syngenta

Propiconazole/Pydiflumetofen

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

Final Report

DATA REQUIREMENT(S): OECD 403 (2009)
EPA 870.1300 (1998)
JMAFF 12-Nousan-8147 (2000)
EC No. 260/2014

AUTHOR(S): Jennifer Durando, BS

COMPLETION DATE: April 16, 2018

PERFORMING LABORATORY: Product Safety Labs
2394 Highway 130
Dayton, NJ 08810 USA

LABORATORY PROJECT ID: Report Number: 46820
Study Number: 46820
Task Number: TK0186804

SPONSOR(S): Syngenta Crop Protection, LLC
410 Swing Road
Post Office Box 18300
Greensboro, NC 27419-8300 USA

VOLUME 1 OF 1 OF STUDY

STATEMENT OF DATA CONFIDENTIALITY CLAIMS

STATEMENT OF NO DATA CONFIDENTIALITY CLAIMS
UNDER SPECIFIED FIFRA PROVISIONS

No claim of confidentiality, on any basis whatsoever, is made for any information contained in this document. I acknowledge that information not designated as within the scope of FIFRA sec. 10(d)(1)(A), (B), or (C) and which pertains to a registered or previously registered pesticide is not entitled to confidential treatment and may be released to the public, subject to the provisions regarding disclosure to multinational entities under FIFRA 10(g).

Company: Syngenta Crop Protection, LLC
410 Swing Road
Post Office Box 18300
Greensboro, NC 27419-8300 USA

Submitter: Adora Clark
Adora Clark, Ph.D.

Date: April 24, 2018

Syngenta is the owner of this information and data. Syngenta has submitted this material to the United States Environmental Protection Agency specifically under the provisions contained in FIFRA as amended and, hereby, consents to use and disclosure of this material by EPA according to FIFRA. In submitting this material to EPA according to method and format requirements contained in PR Notice 2011-3, we do not waive any protection or right involving this material that would have been claimed by the company if this material had not been submitted to the EPA, nor do we waive any protection or right provided under FIFRA Section 3 (concerning data exclusivity and data compensation) or FIFRA Section 10(g) (prohibiting disclosure to foreign and multinational pesticide companies or their agents).

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study meets the requirements of OECD Principles of GLP (as revised in 1997): ENV/MC/CHEM(98)17, OECD, Paris, 1998; U.S. EPA GLP (FIFRA): 40 CFR Part 160, 1989; Japanese Ministry of Agriculture, Forestry and Fisheries: No. 23-Syouan-5173, 2 February, 2012; and EC Directive 2004/10/EC, Official Journal of the European Union, L50/44, Feb. 20, 2004. Specific information related to the characterization of the test substance as received and tested is the responsibility of the study Sponsor (see Test Substance section).

I, the undersigned, declare that the methods, results and data contained in this report faithfully reflect the procedures used and raw data collected during the study.

Jennifer Durando, BS
Study Director, Product Safety Labs

04/16/2018
Date

Performing Laboratory: **Product Safety Labs**
2394 Highway 130
Dayton, NJ 08810 USA

Monique Inforzato, BS
Representative of Submitter/Sponsor

04/24/2018
Date

Submitter/Sponsor: Syngenta Crop Protection, LLC
410 Swing Road
Post Office Box 18300
Greensboro, NC 27419-8300 USA

FLAGGING STATEMENT

This page is intentionally left blank.

QUALITY ASSURANCE STATEMENT

The Product Safety Labs' Quality Assurance Unit has reviewed this final study report to assure the report accurately describes the methods and standard operating procedures, and that the reported results accurately reflect the raw data of the study.

QA activities for this study:

QA Activity	Performed By	Date Conducted	Date Findings Reported To Study Director And Management
Protocol review	A. Adamiec; B. Simms	Dec 22, 2016[1]; Dec 27, 2017	Dec 22, 2016; Dec 27, 2017
Critical phase inspection (Sighting Study – 5.0 mg/L): *Gravimetric sampling #6*	B. Simms	Oct 31, 2017	Oct 31, 2017
Critical phase inspection (Sighting Study – 2.0 mg/L): *Day 12 in-life observations*	B. Simms	Nov 27, 2017	Nov 27, 2017
Critical phase inspection (Main Test – 2.0 mg/L): *Day 8 in-life observations*	B. Simms	Dec 6, 2017	Dec 6, 2017
Raw data audit	B. Simms	Dec 27, 2017	Dec 27, 2017
Draft report review	B. Simms	Dec 27, 2017	Dec 27, 2017

Final report reviewed by:

Barbara Simms
Quality Assurance Auditor
Product Safety Labs

04/16/2018
Date

[1] PSL's "generic" protocol used for this study was reviewed by the Quality Assurance group on this date.

GENERAL INFORMATION

Contributors

The following contributed to this report in the capacities indicated:

Name	Title
Jennifer Durando, BS	Study Director
Monique Inforzato, BS	Syngenta Study Monitor
Matthew Notta	Primary Scientist
Cynthia Bodnar	Scientist
Harry Maselli, ALAT	Scientist
Stephanie Meade, BS	Scientist
Xiomara Portuguez, BS	Scientist
Mark Schooley	Scientist
Matthew Sorber, BS	Scientist

Study dates

Study initiation date: October 26, 2017
Experimental start date: October 31, 2017
Experimental termination date: December 12, 2017

Deviations from the Guidelines

None

Amendments to Final Protocol

1) Protocol Section 12.C. GLP Compliance for JMAFF was updated to:

   JMAFF GLP: Japanese Ministry of Agriculture, Forestry and Fisheries: No. 23-Syouan-5173, 2 February, 2012.

2) Protocol Cover Form Section II.4 was clarified to state that the documentation of the methods of synthesis/fabrication of the test substance is located at the Sponsor's facility.

Deviations from Final Protocol

None

Retention of samples

The test substance is retained for at least 3 months following submission of the final report, unless otherwise specified by the Sponsor. All remaining test substance will be returned to the Sponsor or properly disposed. Records of sample disposition are maintained by Product Safety Labs (PSL).

Other

Information on care of the test system, equipment maintenance and calibration, storage, usage, and disposition of the test substance, and all other records that would demonstrate adherence to the protocol will be maintained. Facility records which are not specific to the subject study will be maintained by the testing facility and archived according to PSL SOP.

The original signed final report and electronic copies (in Microsoft Word and pdf) of the final report, including the signed QA and GLP Compliance pages will be sent to the Sponsor. A copy of the signed report, together with the protocol (P330 SYN), associated amendments and/or deviations if applicable, and all raw data generated at Product Safety Labs, is maintained in the PSL Archives in Notebook No. 46820: pages 1-100. PSL will maintain these records for a period of at least five years. After this time, the Sponsor will be offered the opportunity to take possession of the records or may request continued archiving by PSL.

Performing laboratory test substance reference number

171023-2H

TABLE OF CONTENTS

1.0 EXECUTIVE SUMMARY

1.1 Study Design

This acute inhalation toxicity test was conducted with rats to determine the potential for Propiconazole/Pydiflumetofen SE (A21573C) to produce toxicity from a single exposure via the inhalation (nose-only exposure) route.

After establishing the desired generation procedures during the pre-test trials, sixteen healthy rats were selected for test. As requested by the sponsor, a sighting test with an initial exposure level of 5.0 mg/L was selected for testing using two animals per sex (2 males and 2 females). Since both females died following exposure, the Sponsor requested to run a second sighting test using two females at an exposure level of 2.0 mg/L, in order to determine a more accurate dose selection for the main test. Since the rats survived the second sighting test, the main test was conducted on ten additional animals (5 males and 5 females) at a 2.0 mg/L exposure level. Chamber concentration and particle size distributions of the test atmosphere were determined periodically during the exposure period. The animals were observed for mortality, signs of gross toxicity, and behavioral changes at least once daily for 14 days following exposure or until death occurred. Body weights were recorded prior to exposure (initial) and again on Days 1, 3, 7, and 14 (terminal) or after death. Necropsies were performed on all animals.

1.2 Results

Sighting (5.02 mg/L)
At 5.02 mg/L, one female died and one female was euthanized for humane reasons on the day of exposure to the test substance. Prior to death, the euthanized female was hypoactive and exhibited irregular respiration, gasping, prone posture and a moribund appearance. Since the other female died prior to chamber removal, clinical signs were not noted for this animal due to the position in the exposure tube. Following exposure, the surviving males were hypoactive and exhibited abnormal respiration, ano-genital staining, and/or an unthrifty appearance. However, the surviving animals recovered by Day 6, gained body weight, and appeared active and healthy for the remainder of the study. Gross necropsy of the deceased animals revealed discoloration of the lungs. No gross abnormalities were noted for any of the surviving animals when necropsied at the conclusion of the 14-day observation period.

Sighting (2.07 mg/L)
At 2.07 mg/L, all animals survived exposure to the test atmosphere and gained body weight during the study. Following exposure, all animals exhibited irregular respiration and were hypoactive. However, the animals recovered by Day 2 and appeared active and healthy for the remainder of the study. No gross abnormalities were noted for any of the animals when necropsied at the conclusion of the 14-day observation period.

Main (2.13 mg/L)
At 2.13 mg/L, all animals survived exposure to the test atmosphere and gained body weight during the study. Following exposure three animals were hypoactive and all animals

exhibited abnormal respiration. However, all animals recovered by Day 6 and appeared active and healthy for the remainder of the study. Gross necropsy of one animal revealed discoloration of the lungs. No gross abnormalities were noted for any of the other animals when necropsied at the conclusion of the 14-day observation period.

1.3 Conclusion

Under the experimental conditions of this study, the acute inhalation median lethal concentration (LC 50) of Propiconazole/Pydiflumetofen SE (A21573C) is greater than 2.13 mg/L in Sprague-Dawley derived, albino male and female rats.

The incidence of mortality at each exposure level is summarized below:

Study Phase	Exposure Concentration (mg/L)	Mortality		
		Males	Females	Total
Sighting	5.02	0/2	2/2	2/4
Sighting	2.07	-[1]	0/2	0/2
Main	2.13	0/5	0/5	0/10

2.0 INTRODUCTION

2.1 Purpose

This study was conducted to investigate the acute inhalation toxicity of the test substance, Propiconazole/Pydiflumetofen SE (A21573C) and, if appropriate, to determine its median lethal concentration LC_{50} (4-hour).

2.2 Regulatory Guidelines

The procedures as described in this protocol are based on the most recent version of the following testing guidelines:

- OECD Guidelines for Testing of Chemicals, Test No. 403 (2009)
- U.S. EPA Health Effects Test Guidelines, OPPTS 870.1300 (1998)
- JMAFF 12-Nousan-8147 (2000)
- Official Journal of the European Communities. Methods for the Determination of Toxicity and Other Health Effects, Part B.2 (Acute Toxicity Inhalation) Council Regulation (EC) No. 260/2014

[1] Based on the results of the 5.0 mg/L sighting test, only two females were tested at the 2.0 mg/L sighting test.

2.3 Test Facility

This study was conducted at Product Safety Labs' (PSL) test facility at 2394 US Highway 130, Dayton, New Jersey 08810. In the opinion of the Sponsor and the Study Director, this study did not unnecessarily duplicate any previous work.

3.0 MATERIALS AND METHODS

3.1 Test Substance

The test substance was identified as: Propiconazole/Pydiflumetofen SE
A21573C
Batch ID 1007839

It was received on October 23, 2017 and was further identified with PSL Reference Number 171023-2H. The test substance was stored at room temperature. Documentation of the methods of synthesis, fabrication, or derivation of the test substance is retained by the Sponsor.

Characterization of the test substance was provided to PSL by the Sponsor (see Appendix 1):

Composition: Pydiflumetofen (151 g/L), 13.7% w/w
Propiconazole (128 g/L), 11.6% w/w

Physical Description: Beige liquid

pH: Not available

Stability: Test substance was expected to be stable for the duration of testing.

Recertification Date: End of October 2020

3.2 Experimental Design

3.2.1 Animals

Species/Strain: Rat/Sprague-Dawley derived, albino.

Number of Animals: 16
Sighting (5.02 mg/L): 4
Sighting (2.07 mg/L): 2
Main (2.13 mg/L): 10

Sex: 7 Males and 9 Females. Females assigned to test were nulliparous and non-pregnant.
Sighting (5.02 mg/L): 2 Males and 2 Females
Sighting (2.07 mg/L): 2 Females
Main (2.13 mg/L): 5 Males and 5 Females

Age/Body Weight: Young adult (8-11 weeks)/males 230-373 grams and females 170-231 grams at experimental start.

Source: Received from SAGE® Labs on October 25 and November 8, 2017.

Justification of Test System and Route of Exposure: The rat was the system of choice because, historically, it has been the preferred and most commonly used species for acute inhalation toxicity tests. The inhalation route of administration was used because it is recommended in the referenced guidelines, and because human exposure may occur via this route.

3.2.2 Husbandry

Housing: The animals were singly housed in suspended stainless steel caging, which conforms to the size recommendations in the most recent *Guide for the Care and Use of Laboratory Animals* (Natl. Res. Council, 2011). Enrichment (e.g., toy) was placed in each cage. Litter paper was placed beneath the cage and was changed at least three times per week.

Animal Room Temperature: 19-23ºC

Animal Room Relative Humidity: 41-58%

Animal Room Air Changes: 12 or 13/hour. Airflow measurements are evaluated regularly and the records are kept on file at Product Safety Labs.

Photoperiod: 12-hour light/dark cycle

Acclimation Period: 6, 7, or 20 days

3.2.3 Food and feeding

Food: Envigo Teklad Global 16% Protein Rodent Diet® #2016. The diet was available *ad libitum*, except during the exposure.

Water: Filtered tap water was supplied *ad-libitum*.

Contaminants: There were no known contaminants reasonably expected to be found in the food or water at levels which would have interfered with the results of this study. Analyses of the food and water are conducted regularly and the records are kept on file at Product Safety Labs.

3.2.4 Identification

Cage: Each cage was identified with a cage card indicating at least the study number and identification and sex of the animal.

Animal: A number was allocated to each rat on receipt and a stainless steel ear tag bearing this number was attached to the rat. This number, together with a sequential animal number assigned to study number 46820, constituted unique identification. Only the sequential animal number is presented in this report.

3.3 Preparation of Test Substance

The test substance was aerosolized as received and kept on a magnetic stirrer during aerosolization.

3.4 Pre-Test Trials

Prior to initiation of the study phases, pre-test trials were conducted to establish generation procedures to achieve, to the extent possible, the desired chamber concentration and desired particle size distribution (mass median aerodynamic diameter between 1 and 4 µm). Specific details of the pre-test trials are recorded in Tables 1 through 3. In these trials, the following adjustments were made in an attempt to achieve these objectives:

Air Pressure:	constant
Compressed Generator Airflow:	constant
Compressed Mixing Airflow:	constant
Total Airflow:	constant
Liquid Pump Setting:	varied
Liquid Pump Type:	varied
Tubing Size:	constant
Atomization System:	constant
Clean-Out Needle and Fluid Cap:	constant
Air Cap:	constant
Vacuum Pump:	varied
Concentration Sampling Time:	constant

The procedures and aerosolization equipment used in the study phases below were based on the results of pre-test trial numbers 2, 5 and 8. In each instance, the conditions of generation were modified or confirmed to achieve the targeted chamber concentration with a desirable particle size distribution.

Study Phase	Target Concentration (mg/L)	Trial #	Trial Concentration (mg/L)	MMAD (µm)
Sighting	5.0	2	5.08	3.32
Sighting	2.0	5	2.10	3.64
Main	2.0	8	2.05	3.25

3.5 Inhalation Procedures

For each exposure, the exposure chamber, air supply, and equipment used to measure particle size distribution, airflow, and chamber concentration were the same as used during the respective pre-test trials and are described generally below. Specific details of each exposure are recorded in Tables 4 through 11.

Nose-Only Exposure Chamber: A nose-only inhalation chamber was used for exposure. Animals were individually housed in polycarbonate holding tubes which seal to the chamber with an "O" ring during exposure. The base unit terminates the chamber with a 0.5-inch diameter tube for discharged air.

Air Supply: Filtered generator air was supplied to the spray atomization nozzle by an air compressor, and measured with a Mass Flow Controller. Additional filtered mixing air from the same air compressor, measured with a Mass Flow Controller, was introduced into the chamber to help uniformly distribute the test atmosphere by creating a vortex at the chamber inlet. Chamber airflow was monitored throughout the exposure period and recorded periodically. The exposure was conducted under slight negative pressure.

Ambient Conditions: The temperature and relative humidity within the exposure chamber as well as the room were monitored continuously during exposure, and were measured with a temperature-humidity monitor. Temperature and relative humidity values were recorded every 15 minutes for the first hour of exposure and approximately every 15 or 30 minutes thereafter.

Atmosphere Generation: The test atmosphere was generated using a nebulizer. The test substance was metered to the atomization nozzle through Tygon® tubing, using a peristaltic pump.

Chamber Concentration Measurements: Gravimetric samples were withdrawn at 6 intervals from the breathing zone of the animals. Samples were collected using 37 mm glass fiber filters (Whatman™ GF/B) in a filter holder attached by ¼ inch Tygon® tubing to a vacuum pump. Filter papers were weighed before and after collection to determine the mass collected. This value was divided by the total volume of air sampled to determine the chamber concentration. Sample airflows were measured using a Mass Flow Controller.

Particle Size Distribution: An eight-stage 1 ACFM Andersen Ambient Particle Sizing Sampler was used to assess the particle size distribution of the test atmosphere. Samples were withdrawn from the breathing zone of the animals at two intervals. The filter paper collection stages were weighed before and after sampling to determine the mass collected upon each stage. The mass median aerodynamic diameter (MMAD) and geometric standard deviation (GSD) were determined graphically using two-cycle logarithmic probit axes.

Exposure Period: The animals were exposed to the targeted chamber concentration for at least 4 hours. The exposure period was extended beyond 4 hours to allow the chamber to reach equilibrium (T_{99}). At the end of the exposure period, the generation was terminated and the chamber was operated for at least 15 minutes further with clean air to allow the test

atmosphere to fully dissipate. At the end of this period the animals were removed from the exposure tubes. Prior to being returned to their cages, excess test substance was removed from the fur of each animal by rinsing with tap water and wiping with clean paper towels.

3.6 Selection of Animals

On the day of and prior to each exposure, the rats were examined for health and weighed. Sixteen healthy, naive rats not previously tested were selected for exposure. Two males and four females were selected for the sighting studies at 5.0 mg/L and 2.0 mg/L. Five males and five females were selected for the main study at 2.0 mg/L.

3.7 Body Weights

Individual body weights of the animals were recorded prior to test substance exposure (initial) and again on Days 1, 3, 7, and 14 (terminal) or after death.

3.8 Cage-Side Observations

All animals were observed for mortality during the exposure period. The animals were examined for signs of gross toxicity, and behavioral changes upon removal from the exposure tube and at least once daily thereafter for 14 days or until death occurred. Observations included gross evaluation of skin and fur, eyes and mucous membranes, respiratory, circulatory, autonomic and central nervous systems, somatomotor activity and behavior pattern. Particular attention was directed to observation of tremors, convulsions, salivation, diarrhea, and coma.

3.9 Necropsy

Surviving rats were euthanized on Day 14 via CO_2 inhalation. Gross necropsies were performed on all deceased and euthanized animals. Tissues and organs of the thoracic and abdominal cavities were examined.

3.10 Statistical Analysis

Statistical analysis was limited to the calculation of the mean and standard deviation. Since no death occurred at the limit dose, the LC_{50} was determined without the need of statistical analysis.

4.0 RESULTS AND DISCUSSION

Details of all pre-test exposure trials are described in Tables 1 through 3. A summary of test exposure information is presented in Tables 4 through 11. A summary of mortalities at each exposure level, individual body weights, and cage-side and necropsy observations are presented in Tables 12 through 21, respectively. The Certificate of Analysis is presented in Appendix 1.

4.1 Test Atmosphere Concentration

Sighting (5.02 mg/L)
The gravimetric chamber and nominal chamber concentrations were 5.02 mg/L and 64.03 mg/L, respectively. The average mass median aerodynamic diameter was estimated to be 2.96 µm based on graphic analysis of the particle size distribution as measured with a 1 ACFM Andersen Ambient Particle Sizing Sampler with an average geometric standard deviation of 2.31.

Sighting (2.07 mg/L)
The gravimetric chamber and nominal chamber concentrations were 2.07 mg/L and 23.13 mg/L, respectively. The average mass median aerodynamic diameter was estimated to be 3.49 µm based on graphic analysis of the particle size distribution as measured with a 1 ACFM Andersen Ambient Particle Sizing Sampler with an average geometric standard deviation of 2.49.

Main (2.13 mg/L)
The gravimetric chamber and nominal chamber concentrations were 2.13 mg/L and 24.34 mg/L, respectively. The average mass median aerodynamic diameter was estimated to be 2.89 µm based on graphic analysis of the particle size distribution as measured with a 1 ACFM Andersen Ambient Particle Sizing Sampler with an average geometric standard deviation of 2.25.

Study Phase	Exposure Concentration (mg/L)	Standard Deviation	Nominal Concentration (mg/L)[1]	Mass Median Aerodynamic Diameter[2] (µm)	Geometric Standard Deviation (GSD)
Sighting	5.02	0.15	64.03	2.96	2.31
Sighting	2.07	0.09	23.13	3.49	2.49
Main	2.13	0.13	24.34	2.89	2.25

4.2 Clinical Observations

Sighting (5.02 mg/L)
One female died and one female was euthanized for humane reasons on the day of exposure to the test substance. Prior to death, the euthanized female was hypoactive and exhibited irregular respiration, gasping, prone posture and a moribund appearance. Since the other female died prior to chamber removal, clinical signs were not noted for this animal due to the position in the exposure tube. Following exposure, the surviving males were hypoactive and

[1] Nominal Concentration (mg/L) = Total Test Substance Used (mg) / Total Airflow (Lpm) x Total Time (min)
[2] The mass median aerodynamic diameter was calculated based on graphic analysis of the particle size distribution as measured with 1 ACFM Andersen Ambient Particle Sizing Sampler.

exhibited abnormal respiration, ano-genital staining, and/or an unthrifty appearance. However, the surviving animals recovered by Day 6 and appeared active and healthy for the remainder of the study.

Sighting (2.07 mg/L)
Following exposure, all animals exhibited irregular respiration and were hypoactive. However, all animals recovered by Day 2 and appeared active and healthy for the remainder of the study.

Main (2.13 mg/L)
Following exposure three animals were hypoactive and all animals exhibited abnormal respiration. However, all animals recovered by Day 6 and appeared active and healthy for the remainder of the study.

4.3 Bodyweight

Sighting (5.02 mg/L)
The surviving males gained body weight during the study.

Sighting (2.07 mg/L)
All animals gained body weight during the study.

Main (2.13 mg/L)
All animals gained body weight during the study.

4.4 Necropsy

Sighting (5.02 mg/L)
Gross necropsy of the deceased animals revealed discoloration of the lungs. No gross abnormalities were noted for any of the surviving animals when necropsied at the conclusion of the 14-day observation period.

Sighting (2.07 mg/L)
No gross abnormalities were noted for any of the animals when necropsied at the conclusion of the 14-day observation period.

Main (2.13 mg/L)
Gross necropsy of one animal revealed discoloration of the lungs. No gross abnormalities were noted for any of the surviving animals when necropsied at the conclusion of the 14-day observation period.

5.0 CONCLUSIONS

Under the experimental conditions of this study, the acute inhalation median lethal concentration (LC 50) of Propiconazole/Pydiflumetofen SE (A21573C) is greater than 2.13 mg/L in Sprague-Dawley derived, albino male and female rats.

6.0 REFERENCES

National Research Council. (2011). *Guide for the Care and Use of Laboratory Animals (8th ed.)*. Washington, DC: The National Academies Press.

TABLES SECTION

TABLE 1 Preparation and Generation System for the Pre-Test Trials

Equipment	Type and Model
Chamber	ADG Developments LTD 28 liter (Nose-Only Inhalation Chamber)
Air Supply	Powerex Air Compressor (Model SES050822)
Liquid Pump	Masterflex® Peristaltic Pump (Model 7520-35) Masterflex® Peristaltic Pump (Model 77521-50)
Tubing for Pump	Tygon® Size 14
Atomization	Spraying Systems Co. $^{1}/_{4}$ inch JCO Nebulizer
Clean-Out Needle and Fluid Cap	Spraying Systems Co. FC3
Air Cap	Spraying Systems Co. AC1001
Compressed Generator Air Measurements	Omega Mass Flow Controller (Model FMA-5541)
Compressed Mixing Air Measurements	Omega Mass Flow Controller (Model FMA-5527)
Sample Airflow Measurements	Aalborg Mass Flow Controller (Model GFC-17)
Vacuum Pump	Westech (Model 9803-88) GAST (Model 1531-107B-G557X)

TABLE 2 Pre-Test Exposure Trials

Trial No.	Generator/ Mixing Air Pressure (psi)	Compressed Generator Air (Lpm)	Compressed Mixing Air (Lpm)	Total Air (Lpm)	Pump Setting	Trial Concentration (mg/L)	Particle Size Sampled
1	30/30	50.0	10.0	60.0	15.0	5.08	No
2	30/30	50.0	10.0	60.0	15.0	5.08	Yes
3	30/30	50.0	10.0	60.0	8.0	3.15	No
4	30/30	50.0	10.0	60.0	6.5	2.75	No
5	30/30	50.0	10.0	60.0	5.5	2.10	Yes
6	30/30	50.0	10.0	60.0	6.0	1.00	No
7	30/30	50.0	10.0	60.0	8.0	1.55	No
8	30/30	50.0	10.0	60.0	10.0	2.05	Yes

TABLE 3 Summary of Pre-Test Exposure Trials[1]

Trial No.	Trial Concentration (mg/L)	Mass Median Aerodynamic Diameter[2] (µm)
2	5.08	3.32
5	2.10	3.64
8	2.05	3.25

[1] See Tables 1 and 2 for details of generation system applicable to the trial.
[2] This figure is an estimation based on graphic analysis of the particle size distribution as measured with a 1 ACFM Andersen Ambient Sizing Sampler.

TABLE 4 Generation System for Exposure

Exposure Concentration (mg/L)	5.02	2.07	2.13
Study Phase	**Sighting**	**Sighting**	**Main**
Equipment	**Type and Model**	**Type and Model**	**Type and Model**
Chamber	ADG Developments LTD 28 liter (Nose-Only Inhalation Chamber)	ADG Developments LTD 28 liter (Nose-Only Inhalation Chamber)	ADG Developments LTD 28 liter (Nose-Only Inhalation Chamber)
Air Supply	Powerex Air Compressor (Model SES050822)	Powerex Air Compressor (Model SES050822)	Powerex Air Compressor (Model SES050822)
Liquid Pump	Masterflex® Peristaltic Pump (Model 7520-35)	Masterflex® Peristaltic Pump (Model 7520-35)	Masterflex® Peristaltic Pump (Model 77521-50)
Tubing for Pump	Tygon® Size 14	Tygon® Size 14	Tygon® Size 14
Atomization	Spraying Systems Co. $^1/_4$ inch JCO Nebulizer	Spraying Systems Co. $^1/_4$ inch JCO Nebulizer	Spraying Systems Co. $^1/_4$ inch JCO Nebulizer
Clean-Out Needle and Fluid Cap	Spraying Systems Co. FC3	Spraying Systems Co. FC3	Spraying Systems Co. FC3
Air Cap	Spraying Systems Co. AC1001	Spraying Systems Co. AC1001	Spraying Systems Co. AC1001
Compressed Generator Air Measurements	Omega Mass Flow Controller (Model FMA-5541)	Omega Mass Flow Controller (Model FMA-5541)	Omega Mass Flow Controller (Model FMA-5541)
Compressed Mixing Air Measurements	Omega Mass Flow Controller (Model FMA-5527)	Omega Mass Flow Controller (Model FMA-5527)	Omega Mass Flow Controller (Model FMA-5527)
Sample Airflow Measurements	Aalborg Mass Flow Controller (Model GFC-17)	Aalborg Mass Flow Controller (Model GFC-17)	Aalborg Mass Flow Controller (Model GFC-17)
Vacuum Pump	Westech (Model 9803-88)	Westech (Model 9803-88)	GAST (Model 1531-107B-G557X)
Temperature-Humidity Monitor	Fisher Scientific (Model 11-661-18)	Fisher Scientific (Model 11-661-18)	Fisher Scientific (Model 11-661-18)

TABLE 5 Exposure Conditions

Exposure Concentration (mg/L)	**5.02**	**2.07**	**2.13**
Study Phase	**Sighting**	**Sighting**	**Main**
Compressed Generator Air (Lpm)	50	50	50
Compressed Mixing Air (Lpm)	10	10	10
Total Air (Lpm)[1]	60	60	60
Compressed Generator/Mixing Air (psi)	30/30	30/30	30/30
T_{90} (min)[2]	1.07	1.07	1.07
T_{99} (min)[3]	2.15	2.15	2.15
Exposure Chamber Temp. Range (ºC)	18-19	18-19	20-22
Exposure Chamber Relative Humidity Range (%)	40-43	35	18-24
Ambient Room Temp. Range (ºC)	19	20-21	21-23
Ambient Room Relative Humidity Range (%)	42-43	40-45	40-44
Total Time of Exposure (min)	243	243	243
Number of Air Changes Per Hour	129	129	129

[1] Total air = compressed generator air + compressed mixing air
[2] Time for 90% equilibration of the chamber atmosphere.
[3] Time for 99% equilibration of the chamber atmosphere.

TABLE 6 Gravimetric Chamber Concentrations

Target Concentration (mg/L)	Sample Number	Time of Sample (hour)	Mass Collected (mg)	Airflow Sampled (Lpm)	Collection Time (min)	Exposure Concentration (mg/L)
5.0 mg/L (Sighting)	1	0.5	19.8	4.0	1	4.95
	2	1	20.4	4.0	1	5.10
	3	2	20.2	4.0	1	5.05
	4	2.5	20.2	4.0	1	5.05
	5	3.5	20.8	4.0	1	5.20
	6	3.75	19.0	4.0	1	4.75
Average ± Standard Deviation						5.02 ± 0.16
2.0 mg/L (Sighting)	1	0.5	8.1	4.0	1	2.03
	2	1	8.0	4.0	1	2.00
	3	2	8.0	4.0	1	2.00
	4	2.5	8.1	4.0	1	2.03
	5	3.5	8.4	4.0	1	2.10
	6	3.75	8.9	4.0	1	2.23
Average ± Standard Deviation						2.07 ± 0.09
2.0 mg/L (Main)	1	0.5	9.5	4.0	1	2.38
	2	1	8.5	4.0	1	2.13
	3	2	8.6	4.0	1	2.15
	4	2.5	8.1	4.0	1	2.03
	5	3.5	8.2	4.0	1	2.05
	6	3.75	8.1	4.0	1	2.03
Average ± Standard Deviation						2.13 ± 0.13

TABLE 7 Nominal Chamber Concentration

Study Phase	Exposure Concentration (mg/L)	Total Test Substance Used (g)	Total Airflow (Lpm)	Total Time of Exposure (min)	Nominal Concentration[1] (mg/L)
Sighting	5.02	933.6	60	243	64.03
Sighting	2.07	337.2	60	243	23.13
Main	2.13	354.9	60	243	24.34

[1] Nominal Concentration (mg/L) = $\frac{\text{Total Test Substance Used (mg)}}{\text{Total Airflow (Lpm)} \times \text{Total Time (min)}}$

TABLE 8 Particle Size Distribution (Sighting 5.02 mg/L)

Stage	Effective Cutoff Diameter (µm)	% of Total Particles Captured (by weight)	Cumulative (%)[1]
Sample 1			
0	9.0	2.4	97.6
1	5.8	12.3	85.3
2	4.7	18.0	67.3
3	3.3	29.4	37.9
4	2.1	18.0	19.9
5	1.1	14.2	5.7
6	0.7	1.9	3.8
7	0.4	1.9	1.9
Final	0	1.9	0.0
Sample 2			
0	9.0	4.0	96.0
1	5.8	12.4	83.6
2	4.7	13.8	69.8
3	3.3	29.3	40.4
4	2.1	18.2	22.2
5	1.1	15.1	7.1
6	0.7	3.6	3.6
7	0.4	1.8	1.8
Final	0	1.8	0.0

[1] Percent of particles smaller than corresponding effective cutoff diameter.

TABLE 9 Particle Size Distribution (Sighting 2.07 mg/L)

Stage	Effective Cutoff Diameter (µm)	% of Total Particles Captured (by weight)	Cumulative (%)[1]
Sample 1			
0	9.0	5.3	94.7
1	5.8	18.7	76.0
2	4.7	12.7	63.3
3	3.3	26.0	37.3
4	2.1	18.7	18.7
5	1.1	11.3	7.3
6	0.7	2.0	5.3
7	0.4	2.7	2.7
Final	0	2.7	0.0
Sample 2			
0	9.0	7.3	92.7
1	5.8	21.1	71.6
2	4.7	11.9	59.6
3	3.3	34.9	24.8
4	2.1	0.0	24.8
5	1.1	18.3	6.4
6	0.7	3.7	2.8
7	0.4	1.8	0.9
Final	0	0.9	0.0

[1] Percent of particles smaller than corresponding effective cutoff diameter.

TABLE 10 Particle Size Distribution (Main 2.13 mg/L)

Stage	Effective Cutoff Diameter (µm)	% of Total Particles Captured (by weight)	Cumulative (%)[1]
Sample 1			
0	9.0	5.6	94.4
1	5.8	14.5	79.8
2	4.7	7.3	72.6
3	3.3	17.7	54.8
4	2.1	32.3	22.6
5	1.1	16.9	5.6
6	0.7	3.2	2.4
7	0.4	1.6	0.8
Final	0	0.8	0.0
Sample 2			
0	9.0	3.2	96.8
1	5.8	12.6	84.2
2	4.7	6.3	77.9
3	3.3	23.2	54.7
4	2.1	32.6	22.1
5	1.1	14.7	7.4
6	0.7	3.2	4.2
7	0.4	3.2	1.1
Final	0	1.1	0.0

[1] Percent of particles smaller than corresponding effective cutoff diameter.

TABLE 11 Summary of Particle Size Distribution

Exposure Concentration (mg/L)	Sample No.	Time of Sample (hours)	Collection Time (minutes)	Mass Median Aerodynamic Diameter[1] (µm)	Geometric Standard Deviation
5.02 (Sighting)	1	1.5	1	2.94	2.29
	2	3	1	2.98	2.33
			Average	2.96	2.31
2.07 (Sighting)	1	1.5	1	3.27	2.50
	2	3	1	3.71	2.47
			Average	3.49	2.49
2.13 (Main)	1	1.5	1	3.05	2.27
	2	3	1	2.73	2.22
			Average	2.89	2.25

[1] The mass median aerodynamic diameter was calculated based on graphic analysis of the particle size distribution as measured with 1 ACFM Andersen Ambient Particle Sizing Sampler.

TABLE 12 Summary of Mortality

Study Phase	Exposure Concentration (mg/L)	Number Dead/Number Tested		
		Males	Females	Combined
Sighting	5.02	0/2	2/2	2/4
Sighting	2.07	-[1]	0/2	0/2
Main	2.13	0/5	0/5	0/10
LC_{50} (mg/L):		Is greater than 2.13 mg/L		N/A

N/A – Not applicable

[1] Based on the results of the 5.0 mg/L sighting test, only two females were tested at the 2.0 mg/L sighting test.

TABLE 13 Individual Body Weights/Weight Gains And Mortality (Sighting 5.02 mg/L)

Animal No.	Sex	Body Weight (g)									Mortality	
		Day 0 Weight	Day 1 Weight	Gain*	Day 3 Weight	Gain*	Day 7 Weight	Gain*	Day 14 Weight	Gain*	Day	Weight (g)
3301	M	236	210	-26	226	-10	249	13	296	60	E	-
3302	M	230	220	-10	243	13	274	44	324	94	E	-
3303	F	170	-	-	-	-	-	-	-	-	0	166
3304	F	180	-	-	-	-	-	-	-	-	0	175

* - Body weight gain from Day 0.
E - Euthanized via CO_2 inhalation after weighing on Day 14
M - Male
F - Female

TABLE 14 Individual Cage-Side Observations (Sighting 5.02 mg/L)

Animal Number	Animal Sex	Dose Level (mg/L)	Observation	Day of Observation (x=observation is present)															
				CR[1]	0(2 hrs)	1	2	3	4	5	6	7	8	9	10	11	12	13	14
3301	M	5.02	Active and healthy								x	x	x	x	x	x	x	x	x
			Irregular respiration	x	x	x	x	x	x	x									
			Hypoactivity	x	x	x	x												
			Ano-genital staining			x	x												
			Unthrifty			x	x												
			Dry rales						x										
3302	M	5.02	Active and healthy				x	x	x	x	x	x	x	x	x	x	x	x	x
			Irregular respiration	x	x	x													
			Hypoactivity	x	x	x													
			Ano-genital staining			x													
3303	F	5.02	Dead	x															
3304	F	5.02	Irregular respiration	x															
			Gasping	x															
			Prone	x															
			Hypoactivity	x															
			Moribund	x															
			Euthanized for humane reasons		x														

[1] CR - Removal from the exposure tube.

TABLE 15 Individual Necropsy Observations (Sighting 5.02 mg/L)

Animal Number	Animal Sex	Dose Level (mg/L)	Organ / Tissue	Grade	Observation	Color
3301	M	5.02	All tissues and organs		No gross abnormalities	
3302	M	5.02	All tissues and organs		No gross abnormalities	
3303	F	5.02	Lungs	Extreme		Red
3304	F	5.02	Lungs	Extreme		Red

TABLE 16 Individual Body Weights/Weight Gains (Sighting 2.07 mg/L)

Animal No.	Sex	Body Weight (g)								
		Day 0 Weight	Day 1 Weight	Gain*	Day 3 Weight	Gain*	Day 7 Weight	Gain*	Day 14 Weight	Gain*
3305	F	202	200	-2	204	2	211	9	236	34
3306	F	202	197	-5	203	1	208	6	226	24

* - Body weight gain from Day 0.
F - Female

TABLE 17 Individual Cage-Side Observations (Sighting 2.07 mg/L)

Animal Number	Animal Sex	Dose Level (mg/L)	Observation	Day of Observation (x=observation is present)															
				CR[1]	0(1.5 hrs)	1	2	3	4	5	6	7	8	9	10	11	12	13	14
3305	F	2.07	Active and healthy				x	x	x	x	x	x	x	x	x	x	x	x	x
			Irregular respiration	x	x	x													
			Moist rales	x	x														
			Hypoactivity	x	x														
3306	F	2.07	Active and healthy			x	x	x	x	x	x	x	x	x	x	x	x	x	x
			Irregular respiration	x	x														
			Moist rales	x	x														
			Hypoactivity	x	x														

[1] CR - Removal from the exposure tube.

TABLE 18 Individual Necropsy Observations (Sighting 2.07 mg/L)

Animal Number	Animal Sex	Dose Level (mg/L)	Organ / Tissue	Observation
3305	F	2.07	All tissues and organs	No gross abnormalities
3306	F	2.07	All tissues and organs	No gross abnormalities

TABLE 19 Individual Body Weights/Weight Gains (Main 2.13 mg/L)

Animal No.	Sex	Body Weight (g)								
		Day 0 Weight	Day 1 Weight	Gain*	Day 3 Weight	Gain*	Day 7 Weight	Gain*	Day 14 Weight	Gain*
3307	M	363	351	-12	349	-14	362	-1	385	22
3308	M	373	368	-5	380	7	392	19	421	48
3309	M	327	323	-4	323	-4	333	6	353	26
3310	M	365	353	-12	351	-14	369	4	399	34
3311	M	332	327	-5	330	-2	342	10	364	32
3312	F	228	220	-8	221	-7	229	1	235	7
3313	F	220	222	2	222	2	227	7	236	16
3314	F	210	212	2	219	9	225	15	237	27
3315	F	231	230	-1	239	8	239	8	248	17
3316	F	207	203	-4	210	3	214	7	228	21

* - Body weight gain from Day 0.
M -Male
F - Female

TABLE 20 Individual Cage-Side Observations (Main 2.13 mg/L)

Animal Number	Animal Sex	Dose Level (mg/L)	Observation	Day of Observation (x=observation is present)															
				CR[1]	0(1 hr)	1	2	3	4	5	6	7	8	9	10	11	12	13	14
3307	M	2.13	Active and healthy								x	x	x	x	x	x	x	x	x
			Moist rales	x	x	x	x												
			Irregular respiration	x	x	x	x	x	x	x									
			Facial staining	x	x														
3308	M	2.13	Active and healthy			x	x	x	x	x	x	x	x	x	x	x	x	x	x
			Moist rales	x	x														
			Irregular respiration	x	x														
			Facial staining	x	x														
3309	M	2.13	Active and healthy					x	x	x	x	x	x	x	x	x	x	x	x
			Moist rales	x	x	x													
			Irregular respiration	x	x	x	x												
			Facial staining	x	x														
3310	M	2.13	Active and healthy								x	x	x	x	x	x	x	x	x
			Moist rales	x	x	x	x	x	x	x									
			Irregular respiration	x	x	x	x	x	x	x									
			Facial staining	x	x														

[1] CR - Removal from the exposure tube.

TABLE 20 Individual Cage-Side Observations (Main 2.13 mg/L) (Continued)

Animal Number	Animal Sex	Dose Level (mg/L)	Observation	Day of Observation (x=observation is present)															
				CR[1]	0(1 hr)	1	2	3	4	5	6	7	8	9	10	11	12	13	14
3311	M	2.13	Active and healthy								x	x	x	x	x	x	x	x	x
			Moist rales	x	x														
			Irregular respiration	x	x	x	x	x	x	x									
			Facial staining	x	x														
3312	F	2.13	Active and healthy								x	x	x	x	x	x	x	x	x
			Moist rales	x	x	x	x	x	x	x									
			Irregular respiration	x	x	x													
			Hypoactivity	x															
			Facial staining	x	x														
3313	F	2.13	Active and healthy								x	x	x	x	x	x	x	x	x
			Moist rales	x	x														
			Irregular respiration	x	x	x	x	x	x	x									
			Facial staining	x	x														

[1] CR - Removal from the exposure tube.

TABLE 20 Individual Cage-Side Observations (Main 2.13 mg/L) (Continued)

Animal Number	Animal Sex	Dose Level (mg/L)	Observation	Day of Observation (x=observation is present)															
				CR[1]	0(1 hr)	1	2	3	4	5	6	7	8	9	10	11	12	13	14
3314	F	2.13	Active and healthy								x	x	x	x	x	x	x	x	x
			Moist rales	x	x	x													
			Irregular respiration	x	x	x	x	x	x	x									
			Facial staining	x	x														
3315	F	2.13	Active and healthy					x	x	x	x	x	x	x	x	x	x	x	x
			Moist rales	x	x														
			Irregular respiration	x	x	x	x												
			Hypoactivity	x															
			Facial staining	x	x														
3316	F	2.13	Active and healthy								x	x	x	x	x	x	x	x	x
			Moist rales	x	x	x													
			Irregular respiration	x	x	x	x	x	x	x									
			Hypoactivity		x														
			Facial staining	x	x														

[1] CR - Removal from the exposure tube.

TABLE 21 Individual Necropsy Observations (Main 2.13 mg/L)

Animal Number	Animal Sex	Dose Level (mg/L)	Organ / Tissue	Grade	Observation	Color
3307	M	2.13	All tissues and organs		No gross abnormalities	
3308	M	2.13	All tissues and organs		No gross abnormalities	
3309	M	2.13	All tissues and organs		No gross abnormalities	
3310	M	2.13	All tissues and organs		No gross abnormalities	
3311	M	2.13	All tissues and organs		No gross abnormalities	
3312	F	2.13	All tissues and organs		No gross abnormalities	
3313	F	2.13	Lungs	Extreme		Red
3314	F	2.13	All tissues and organs		No gross abnormalities	
3315	F	2.13	All tissues and organs		No gross abnormalities	
3316	F	2.13	All tissues and organs		No gross abnormalities	

APPENDICES SECTION

APPENDIX 1 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 1 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
Analytical and Product Chemistry Department

Date

COA Number: USGR170462

Page 2 of 2