SYN545192

SYN545192 - 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: 08 June 2010

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

LABORATORY PROJECT ID: Report Number: 09/265-001P
Study Number: 09/265-001P
Task Number: TK0002629

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 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: 08 June 2010

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: 09/265-001P

Study Title: SYN545192 – Acute Oral Toxicity Study in the Rat (Up and Down Procedure)

Test Item: SYN545192

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
09 December 2009	Study Plan	09 December 2009	09 December 2009
12 January 2010	Clinical Observations	12 January 2010	12 January 2010
22 March 2010	Draft Report	22 March 2010	22 March 2010
08 June 2010	Final Report	08 June 2010	08 June 2010

Signature: Kim Istvánné Date: 08 June 2010

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., the study titled "SYN545192 - 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: 08 June 2010

David J. Esdaile, M.Sc.
Scientific 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
István Pásztor, DVM	Veterinary control
Peter Maslej, DVM, PhD	Head of Pathology Unit
András Mátyás	Technical Team Leader of Central Dispensary (experimental phase)
Tamás Mészáros, PhD	Head of Central Dispensary (reporting phase)
Eric Yau	Syngenta Study Manager

Study dates

Experimental Starting Date	06 January 2010
Experimental Completion Date	02 February 2010
Reception of Animals	30 December 2009
Acclimatization	At least 7 days
Treatment	06 January 2010 (female no. 7004) 07 January 2010 (female no. 7002) 08 January 2010 (female no. 7003) 12 January 2010 (female no. 7006) 13 January 2010 (female no. 7008) 14 January 2010 (female no. 7010) 15 January 2010 (female no. 7009) 19 January 2010 (female no. 7011)
Observation	06 January 2010 (female no. 7004) 07 - 21 January 2010 (female no. 7002) 08 - 09 January 2010 (female no. 7003) 12 - 26 January 2010 (female no. 7006) 13 - 14 January 2010 (female no. 7008) 14 January 2010 (female no. 7010) 15 - 29 January 2010 (female no. 7009) 19 Jan. – 02 Febr. 2010 (female no. 7011)

Deviations from the study plan

Márta Tenk was not involved in the study.

Interpretation of the results will not be performed according to the EU labelling regulations.

Due to personnel changes, Tamás Mészáros acts as the Head of Central Dispensary at the reporting phase.

The Draft Report was sent on 24 March 2010 instead of 10 March 2010 as indicated in the Study Plan.

These deviations are considered to have no impact on the outcome of the study and interpretation of the results.

Performing laboratory test substance reference number

09/268K/1 091121

Other

The study documents:
- study plan and amendment,
- 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 24 hour intervals. The time intervals between dosing were determined by the onset, duration and severity of toxic signs.

Limit test was not performed as the Sponsor had information which indicated the test item was likely to cause mortality at a dose level of 2000 mg/kg. The starting dose was 175 mg/kg as requested by the Sponsor.

Dosages

The test substance was formulated in 1% Carboxymethylcellulose.

Animal Number	Dosage [mg/kg body weight]	Volume [mL/kg body weight]
7004	175	10
7002	55	10
7003	175	10
7006	55	10
7008	175	10
7010	55	10
7009	17.5	10
7011	55	10

Observations

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

SYN545192 caused mortalities at 175 mg/kg bw (3/3) and at 55 mg/kg bw (1/4).

Clinical signs included decreased activity (3/3), prone position (3/3), incoordination (3/3), piloerection (3/3), dyspnoea (3/3), decreased respiratory rate (1/3), clonic convulsion (1/3), decreased body temperature (3/3) and mortality (3/3) at a dose level of 175 mg/kg bw and decreased activity (4/4), dyspnoea (4/4), incoordination (4/4), hunched back (1/4) and

mortality (1/4) at 55 mg/kg. There were no adverse signs observed in the animal dosed at 17.5 mg/kg bw.
Body weight and body weight gain of the surviving animals during the study showed no indication of a treatment-related effect.

Necropsy of intercurrent deaths (animals dosed at 175 mg/kg and 55 mg/kg) observed macroscopic findings including non-collapsing or dark/red discoloration of the lungs and/or thymus, frothy material in the trachea or enlarged atria in the heart were seen in these animals. These findings were considered to be due to agonal or post mortem changes. At terminal necropsy, 1 animal dosed at 55 mg/kg showed dark/red discoloration of the lungs. No macroscopic findings were observed in the other surviving animals at dose levels of 55 mg/kg and 17.5 mg/kg.

1.3 Conclusion

Under the conditions of this study, the acute oral median lethal dose (LD_{50}) of SYN545192 was calculated to be 55 mg/kg bw in female CRL:(WI) BR rats.

2.0 INTRODUCTION

2.1 Purpose

The purpose of the study was to assess the oral toxicity of the test item SYN545192 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. Revewed 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:	SYN545192
Batch number:	SMU9BP005
Product code:	SYN545192
Appearance:	powder/ beige
Reanalysis date:	End of February 2013
Storage conditions:	< 30˚C
Safety Precautions:	Routine safety precautions (lab coat, safety glasses, gloves, face mask) for unknown materials were applied to assure personnel health and safety
Vehicle:	1% Carboxymethylcellulose (high viscosity)
Batch number:	Lot:1336453
Expiry Date:	30 January 2010
Produced by:	Fluka zRt.

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

SYN545192 was formulated for treatment doses at 175, 55 and 17.5 mg/kg (dose volume of 10 mL). The test substance was formulated in 1% Carboxymethylcellulose.

3.2 Experimental Animals

Species and strain:	CRL:(WI)BR rats
Source:	Toxi Coop, Cserkesz u. 90. 1103 Budapest, Hungary
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, 8-9 weeks old.
Body weight (at dosing):	220 - 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.
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 *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:

Limit test was not performed. The starting dose in the main study was 175 mg/kg bw.

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 at least 24 hours. 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 only performed when no significant clinical signs were noted in the previous animal.

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 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

SYN545192 caused mortalities at 175 mg/kg bw (3/3) and at 55 mg/kg bw (1/4).

4.2 Body Weights

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

4.3 Clinical Signs

Clinical signs included decreased activity (3/3), prone position (3/3), incoordination (3/3), piloerection (3/3), dyspnoea (3/3), decreased respiratory rate(1/3), clonic convulsion (1/3), decreased body temperature (3/3) and mortality (3/3) at a dose level of 175 mg/kg bw and decreased activity (4/4), dyspnoea (4/4), incoordination (4/4), hunched back (1/4) and mortality (1/4) at 55 mg/kg. There were no adverse signs observed in the animal dosed at 17.5 mg/kg bw.

4.4 Macroscopic Findings

Necropsy of intercurrent deaths (animals dosed at 175 mg/kg and 55 mg/kg) observed macroscopic findings including non-collapsing or dark/red discoloration of the lungs and/or thymus, frothy material in the trachea or enlarged atria in the heart were seen in these animals. These findings were considered to be due to agonal or post mortem changes. At terminal necropsy, 1 animal dosed at 55 mg/kg showed dark/red discoloration of the lungs. No macroscopic findings were observed in the other surving animals at dosed level of 55 mg/kg and 17.5 mg/kg.

5.0 CONCLUSIONS

Under the conditions of this study, the acute oral median lethal dose (LD_{50}) of SYN545192 was calculated to be 55 mg/kg bw in female CRL:(WI) BR rats.

TABLES SECTION

TABLE 1 Individual Findings – Clinical Signs

Cage	Sex	Dose Level (mg/kg)	Animal Number	Observations	Observation days																
					0						1	2	3	4	5	6	7	8	9	10	11	12	13	14
					30'	1h	2h	3h	4h	6h														
1	Female	175	7004	Symptom Free	+	-	-	-	-	-	**animal dead on day 0**													
				Activity decreased	-	+2	+3	+3	+3	-														
				Prone position	-	-	+	+	+	-														
				Incoordination	-	+2	-	-	-	-														
				Piloerection	-	-	+	+	+	-														
				Cold to touch (whole body)	-	-	+	+	+	-														
				Respiratory rate decreased	-	-	-	-	+2	-														
				Dyspnoea	-	+1	+2	+2	+3	-														
				Found Dead	-	-	-	-	-	+														
3			7003*	Activity decreased	+1	+1	+3	+3	+3	+3	-	**animal dead on day 1**												
				Prone position	-	-	+	+	+	+	-													
				Incoordination	+1	+3	-	-	-	-	-													
				Clonic convulsion (whole body)	-	-	-	+2	-	-	-													
				Piloerection	-	-	+	+	+	+	-													
				Cold to touch (whole body)	-	-	+	+	+	+	-													
				Dyspnoea	+1	+1	+1	+1	+3	+3	-													
				Found Dead	-	-	-	-	-	-	+													
5			7008	Activity decreased	+1	+2	+3	+3	+3	+3	-	**animal dead on day 1**												
				Prone position	-	-	+	+	+	+	-													
				Incoordination	+2	+3	-	-	-	-	-													
				Piloerection	-	+	+	+	+	+	-													
				Cold to touch (whole body)	-	-	+	+	+	+	-													
				Dyspnoea	+1	+1	+1	+2	+2	+2	-													
				Found Dead	-	-	-	-	-	-	+													

*: the animal circles to left and right

TABLE 1 Individual Findings – Clinical Signs (Continued)

Cage	Sex	Dose Level (mg/kg)	Animal Number	Observations	Observation days																			
					0						1	2	3	4	5	6	7	8	9	10	11	12	13	14
					30'	1h	2h	3h	4h	6h														
2	Female	55	7002	Symptom Free	+	-	-	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
				Activity decreased	-	+2	+2	+2	+1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
				Incoordination	-	+1	+1	+1	+1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
				Dyspnoea	-	+1	+1	+1	+1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4			7006	Symptom Free	+	-	-	-	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
				Activity decreased	-	+2	+2	+2	+3	+2	-	-	-	-	-	-	-	-	-	-	-	-	-	-
				Hunched back	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-
				Incoordination	-	+2	+2	+2	+3	+3	-	-	-	-	-	-	-	-	-	-	-	-	-	-
				Dyspnoea	-	+1	+1	+1	+1	+1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6			7010	Activity decreased	+2	+2	-																	
				Incoordination	+1	+2*	-																	
				Dyspnoea	-	+1	-																	
				Found Dead	-	-	+	**animal dead on day 0**																
8			7011	Symptom Free	-	-	-	-	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
				Activity decreased	+1	+1	+1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
				Incoordination	-	-	+1	+1	+1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
				Dyspnoea	+1	+1	+1	+1	+1	+1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
7	Female	17.5	7009	Symptom Free	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

Remarks:

Severities: 1=Slight/Small/Few; 2=Moderate/Medium; 3=Marked/Large/Many +: increased, or present; -: decreased, or absent

Treatment day = Day 0

*: circling to right (not continuous)

TABLE 2 Body Weight and Body Weight Gain

Group	Dose Level (mg/kg)	Sex	Animal No.	Body weight (g) Days					Body Weight Gain (g)			
				-1	0	7	14	B.W. Death	-1-0	0-7	7- 14	-1 - 14
1	175	Female	7004	244	228	-	-	218	-16	-	-	-
3		Female	7003	239	220	-	-	210	-19	-	-	-
5		Female	7008	246	230	-	-	215	-16	-	-	-
Mean: (Body Weight (g)				243.0	226.0	-	-	214.3	-17.0	-	-	-
Standard deviation:				3.6	5.3	-	-	4.0	1.7	-	-	-

Group	Dose Level (mg/kg)	Sex	Animal No.	Body weight (g) Days					Body Weight Gain (g)			
				-1	0	7	14	B.W. Death	-1-0	0-7	7- 14	-1 - 14
2	55	Female	7002	238	227	257	270	-	-11	30	13	32
4		Female	7006	254	228	262	275	-	-26	34	13	21
6		Female	7010	242	226	-	-	219	-16	-	-	-
8		Female	7011	246	228	257	265	-	-18	29	8	19
Mean: (Body Weight (g)				245.0	227.3	258.7	270.0	219.0	-17.8	31.0	11.3	24.0
Standard deviation:				6.8	1.0	2.9	5.0	-	6.2	2.6	2.9	7.0

Group	Dose Level (mg/kg)	Sex	Animal No.	Body weight (g) Days					Body Weight Gain (g)			
				-1	0	7	14	B.W. Death	-1-0	0-7	7- 14	-1 - 14
7	17.5	Female	7009	248	234	260	276	-	-14	26	16	28

TABLE 3 Macroscopic Findings

Cage	Sex	Dose Level (mg/kg)	Animal Number	Necropsy Date	External Observations	Internal Observations	Location
1	Female	175	7004*	06 January 2010	No external observations recorded	Dark discoloration, red, diffuse, all lobes	Lungs
3			7003*	09 January 2010	No external observations recorded	Dark discoloration, red, diffuse, all lobes	Lungs
						Dark discoloration, red, diffuse	Thymus
5			7008*	14 January 2010	No external observations recorded	Non collapsed	Lungs
						Dark discoloration, red, diffuse, all lobes	
						Enlargement, left and right atria	Heart
						Frothy material, white	Trachea
						Dark discoloration, red, diffuse	Thymus
2	Female	55	7002	21 January 2010	No external observations recorded	No internal observations recorded	Not applicable
4			7006	26 January 2010	No external observations recorded	Dark discoloration, red, diffuse, all lobes	Lungs
6			7010*	14 January 2010	No external observations recorded	Non collapsed	Lungs
						Dark discoloration, red, diffuse, all lobes	
8			7011	02 February 2010	No external observations recorded	No internal observations recorded	Not applicable
7	Female	17.5	7009	29 January 2010	No external observations recorded	No internal observations recorded	Not applicable

*: Found dead

APPENDICES SECTION

APPENDIX 1 Pathology Report

LAB Study code. 09/265-001P

PATHOLOGY REPORT

INTRODUCTION

The objective of the study was to assess the acute oral toxicity of SYN545192 when administered in a single dose to 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

Four animals were found dead on Days 0 or 1. Affected animals included 3 females (7003, 7004 and 7008) at a dose level of 175 mg/kg and one female (7010) dosed at 55 mg/kg.

FOUND DEAD

Macroscopic Findings

Non-collapsing or dark/red discoloration of the lungs and/or thymus, frothy material in the trachea or enlarged atria in the heart seen in these found dead animals were considered to be agonal or post mortem changes.

TERMINAL (DAY 14)

Macroscopic Findings

Dark/red discoloration of the lungs was observed in the female 7006 dosed at 55 mg/kg.

APPENDIX 1 Pathology Report (Continued)

CONCLUSION

A single oral gavage of SYN545192 to the CRL: (WI) BR rat led to the death of 3 female rats at a dose level of 175 mg/kg and one animal dosed at 55 mg/kg bw. A specific cause of death was not determined for these animals.

Following a 14 day observation period, administration of SYN545192 was not associated with test item-related macroscopic findings.

09 June 2010

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

APPENDIX 2 Certificate of Analysis

09/265-001P

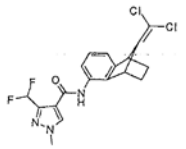
syngenta

GLP Testing Facility WMU
Analytical Development &
Product Chemistry GS2131

Syngenta Crop Protection
Münchwilen AG
Breitenloh 5
CH-4333 Münchwilen

Certificate of Analysis

SYN545192 tech.



SMU9BP005 - Purity 97.0 %

Batch Identification	**SMU9BP005**
Product Code	**SYN545192 tech.**
Other Product Code(s)	---
ISO Common Name	---
CA Reg. No.	---
CA Index Name	---
IUPAC Name	3-difluoromethyl-1-methyl-1H-pyrazole-4-carboxylic acid (9-dichloromethen-1,2,3,4-tetrahydro-1,4-methano-naphthalen-5-yl)-amide
Molecular formula	$C_{18}H_{15}Cl_2F_2N_3O$
Molecular mass	398.2
Chemical Analysis	
– **Identity ***	**confirmed**
– **Content of SYN545192 ***	**97.0 %**
Methodology used for Characterisation	HPLC
Physical Analysis	
– **Appearance ***	**beige powder**
– **Particle Size ***	**1.1 µm (10%), 6.1 µm (50%), 41.4 µm (90%)**
Stability:	
– **Storage Temperature**	**< 30°C**
– **Reanalysis Date**	**End of February 2013**

KKE
It's a true copy
Hiteles másolat
Date / Dátum: 2009 DEC 01
Signature/Aláírás:
Eredeti helye: 8.sz. dosszié

The stability of this test substance will be controlled by reanalysis of material held in the inventory at Syngenta Crop Protection AG at the appropriate time.

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.

Characterisation: 119677
Authorisation:

25-Feb-2009
Dr. R. Kettner
Analytical Development & Product Chemistry

10382606

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APPENDIX 3 GLP-Certificate

ORSZÁGOS GYÓGYSZERÉSZETI INTÉZET
National Institute of Pharmacy

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Budapest, 20th December 2008
No: 38625/48/2007
Our ref.: Szilvia Karsai
Subject: GLP Certificate

GOOD LABORATORY PRACTICE (GLP)
CERTIFICATE

Based on the Inspection report and the discussion of follow up activities it is hereby certified that the test facility

LAB Research Ltd.
H-8201 Veszprém, Szabadságpuszta, Hungary

is able to carry out **Physical-chemical testing, Toxicity studies, Mutagenicity studies, Environmental toxicity studies on aquatic and terrestrial organisms, Studies on behaviour in water, soil and air; bioaccumulation, Bioanalytical, Analytical and clinical chemistry testing** compliance with the Principles of GLP (Good Laboratory Practice).

Date of the inspection: **13-22 October 2008.**

This GLP Certificate is valid for 2 years.

Zsuzsanna Szepezdi, Ph. D.
Director-General