SYN520453

SYN520453 EC (A15149AC) - Acute Oral Toxicity Study in the Rat (Up and Down Procedure)

Final Report

DATA REQUIREMENT(S): OECD [Test Guideline, Number 425]
Directive 2004/73/EC, B.1 tris
EPA [OPPTS 870.1100]
Japanese MAFF [12 NohSan No. 8147]

AUTHOR(S): Dr. C. Simon

STUDY COMPLETION DATE: 11-JUL-2008

PERFORMING LABORATORY: RCC Ltd
Wölferstrasse 4
4414 Füllinsdorf, Switzerland

LABORATORY PROJECT ID: Report Number: B83823
Study Number: B83823
Task Number: T011358-05

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

STATEMENTS OF DATA CONFIDENTIALITY CLAIMS

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GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

RCC Study Number:	B83823
Syngenta Task Number:	T011358-05
Test Item:	SYN520453 EC (A15149AC)
Study Director:	Dr. C. Simon
Study Title:	SYN520453 EC (A15149AC) - Acute Oral Toxicity Study in the Rat (Up and Down Procedure)

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

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

C Simon — 11-Jul-2008

Dr. C. Simon
Study Director
Acute Toxicology

Date

Performing Laboratory:

RCC Ltd,
Wölferstrasse 4
4414 Füllinsdorf / Switzerland

FLAGGING STATEMENT

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QUALITY ASSURANCE STATEMENT

RCC Ltd, Zelgliweg 1, 4452 Itingen / Switzerland

RCC Study Number:	B83823
Syngenta Task Number:	T011358-05
Test Item:	SYN520453 EC (A15149AC)
Study Director:	Dr. C. Simon
Study Title:	SYN520453 EC (A15149AC) - Acute Oral Toxicity Study in the Rat (Up and Down Procedure)

The general facilities and activities are inspected periodically 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
20-FEB-2008	Study Plan	20-FEB-2008
04-MAR-2008	Process Based (Test System, Test Item, Raw Data, Dose Preparation, Treatment)	04-MAR-2008
23-JUN-2008	Report	23-JUN-2008

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

Quality Assurance: S. van Dongen

S. van Dongen

Date: 11-Jul-2008

GENERAL INFORMATION

Contributors

The following contributed to this report in the capacities indicated:

Name	Function
Dr. C. Simon	Study Director
G. Arcelin	Deputy Study Director
I. Wüthrich	Head of RCC Quality Assurance
R. Sheldon	Syngenta Study Manager

Study dates

Experimental Starting Date	26-FEB-2008
Experimental Completion Date	30-APR-2008
Delivery of Animals	26-FEB-2008 (female no. 1) 28-FEB-2008 (female no. 2) 04-MAR-2008 (female no. 3) 13-MAR-2008 (female no. 4) 18-MAR-2008 (female no. 5) 19-MAR-2008 (female no. 6) 20-MAR-2008 (female no. 7) 27-MAR-2008 (female no. 8) 01-APR-2008 (female no. 9) 09-APR-2008 (female no. 10) 11-APR-2008 (female no. 11)
Acclimatization	26-FEB-2008 to 03-MAR-2008 (female no. 1) 28-FEB-2008 to 05-MAR-2008 (female no. 2) 04-MAR-2008 to 10-MAR-2008 (female no. 3) 13-MAR-2008 to 19-MAR-2008 (female no. 4) 18-MAR-2008 to 24-MAR-2008 (female no. 5) 19-MAR-2008 to 26-MAR-2008 (female no. 6) 20-MAR-2008 to 31-MAR-2008 (female no. 7) 27-MAR-2008 to 02-APR-2008 (female no. 8) 01-APR-2008 to 08-APR-2008 (female no. 9) 09-APR-2008 to 15-APR-2008 (female no. 10) 11-APR-2008 to 17-APR-2008 (female no. 11)

Treatment	04-MAR-2008 (female no. 1) 06-MAR-2008 (female no. 2) 11-MAR-2008 (female no. 3) 20-MAR-2008 (female no. 4) 25-MAR-2008 (female no. 5) 27-MAR-2008 (female no. 6) 01-APR-2008 (female no. 7) 03-APR-2008 (female no. 8) 09-APR -2008 (female no. 9) 16-APR -2008 (female no. 10) 18-APR-2008 (female no. 11)
Observation	26-FEB-2008 to 04-MAR-2008 (female no. 1) 28-FEB-2008 to 20-MAR-2008 (female no. 2) 04-MAR-2008 to 25-MAR-2008 (female no. 3) 13-MAR-2008 to 03-APR-2008 (female no. 4) 18-MAR-2008 to 26-MAR-2008 (female no. 5) 19-MAR-2008 to 10-APR-2008 (female no. 6) 20-MAR-2008 to 01-APR-2008 (female no. 7) 27-MAR-2008 to 03-APR-2008 (female no. 8) 01-APR-2008 to 23-APR-2008 (female no. 9) 09-APR-2008 to 30-APR-2008 (female no. 10) 11-APR-2008 to 18-APR-2008 (female no. 11)

Deviations from the guidelines

None

Retention of samples

See below under Other.

Performing Laboratory Test Substance Reference Number

205173

Other

RCC Ltd (CH-4452 Itingen / Switzerland) will retain the study plan, raw data, sample of test item(s) and the original final report of the present study for a minimum of five years. Thereafter, all items described above must be archived for at least a further five years. In agreement with the Sponsor, this may be at RCC Ltd or at another GLP compliant archive facility. A report amendment need only be written if the archived items are transferred to another facility.

No data will be discarded without the Sponsor's written consent.

TABLE OF CONTENTS

1.0 EXECUTIVE SUMMARY

1.1 Study design

A limit test with 1 animal and a main study with 10 animals (female HanRcc:WIST (SPF) rat) was conducted. These animals were treated with SYN520453 EC (A15149AC) by gavage at the limit dosage (5000 mg/kg body weight) as well as 175, 550, 1750 mg/kg body weight. The test item was applied undiluted at a volume of 5.23, 0.183, 0.575 mL/kg or 1.83 mL/kg (see table below).

Application scheme

Animal Number	Dosage [mg/kg body weight]	Volume [mL/kg body weight]
1	5000	5.23
2	175	0.183
3	550	0.575
4	1750	1.83
5	5000	5.23
6	1750	1.83
7	5000	5.23
8	1750	1.83
9	550	0.575
10	1750	1.83
11	5000	5.23

The animals were examined daily during the acclimatization period and mortality, viability and clinical signs were recorded. All animals were examined for clinical signs 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 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 after being killed in extremis or at the end of the study.

1.2 Results

175 mg/kg (1 animal)
This animal survived. It had slightly ruffled fur 2 to 4 days post-dose and a hunched posture was present on test day 2. Thereafter this animal was free of clinical signs up to test day 15 and gained body weight up to the end of the observation period.
No gross abnormalities were noted when necropsied following the 14-day observation period.

550 mg/kg (2 animals)
Both animals survived. One of them had a slightly ruffled fur 1 hour after dosing up to test day 2. The second animal did not show any clinical signs. Both gained body weight up to the end of the observation period.
No gross abnormalities were noted at necropsy.

1750 mg/kg (4 animals)
Three animals survived. All animals treated at 1750 mg/kg showed clinical signs including slightly ruffled fur, slight to marked sedation, slight to moderate poor coordination and hunched posture from test day 1 to test day 2. Additionally, two animals had ventral recumbency and labored respiration on test day 1 and/or 2. One animal (No. 8) was observed with grinding teeth before it was humanely sacrificed for ethical reasons on test day 2.
The animals that survived gained body weight to the end of the observation period.
At necropsy, the stomach of the sacrificed animal (No. 8) was distended with gas, and liquid, yellowish contents were found in the duodenum and jejunum. No gross abnormalities were noted in the remaining animals.

5000 mg/kg (4 animals)
All animals were sacrificed for ethical reasons on test days 1 or 2.
The animals showed clinical signs including slight to moderate ruffled fur, slight to marked sedation, slight to marked poor coordination, ventral recumbency, tachypnea, bradypnea, deep respiration, rales, labored respiration, slight to moderate tremor, convulsions, vocalisation and being cold to touch before being sacrificed.
At necropsy, congested lungs, liquid contents in the stomach, duodenum and/or jejunum and/or a discoloration (tan) of the liver or the kidneys were observed in three of these animals.

1.3 Conclusion

The median lethal dose of SYN520453 EC (A15149AC) after single oral administration to female rats, observed over a period of 14 days is:

LD_{50} (female rat): 1750 mg/kg body weight
(Approximate 95 % PL[1] confidence interval: 1239 to 4450 mg/kg)

[1] Profile-likelihood based confidence interval

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).

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

2.2 Guidelines

The study was done according to the following guidelines:

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

Directive 2004/73/EC, B.1 tris "Acute Oral Toxicity", April 29, 2004.

Japanese MAFF Test Data for Registration of Agricultural Chemicals, Test Guidelines, Acute oral toxicity studies, 12 NohSan No. 8147, Agricultural Production Bureau, November 24, 2000 [English translation by IAI:ACIS, revised on June 26, 2001 (13 Seisan No. 1739) and December 10, 2002 (14 Seisan No. 7269)].

EPA Health Effects Test Guidelines, OPPTS 870.1100 Acute Oral Toxicity EPA 712-C-03-190, December 2002.

3.0 MATERIALS AND METHODS

3.1 Test substance

Data as supplied by the Sponsor.

Identification:	SYN520453 EC (A15149AC)
Design Code:	A15149AC
Description:	Liquid; uniform mobile clear brown
Batch Number:	J8092/056
Formulation:	SYN520453: 13.4% w/w corresponding to 128 g/l
Density:	0.956 g/cm^3
Stability of Test Item:	Stable under storage conditions.
Expiry Date:	December 2009
Storage Conditions:	At a temperature > 0°C and < 40°C; light protected.
Safety Precautions:	Routine hygienic procedures were used to ensure the health and safety of the personnel.

The certificate of analysis as attached in Appendix 1.

3.2 Experimental design

The animals received a single dose of the test item by oral gavage administration after being fasted for approximately 16 ½ to 19 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.

Homogeneity of the test item in the vehicle was maintained during administration using a magnetic stirrer.

Dosing started in one female animal at a dosage level of 5000 mg/kg. The application volume was 5.23 mL/kg body weight.

Application scheme:

Animal Number	Dosage [mg/kg body weight]	Volume [mL/kg body weight]	Viability/Mortality
1	5000	5.23	Killed in extremis
2	175	0.183	Survived
3	550	0.575	Survived
4	1750	1.83	Survived
5	5000	5.23	Killed in extremis
6	1750	1.83	Survived
7	5000	5.23	Killed in extremis
8	1750	1.83	Killed in extremis
9	550	0.575	Survived
10	1750	1.83	Survived
11	5000	5.23	Killed in extremis

Rational: 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 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 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 after being killed at the end of the study.

3.2.1 Animals

Animal species and strain:	Rat, HanRcc:WIST (SPF)
Rationale:	Recognized by international guidelines as a recommended test system.
Breeder/supplier:	RCC Ltd, Laboratory Animal Services CH-4414 Füllinsdorf / Switzerland
Number of animals per group:	One female
Total number of animals:	11 females
Age when treated:	11 weeks
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. Only animals without any visible signs of illness were used for the study.

3.2.2 Husbandry

Room Number:	0105 / RCC Ltd, Füllinsdorf
Conditions:	Standard Laboratory Conditions. Air-conditioned with 10-15 air changes per hour, and continuously monitored environment with ranges for room temperature 22 ± 3 °C and for relative humidity between 30-70 % (values above 70 % during cleaning process possible), automatically controlled light cycle of 12 hours light and 12 hours dark, music during the daytime light period.
Accommodation:	Individually in Makrolon type-3 cages with standard softwood bedding ('Lignocel' Schill AG, CH-4132 Muttenz/Switzerland) during treatment and observation.
Diet:	Pelleted standard Provimi Kliba 3433 rat/mouse maintenance diet, batch nos. 77/07 and 12/08 (Provimi Kliba AG, CH-4303 Kaiseraugst/Switzerland) ad libitum. Results of analyses for contaminants are archived at RCC Ltd.
Water:	Community tap water from Füllinsdorf ad libitum. Results of bacteriological, chemical and contaminant analyses are archived at RCC Ltd.

3.3 *Post mortem* investigations

The four animals treated at 5000 mg/kg as well as one animal treated at 1750 mg/kg were killed in extremis by intravenous injection of pentobarbitone into the ear vein at a dose of at least 1 mL/kg body weight (162 mg sodium pentobarbitone/kg body weight) and necropsied as soon as they were killed.

All surviving animals were killed at the end of the observation period by carbon dioxide asphyxiation and discarded after macroscopic examinations were performed.

No organs or tissues were retained.

3.4 Data evaluation

Body weights were recorded on-line.

Clinical signs were recorded on data sheets.

Mortality/viability were compiled into the RCC Tox Computer System during recording and/ or recorded on data sheets.

Macroscopic findings were compiled into the RCC Tox Computer System during recording. The RCC Tox Computer System (RCC-Tox-Lims) has been validated with respect to data collection, 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

4.1 Results

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.

4.1.1 Mortality

Four animals had to be sacrificed during the course of the study.

4.1.2 Body weights

The body weight of the animals was within the range commonly recorded for this strain and age.

4.1.3 Clinical signs

175 mg/kg (1 animal)
This animal survived. It had slightly ruffled fur 2 to 4 days post-dose and a hunched posture was present on test day 2. Thereafter this animal was free of clinical signs up to test day 15 and gained body weight up to the end of the observation period.

550 mg/kg (2 animals)
Both animals survived. One of them had a slightly ruffled fur 1 hour after dosing up to test day 2. The second animal did not show any clinical signs. Both gained body weight up to the end of the observation period.

1750 mg/kg (4 animals)
Three animals survived. All animals treated at 1750 mg/kg showed clinical signs including slightly ruffled fur, slight to marked sedation, slight to moderate poor coordination and hunched posture from test day 1 to test day 2. Additionally, two animals had ventral recumbency and labored respiration on test day 1 and/or 2. One animal (No. 8) was observed with grinding teeth before it was humanely sacrificed for ethical reasons on test day 2. The animals that survived gained body weight to the end of the observation period.

5000 mg/kg (4 animals)
All animals were sacrificed for ethical reasons on test days 1 or 2.
The animals showed clinical signs including slight to moderate ruffled fur, slight to marked sedation, slight to marked poor coordination, ventral recumbency, tachypnea, bradypnea, deep respiration, rales, labored respiration, slight to moderate tremor, convulsions, vocalisation and being cold to touch before being sacrificed.

4.1.4 Macroscopic findings

At necropsy, the stomach of one animal treated at 1750 mg/kg (No. 8) was distended with gas and liquid, yellowish contents were found in the duodenum and jejunum. Congested lungs, liquid contents in the stomach, duodenum and/or jejunum and/or a discoloration (tan) of the liver or the kidneys were observed in three out of the four animals treated at 5000 mg/kg.

5.0 CONCLUSIONS

The median lethal dose of SYN520453 EC (A15149AC) after single oral administration to female rats, observed over a period of 14 days is:

LD_{50} (female rat): 1750 mg/kg body weight
(Approximate 95 % PL[2] confidence interval: 1239 to 4450 mg/kg)

[2] Profile-likelihood based confidence interval

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).

TABLES SECTION

TABLE 1 **Individual Findings – Mortality / Clinical Signs**

Dose mg/kg bw	Animal No.	Sex	Signs	Test days																	
				1					2	3	4	5	6	7	8	9	10	11	12	13	14	15
				0.5*	1*	2*	3*	5*														
5000	1	F	Ruffled fur	1	1	1	2	2[K]														
			Poor coordination		3																	
			Sedation		3	3	3	3														
			Ventral recumbency		√	√	√	√														
			Tachypnea		√	√	√															
			Deep respiration		√	√	√	√														
			Bradypnea					√														
			Labored respiration					√°														
			Vocalization					√°														
			Rales					√°														
175	2	F	No clinical signs	√	√	√	√	√				√	√	√	√	√	√	√	√	√	√	√
			Ruffled fur						1	1	1											
			Hunched posture						√													
550	3	F	No clinical signs	√						√	√	√	√	√	√	√	√	√	√	√	√	√
			Ruffled fur		1	1	1	1	1													
1750	4	F	No clinical signs	√	√					√	√	√	√	√	√	√	√	√	√	√	√	√
			Ruffled fur			1	1	1	1													
5000	5	F	Ruffled fur	1	1	1	1	1	2[K]													
			Sedation	1	1	2	2	3	3													
			Poor coordination	2	2	2	2	2														
			Ventral recumbency					√	√													
			Labored respiration						√													

Key: 1 slight, 2 moderate, 3 marked, √ noted, [K] killed in extremis

* Examinations were performed during the first 30 minutes and approximately 1, 2, 3 and 5 hours after treatment

°These symptoms were additionally observed approximately 7 hours after dosing and the animal was killed shortly thereafter

No clinical signs were evident in any animal during the acclimatization period.

TABLE 1 **Mortality / Clinical Signs (Continued)**

Dose mg/kg bw	Animal No.	Sex	Signs	Test days																	
				1					2	3	4	5	6	7	8	9	10	11	12	13	14	15
				0.5 *	1*	2*	3*	5*														
1750	6	F	No clinical signs	√						√	√	√	√	√	√	√	√	√	√	√	√	√
			Ruffled fur		1	1	1	1	1													
			Sedation		1	1	1	1														
			Poor coordination			1	1	1														
			Hunched posture				√	√														
5000	7	F	Ruffled fur	1	1	K																
			Sedation	1	2	3																
			Poor coordination	1	2																	
			Ventral recumbency		√	√																
			Tremor			2																
			Deep respiration		√	√																
			Bradypnea		√	√																
			Rales			√																
1750	8	F	Poor coordination	1	1			K														
			Sedation	1	1	2	3	3														
			Ruffled fur	1	1	1	1	2														
			Ventral recumbency	√	√	√	√	√														
			Labored respiration			√	√	√														
			Grinding teeth					√														
550	9	F	No clinical signs	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√

Key: 1 slight, 2 moderate, 3 marked, √ noted, K killed in extremis

* Examinations were performed during the first 30 minutes and approximately 1, 2, 3 and 5 hours after treatment

No clinical signs were evident in any animal during the acclimatization period.

TABLE 1 **Mortality / Clinical Signs (Continued)**

Dose mg/kg bw	Animal No.	Sex	Signs	Test days																	
				1					2	3	4	5	6	7	8	9	10	11	12	13	14	15
				0.5 *	1*	2*	3*	5*														
1750	10	F	No clinical signs							√	√	√	√	√	√	√	√	√	√	√	√	√
			Ruffled fur	1	1	1	1	1	1													
			Sedation	1	2	2	2	2														
			Poor coordination	1	2	2	2	2														
			Ventral recumbency	√	√	√	√	√														
			Labored respiration				√	√														
5000	11	F	Poor coordination	1	1	2	2	K														
			Sedation	1	1	1	1	2														
			Ruffled fur		1	1	1	2														
			Ventral recumbency	√	√	√	√	√														
			Labored respiration					√														
			Convulsions					1														
			Cold to touch					√														

Key: 1 slight, 2 moderate, √ noted, K killed in extremis

* Examinations were performed during the first 30 minutes and approximately 1, 2, 3 and 5 hours after treatment

No clinical signs were evident in any animal during the acclimatization period.

TABLE 2 **Body Weights**

Dose mg/kg bw	Animal No.	Sex	Day -1 (prior to removal of food)	Day 1 (prior to treatment)	Day 8	Day 15
5000	1	F	194.2	193.3	---	---
175	2	F	197.7	189.4	213.2	225.6
550	3	F	189.6	184.7	196.7	204.6
1750	4	F	176.1	173.1	187.8	196.7
5000	5	F	196.1	193.6	---	---
1750	6	F	195.8	191.4	204.0	208.5
5000	7	F	201.0	195.1	---	---
1750	8	F	203.3	202.1	---	---
550	9	F	203.7	193.7	209.1	219.2
1750	10	F	193.7	188.0	198.9	210.7
5000	11	F	190.0	180.1	---	---

Body weights are presented in grams.

TABLE 3 **Macroscopic Findings**

Dose mg/kg body weight	Animal No.	Sex	Mode of death	Findings
5000	1	F	K	Lungs: congested Stomach: liquid contents Duodenum: liquid contents Jejunum: liquid contents
175	2	F	S	No macroscopic findings
550	3	F	S	No macroscopic findings
1750	4	F	S	No macroscopic findings
5000	5	F	K	Stomach: liquid contents Liver: tan discoloration
1750	6	F	S	No macroscopic findings
5000	7	F	K	No macroscopic findings
1750	8	F	K	Stomach: distended with gas Duodenum: contents liquid and yellowish Jejunum: contents liquid and yellowish
550	9	F	S	No macroscopic findings
1750	10	F	S	No macroscopic findings
5000	11	F	K	Stomach: distended with liquid contents Kidneys: tan discoloration

S: scheduled necropsy, K: killed in extremis

APPENDICES SECTION

APPENDIX 1 Certificate of Analysis

syngenta

GLP Testing Facility JH
Analytical Development & Product Chemistry

Jealott's Hill International Research Centre,
Bracknell, Berkshire
RG42 6EY
United Kingdom

Certificate of Analysis

Formulated Material

SYN520453(125 g/L) EC

Batch Identification	**J8092/056**
Design Code	**A15149AC**
Other Product Code(s)	-

Chemical Analysis
(Active Ingredient Content)

– **Identity of the Active Ingredient(s)***	**confirmed**
– **Content of SYN520453 ***	**13.4% w/w corresponding to 128 g/L.** **4.1% w/w SYN534968 corresponding to 39 g/L)** **9.3% w/w SYN534969 corresponding to 89 g/L))**
Methodology used for Characterisation / Reanalysis	Capillary GC

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

Physical Analysis

– **Appearance**	**A uniform mobile clear brown liquid**
– **Density ***	**0.956 g/cm^3**

Stability:

– **Storage Temperature**	**0 < t < 40°C, keep away from direct sunlight**
– **Expiry date**	**December 2009 (Temperate and sub-tropical climates)**

The stability of this test substance will be controlled by reanalysis of material held in the inventory at Syngenta Crop Protection Muenchwilen 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 under GLP protocol. Raw data, documentation, 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 JH at Syngenta, Jealott's Hill International Research Centre, Bracknell, Berkshire, RG42 6EY.

Study Number(s):	08AS001, NS00979
IDS Report Number(s):	10343850
Supplementary Information:	Initial characterisation January 2008. Where applicable, spray tank dilutions should be used within one working day. Handling of the material will follow the guidelines within the appropriate MSDS

Authorisation:

P. Clarke — P M Clarke

15 Jan 2008 — Date

APPENDIX 2 GLP-Certificate

The Swiss GLP Monitoring Authorities

Swiss Federal Office of Public Health

Swiss Agency for the Environment, Forests and Landscape

Swissmedic Swiss Agency for Therapeutic Products

Statement of GLP Compliance

It is hereby confirmed that

during the period of — April 22, 25 – 29, 2005
May 09 – 13, 2005

the following Facilities of — **RCC Ltd**
4452 Itingen
Switzerland

were inspected by the Federal Office of Public Health, the Swiss Agency for Therapeutic Products and the Swiss Agency for the Environment, Forests and Landscape with respect to the compliance with the Swiss legislation on Good Laboratory Practice.

Facilities	**Areas of expertise ***
- Test Facility: Toxicology	**TOX, ACC, OTH (Safety Pharmacology, Alternative Test Systems)**
- Test Facility: Environmental Chemistry & Pharmanalytics	**ACC, ECT, ENF, EMN, PCT, RES, OTH (Animal Metabolism)**
- Archive Facilities	

The inspections were performed in agreement with the OECD Guidelines for National GLP Inspections and Audits. It was found that the aforementioned test facilities were operating in compliance with the Swiss Ordinance relating to Good Laboratory Practice [RS 813.016.5] at the time they were inspected.

Federal Office of Public Health
The Director

Bern, November 2005

Prof. Th. Zeltner

* TOX = Toxicology ; ACC = Analytical and Clinical Chemistry ; ECT = Environmental toxicity on aquatic and terrestrial organisms ; ENF = Behaviour in water, soil and air. Bioaccumulation ; EMN = Studies on effects on mesocosms and natural ecosystems; PCT = Physical-chemical testing ; RES = Residue studies ; OTH = Other, to be specified.