal application of Propiconazole/Pydiflumetofen SE (A21573C) to male and female Crl:WI Wistar rats at a dose level of 5000 mg/kg bw followed by 14 days observation, was not associated with any macroscopic findings.

Peter Maslej, D.V.M., Ph.D.
Director of Pathology

02 May 2018
Date

APPENDIX 2 Certificate of Analysis

syngenta

Syngenta Crop Protection, LLC
Analytical and Product Chemistry
Greensboro, NC 27409

Certificate of Analysis

A21573C

Batch ID 1007839 (GP170913)

Test Substance Name:	CGA64250/SYN545974 SE (125/150)
Common Name:	Propiconazole/Pydiflumetofen SE (125/150)
Design Code:	A21573C
Batch ID:	1007839
Other ID:	GP170913
Source:	Syngenta Crop Protection LLC.,US .410 Swing Road,Greensboro, NC 27409,

Chemical Analysis

AI	% w/w	g/L
Pydiflumetofen	13.7	151
Propiconazole	11.6	128

Identity of the Active Ingredients: Confirmed

Methodology Used for Characterization: LC , mass spectrometry, oscillating density meter

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

Isomer Assay

Analyte	Isomer	% w/w	g/L
CGA93590	1H-1,2,4-triazole, 1-{[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]methyl}-, cis-	6.73	74
CGA93591	1H-1,2,4-triazole, 1-{[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]methyl}-, trans-	4.84	53.2

COA Number: USGR170462

Page 1 of 2

APPENDIX 2 Certificate of Analysis (Continued)

Physical Analysis

Property	Value	Units
Density	1.100	g/cm3

Appearance: Beige liquid

Storage Temperature: <30°C

Re-certification Date:End of Oct/2020

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

The stability of this test substance will be determined concurrently through reanalysis of material held in inventory under GLP conditions at Syngenta Crop Protection, LLC, Greensboro, NC.

This Certificate of Analysis is summarizing data from a study that has been performed in compliance with Good Laboratory Practices per 40 CFR Part 160. Raw data, documentation, protocols, any amendments to study protocols and reports pertaining to this study are maintained in the Syngenta Crop Protection Archives in Greensboro, NC.

Study Number: USGR170462

Authorization: Kirt Durand

Oct. 13, 2017

Kirt Durand — Date

Analytical and Product Chemistry Department

COA Number: USGR170462 Page 2 of 2

APPENDIX 3 GLP Certificates

OGYÉI
National Institute of
Pharmacy and Nutrition

H-1051 Budapest, Zrínyi u. 3.
1372 P.O. Box:450.
Tel: +36 1 88 69-300, Fax: +36 1 88 69 460
E-mail: ogyei@ogyei.gov.hu, Web: www.ogyei.gov.hu

Ref. no: OGYI/19440-7/2015
Admin.: Szatmári Andrea
Date: 22 September, 2015

GOOD LABORATORY PRACTICE (GLP)
CERTIFICATE

It is hereby certified that the test facility

CiToxLAB Hungary Ltd.

H-8200 Veszprém, Szabadságpuszta

is able to carry out

physico-chemical testing, toxicity studies, in vitro studies and mutagenicity studies, environmental toxicity studies on aquatic or terrestrial organisms, studies on behaviour in water, soil and air; bio-accumulation, 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: **02-04. June 2015.**

Dr. József Reiter
Deputy Director-General

Note: Translation of the Stamp on the official document ("Országos Gyógyszerészeti és Élelmezés-egészségügyi Intézet"): "National Institute of Pharmacy and Nutrition"

APPENDIX 3 GLP Certificates (Continued)

OGYÉI
National Institute of
Pharmacy and Nutrition

H-1051 Budapest, Zrínyi u. 3.
1372 P.O. Box:450.
Tel: +36 1 88 69-300, Fax: +36 1 88 69 460
E-mail: ogyei@ogyei.gov.hu, Web: www.ogyei.gov.hu

Ref. no: OGYÉI/22762-5/2018
Admin.: Dr. Juhász Uzonka
Date: 03 August 2018

GOOD LABORATORY PRACTICE (GLP) CERTIFICATE

It is hereby certified that the test facility

CiToxLAB Hungary Ltd.

H-8200 Veszprém, Szabadságpuszta

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, analytical and clinical chemistry, pathology studies, preparation of microscopic tissue sections, reproduction toxicology, in vitro studies, inhalation toxicology, 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: **07-11 May 2018.**

Tarjáni Ibolya
Head of Inspectorate

Note: Translation of the Stamp on the official document ("Országos Gyógyszerészeti és Élelmezés-egészségügyi Intézet"): "National Institute of Pharmacy and Nutrition"