DP Barcode: 444982 MRID No.: 50449801 & 50449802

DATA EVALUATION RECORD
CHRONIC (REPEAT DOSE) TOXICITY TESTS WITH THE HONEY BEE (*Apis mellifera*) LARVAE
NON-GUIDELINE

1. CHEMICAL: Difenoconazole PC Code No.: 128847

2. TEST MATERIAL: Difenoconazole (CGA 169374) Technical Purity: 93.9%

3. CITATION

Authors:	Kling, A.
Title:	Difenoconazole: Honey Bee (*Apis mellifera* L.) 22 Day Larval Toxicity Test (Repeated Exposure).
Study Completion Date:	December 20, 2017
Laboratory:	Eurofins Agroscience Services EcoChem GmbH / Eurofins Agroscience Services Ecotox GmbH Niefern, Öschelbronn, Germany
Sponsor:	Syngenta Ltd Jealott's Hill International Research Centre Bracknell, Berkshire, RG42 6EY, United Kingdom
Laboratory Report ID:	S17-01517
MRID:	50449801 & 50449802
DP Barcode:	444982

4. REVIEWED BY: Rebecca L. Bryan, Staff Scientist, CDM/CSS-Dynamac JV

Signature: Rebecca L. Bryan **Date:** 5/15/2018

5. REVIEWED BY: Moncie V. Wright, Environmental Scientist, CDM/CSS-Dynamac JV

Signature: Moncie V Wright **Date:** 5/16/2018

(Stats and DER update completed 11/12/2019)

REVIEWED BY: Melissa E. Bridges, Ph.D., Biologist, EPA/OPP/EFED/EISB

Signature: Bridges, Melissa Digitally signed by Bridges, Melissa Date: 2020.05.11 15:15:40 -04'00' **Date:**

Frank T. Farruggia, Ph.D., Senior Biologist, EPA/OPP/EFED/ERB1

Signature: 2020.05.11 16:56:19 -04'00' **Date:**

This Data Evaluation Record may have been altered by the Environmental Fate and Effects Division subsequent to signing by CDM Smith/CSS-Dynamac JV personnel. The CDM/CSS-Dynamac Joint Venture role does not include establishing Agency policies.

6. STUDY PARAMETERS

Test Species: Honey bees (*Apis mellifera carnica* Pollmann)
Age of Test Organisms at Test Initiation: First instar (L1) larvae
Exposure Duration: 22 days

7. CONCLUSIONS:

Individual synchronized honey bee (*Apis mellifera* L.) larvae (first instar) were exposed *in vitro* to **Difenoconazole Technical** at the concentrations and doses reported in the table below on Days 3 (D3) through Day 6 (D6) of the study. The reviewer used the nominal cumulative doses (µg ai/larva/developmental period), % recovery from the analytical data, and number of days of exposure to calculate the measured daily dietary doses. The measured dietary concentrations were reported by the study author.

Nominal Daily Dose (µg ai/larva/day)	Measured Daily Dose (µg ai/larva/day)	Nominal Diet Concentration (mg ai/kg diet)	Measured Diet Concentration (mg ai/kg diet)
0.640	0.646	16.6	16.8
1.60	1.47	41.6	38.2
4.00	3.79	104	98.7
10.0	9.28	260	242
25.0	20.9	650	542

Larvae used in the study were obtained from in-house colonies. A negative and solvent (solvent; 0.5% v/v acetone) control were run; dimethoate technical (99.9% purity) was used as a reference toxicant at 48 mg/kg diet. All groups consisted of 48 replicates of individual larva; each larva was contained within a polystyrene grafting cell that was within a 48-well cell culture plate.

Significant effects were detected in the highest test level for Day 8 and Day 15 mortality and Day 22 emergence. The effects were not dose responsive. The adult emergence rate NOAEC and EC_{50} were 242 and 501 mg ai/kg diet, respectively. The NOAEL and ED_{50} were 9.28 and 19.3 µg ai/larva/day, respectively.

The study **is scientifically sound** and **is consistent** with the OECD Guidance Document for measuring chronic (repeat dose) toxicity to honey bee larvae. The study is classified as **acceptable**.

	Mortality (Day 8)	**Mortality (Day 15)**	**Adult emergence rate**
Dietary Concentration (mg ai/kg diet)	LC_{50}: >542 95% CI: N/A Slope: N/A NOAEC: 242 LOAEC: 542	LC_{50}: 532 95% CI: 421 to 671 Slope: N/A NOAEC: 242 LOAEC: 542	EC_{50}: 501 95% CI: 414 to 607 Slope: N/A NOAEC: 242 LOAEC: 542
Daily Dietary Dose (µg ai/larva/day)	LD_{50}: >20.9 95% CI: N/A Slope: N/A NOAEL: 9.28 LOAEL: 20.9	LD_{50}: 20.5 95% CI: 16.2 to 25.9 Slope: N/A NOAEL: 9.28 LOAEL: 20.9	ED_{50}: 19.3 95% CI: 15.9 to 23.4 Slope: N/A NOAEL: 9.28 LOAEL: 20.9

8. ADEQUACY OF THE STUDY

A. Classification: This study **is scientifically sound** and is classified as **acceptable**.

B. Rationale: NA

C. Repairability: NA

9. GUIDANCE DEVIATIONS:

Deviations from OECD Draft Guidance Document for the Honey Bee (*Apis mellifera*) Larval Toxicity Test, Repeated Exposure (February 25, 2014) were noted by the reviewer:

1. The relative humidity at all bee development stages in this test was below the suggested ranges:

Day 1 to Day 8
49.8 to 100% (recommended 95 ± 5%)
Day 8 to Day 15
60.6 to 94.5% (recommended 80 ± 5%)
Day 15 to Day 22
43.7 to 66.8% (recommended 50 - 80%)

2. The study author did not report randomly assigning larvae to the replicates of each control and treatment group.

These deviations **did not** have an impact on the scientific integrity of this study.

10. SUBMISSION PURPOSE: To determine the chronic effects on growth, development and survival and sublethal effects of **Difenoconazole** on the honey bee (*A. mellifera* L) larvae from chronic [repeat dose] exposure following the OECD Guidance Document for the purpose of chemical re-registration.

11. MATERIALS AND METHODS

A. Test Material

Test Material:	**Difenoconazole tech. (CGA169374 tech.)**
Description:	Off-white solid
Lot No./Batch No.:	SMO3E4125
Purity	93.9% w/w
Stability of compound under test conditions.	Stable.
Storage conditions of test chemical:	Ambient (5-30°C).

Range finding test yes/no (if yes, describe): No.

OECD recommends a preliminary study with doses of the test chemical in a geometric ratio from 5 to 10.

Physicochemical properties of Difenoconazole.

Parameter	Values	Comments
Molecular Weight	Not reported.	
Water solubility at 20°C (mg/L)	Not reported.	
Vapor pressure (torr, at 25°C)	Not reported.	
Structure	Not reported.	
Mean organic carbon partition coefficient K_{oc} (L/kg_{oc})	Not reported.	
Log octanol-water partition coefficient Log K_{ow}	Not reported.	

B. Test Organisms

Guidance Criteria	Reported Information	Comments
Species	Honey bees (*Apis mellifera carnica* Pollmann)	

Guidance Criteria	Reported Information	Comments
		OECD recommends European honey bee (Apis mellifera)
Age at beginning of test Worker bees of uniform age.	First instar (L1) larvae	_____ *OECD recommends that on D1 of study, first instar (L1) synchronized larvae (i.e., larvae of the same age) are taken from comb of three colonies.*
Source	In-house bee hives maintained by the testing laboratory.	_____ *OECD recommends larvae are collected from three different colonies.*
Were bees from disease-free colonies?	The colonies were examined for reportable bee epidemics by an authorized bee specialist. The hives were parasite-free and queen-right (as far as possible). No chemical substances (antibiotics, anti-Varroa treatments, pesticides, etc.) were used in the hive within 4 weeks prior to test initiation.	_____ *OECD recommends that colonies used to obtain larvae should be adequately fed, health (i.e., as far as disease- and parasite-free), with a known history and physiological status.*
Were bees kept in conditions conforming to proper cultural practices?	The colonies were inspected periodically according to standard bee-keeping practices by an experienced apiarist. The hives were adequately fed and healthy.	

B. Test System

Guidance Criteria	Reported Information	
Test Chambers	Crystal polystyrene grafting cells (NICOTPLAST) with a diameter of 9 mm, placed into individual wells of sterile 48-well cellular culture plates (Greiner Bio	_____ *OECD recommends 48-well plate with each well containing a crystal*

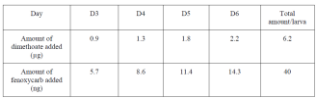
Guidance Criteria	Reported Information	
	One).	*polystyrene grafting cell.*
Temperature during exposure	Grafting on Day 1 until Day 8 33.3 to 34.3°C Day 8 to Day 15 33.1 to 33.9°C Day 15 to Day 22 33.6 to 34.6°C	*OECD recommends incubator at 34 – 35°C. (34.5 ± 0.5°C). Deviations may occur but temperature should not be lower that 23°C or higher than 40°C; deviations not last more than 15 minutes once every 24 hrs.*
Relative humidity during exposure	Grafting on Day 1 until Day 8 55.6 to 100% Day 8 to Day 15 60.6 to 94.5% Day 15 to Day 22 43.7 to 66.8% The open plates were placed into a hermetically sealed desiccator that contained a dish filled with saturated potassium sulfate (K_2SO_4) solution (to maintain a water-saturated atmosphere from Day 1 to Day 8). On Day 8, the plates were transferred to a second desiccator containing a dish filled with a saturated sodium chloride (NaCl) solution. The desiccators were placed in an incubator with forced air circulation. On Day 15 each plate was covered by its lid and transferred to an incubator with automated humidity control.	*OECD recommends use of K_2SO_4 to maintain water saturated atmosphere (95 ± 5%) from D1 – D8. On D8, dental rolls removed from exposure wells, pupal plates placed in incubator containing saturated NaCl to maintain relative humidity of 80% ± 5%.*
Lighting	None, except during grafting, feeding, and assessments.	*OECD recommends that plates should be maintained in darkness.*

Guidance Criteria	Reported Information	
Feeding	20 µL of untreated Diet A on Day 1; 20 µL of untreated or treated Diet B on Day 3; and 30, 40, and 50 µL of untreated or treated Diet C on Days 4, 5, and 6, respectively. Food was dropped next to the larva using a multi-stepper pipette, along the wall of the grafting cell. Diet A: 50% wt fresh royal jelly + 50% wt of aqueous solution (2% wt yeast extract + 12% wt glucose + 12% wt fructose) Diet B: 50% wt fresh royal jelly + 50% wt of aqueous solution (3% wt yeast extract + 15% wt glucose + 15% wt fructose) Diet C: 50% wt fresh royal jelly + 50% wt of aqueous solution (4% wt yeast extract + 18% wt glucose + 18% wt fructose)	——————————— *OECD recommends that all larvae are fed once a day. Volume of diet is adjusted each day. Additional food should be added to the cell even if previous allocation has not been totally consumed. Presence of uneaten food at termination of test should be reported.* *OECD recommends:* *Diet A (D1): 50% weight of fresh royal jelly + 50% weight of an aqueous solution containing 2% weight of yeast extract, 12% weight of glucose, and 12% weight fructose.* *Diet B (D3): 50% weight of fresh royal jelly + 50% weight of an aqueous solution containing 3% weight of yeast extract, 15% weight of glucose and 15% weight of fructose.* *Diet C (from D4 to D6): 50% weight of fresh royal jelly + 50% weight of an aqueous solution containing 4% weight of yeast extract, 18% weight of glucose, and 18% weight of fructose.* *OECD recommends the following feeding schedule:* 

C. Test Design

Guidance Criteria	Reported Information	Comments
Nominal dosage levels tested	Dietary concentrations: 16.6, 41.6, 104, 260, and 650 mg ai/kg diet Daily dietary doses: 0.640, 1.60, 4.00, 10.0, and 25.0 µg ai/larva/day	*OECD recommends 5 treatments of increasing test concentrations in geometric series spaced by a factor not exceeding 3. Alternatively, when a limit test is performed, a single dose of 40 mg ai/kg diet or the maximum achievable solubility (whichever is lower).* *Maximum reference toxicant: 40 mg dimethoate/kg diet or 0.25 mg fenoxycarb/kg diet.*
Measured test concentrations	Dietary concentrations: 16.8, 38.2, 98.7, 242, and 542 mg ai/kg diet Dietary doses: 0.646, 1.47, 3.79, 9.28, and 20.9 µg ai/larva/day	*OECD recommends test concentrations measured in the stock solution and should be within 20% of nominal.*
Number of bees exposed per dosage level	48 individual larva (replicates) per treatment group	*OECD recommends minimum of 12 larvae from each of 3 colonies allocated on the same plate to each treatment, i.e., minimum of 36 larvae per treatment.*
Other experimental design information	Four days prior to grafting, queens of eight colonies were confined in their respective colonies in excluder cages containing combs with empty cells. Three days prior to grafting, the queens were released from the cages. On Day 1, the combs were	*OECD recommends that newly hatched larvae are selected that have not yet formed a "C" shape and*

Guidance Criteria	Reported Information	Comments
	transferred to the laboratory using an insulated container equipped with a moist wipe to avoid temperature variation. Three of eight combs were selected for grafting, on the basis of the highest number of synchronized larvae. Larvae were transferred to the surface of the diet in the grafting cells using a grafting tool. The grafted larvae had not yet formed a circular "C" shape. In addition, reserve plates were prepared using larvae of the same replicate hives. Before exposure initiation on Day 3, non-suitable larvae were replaced using individuals from their respective hive reserves.	*randomizing the allocation of larvae into the plates for each colony. On Day 1, larva is deposited in cell containing 20 µL diet.*
Bees randomly or impartially assigned to test groups	Not reported.	*OECD recommends that each group of a minimum of 12 larvae from each of the three colonies is considered a replicate for a given treatment level and identified as such on the microplate.*
Control	Untreated Diet 48 individual larva (replicates) per treatment group	*OECD recommends 12 larvae x 3 colonies=36 larvae minimum and that control mortality from D3 to D8 should be ≤15%. Adult emergence should be ≥70% on Day 22,*
Solvent control	Diet with acetone, 0.5% v/v 48 individual larva (replicates) per treatment group	*OECD recommends maximum of 2% of diet.*

Guidance Criteria	Reported Information	Comments
Reference Toxicant	Dimethoate technical (99.9% w/w), provided as 48 mg/kg diet	*OECD recommends technical grade dimethoate or fenoxycarb at the constant concentration of 40 mg ai/kg diet or 0.25 mg ai/kg diet, respectively and provided at the following amounts:*  *Dimethoate larval mortality ≥50% on Day 8; fenoxycarb emergence rate ≤15%.*
Total observation period and frequency of interim observations	22 days Mortality assessed daily during the larval phase (Day 4 to Day 8). Mortality assessed on Day 15 and 22 of the pupation phase. Emergence assessed on Day 22. Behavioral and other adverse effects assessed on Day 22. Uneaten food qualitatively assessed on Day 8.	*OECD recommends that following chemical exposure on Days 3 - 6, mortalities are checked at time of feeding on D4 – D8, D15, and D22 (test termination). Adult emergence at D22; non-emerged bees on D22 are recorded as pupal mortality. Other observations including presence of uneaten food on D8 should be qualitatively reported. Morphological differences (from controls) should also be recored.*

12. REPORTED RESULTS

Guidance Criteria	Reported Information
Quality assurance and GLP compliance statements were included in the report?	Yes. This study was conducted in compliance with the German and OECD Principles of GLP, which are compatible with the U.S. and Japan Principles of GLP. There were two

Guidance Criteria	Reported Information
	exceptions: 1.) inspections of colonies according to standard beekeeping practices and stock keeping; and 2.) multi-residue analysis of royal jelly for antibiotics, pesticides, and heavy metals.
Observed adverse effects on bees at respective dosages	Yes; details provided in the Mortality and Observations section.
Control and Solvent Control Mortality	8-Day Larval Mortality Negative control: 0% Solvent control: 4.2% 15-Day Cumulative Mortality Negative control: 10.4% Solvent control: 12.5% 22-Day Cumulative Mortality Negative control: 20.8% Solvent control: 20.8%
Were raw data included?	Yes.
Analytical Analysis?	Analytical verification performed using LC-MS/MS. LOD = 0.450 mg/kg diet

Mortality and Observations:

At Day 8, larval mortality averaged 0% in the negative control and 4.2% in the solvent control, compared to 2.1, 0, 0, 2.1, and 37.5% in the measured 16.8, 38.2, 98.7, 242, and 542 mg ai/kg diet groups, respectively.

At Day 15, cumulative mortality averaged 10.4% in the negative control and 12.5% in the solvent control, compared to 10.4, 14.6, 10.4, 12.4, and 56.3% in the measured 16.8, 38.2, 98.7, 242, and 542 mg ai/kg diet groups, respectively.

Day 22 emergence averaged 79.2% in the negative and solvent controls, compared to 77.1, 79.2, 79.2, 79.2, and 35.4% in the measured 16.8, 38.2, 98.7, 242, and 542 mg ai/kg diet groups, respectively.

Mortality at Days 8, 15, and 22 were significantly increased in the 542 mg ai/kg diet group, and Day 22 emergence was significantly reduced in the 542 mg ai/kg diet group.

Table 1. Cumulative honey bee larval and pupal mortality data after repeat dietary exposure (dose).[a]

Measured Dietary Concentration (mg ai/kg diet)	Number Exposed	Day 8 (%)	Day 15 (%)
Negative Control	48	0.0	10.4
Solvent Control	48	4.2	12.5
16.8	48	2.1	10.4
38.2	48	0.0	14.6
98.7	48	0.0	10.4
242	48	2.1	12.4
542	48	37.5	56.3*
Dimethoate, 48 mg/kg diet	48	87.5	N/A

a Data from pages 27-28 of the study report

* Significantly different from the solvent control group (Cochran-Armitage test5 for Day 8 and 15 mortality or multiple Chi^2 -test with Bonferoni-Holms adjustment for Day 22 pupal mortality. Both tests were one sided greater, α=0.05).

Table 2. Cumulative honey bee adult emergence data after repeat dietary exposure (dose).[a]

Measured Dietary Concentration (mg ai/kg diet)	Number Exposed	Day 22 (%)
Negative Control	48	79.2
Solvent Control	48	79.2
16.8	48	77.1
38.2	48	79.2
98.7	48	79.2
242	48	79.2
542	48	35.4*
Dimethoate, 48 mg/kg diet	48	N/A

a Data from pages 27-28 of the study report

* Significantly different from the solvent control group (Cochran-Armitage test, one sided greater, α=0.05).

Reported Statistical Analysis

Cochran-Armitage test (one-sided greater, $\alpha = 0.05$) was used to evaluate whether there was a statistically significant difference between mortality data of the test item groups and the solvent control group for larval mortality on Day 8, larval and pupal mortality on Day 15, and adult emergence on Day 22. The multiple Chi^2 -test with Bonferroni-Holms adjustment was used to evaluate pupal mortality between Days 8 and 22. The Day 8 LC_{50} value could not be calculated due to a lack of mortality above 50 %. The NOAEC was determined for adult emergence on Day 22, and the corresponding NOAEL values were calculated by accounting for the density of the larval diet (1.1 g/cm3) and the cumulative feeding volume per larva (140 µL diet). The Day 22 EC_{10}/ED_{10} and EC_{20}/ED_{20} for adult emergence could not be determined due to the lack of a clear dose response relationship. The Day 22 EC_{50} for adult emergence with 95 % confidence limits was determined with Spearman-Karber procedure. The calculation was performed using the solvent control corrected percentage of non-emerged bees. All analyses were conducted using ToxRat professional, Version 3.2.1.

Reviewer's Statistical Analysis

Mortality and emergence data were analyzed using CETIS statistical software version 1.9.2.8 and 1.9.5.3 with database backend settings implemented by EFED on 7/25/17. The measured diet concentrations and measured daily doses were used for the analyses and separate test records were created for each.

The negative and solvent control data were compared using Fisher's Exact Test. No significant differences were detected. The exposure data were compared to the negative control using the Fisher Exact Test with a Bonferroni-Holm Adjustment due to a lack of monotonicity.

The Day 15 LD/LC_{50} estimates, Day 22 ED/EC_{50} estimates, and corresponding 95% confidence intervals were determined using the Trimmed Spearman-Karber method because the data were not distributed appropriately for a probit regression. The maximum effect for Day 8 mortality was 37%; so, the LC/LD_{50} values were visually estimated as being greater than the highest concentration/dose.

	Mortality (Day 8)	**Mortality (Day 15)**	**Adult emergence rate**
Dietary Concentration (mg ai/kg diet)	LC_{50}: >542 95% CI: N/A Slope: N/A NOAEC: 242 LOAEC: 542	LC_{50}: 532 95% CI: 421 to 671 Slope: N/A NOAEC: 242 LOAEC: 542	EC_{50}: 501 95% CI: 414 to 607 Slope: N/A NOAEC: 242 LOAEC: 542
Daily Dietary Dose (µg ai/larva)	LD_{50}: >20.9 95% CI: N/A Slope: N/A NOAEL: 9.28 LOAEL: 20.9	LD_{50}: 20.5 95% CI: 16.2 to 25.9 Slope: N/A NOAEL: 9.28 LOAEL: 20.9	ED_{50}: 19.3 95% CI: 15.9 to 23.4 Slope: N/A NOAEL: 9.28 LOAEL: 20.9

13.

REVIEWER'S COMMENTS:

The reviewer's and the study author's determinations of the NOAEC/NOAEL values agreed when accounting for the differences in the concentrations/doses used for those determinations. The EC/ED_{50} values were not in agreement due to the following factors: 1.) the study author used the nominal dietary concentrations and nominal cumulative dietary doses for the analyses and reporting, whereas the reviewer used the measured dietary concentrations and measured daily dietary doses; and 2.) the study author used the solvent control data for comparisons to treatment groups; whereas, the reviewer used the negative control data. The reviewer's results are reported in the Conclusions section of this DER.

Larval mortality from days 3 to 8 in the negative and solvent control should be ≤15% prior to pupation. In this study, larval mortality in the negative control was 0% (the criterion was met). Adult emergence should be ≥70% in the control on Day 22. In the present study, adult emergence was 79.2% in the negative control. Larval mortality in the positive control (dimethoate) should be ≥50% on Day 8. In this test, larval mortality was 87.5% and meets this criterion.

The analytical method was verified for difenoconazole in larval diet (supplemental MRID 50449802). Larval diet recovery samples were extracted with acetonitrile/water (80:20, v/v) and diluted with acetonitrile/water (50:50, v/v). The samples were further diluted with blank matrix extract. Quantification was performed using LC-MS/MS. Two mass transitions were evaluated to demonstrate the method achieves a high level of selectivity. No significant interference >30% of the LOQ was detected in any control samples. A matrix effect was not determined, and the linearity of the detector response was demonstrated. The calibration curves obtained for both mass transitions were linear with correlation coefficients ≥0.999. Accuracy was determined by fortification of control samples with known amounts of test material (1.5 and 850 mg/kg), and the mean recoveries using the method were 100-110% (both mass transitions). The LOQ was established at 1.5 mg/kg difenoconazole.

14. REVIEWER'S CONCLUSIONS:

This study **is scientifically sound** and is classified as **acceptable**. Significant effects were detected in the highest test level for Day 8 and Day 15 mortality and Day 22 emergence. The NOAEC and EC_{50} were 242 and 501 mg ai/kg diet, respectively. The NOAEL and ED_{50} were 9.28 and 19.3 µg ai/larva/day, respectively.

References

Gaus, J. (2017): Difenoconazole – Validation and Development of Analytical Method ECO_022_03A for the Determination of Difenoconazole in Honey Bee Larval Diet from Ecotoxicology Studies. Eurofins Agroscience Services EcoChem GmbH/Eurofins Agroscience Services Ecotox GmbH, Eutinger Str. 24, D-75223 Niefern Öschelbronn, Germany. Unpublished report No S17-06079.

All other references were standard guidelines or methodologies.

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Eurofins Agroscience Service GmbH**

Batch ID:	13-1639-2584	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	26 Jun-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	Royal Jelly
Ending Date:	21 Sep-17	**Species:**	Apis mellifera	**Brine:**	
Duration:	87d 0h	**Source:**	Lab In-House Culture	**Age:**	

Sample ID:	06-9108-4422	**Code:**	50449801	**Client:**	CDM Smith - E. Krupka
Sample Date:	26 Jun-17	**Material:**	Difenoconazole	**Project:**	Fungicide
Receipt Date:	07 May-18 00:40	**Source:**	Syngenta		
Sample Age:	n/a	**Station:**			

Comments:
PC Code 044200 MRID 50218644 mean-measured daily dietary dose

Point Estimate Summary

Analysis ID	Endpoint	Point Estimate Method	Level	ug ai/larv	95% LCL	95% UCL	TU	✓
10-2301-8758	Adult Emergence Rate	Regression: Log-Normal (Probit)	EC5	0.06448	n/a	0.5005		✓
			EC10	0.2477	2.95E-07	1.118		✓
			EC15	0.614	4.66E-05	2.017		✓
			EC20	1.263	0.002392	3.504		✓
			EC25	2.346	0.05785	6.828		✓
			EC40	11.16	4.087	1592		✓
			EC50	28.53	8.924	250800		
00-4959-5362	Adult Emergence Rate	Trimmed Spearman-Kärber	EC50	19.33	15.94	23.44		✓
01-4334-5343	Day 15 Mortality	Regression: Log-Normal (Probit)	LC5	0.4625	0.003326	1.462		
			LC10	1.26	0.05731	2.987		
			LC15	2.478	0.3514	5.385		
			LC20	4.242	1.231	10.38		
			LC25	6.728	2.775	23.68		
			LC40	21.5	9.137	446.4		
			LC50	43.26	15.23	3209		
12-0178-4519	Day 15 Mortality	Trimmed Spearman-Kärber	LC50	20.5	16.22	25.91		
00-5707-0817	Larval Mortality	Regression: Log-Normal (Probit)	LC5	5.648	n/a	n/a		
			LC10	8.844	n/a	n/a		
			LC15	11.97	n/a	n/a		
			LC20	15.22	n/a	n/a		
			LC25	18.71	n/a	n/a		
			LC40	31.46	n/a	n/a		
			LC50	43	n/a	n/a		

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Eurofins Agroscience Service GmbH**

Adult Emergence Rate Summary

Conc-ug ai/larv	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	%Effect
0	S	3	0.7917	0.4331	1.0000	0.6250	0.8750	0.0833	0.1443	18.23%	0.00%
0	N	3	0.7917	0.6124	0.9709	0.7500	0.8750	0.0417	0.0722	9.12%	0.00%
0.646		3	0.7708	0.4476	1.0000	0.6250	0.8750	0.0751	0.1301	16.88%	2.63%
1.47		3	0.7917	0.4685	1.0000	0.6875	0.9375	0.0751	0.1301	16.43%	0.00%
3.79		3	0.7917	0.7020	0.8813	0.7500	0.8125	0.0208	0.0361	4.56%	0.00%
9.28		3	0.7917	0.7020	0.8813	0.7500	0.8125	0.0208	0.0361	4.56%	0.00%
20.9		3	0.3542	0.0000	0.7449	0.1875	0.5000	0.0908	0.1573	44.41%	55.26%

Day 15 Mortality Summary

Conc-ug ai/larv	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	%Effect
0	S	3	0.1250	0.0000	0.2803	0.0625	0.1875	0.0361	0.0625	50.00%	0.00%
0	N	3	0.1042	0.0145	0.1938	0.0625	0.1250	0.0208	0.0361	34.64%	-2.38%
0.646		3	0.1042	0.0145	0.1938	0.0625	0.1250	0.0208	0.0361	34.64%	-2.38%
1.47		3	0.1458	0.0000	0.3830	0.0625	0.2500	0.0551	0.0955	65.47%	2.38%
3.79		3	0.1042	0.0145	0.1938	0.0625	0.1250	0.0208	0.0361	34.64%	-2.38%
9.28		3	0.1250	0.0000	0.2803	0.0625	0.1875	0.0361	0.0625	50.00%	0.00%
20.9		3	0.5625	0.1517	0.9733	0.3750	0.6875	0.0955	0.1654	29.40%	50.00%

Larval Mortality Summary

Conc-ug ai/larv	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	%Effect
0	S	3	0.0417	0.0000	0.1313	0.0000	0.0625	0.0208	0.0361	86.60%	0.00%
0	N	3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000		-4.35%
0.646		3	0.0208	0.0000	0.1105	0.0000	0.0625	0.0208	0.0361	173.21%	-2.17%
1.47		3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000		-4.35%
3.79		3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000		-4.35%
9.28		3	0.0208	0.0000	0.1105	0.0000	0.0625	0.0208	0.0361	173.21%	-2.17%
20.9		3	0.3750	0.0645	0.6855	0.2500	0.5000	0.0722	0.1250	33.33%	34.78%

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Eurofins Agroscience Service GmbH**

Adult Emergence Rate Detail

Conc-ug ai/larv	Code	Rep 1	Rep 2	Rep 3
0	S	0.8750	0.6250	0.8750
0	N	0.8750	0.7500	0.7500
0.646		0.8750	0.8125	0.6250
1.47		0.6875	0.9375	0.7500
3.79		0.8125	0.7500	0.8125
9.28		0.8125	0.8125	0.7500
20.9		0.1875	0.5000	0.3750

Day 15 Mortality Detail

Conc-ug ai/larv	Code	Rep 1	Rep 2	Rep 3
0	S	0.0625	0.1875	0.1250
0	N	0.1250	0.1250	0.0625
0.646		0.1250	0.0625	0.1250
1.47		0.1250	0.0625	0.2500
3.79		0.0625	0.1250	0.1250
9.28		0.1250	0.0625	0.1875
20.9		0.6875	0.3750	0.6250

Larval Mortality Detail

Conc-ug ai/larv	Code	Rep 1	Rep 2	Rep 3
0	S	0.0625	0.0625	0.0000
0	N	0.0000	0.0000	0.0000
0.646		0.0000	0.0625	0.0000
1.47		0.0000	0.0000	0.0000
3.79		0.0000	0.0000	0.0000
9.28		0.0000	0.0625	0.0000
20.9		0.5000	0.2500	0.3750

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Eurofins Agroscience Service GmbH**

Batch ID:	01-5595-9885	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**			
Start Date:	26 Jun-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	Royal Jelly		
Ending Date:	21 Sep-17	**Species:**	Apis mellifera	**Brine:**			
Test Length:	87d 0h	**Taxon:**		**Source:**	Lab In-House Culture	**Age:**	

Sample ID:	07-9424-3951	**Code:**	50449801	**Project:**	Fungicide
Sample Date:	26 Jun-17	**Material:**	Difenoconazole	**Source:**	Syngenta
Receipt Date:		**CAS (PC):**		**Station:**	
Sample Age:	n/a	**Client:**	CDM Smith - E. Krupka		

PC Code 044200 MRID 50218644 mean-measured concentration

SIngle Comparison Summary

Analysis ID	Endpoint	Comparison Method	P-Value	Comparison Result	S
11-2084-9123	Adult Emergence Rate	Fisher Exact Test	1.0000	Solvent Blank passed adult emergence rat	1
02-7986-8374	Day 15 Mortality	Fisher Exact Test	1.0000	Solvent Blank passed day 15 mortality	1
15-8642-9495	Larval Mortality	Fisher Exact Test	0.4947	Solvent Blank passed larval mortality	1

Multiple Comparison Summary

Analysis ID	Endpoint	Comparison Method	✓	NOEL	LOEL	TOEL	TU	PMSD	S
01-4676-3039	Adult Emergence Rate	Cochran-Armitage (N) Trend Test	✓	242	542	362.2		n/a	1
00-4440-7402	Adult Emergence Rate	Fisher Exact/Bonferroni-Holm Test	✓	242	542	362.2		n/a	1
08-3355-8159	Day 15 Mortality	Cochran-Armitage (N) Trend Test	✓	242	542	362.2		n/a	1
20-3253-7553	Day 15 Mortality	Fisher Exact/Bonferroni-Holm Test	✓	242	542	362.2		n/a	1
21-4004-8321	Larval Mortality	Cochran-Armitage (N) Trend Test	✓	242	542	362.2		n/a	1
01-5622-0205	Larval Mortality	Fisher Exact/Bonferroni-Holm Test	✓	242	542	362.2		n/a	1

Point Estimate Summary

Analysis ID	Endpoint	Point Estimate Method	✓	Level	mg ai/kg d	95% LCL	95% UCL	TU	S
17-3816-7853	Adult Emergence Rate	GLM: Log-Normal (Probit)	✓	EC5	1.67	n/a	13		1
			✓	EC10	6.42	6.35E-06	29.1		
			✓	EC25	61	1.44	178		
				EC50	744	232	7390000		
11-3728-2103	Adult Emergence Rate	Trimmed Spearman-Kärber	✓	EC50	501	414	607		1
15-4867-6260	Day 15 Mortality	GLM: Log-Normal (Probit)		LC5	12	0.0829	38		1
				LC10	32.7	1.45	77.7		
				LC25	175	72	620		
				LC50	1130	396	86600		
08-5814-6348	Day 15 Mortality	Trimmed Spearman-Kärber		LC50	532	421	671		1
11-8533-0296	Larval Mortality	GLM: Log-Normal (Probit)		LC5	147	n/a	n/a		1
				LC10	230	n/a	n/a		
				LC25	486	n/a	n/a		
				LC50	1120	n/a	n/a		

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Eurofins Agroscience Service GmbH**

Adult Emergence Rate Summary

Conc-mg ai/kg d	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	%Effect
0	S	3	0.792	0.433	1.000	0.625	0.875	0.083	0.144	18.23%	0.00%
0	N	3	0.792	0.612	0.971	0.750	0.875	0.042	0.072	9.12%	0.00%
16.8		3	0.771	0.448	1.000	0.625	0.875	0.075	0.130	16.88%	2.63%
38.2		3	0.792	0.468	1.000	0.688	0.938	0.075	0.130	16.43%	0.00%
98.7		3	0.792	0.702	0.881	0.750	0.812	0.021	0.036	4.56%	0.00%
242		3	0.792	0.702	0.881	0.750	0.812	0.021	0.036	4.56%	0.00%
542		3	0.354	0.000	0.745	0.188	0.500	0.091	0.157	44.41%	55.26%

Day 15 Mortality Summary

Conc-mg ai/kg d	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	%Effect
0	S	3	0.125	0.000	0.280	0.063	0.188	0.036	0.063	50.00%	0.00%
0	N	3	0.104	0.015	0.194	0.063	0.125	0.021	0.036	34.64%	-2.38%
16.8		3	0.104	0.015	0.194	0.063	0.125	0.021	0.036	34.64%	-2.38%
38.2		3	0.146	0.000	0.383	0.063	0.250	0.055	0.096	65.47%	2.38%
98.7		3	0.104	0.015	0.194	0.063	0.125	0.021	0.036	34.64%	-2.38%
242		3	0.125	0.000	0.280	0.063	0.188	0.036	0.063	50.00%	0.00%
542		3	0.562	0.152	0.973	0.375	0.688	0.096	0.165	29.40%	50.00%

Larval Mortality Summary

Conc-mg ai/kg d	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	%Effect
0	S	3	0.042	0.000	0.131	0.000	0.063	0.021	0.036	86.60%	0.00%
0	N	3	0.000	0.000	0.000	0.000	0.000	0.000	0.000		-4.35%
16.8		3	0.021	0.000	0.110	0.000	0.063	0.021	0.036	173.21%	-2.17%
38.2		3	0.000	0.000	0.000	0.000	0.000	0.000	0.000		-4.35%
98.7		3	0.000	0.000	0.000	0.000	0.000	0.000	0.000		-4.35%
242		3	0.021	0.000	0.110	0.000	0.063	0.021	0.036	173.21%	-2.17%
542		3	0.375	0.065	0.686	0.250	0.500	0.072	0.125	33.33%	34.78%

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Eurofins Agroscience Service GmbH**

Adult Emergence Rate Detail

Conc-mg ai/kg d	Code	Rep 1	Rep 2	Rep 3
0	S	0.875	0.625	0.875
0	N	0.875	0.750	0.750
16.8		0.875	0.812	0.625
38.2		0.688	0.938	0.750
98.7		0.812	0.750	0.812
242		0.812	0.812	0.750
542		0.188	0.500	0.375

Day 15 Mortality Detail

Conc-mg ai/kg d	Code	Rep 1	Rep 2	Rep 3
0	S	0.063	0.188	0.125
0	N	0.125	0.125	0.063
16.8		0.125	0.063	0.125
38.2		0.125	0.063	0.250
98.7		0.063	0.125	0.125
242		0.125	0.063	0.188
542		0.688	0.375	0.625

Larval Mortality Detail

Conc-mg ai/kg d	Code	Rep 1	Rep 2	Rep 3
0	S	0.063	0.063	0.000
0	N	0.000	0.000	0.000
16.8		0.000	0.063	0.000
38.2		0.000	0.000	0.000
98.7		0.000	0.000	0.000
242		0.000	0.063	0.000
542		0.500	0.250	0.375

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Eurofins Agroscience Service GmbH**

Analysis ID:	00-4440-7402	**Endpoint:**	Adult Emergence Rate	**CETIS Version:**	CETISv1.9.5
Analyzed:	12 Nov-19 17:57	**Analysis:**	STP 2xK Contingency Tables	**Status Level:**	1
Batch ID:	01-5595-9885	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	26 Jun-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	Royal Jelly
Ending Date:	21 Sep-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	87d 0h	**Taxon:**		**Source:**	Lab In-House Culture **Age:**

Data Transform	Alt Hyp	NOEL	LOEL	TOEL	TU
Untransformed	C > T	242	542	362.2	

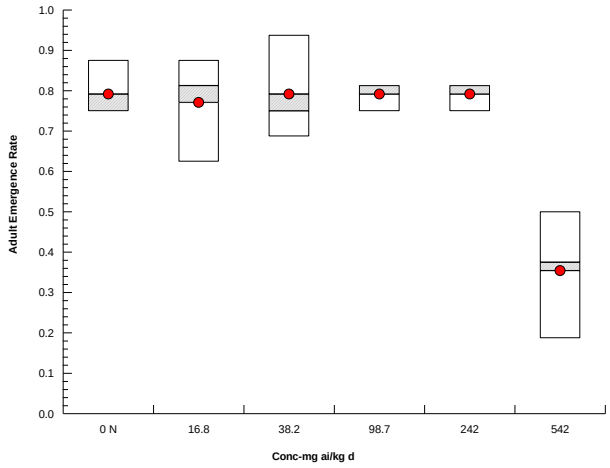
Fisher Exact/Bonferroni-Holm Test

Control	vs	Group	Test Stat	P-Type	P-Value	Decision(α:5%)
Negative Control		16.8	0.500	Exact	1.0000	Non-Significant Effect
		38.2	0.599	Exact	1.0000	Non-Significant Effect
		98.7	0.599	Exact	1.0000	Non-Significant Effect
		242	0.599	Exact	1.0000	Non-Significant Effect
		542*	0.000	Exact	6.9E-05	Significant Effect

Data Summary

Conc-mg ai/kg d	Code	NR	R	NR + R	Prop NR	Prop R	%Effect
0	N	38	10	48	0.792	0.208	0.0%
16.8		37	11	48	0.771	0.229	2.63%
38.2		38	10	48	0.792	0.208	0.0%
98.7		38	10	48	0.792	0.208	0.0%
242		38	10	48	0.792	0.208	0.0%
542		17	31	48	0.354	0.646	55.3%

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Eurofins Agroscience Service GmbH**

Analysis ID:	01-4676-3039	**Endpoint:**	Adult Emergence Rate	**CETIS Version:**	CETISv1.9.5
Analyzed:	12 Nov-19 17:58	**Analysis:**	STP 2xK Contingency Tables-Numerical Sc	**Status Level:**	1
Batch ID:	01-5595-9885	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	26 Jun-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	Royal Jelly
Ending Date:	21 Sep-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	87d 0h	**Taxon:**		**Source:**	Lab In-House Culture **Age:**

Data Transform	Alt Hyp	NOEL	LOEL	TOEL	TU
Untransformed	C > T	242	542	362.2	

Cochran-Armitage (N) Trend Test

Control vs	Group	Test Stat	P-Type	P-Value	Decision(α:5%)
Negative Control	16.8	0.247	Asymp	0.5445	Non-Significant Effect
	38.2	-0.020	Asymp	0.5445	Non-Significant Effect
	98.7	-0.102	Asymp	0.5445	Non-Significant Effect
	242	-0.112	Asymp	0.5445	Non-Significant Effect
	542*	5.462	Asymp	<1.0E-37	Significant Effect

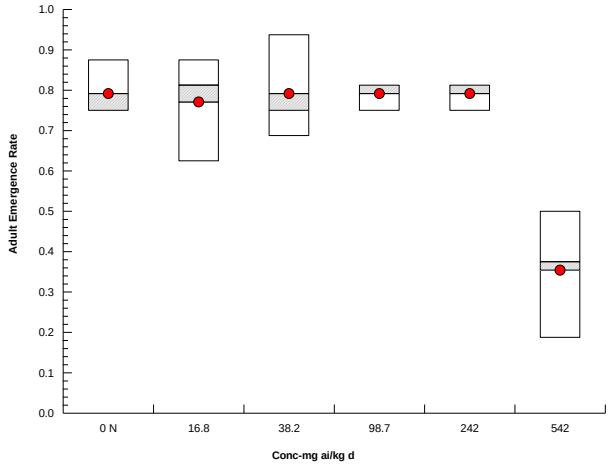
Auxiliary Tests

Attribute	Test	Test Stat	Critical	P-Value	Decision(α:5%)
Overall Effect	Pearson Chi-Square Test	37	11.1	6.4E-07	Significant Overall Effect
Nonlinearity	Chi-Square Lack of Fit Test	7.13	9.49	0.1294	Non-Significant Lack of Linearity
Overdispersion	Tarone C(α) Binomial Overdispersion Test	1.16	1.64	0.1234	Non-Significant Overdispersion

Data Summary

Conc-mg ai/kg d	Code	NR	R	NR + R	Prop NR	Prop R	%Effect
0	N	38	10	48	0.792	0.208	0.0%
16.8		37	11	48	0.771	0.229	2.63%
38.2		38	10	48	0.792	0.208	0.0%
98.7		38	10	48	0.792	0.208	0.0%
242		38	10	48	0.792	0.208	0.0%
542		17	31	48	0.354	0.646	55.3%

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Eurofins Agroscience Service GmbH**

Analysis ID:	11-2084-9123	**Endpoint:**	Adult Emergence Rate	**CETIS Version:**	CETISv1.9.5
Analyzed:	12 Nov-19 17:58	**Analysis:**	Single 2x2 Contingency Table	**Status Level:**	1
Batch ID:	01-5595-9885	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	26 Jun-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	Royal Jelly
Ending Date:	21 Sep-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	87d 0h	**Taxon:**		**Source:**	Lab In-House Culture **Age:**

Data Transform	Alt Hyp	Comparison Result
Untransformed	C <> T	Solvent Blank passed adult emergence rate

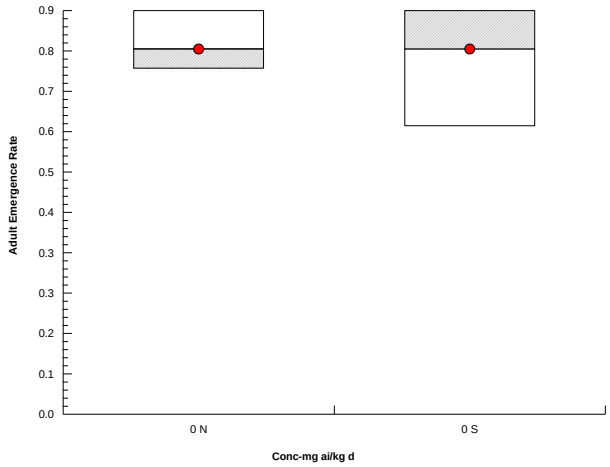
Fisher Exact Test

Control	vs	Control	Test Stat	P-Type	P-Value	Decision(α:5%)
Negative Control		Solvent Blank	1.000	Exact	1.0000	Non-Significant Effect

Data Summary

Conc-mg ai/kg d	Code	NR	R	NR + R	Prop NR	Prop R	%Effect
0	S	38	10	48	0.792	0.208	0.0%
0	N	38	10	48	0.792	0.208	0.0%

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Eurofins Agroscience Service GmbH**

Analysis ID:	20-3253-7553	**Endpoint:**	Day 15 Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	12 Nov-19 17:57	**Analysis:**	STP 2xK Contingency Tables	**Status Level:**	1
Batch ID:	01-5595-9885	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	26 Jun-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	Royal Jelly
Ending Date:	21 Sep-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	87d 0h	**Taxon:**		**Source:**	Lab In-House Culture **Age:**

Data Transform	Alt Hyp	NOEL	LOEL	TOEL	TU
Untransformed	C < T	242	542	362.2	

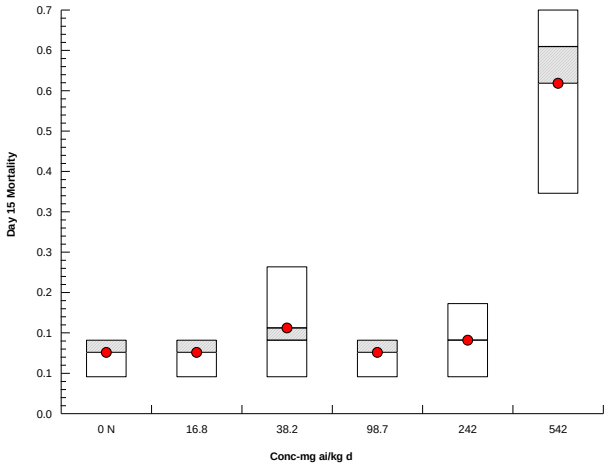
Fisher Exact/Bonferroni-Holm Test

Control	vs	Group	Test Stat	P-Type	P-Value	Decision(α:5%)
Negative Control		16.8	0.630	Exact	1.0000	Non-Significant Effect
		38.2	0.379	Exact	1.0000	Non-Significant Effect
		98.7	0.630	Exact	1.0000	Non-Significant Effect
		242	0.500	Exact	1.0000	Non-Significant Effect
		542*	0.000	Exact	7.0E-06	Significant Effect

Data Summary

Conc-mg ai/kg d	Code	NR	R	NR + R	Prop NR	Prop R	%Effect
0	N	43	5	48	0.896	0.104	0.0%
16.8		43	5	48	0.896	0.104	0.0%
38.2		41	7	48	0.854	0.146	-40.0%
98.7		43	5	48	0.896	0.104	0.0%
242		42	6	48	0.875	0.125	-20.0%
542		21	27	48	0.438	0.562	-440.0%

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Eurofins Agroscience Service GmbH**

Analysis ID:	08-3355-8159	**Endpoint:**	Day 15 Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	12 Nov-19 17:57	**Analysis:**	STP 2xK Contingency Tables-Numerical Sc	**Status Level:**	1
Batch ID:	01-5595-9885	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	26 Jun-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	Royal Jelly
Ending Date:	21 Sep-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	87d 0h	**Taxon:**		**Source:**	Lab In-House Culture **Age:**

Data Transform	Alt Hyp	NOEL	LOEL	TOEL	TU
Untransformed	C < T	242	542	362.2	

Cochran-Armitage (N) Trend Test

Control vs	Group	Test Stat	P-Type	P-Value	Decision(α:5%)
Negative Control	16.8	0.000	Asymp	0.5011	Non-Significant Effect
	38.2	0.656	Asymp	0.5011	Non-Significant Effect
	98.7	-0.003	Asymp	0.5011	Non-Significant Effect
	242	0.185	Asymp	0.4266	Non-Significant Effect
	542*	6.567	Asymp	<1.0E-37	Significant Effect

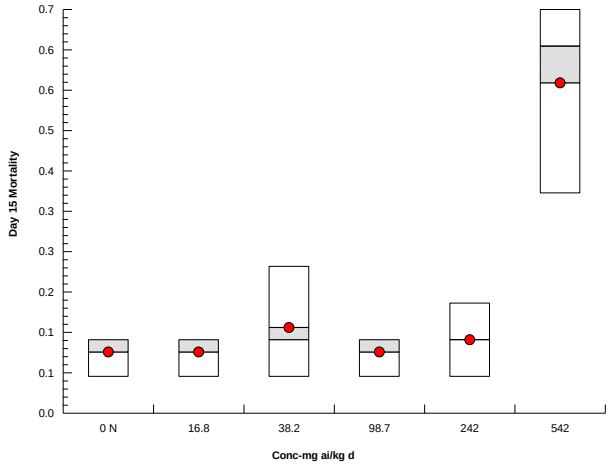
Auxiliary Tests

Attribute	Test	Test Stat	Critical	P-Value	Decision(α:5%)
Overall Effect	Pearson Chi-Square Test	51.9	11.1	<1.0E-37	Significant Overall Effect
Nonlinearity	Chi-Square Lack of Fit Test	8.77	9.49	0.0671	Non-Significant Lack of Linearity
Overdispersion	Tarone C(α) Binomial Overdispersion Test	1.08	1.64	0.1408	Non-Significant Overdispersion

Data Summary

Conc-mg ai/kg d	Code	NR	R	NR + R	Prop NR	Prop R	%Effect
0	N	43	5	48	0.896	0.104	0.0%
16.8		43	5	48	0.896	0.104	0.0%
38.2		41	7	48	0.854	0.146	-40.0%
98.7		43	5	48	0.896	0.104	0.0%
242		42	6	48	0.875	0.125	-20.0%
542		21	27	48	0.438	0.562	-440.0%

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Eurofins Agroscience Service GmbH**

Analysis ID:	02-7986-8374	**Endpoint:**	Day 15 Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	12 Nov-19 17:58	**Analysis:**	Single 2x2 Contingency Table	**Status Level:**	1
Batch ID:	01-5595-9885	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	26 Jun-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	Royal Jelly
Ending Date:	21 Sep-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	87d 0h	**Taxon:**		**Source:**	Lab In-House Culture **Age:**

Data Transform	Alt Hyp	Comparison Result
Untransformed	C <> T	Solvent Blank passed day 15 mortality

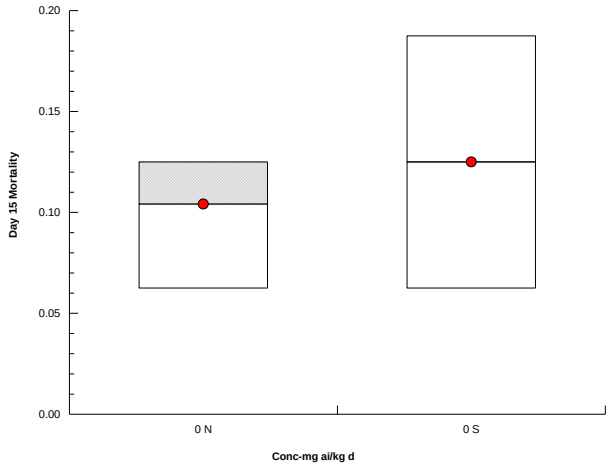
Fisher Exact Test

Control	vs	Control	Test Stat	P-Type	P-Value	Decision(α:5%)
Negative Control		Solvent Blank	1.000	Exact	1.0000	Non-Significant Effect

Data Summary

Conc-mg ai/kg d	Code	NR	R	NR + R	Prop NR	Prop R	%Effect
0	S	42	6	48	0.875	0.125	-20.0%
0	N	43	5	48	0.896	0.104	0.0%

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Eurofins Agroscience Service GmbH**

Analysis ID:	01-5622-0205	**Endpoint:**	Larval Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	12 Nov-19 17:57	**Analysis:**	STP 2xK Contingency Tables	**Status Level:**	1
Batch ID:	01-5595-9885	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	26 Jun-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	Royal Jelly
Ending Date:	21 Sep-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	87d 0h	**Taxon:**		**Source:**	Lab In-House Culture **Age:**

Data Transform	Alt Hyp	NOEL	LOEL	TOEL	TU
Untransformed	C < T	242	542	362.2	

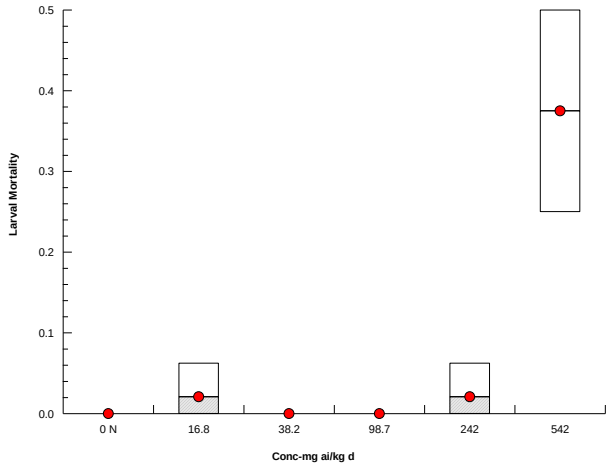
Fisher Exact/Bonferroni-Holm Test

Control	vs	Group	Test Stat	P-Type	P-Value	Decision(α:5%)
Negative Control		16.8	0.500	Exact	1.0000	Non-Significant Effect
		38.2	1.000	Exact	1.0000	Non-Significant Effect
		98.7	1.000	Exact	1.0000	Non-Significant Effect
		242	0.500	Exact	1.0000	Non-Significant Effect
		542*	0.000	Exact	2.7E-06	Significant Effect

Data Summary

Conc-mg ai/kg d	Code	NR	R	NR + R	Prop NR	Prop R	%Effect
0	N	48	0	48	1	0	
16.8		47	1	48	0.979	0.0208	
38.2		48	0	48	1	0	
98.7		48	0	48	1	0	
242		47	1	48	0.979	0.0208	
542		30	18	48	0.625	0.375	

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Eurofins Agroscience Service GmbH**

Analysis ID:	21-4004-8321	**Endpoint:**	Larval Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	12 Nov-19 17:57	**Analysis:**	STP 2xK Contingency Tables-Numerical Sc	**Status Level:**	1
Batch ID:	01-5595-9885	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	26 Jun-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	Royal Jelly
Ending Date:	21 Sep-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	87d 0h	**Taxon:**		**Source:**	Lab In-House Culture **Age:**

Data Transform	Alt Hyp	NOEL	LOEL	TOEL	TU
Untransformed	C < T	242	542	362.2	

Cochran-Armitage (N) Trend Test

Control vs	Group	Test Stat	P-Type	P-Value	Decision(α:5%)
Negative Control	16.8	1.005	Asymp	0.7193	Non-Significant Effect
	38.2	-0.099	Asymp	0.7193	Non-Significant Effect
	98.7	-0.581	Asymp	0.7193	Non-Significant Effect
	242	0.811	Asymp	0.2087	Non-Significant Effect
	542*	8.392	Asymp	<1.0E-37	Significant Effect

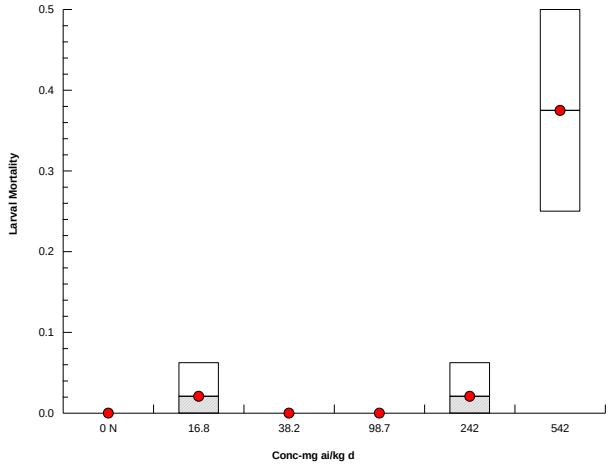
Auxiliary Tests

Attribute	Test	Test Stat	Critical	P-Value	Decision(α:5%)
Overall Effect	Pearson Chi-Square Test	83.6	11.1	<1.0E-37	Significant Overall Effect
Nonlinearity	Chi-Square Lack of Fit Test	13.2	9.49	0.0104	Significant Lack of Linearity
Overdispersion	Tarone C(α) Binomial Overdispersion Test	0.404	1.64	0.3432	Non-Significant Overdispersion

Data Summary

Conc-mg ai/kg d	Code	NR	R	NR + R	Prop NR	Prop R	%Effect
0	N	48	0	48	1	0	
16.8		47	1	48	0.979	0.0208	
38.2		48	0	48	1	0	
98.7		48	0	48	1	0	
242		47	1	48	0.979	0.0208	
542		30	18	48	0.625	0.375	

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Eurofins Agroscience Service GmbH**

Analysis ID:	15-8642-9495	**Endpoint:**	Larval Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	12 Nov-19 17:58	**Analysis:**	Single 2x2 Contingency Table	**Status Level:**	1
Batch ID:	01-5595-9885	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	26 Jun-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	Royal Jelly
Ending Date:	21 Sep-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	87d 0h	**Taxon:**		**Source:**	Lab In-House Culture **Age:**

Data Transform	Alt Hyp	Comparison Result
Untransformed	C <> T	Solvent Blank passed larval mortality

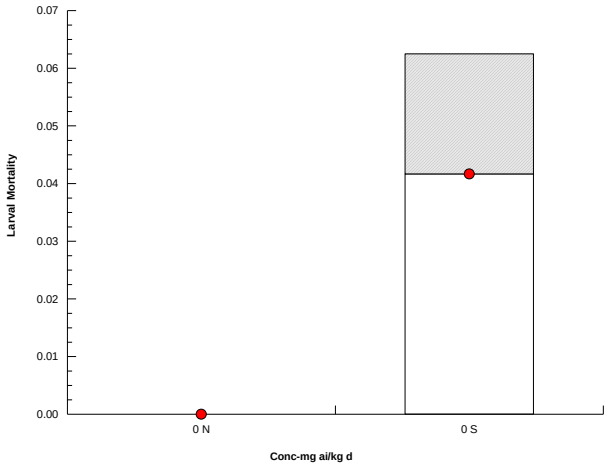
Fisher Exact Test

Control	vs	Control	Test Stat	P-Type	P-Value	Decision(α:5%)
Negative Control		Solvent Blank	0.495	Exact	0.4947	Non-Significant Effect

Data Summary

Conc-mg ai/kg d	Code	NR	R	NR + R	Prop NR	Prop R	%Effect
0	S	46	2	48	0.958	0.0417	
0	N	48	0	48	1	0	

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Eurofins Agroscience Service GmbH**

Analysis ID:	10-2301-8758	**Endpoint:**	Adult Emergence Rate	**CETIS Version:**	CETISv1.9.2
Analyzed:	07 May-18 0:51	**Analysis:**	Linear Regression (GLM)	**Official Results:**	Yes
Batch ID:	13-1639-2584	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	26 Jun-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	Royal Jelly
Ending Date:	21 Sep-17	**Species:**	Apis mellifera	**Brine:**	
Duration:	87d 0h	**Source:**	Lab In-House Culture	**Age:**	
Sample ID:	06-9108-4422	**Code:**	50449801	**Client:**	CDM Smith - E. Krupka
Sample Date:	26 Jun-17	**Material:**	Difenoconazole	**Project:**	Fungicide
Receipt Date:	07 May-18 00:40	**Source:**	Syngenta		
Sample Age:	n/a	**Station:**			

Comments:
PC Code 044200 MRID 50218644 mean-measured daily dietary dose

Linear Regression Options

Model Name	Link Function	Threshold Option	Thresh	Optimized	Pooled	Het Corr	Weighted
Log-Normal (Probit)	η=inv Φ[π]	Zero Threshold	0	No	No	Yes	Yes

Regression Summary

Iters	LL	AICc	BIC	Mu	Sigma	Adj R2	F Stat	Critical	P-Value	Decision(α:5%)
5	-35.12	75.25	75.66	1.455	1.609	0.5795	4.874	3.708	0.0243	Significant Lack of Fit

Point Estimates

Level	ug ai/larv	95% LCL	95% UCL
EC5	0.06448	n/a	0.5005
EC10	0.2477	2.95E-07	1.118
EC15	0.614	4.66E-05	2.017
EC20	1.263	0.002392	3.504
EC25	2.346	0.05785	6.828
EC40	11.16	4.087	1592
EC50	28.53	8.924	250800

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision(α:5%)
Slope	0.6217	0.2371	0.1095	1.134	2.622	0.0211	Significant Parameter
Intercept	-0.9047	0.1971	-1.33	-0.479	-4.591	5.1E-04	Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision(α:5%)
Model	42.2	42.2	1	20.29	5.9E-04	Significant
Lack of Fit	16.05	5.351	3	4.874	0.0243	Significant
Pure Error	10.98	1.098	10			
Residual	27.03	2.08	13			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision(α:5%)
Goodness-of-Fit	Pearson Chi-Sq GOF Test	27.03	22.36	0.0123	Significant Heterogeneity
	Likelihood Ratio GOF Test	27.41	22.36	0.0109	Significant Heterogeneity
Variances	Bartlett Equality of Variance Test	5.844	9.488	0.2111	Equal Variances
	Mod Levene Equality of Variance	1.496	5.192	0.3302	Equal Variances
Distribution	Shapiro-Wilk W Normality Test	0.9171	0.8815	0.1738	Normal Distribution
	Anderson-Darling A2 Normality Te	0.48	2.492	0.2377	Normal Distribution

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Eurofins Agroscience Service GmbH**

Analysis ID: 10-2301-8758 **Endpoint:** Adult Emergence Rate **CETIS Version:** CETISv1.9.2
Analyzed: 07 May-18 0:51 **Analysis:** Linear Regression (GLM) **Official Results:** Yes

Adult Emergence Rate Summary

			Calculated Variate(A/B)								
Conc-ug ai/larv	**Code**	**Count**	**Mean**	**Min**	**Max**	**Std Err**	**Std Dev**	**CV%**	**%Effect**	**A**	**B**
0.646		3	0.7708	0.6250	0.8750	0.0751	0.1301	16.88%	0.0%	37	48
1.47		3	0.7917	0.6875	0.9375	0.0751	0.1301	16.43%	-2.7%	38	48
3.79		3	0.7917	0.7500	0.8125	0.0208	0.0361	4.56%	-2.7%	38	48
9.28		3	0.7917	0.7500	0.8125	0.0208	0.0361	4.56%	-2.7%	38	48
20.9		3	0.3542	0.1875	0.5000	0.0908	0.1573	44.41%	54.05%	17	48

Adult Emergence Rate Detail

Conc-ug ai/larv	**Code**	**Rep 1**	**Rep 2**	**Rep 3**
0.646		0.8750	0.8125	0.6250
1.47		0.6875	0.9375	0.7500
3.79		0.8125	0.7500	0.8125
9.28		0.8125	0.8125	0.7500
20.9		0.1875	0.5000	0.3750

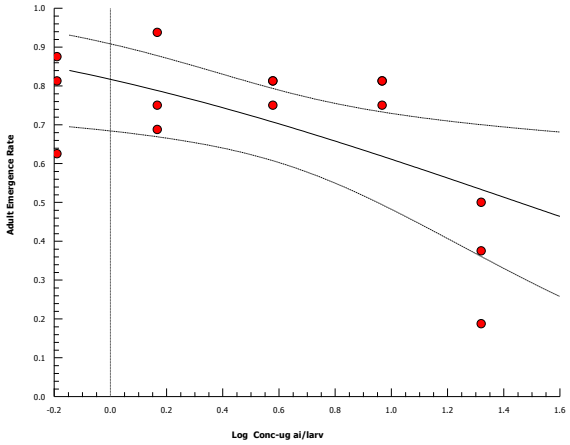
Adult Emergence Rate Binomials

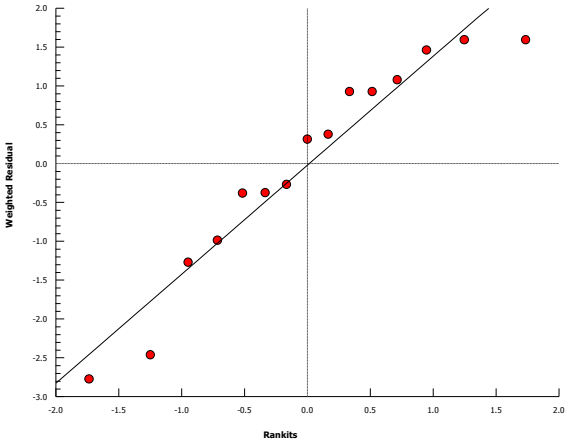
Conc-ug ai/larv	**Code**	**Rep 1**	**Rep 2**	**Rep 3**
0.646		0/16	1/16	0/16
1.47		0/16	0/16	0/16
3.79		0/16	0/16	0/16
9.28		0/16	1/16	0/16
20.9		8/16	4/16	6/16

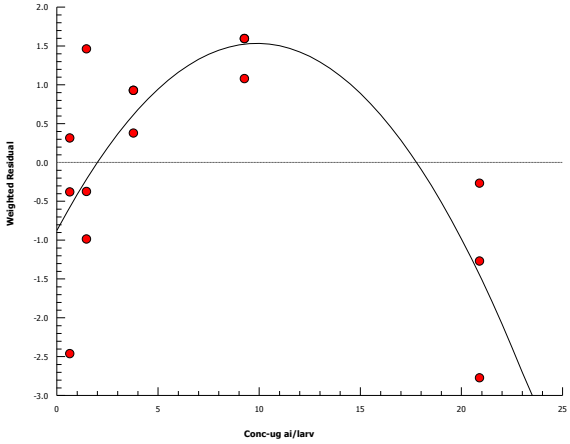
Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Eurofins Agroscience Service GmbH**

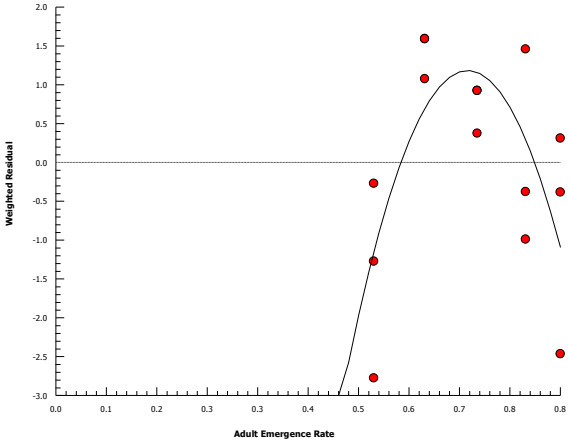
Analysis ID:	10-2301-8758	**Endpoint:**	Adult Emergence Rate	**CETIS Version:**	CETISv1.9.2
Analyzed:	07 May-18 0:51	**Analysis:**	Linear Regression (GLM)	**Official Results:**	Yes

Graphics — Log-Normal: inv Φ[π]=α+β·log[x]









Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Eurofins Agroscience Service GmbH**

Analysis ID:	01-4334-5343	**Endpoint:**	Day 15 Mortality	**CETIS Version:**	CETISv1.9.2
Analyzed:	07 May-18 0:52	**Analysis:**	Linear Regression (GLM)	**Official Results:**	Yes
Batch ID:	13-1639-2584	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	26 Jun-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	Royal Jelly
Ending Date:	21 Sep-17	**Species:**	Apis mellifera	**Brine:**	
Duration:	87d 0h	**Source:**	Lab In-House Culture	**Age:**	
Sample ID:	06-9108-4422	**Code:**	50449801	**Client:**	CDM Smith - E. Krupka
Sample Date:	26 Jun-17	**Material:**	Difenoconazole	**Project:**	Fungicide
Receipt Date:	07 May-18 00:40	**Source:**	Syngenta		
Sample Age:	n/a	**Station:**			

Comments:
PC Code 044200 MRID 50218644 mean-measured daily dietary dose

Linear Regression Options

Model Name	Link Function	Threshold Option	Thresh	Optimized	Pooled	Het Corr	Weighted
Log-Normal (Probit)	η=inv Φ[π]	Zero Threshold	0	No	No	Yes	Yes

Regression Summary

Iters	LL	AICc	BIC	Mu	Sigma	Adj R2	F Stat	Critical	P-Value	Decision(α:5%)
6	-31.5	67.99	68.41	1.636	1.198	0.8747	6.489	3.708	0.0103	Significant Lack of Fit

Point Estimates

Level	ug ai/larv	95% LCL	95% UCL
LC5	0.4625	0.003326	1.462
LC10	1.26	0.05731	2.987
LC15	2.478	0.3514	5.385
LC20	4.242	1.231	10.38
LC25	6.728	2.775	23.68
LC40	21.5	9.137	446.4
LC50	43.26	15.23	3209

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision(α:5%)
Slope	0.8345	0.2554	0.2828	1.386	3.268	0.0061	Significant Parameter
Intercept	-1.365	0.226	-1.854	-0.8771	-6.041	4.2E-05	Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision(α:5%)
Model	183.7	183.7	1	98.69	1.9E-07	Significant
Lack of Fit	15.99	5.329	3	6.489	0.0103	Significant
Pure Error	8.213	0.8213	10			
Residual	24.2	1.862	13			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision(α:5%)
Goodness-of-Fit	Pearson Chi-Sq GOF Test	24.2	22.36	0.0293	Significant Heterogeneity
	Likelihood Ratio GOF Test	25.09	22.36	0.0225	Significant Heterogeneity
Variances	Bartlett Equality of Variance Test	3.752	9.488	0.4406	Equal Variances
	Mod Levene Equality of Variance	0.8533	5.192	0.5485	Equal Variances
Distribution	Shapiro-Wilk W Normality Test	0.952	0.8815	0.5557	Normal Distribution
	Anderson-Darling A2 Normality Te	0.3776	2.492	0.4132	Normal Distribution

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Eurofins Agroscience Service GmbH**

Analysis ID: 01-4334-5343 **Endpoint:** Day 15 Mortality **CETIS Version:** CETISv1.9.2
Analyzed: 07 May-18 0:52 **Analysis:** Linear Regression (GLM) **Official Results:** Yes

Day 15 Mortality Summary

			Calculated Variate(A/B)								
Conc-ug ai/larv	**Code**	**Count**	**Mean**	**Min**	**Max**	**Std Err**	**Std Dev**	**CV%**	**%Effect**	**A**	**B**
0.646		3	0.1042	0.0625	0.1250	0.0208	0.0361	34.64%	0.0%	5	48
1.47		3	0.1458	0.0625	0.2500	0.0551	0.0955	65.47%	4.65%	7	48
3.79		3	0.1042	0.0625	0.1250	0.0208	0.0361	34.64%	0.0%	5	48
9.28		3	0.1250	0.0625	0.1875	0.0361	0.0625	50.00%	2.33%	6	48
20.9		3	0.5625	0.3750	0.6875	0.0955	0.1654	29.40%	51.16%	27	48

Day 15 Mortality Detail

Conc-ug ai/larv	**Code**	**Rep 1**	**Rep 2**	**Rep 3**
0.646		0.1250	0.0625	0.1250
1.47		0.1250	0.0625	0.2500
3.79		0.0625	0.1250	0.1250
9.28		0.1250	0.0625	0.1875
20.9		0.6875	0.3750	0.6250

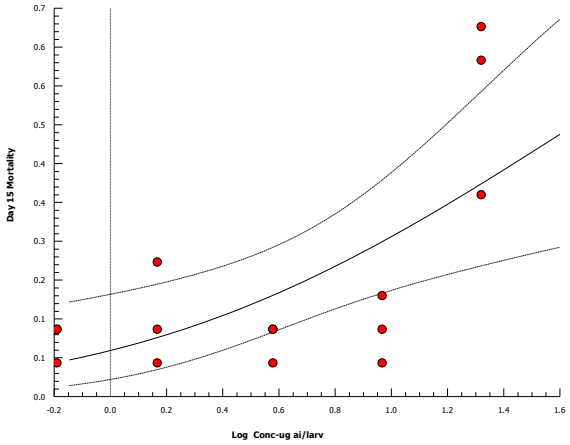
Day 15 Mortality Binomials

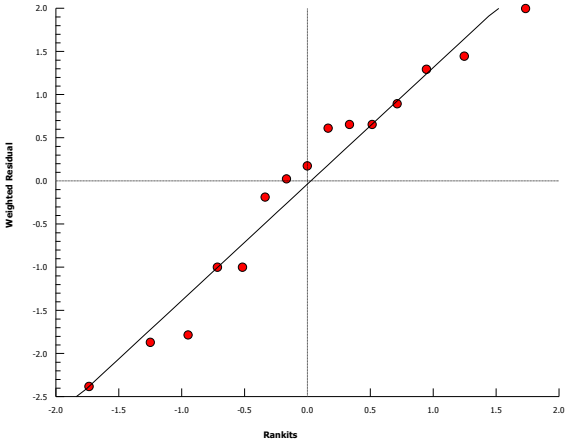
Conc-ug ai/larv	**Code**	**Rep 1**	**Rep 2**	**Rep 3**
0.646		0/16	1/16	0/16
1.47		0/16	0/16	0/16
3.79		0/16	0/16	0/16
9.28		0/16	1/16	0/16
20.9		8/16	4/16	6/16

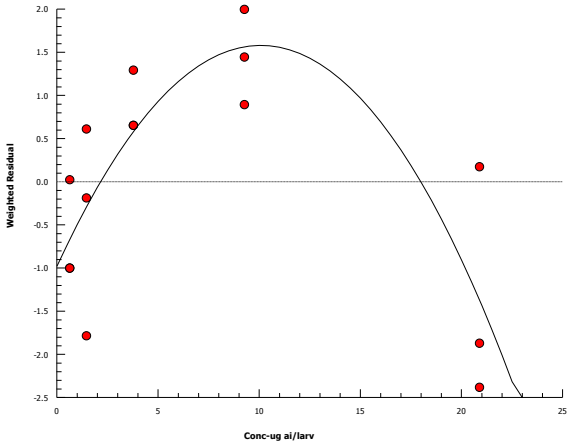
Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Eurofins Agroscience Service GmbH**

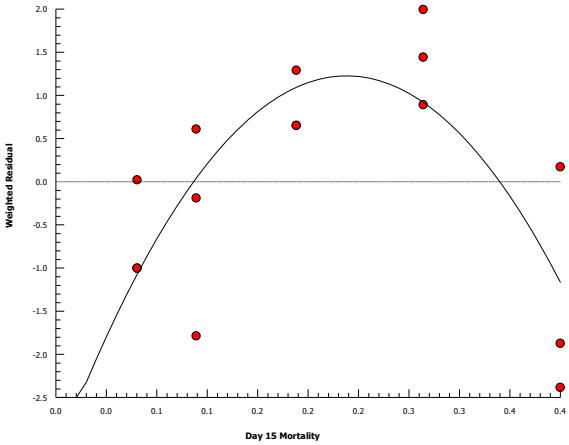
Analysis ID:	01-4334-5343	**Endpoint:**	Day 15 Mortality	**CETIS Version:**	CETISv1.9.2
Analyzed:	07 May-18 0:52	**Analysis:**	Linear Regression (GLM)	**Official Results:**	Yes

Graphics — Log-Normal: inv Φ[π]=α+β·log[x]









Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Eurofins Agroscience Service GmbH**

Analysis ID:	00-5707-0817	**Endpoint:**	Larval Mortality	**CETIS Version:**	CETISv1.9.2
Analyzed:	07 May-18 0:52	**Analysis:**	Linear Regression (GLM)	**Official Results:**	Yes
Batch ID:	13-1639-2584	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	26 Jun-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	Royal Jelly
Ending Date:	21 Sep-17	**Species:**	Apis mellifera	**Brine:**	
Duration:	87d 0h	**Source:**	Lab In-House Culture	**Age:**	
Sample ID:	06-9108-4422	**Code:**	50449801	**Client:**	CDM Smith - E. Krupka
Sample Date:	26 Jun-17	**Material:**	Difenoconazole	**Project:**	Fungicide
Receipt Date:	07 May-18 00:40	**Source:**	Syngenta		
Sample Age:	n/a	**Station:**			

Comments:
PC Code 044200 MRID 50218644 mean-measured daily dietary dose

Linear Regression Options

Model Name	Link Function	Threshold Option	Thresh	Optimized	Pooled	Het Corr	Weighted
Log-Normal (Probit)	η=inv Φ[π]	Zero Threshold	0	No	No	Yes	Yes

Regression Summary

Iters	LL	AICc	BIC	Mu	Sigma	Adj R2	F Stat	Critical	P-Value	Decision(α:5%)
11	-18.19	41.39	41.8	1.634	0.536	0.9977	1.767	3.708	0.2169	Non-Significant Lack of Fit

Point Estimates

Level	ug ai/larv	95% LCL	95% UCL
LC5	5.648	n/a	n/a
LC10	8.844	n/a	n/a
LC15	11.97	n/a	n/a
LC20	15.22	n/a	n/a
LC25	18.71	n/a	n/a
LC40	31.46	n/a	n/a
LC50	43	n/a	n/a

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision(α:5%)
Slope	1.866	1.743	-1.9	5.631	1.07	0.3039	Non-Significant Parameter
Intercept	-3.048	1.947	-7.255	1.159	-1.565	0.1416	Non-Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision(α:5%)
Model	90170	90170	1	6012	<1.0E-37	Significant
Lack of Fit	67.55	22.52	3	1.767	0.2169	Non-Significant
Pure Error	127.4	12.74	10			
Residual	195	15	13			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision(α:5%)
Goodness-of-Fit	Pearson Chi-Sq GOF Test	195	22.36	1.6E-07	Significant Heterogeneity
	Likelihood Ratio GOF Test	23.08	22.36	0.0407	Significant Heterogeneity
Variances	Mod Levene Equality of Variance	0.911	5.192	0.5227	Equal Variances
Distribution	Shapiro-Wilk W Normality Test	0.4702	0.8815	2.0E-06	Non-Normal Distribution
	Anderson-Darling A2 Normality Te	3.745	2.492	<1.0E-37	Non-Normal Distribution

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Eurofins Agroscience Service GmbH**

Analysis ID: 00-5707-0817 **Endpoint:** Larval Mortality **CETIS Version:** CETISv1.9.2
Analyzed: 07 May-18 0:52 **Analysis:** Linear Regression (GLM) **Official Results:** Yes

Larval Mortality Summary

			Calculated Variate(A/B)								
Conc-ug ai/larv	**Code**	**Count**	**Mean**	**Min**	**Max**	**Std Err**	**Std Dev**	**CV%**	**%Effect**	**A**	**B**
0.646		3	0.0208	0.0000	0.0625	0.0208	0.0361	173.20%	0.0%	1	48
1.47		3	0.0000	0.0000	0.0000	0.0000	0.0000		-2.13%	0	48
3.79		3	0.0000	0.0000	0.0000	0.0000	0.0000		-2.13%	0	48
9.28		3	0.0208	0.0000	0.0625	0.0208	0.0361	173.20%	0.0%	1	48
20.9		3	0.3750	0.2500	0.5000	0.0722	0.1250	33.33%	36.17%	18	48

Larval Mortality Detail

Conc-ug ai/larv	**Code**	**Rep 1**	**Rep 2**	**Rep 3**
0.646		0.0000	0.0625	0.0000
1.47		0.0000	0.0000	0.0000
3.79		0.0000	0.0000	0.0000
9.28		0.0000	0.0625	0.0000
20.9		0.5000	0.2500	0.3750

Larval Mortality Binomials

Conc-ug ai/larv	**Code**	**Rep 1**	**Rep 2**	**Rep 3**
0.646		0/16	1/16	0/16
1.47		0/16	0/16	0/16
3.79		0/16	0/16	0/16
9.28		0/16	1/16	0/16
20.9		8/16	4/16	6/16

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Eurofins Agroscience Service GmbH**

Analysis ID:	00-5707-0817	**Endpoint:**	Larval Mortality	**CETIS Version:**	CETISv1.9.2
Analyzed:	07 May-18 0:52	**Analysis:**	Linear Regression (GLM)	**Official Results:**	Yes

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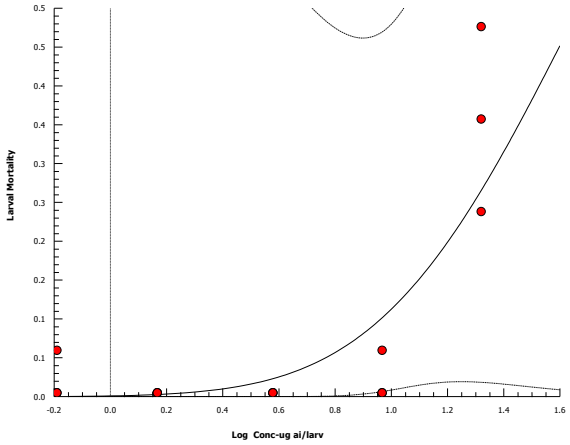
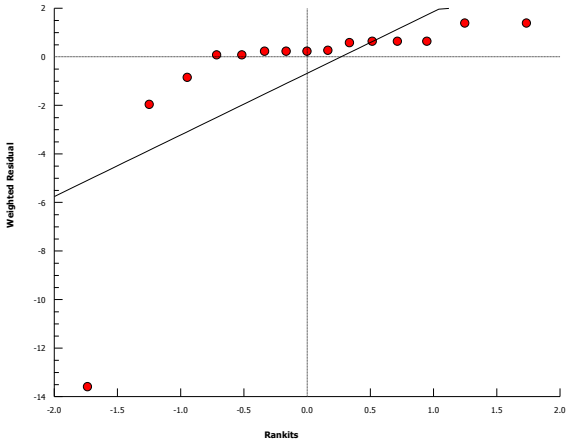
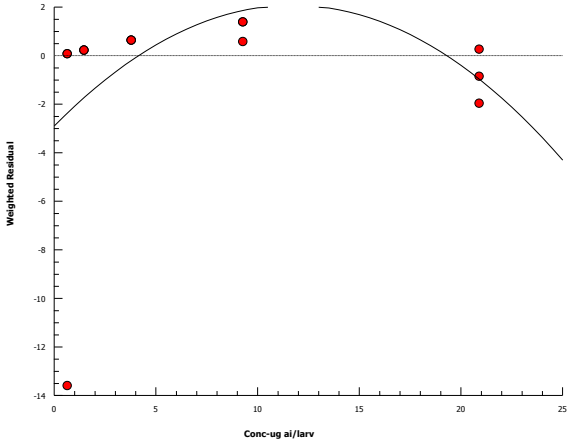
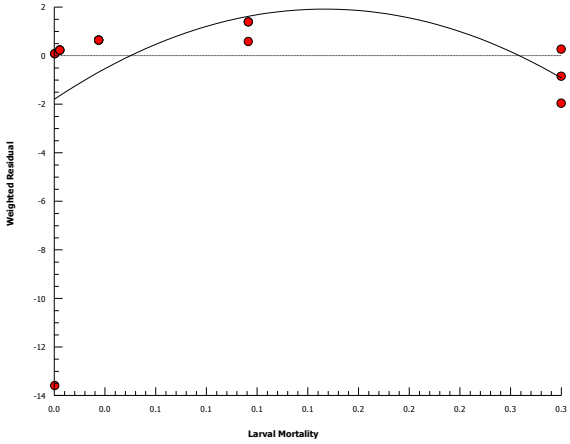








Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Eurofins Agroscience Service GmbH**

Analysis ID:	00-4959-5362	**Endpoint:**	Adult Emergence Rate	**CETIS Version:**	CETISv1.9.2
Analyzed:	07 May-18 0:51	**Analysis:**	Trimmed Spearman-Kärber	**Official Results:**	Yes
Batch ID:	13-1639-2584	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	26 Jun-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	Royal Jelly
Ending Date:	21 Sep-17	**Species:**	Apis mellifera	**Brine:**	
Duration:	87d 0h	**Source:**	Lab In-House Culture	**Age:**	
Sample ID:	06-9108-4422	**Code:**	50449801	**Client:**	CDM Smith - E. Krupka
Sample Date:	26 Jun-17	**Material:**	Difenoconazole	**Project:**	Fungicide
Receipt Date:	07 May-18 00:40	**Source:**	Syngenta		
Sample Age:	n/a	**Station:**			

Comments:
PC Code 044200 MRID 50218644 mean-measured daily dietary dose

Trimmed Spearman-Kärber Estimates

Threshold Option	Threshold	Trim	Mu	Sigma	EC50	95% LCL	95% UCL
Control Threshold	0.2083	44.74%	1.286	0.04188	19.33	15.94	23.44

Adult Emergence Rate Summary

			Calculated Variate(A/B)								
Conc-ug ai/larv	**Code**	**Count**	**Mean**	**Min**	**Max**	**Std Err**	**Std Dev**	**CV%**	**%Effect**	**A**	**B**
0	N	3	0.7917	0.7500	0.8750	0.0417	0.0722	9.12%	0.0%	38	48
0.646		3	0.7708	0.6250	0.8750	0.0751	0.1301	16.88%	2.63%	37	48
1.47		3	0.7917	0.6875	0.9375	0.0751	0.1301	16.43%	0.0%	38	48
3.79		3	0.7917	0.7500	0.8125	0.0208	0.0361	4.56%	0.0%	38	48
9.28		3	0.7917	0.7500	0.8125	0.0208	0.0361	4.56%	0.0%	38	48
20.9		3	0.3542	0.1875	0.5000	0.0908	0.1573	44.41%	55.26%	17	48

Adult Emergence Rate Detail

Conc-ug ai/larv	Code	Rep 1	Rep 2	Rep 3
0	N	0.8750	0.7500	0.7500
0.646		0.8750	0.8125	0.6250
1.47		0.6875	0.9375	0.7500
3.79		0.8125	0.7500	0.8125
9.28		0.8125	0.8125	0.7500
20.9		0.1875	0.5000	0.3750

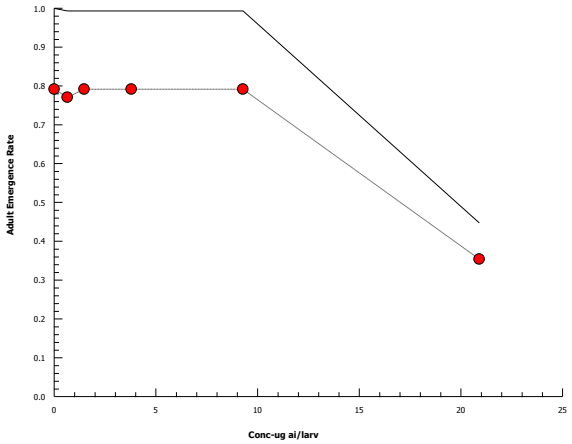
Adult Emergence Rate Binomials

Conc-ug ai/larv	Code	Rep 1	Rep 2	Rep 3
0	S	1/16	1/16	0/16
0	N	0/16	0/16	0/16
0.646		0/16	1/16	0/16
1.47		0/16	0/16	0/16
3.79		0/16	0/16	0/16
9.28		0/16	1/16	0/16
20.9		8/16	4/16	6/16

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Eurofins Agroscience Service GmbH**

Analysis ID:	00-4959-5362	**Endpoint:**	Adult Emergence Rate	**CETIS Version:**	CETISv1.9.2
Analyzed:	07 May-18 0:51	**Analysis:**	Trimmed Spearman-Kärber	**Official Results:**	Yes

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Eurofins Agroscience Service GmbH**

Analysis ID:	12-0178-4519	**Endpoint:**	Day 15 Mortality	**CETIS Version:**	CETISv1.9.2
Analyzed:	07 May-18 0:52	**Analysis:**	Trimmed Spearman-Kärber	**Official Results:**	Yes
Batch ID:	13-1639-2584	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	26 Jun-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	Royal Jelly
Ending Date:	21 Sep-17	**Species:**	Apis mellifera	**Brine:**	
Duration:	87d 0h	**Source:**	Lab In-House Culture	**Age:**	
Sample ID:	06-9108-4422	**Code:**	50449801	**Client:**	CDM Smith - E. Krupka
Sample Date:	26 Jun-17	**Material:**	Difenoconazole	**Project:**	Fungicide
Receipt Date:	07 May-18 00:40	**Source:**	Syngenta		
Sample Age:	n/a	**Station:**			

Comments:
PC Code 044200 MRID 50218644 mean-measured daily dietary dose

Trimmed Spearman-Kärber Estimates

Threshold Option	Threshold	Trim	Mu	Sigma	LC50	95% LCL	95% UCL
Control Threshold	0.1042	48.84%	1.312	0.05085	20.5	16.22	25.91

Day 15 Mortality Summary

			Calculated Variate(A/B)								
Conc-ug ai/larv	**Code**	**Count**	**Mean**	**Min**	**Max**	**Std Err**	**Std Dev**	**CV%**	**%Effect**	**A**	**B**
0	N	3	0.1042	0.0625	0.1250	0.0208	0.0361	34.64%	0.0%	5	48
0.646		3	0.1042	0.0625	0.1250	0.0208	0.0361	34.64%	0.0%	5	48
1.47		3	0.1458	0.0625	0.2500	0.0551	0.0955	65.47%	4.65%	7	48
3.79		3	0.1042	0.0625	0.1250	0.0208	0.0361	34.64%	0.0%	5	48
9.28		3	0.1250	0.0625	0.1875	0.0361	0.0625	50.00%	2.33%	6	48
20.9		3	0.5625	0.3750	0.6875	0.0955	0.1654	29.40%	51.16%	27	48

Day 15 Mortality Detail

Conc-ug ai/larv	Code	Rep 1	Rep 2	Rep 3
0	N	0.1250	0.1250	0.0625
0.646		0.1250	0.0625	0.1250
1.47		0.1250	0.0625	0.2500
3.79		0.0625	0.1250	0.1250
9.28		0.1250	0.0625	0.1875
20.9		0.6875	0.3750	0.6250

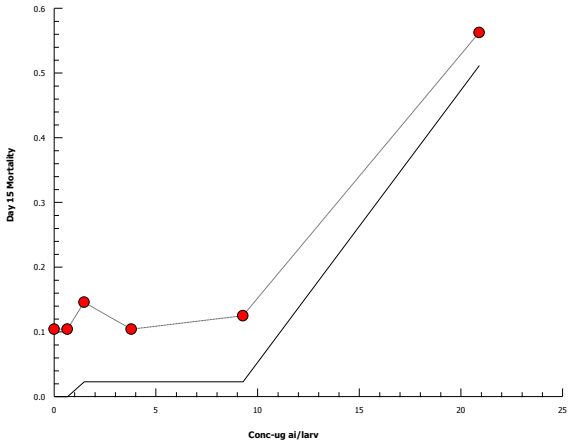
Day 15 Mortality Binomials

Conc-ug ai/larv	Code	Rep 1	Rep 2	Rep 3
0	S	1/16	1/16	0/16
0	N	0/16	0/16	0/16
0.646		0/16	1/16	0/16
1.47		0/16	0/16	0/16
3.79		0/16	0/16	0/16
9.28		0/16	1/16	0/16
20.9		8/16	4/16	6/16

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Eurofins Agroscience Service GmbH**

Analysis ID:	12-0178-4519	**Endpoint:**	Day 15 Mortality	**CETIS Version:**	CETISv1.9.2
Analyzed:	07 May-18 0:52	**Analysis:**	Trimmed Spearman-Kärber	**Official Results:**	Yes

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Eurofins Agroscience Service GmbH**

Analysis ID:	17-3816-7853	**Endpoint:**	Adult Emergence Rate	**CETIS Version:**	CETISv1.9.2
Analyzed:	07 May-18 0:46	**Analysis:**	Linear Regression (GLM)	**Official Results:**	Yes
Batch ID:	01-5595-9885	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	26 Jun-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	Royal Jelly
Ending Date:	21 Sep-17	**Species:**	Apis mellifera	**Brine:**	
Duration:	87d 0h	**Source:**	Lab In-House Culture	**Age:**	
Sample ID:	07-9424-3951	**Code:**	50449801	**Client:**	CDM Smith - E. Krupka
Sample Date:	26 Jun-17	**Material:**	Difenoconazole	**Project:**	Fungicide
Receipt Date:		**Source:**	Syngenta		
Sample Age:	n/a	**Station:**			

Comments:
PC Code 044200 MRID 50218644 mean-measured concentration

Linear Regression Options

Model Name	Link Function	Threshold Option	Thresh	Optimized	Pooled	Het Corr	Weighted
Log-Normal (Probit)	η=inv Φ[π]	Zero Threshold	0	No	No	Yes	Yes

Regression Summary

Iters	LL	AICc	BIC	Mu	Sigma	Adj R2	F Stat	Critical	P-Value	Decision(α:5%)
5	-35.15	75.29	75.71	2.872	1.611	0.5785	4.888	3.708	0.0241	Significant Lack of Fit

Point Estimates

Level	mg ai/kg	95% LCL	95% UCL
EC5	1.668	n/a	13.01
EC10	6.418	6.35E-06	29.07
EC15	15.93	0.001064	52.45
EC20	32.81	0.05731	91.16
EC25	60.98	1.442	177.9
EC40	290.7	106.2	44120
EC50	743.9	232.1	7392000

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision(α:5%)
Slope	0.6209	0.2373	0.1083	1.133	2.617	0.0213	Significant Parameter
Intercept	-1.783	0.5038	-2.871	-0.6945	-3.539	0.0036	Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision(α:5%)
Model	42.1	42.1	1	20.22	6.0E-04	Significant
Lack of Fit	16.1	5.366	3	4.888	0.0241	Significant
Pure Error	10.98	1.098	10			
Residual	27.07	2.083	13			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision(α:5%)
Goodness-of-Fit	Pearson Chi-Sq GOF Test	27.07	22.36	0.0122	Significant Heterogeneity
	Likelihood Ratio GOF Test	27.46	22.36	0.0108	Significant Heterogeneity
Variances	Bartlett Equality of Variance Test	5.843	9.488	0.2112	Equal Variances
	Mod Levene Equality of Variance	1.496	5.192	0.3302	Equal Variances
Distribution	Shapiro-Wilk W Normality Test	0.9172	0.8815	0.1745	Normal Distribution
	Anderson-Darling A2 Normality Te	0.48	2.492	0.2376	Normal Distribution

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Eurofins Agroscience Service GmbH**

Analysis ID: 17-3816-7853 **Endpoint:** Adult Emergence Rate **CETIS Version:** CETISv1.9.2
Analyzed: 07 May-18 0:46 **Analysis:** Linear Regression (GLM) **Official Results:** Yes

Adult Emergence Rate Summary

			Calculated Variate(A/B)								
Conc-mg ai/kg d	**Code**	**Count**	**Mean**	**Min**	**Max**	**Std Err**	**Std Dev**	**CV%**	**%Effect**	**A**	**B**
16.8		3	0.7708	0.6250	0.8750	0.0751	0.1301	16.88%	0.0%	37	48
38.2		3	0.7917	0.6875	0.9375	0.0751	0.1301	16.43%	-2.7%	38	48
98.7		3	0.7917	0.7500	0.8125	0.0208	0.0361	4.56%	-2.7%	38	48
242		3	0.7917	0.7500	0.8125	0.0208	0.0361	4.56%	-2.7%	38	48
542		3	0.3542	0.1875	0.5000	0.0908	0.1573	44.41%	54.05%	17	48

Adult Emergence Rate Detail

Conc-mg ai/kg d	**Code**	**Rep 1**	**Rep 2**	**Rep 3**
16.8		0.8750	0.8125	0.6250
38.2		0.6875	0.9375	0.7500
98.7		0.8125	0.7500	0.8125
242		0.8125	0.8125	0.7500
542		0.1875	0.5000	0.3750

Adult Emergence Rate Binomials

Conc-mg ai/kg d	**Code**	**Rep 1**	**Rep 2**	**Rep 3**
16.8		0/16	1/16	0/16
38.2		0/16	0/16	0/16
98.7		0/16	0/16	0/16
242		0/16	1/16	0/16
542		8/16	4/16	6/16

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Eurofins Agroscience Service GmbH**

Analysis ID:	17-3816-7853	**Endpoint:**	Adult Emergence Rate	**CETIS Version:**	CETISv1.9.2
Analyzed:	07 May-18 0:46	**Analysis:**	Linear Regression (GLM)	**Official Results:**	Yes

Graphics

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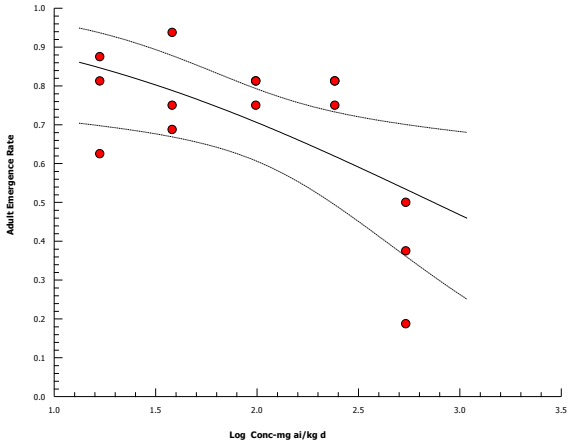
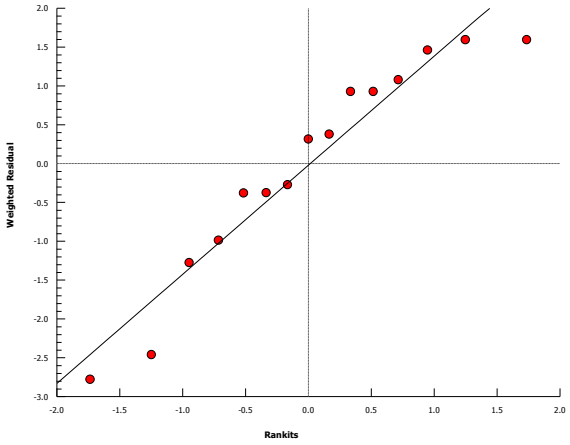
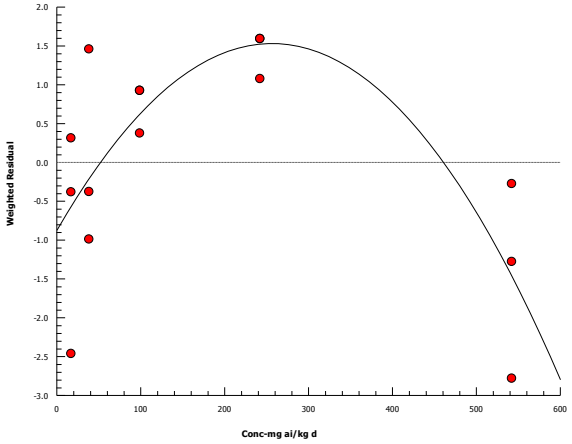
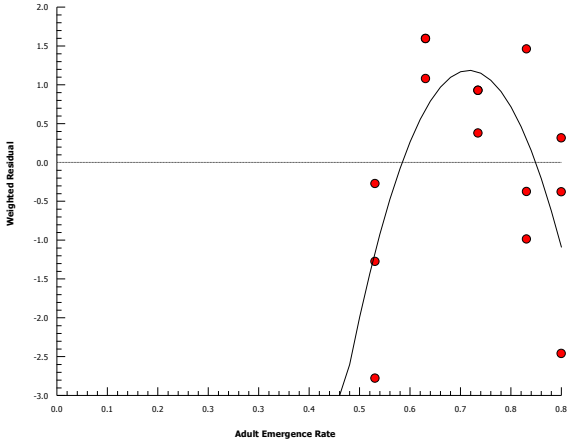








Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Eurofins Agroscience Service GmbH**

Analysis ID:	15-4867-6260	**Endpoint:**	Day 15 Mortality	**CETIS Version:**	CETISv1.9.2
Analyzed:	07 May-18 0:47	**Analysis:**	Linear Regression (GLM)	**Official Results:**	Yes
Batch ID:	01-5595-9885	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	26 Jun-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	Royal Jelly
Ending Date:	21 Sep-17	**Species:**	Apis mellifera	**Brine:**	
Duration:	87d 0h	**Source:**	Lab In-House Culture	**Age:**	
Sample ID:	07-9424-3951	**Code:**	50449801	**Client:**	CDM Smith - E. Krupka
Sample Date:	26 Jun-17	**Material:**	Difenoconazole	**Project:**	Fungicide
Receipt Date:		**Source:**	Syngenta		
Sample Age:	n/a	**Station:**			

Comments:
PC Code 044200 MRID 50218644 mean-measured concentration

Linear Regression Options

Model Name	Link Function	Threshold Option	Thresh	Optimized	Pooled	Het Corr	Weighted
Log-Normal (Probit)	η=inv Φ[π]	Zero Threshold	0	No	No	Yes	Yes

Regression Summary

Iters	LL	AICc	BIC	Mu	Sigma	Adj R2	F Stat	Critical	P-Value	Decision(α:5%)
6	-31.53	68.05	68.47	3.052	1.199	0.8741	6.512	3.708	0.0102	Significant Lack of Fit

Point Estimates

Level	mg ai/kg	95% LCL	95% UCL
LC5	12	0.08295	38.03
LC10	32.73	1.454	77.71
LC15	64.41	9.015	140.2
LC20	110.3	31.81	270.7
LC25	175	72.01	620.2
LC40	560	237.5	11910
LC50	1127	395.9	86630

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision(α:5%)
Slope	0.8337	0.2558	0.2812	1.386	3.26	0.0062	Significant Parameter
Intercept	-2.545	0.5622	-3.759	-1.33	-4.526	5.7E-04	Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision(α:5%)
Model	183.3	183.3	1	98.23	2.0E-07	Significant
Lack of Fit	16.04	5.348	3	6.512	0.0102	Significant
Pure Error	8.212	0.8212	10			
Residual	24.26	1.866	13			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision(α:5%)
Goodness-of-Fit	Pearson Chi-Sq GOF Test	24.26	22.36	0.0288	Significant Heterogeneity
	Likelihood Ratio GOF Test	25.15	22.36	0.0220	Significant Heterogeneity
Variances	Bartlett Equality of Variance Test	3.756	9.488	0.4401	Equal Variances
	Mod Levene Equality of Variance	0.854	5.192	0.5481	Equal Variances
Distribution	Shapiro-Wilk W Normality Test	0.9522	0.8815	0.5592	Normal Distribution
	Anderson-Darling A2 Normality Te	0.3759	2.492	0.4169	Normal Distribution

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Eurofins Agroscience Service GmbH**

Analysis ID: 15-4867-6260 **Endpoint:** Day 15 Mortality **CETIS Version:** CETISv1.9.2
Analyzed: 07 May-18 0:47 **Analysis:** Linear Regression (GLM) **Official Results:** Yes

Day 15 Mortality Summary

			Calculated Variate(A/B)								
Conc-mg ai/kg d	**Code**	**Count**	**Mean**	**Min**	**Max**	**Std Err**	**Std Dev**	**CV%**	**%Effect**	**A**	**B**
16.8		3	0.1042	0.0625	0.1250	0.0208	0.0361	34.64%	0.0%	5	48
38.2		3	0.1458	0.0625	0.2500	0.0551	0.0955	65.47%	4.65%	7	48
98.7		3	0.1042	0.0625	0.1250	0.0208	0.0361	34.64%	0.0%	5	48
242		3	0.1250	0.0625	0.1875	0.0361	0.0625	50.00%	2.33%	6	48
542		3	0.5625	0.3750	0.6875	0.0955	0.1654	29.40%	51.16%	27	48

Day 15 Mortality Detail

Conc-mg ai/kg d	**Code**	**Rep 1**	**Rep 2**	**Rep 3**
16.8		0.1250	0.0625	0.1250
38.2		0.1250	0.0625	0.2500
98.7		0.0625	0.1250	0.1250
242		0.1250	0.0625	0.1875
542		0.6875	0.3750	0.6250

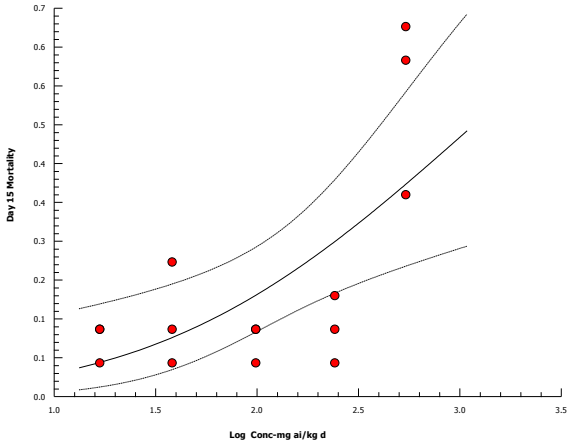
Day 15 Mortality Binomials

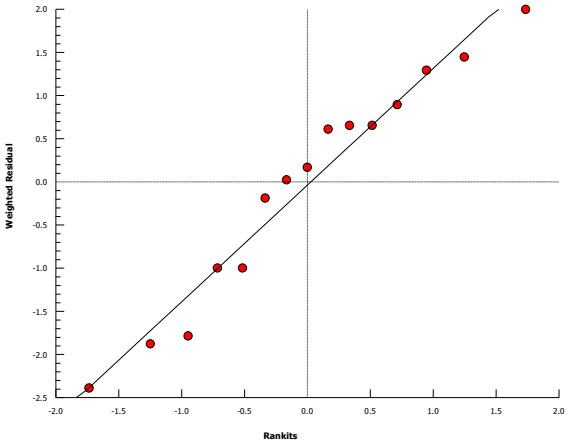
Conc-mg ai/kg d	**Code**	**Rep 1**	**Rep 2**	**Rep 3**
16.8		0/16	1/16	0/16
38.2		0/16	0/16	0/16
98.7		0/16	0/16	0/16
242		0/16	1/16	0/16
542		8/16	4/16	6/16

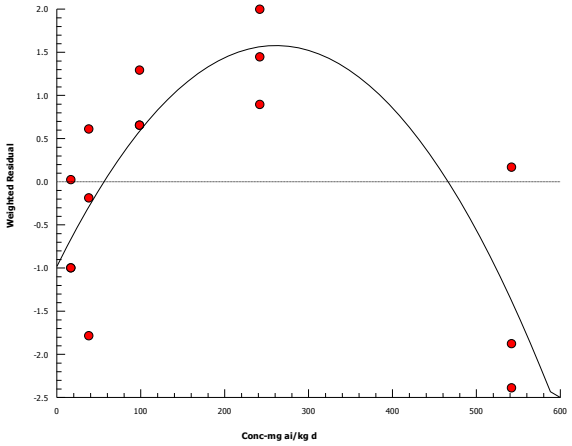
Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Eurofins Agroscience Service GmbH**

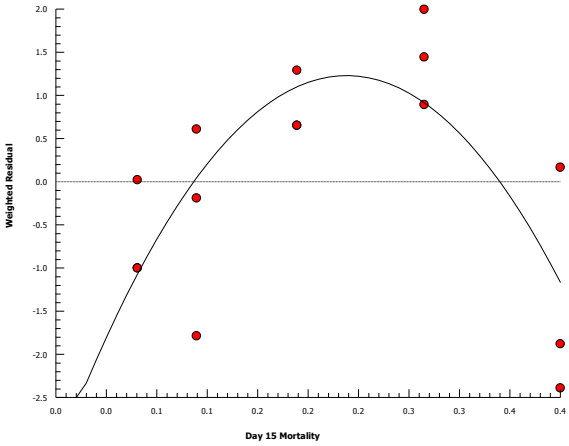
Analysis ID:	15-4867-6260	**Endpoint:**	Day 15 Mortality	**CETIS Version:**	CETISv1.9.2
Analyzed:	07 May-18 0:47	**Analysis:**	Linear Regression (GLM)	**Official Results:**	Yes

Graphics Log-Normal: inv Φ[π]=α+β·log[x]









Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Eurofins Agroscience Service GmbH**

Analysis ID:	11-8533-0296	**Endpoint:**	Larval Mortality	**CETIS Version:**	CETISv1.9.2
Analyzed:	07 May-18 0:47	**Analysis:**	Linear Regression (GLM)	**Official Results:**	Yes
Batch ID:	01-5595-9885	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	26 Jun-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	Royal Jelly
Ending Date:	21 Sep-17	**Species:**	Apis mellifera	**Brine:**	
Duration:	87d 0h	**Source:**	Lab In-House Culture	**Age:**	
Sample ID:	07-9424-3951	**Code:**	50449801	**Client:**	CDM Smith - E. Krupka
Sample Date:	26 Jun-17	**Material:**	Difenoconazole	**Project:**	Fungicide
Receipt Date:		**Source:**	Syngenta		
Sample Age:	n/a	**Station:**			

Comments:
PC Code 044200 MRID 50218644 mean-measured concentration

Linear Regression Options

Model Name	Link Function	Threshold Option	Thresh	Optimized	Pooled	Het Corr	Weighted
Log-Normal (Probit)	η=inv Φ[π]	Zero Threshold	0	No	No	Yes	Yes

Regression Summary

Iters	LL	AICc	BIC	Mu	Sigma	Adj R2	F Stat	Critical	P-Value	Decision(α:5%)
11	-18.23	41.46	41.88	3.048	0.5359	0.9977	1.768	3.708	0.2165	Non-Significant Lack of Fit

Point Estimates

Level	mg ai/kg	95% LCL	95% UCL
LC5	146.8	n/a	n/a
LC10	229.9	n/a	n/a
LC15	311	n/a	n/a
LC20	395.6	n/a	n/a
LC25	486.2	n/a	n/a
LC40	817.5	n/a	n/a
LC50	1118	n/a	n/a

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision(α:5%)
Slope	1.866	1.746	-1.907	5.639	1.068	0.3047	Non-Significant Parameter
Intercept	-5.688	4.379	-15.15	3.772	-1.299	0.2165	Non-Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision(α:5%)
Model	90110	90110	1	6010	<1.0E-37	Significant
Lack of Fit	67.56	22.52	3	1.768	0.2165	Non-Significant
Pure Error	127.3	12.73	10			
Residual	194.9	14.99	13			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision(α:5%)
Goodness-of-Fit	Pearson Chi-Sq GOF Test	194.9	22.36	1.5E-07	Significant Heterogeneity
	Likelihood Ratio GOF Test	23.16	22.36	0.0398	Significant Heterogeneity
Variances	Mod Levene Equality of Variance	0.911	5.192	0.5227	Equal Variances
Distribution	Shapiro-Wilk W Normality Test	0.4708	0.8815	2.1E-06	Non-Normal Distribution
	Anderson-Darling A2 Normality Te	3.738	2.492	<1.0E-37	Non-Normal Distribution

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Eurofins Agroscience Service GmbH**

Analysis ID: 11-8533-0296 **Endpoint:** Larval Mortality **CETIS Version:** CETISv1.9.2
Analyzed: 07 May-18 0:47 **Analysis:** Linear Regression (GLM) **Official Results:** Yes

Larval Mortality Summary

			Calculated Variate(A/B)								
Conc-mg ai/kg d	**Code**	**Count**	**Mean**	**Min**	**Max**	**Std Err**	**Std Dev**	**CV%**	**%Effect**	**A**	**B**
16.8		3	0.0208	0.0000	0.0625	0.0208	0.0361	173.20%	0.0%	1	48
38.2		3	0.0000	0.0000	0.0000	0.0000	0.0000		-2.13%	0	48
98.7		3	0.0000	0.0000	0.0000	0.0000	0.0000		-2.13%	0	48
242		3	0.0208	0.0000	0.0625	0.0208	0.0361	173.20%	0.0%	1	48
542		3	0.3750	0.2500	0.5000	0.0722	0.1250	33.33%	36.17%	18	48

Larval Mortality Detail

Conc-mg ai/kg d	**Code**	**Rep 1**	**Rep 2**	**Rep 3**
16.8		0.0000	0.0625	0.0000
38.2		0.0000	0.0000	0.0000
98.7		0.0000	0.0000	0.0000
242		0.0000	0.0625	0.0000
542		0.5000	0.2500	0.3750

Larval Mortality Binomials

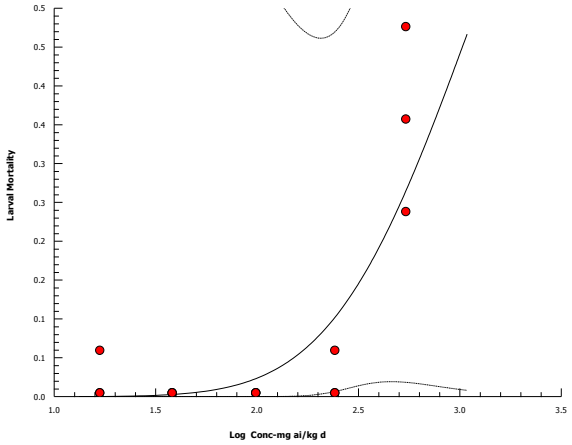
Conc-mg ai/kg d	**Code**	**Rep 1**	**Rep 2**	**Rep 3**
16.8		0/16	1/16	0/16
38.2		0/16	0/16	0/16
98.7		0/16	0/16	0/16
242		0/16	1/16	0/16
542		8/16	4/16	6/16

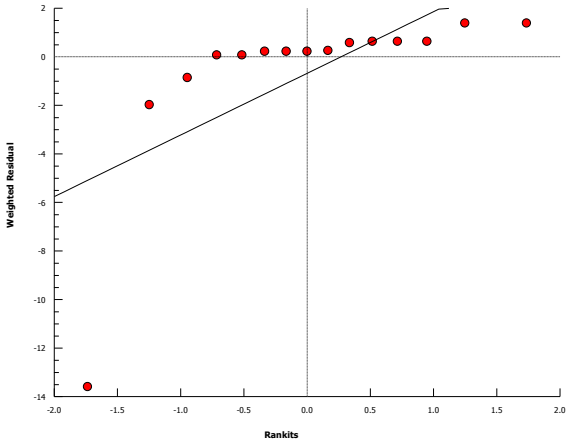
Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Eurofins Agroscience Service GmbH**

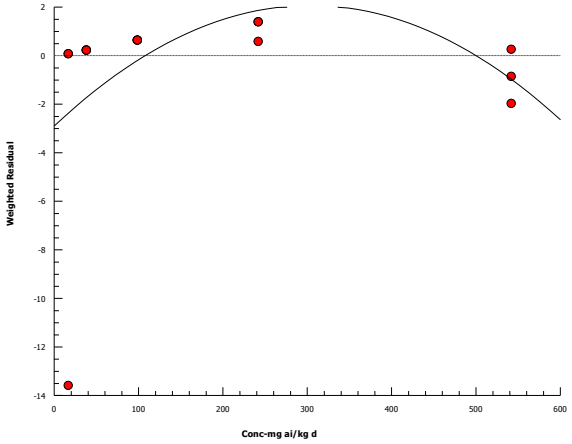
Analysis ID:	11-8533-0296	**Endpoint:**	Larval Mortality	**CETIS Version:**	CETISv1.9.2
Analyzed:	07 May-18 0:47	**Analysis:**	Linear Regression (GLM)	**Official Results:**	Yes

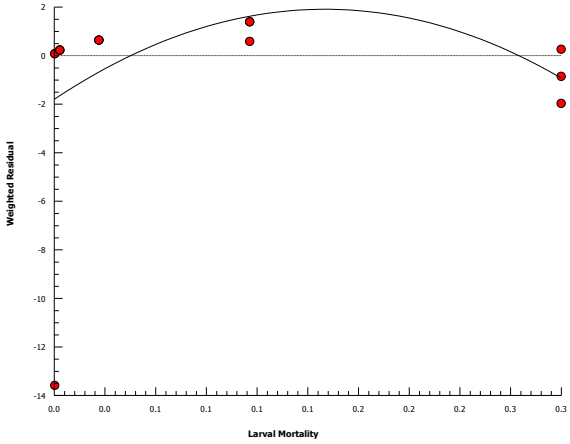
Graphics

Log-Normal: inv Φ[π]=α+β·log[x]









Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Eurofins Agroscience Service GmbH**

Analysis ID:	11-3728-2103	**Endpoint:**	Adult Emergence Rate	**CETIS Version:**	CETISv1.9.2
Analyzed:	07 May-18 0:46	**Analysis:**	Trimmed Spearman-Kärber	**Official Results:**	Yes
Batch ID:	01-5595-9885	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	26 Jun-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	Royal Jelly
Ending Date:	21 Sep-17	**Species:**	Apis mellifera	**Brine:**	
Duration:	87d 0h	**Source:**	Lab In-House Culture	**Age:**	
Sample ID:	07-9424-3951	**Code:**	50449801	**Client:**	CDM Smith - E. Krupka
Sample Date:	26 Jun-17	**Material:**	Difenoconazole	**Project:**	Fungicide
Receipt Date:		**Source:**	Syngenta		
Sample Age:	n/a	**Station:**			

Comments:
PC Code 044200 MRID 50218644 mean-measured concentration

Trimmed Spearman-Kärber Estimates

Threshold Option	Threshold	Trim	Mu	Sigma	EC50	95% LCL	95% UCL
Control Threshold	0.2083	44.74%	2.7	0.04159	501.5	414.1	607.3

Adult Emergence Rate Summary

			Calculated Variate(A/B)								
Conc-mg ai/kg d	**Code**	**Count**	**Mean**	**Min**	**Max**	**Std Err**	**Std Dev**	**CV%**	**%Effect**	**A**	**B**
0	N	3	0.7917	0.7500	0.8750	0.0417	0.0722	9.12%	0.0%	38	48
16.8		3	0.7708	0.6250	0.8750	0.0751	0.1301	16.88%	2.63%	37	48
38.2		3	0.7917	0.6875	0.9375	0.0751	0.1301	16.43%	0.0%	38	48
98.7		3	0.7917	0.7500	0.8125	0.0208	0.0361	4.56%	0.0%	38	48
242		3	0.7917	0.7500	0.8125	0.0208	0.0361	4.56%	0.0%	38	48
542		3	0.3542	0.1875	0.5000	0.0908	0.1573	44.41%	55.26%	17	48

Adult Emergence Rate Detail

Conc-mg ai/kg d	Code	Rep 1	Rep 2	Rep 3
0	N	0.8750	0.7500	0.7500
16.8		0.8750	0.8125	0.6250
38.2		0.6875	0.9375	0.7500
98.7		0.8125	0.7500	0.8125
242		0.8125	0.8125	0.7500
542		0.1875	0.5000	0.3750

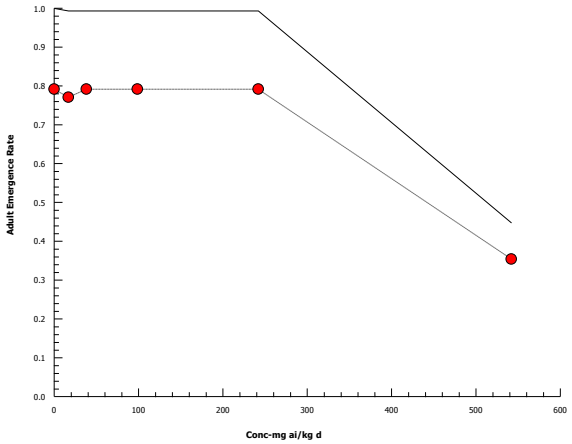
Adult Emergence Rate Binomials

Conc-mg ai/kg d	Code	Rep 1	Rep 2	Rep 3
0	S	1/16	1/16	0/16
0	N	0/16	0/16	0/16
16.8		0/16	1/16	0/16
38.2		0/16	0/16	0/16
98.7		0/16	0/16	0/16
242		0/16	1/16	0/16
542		8/16	4/16	6/16

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Eurofins Agroscience Service GmbH**

Analysis ID:	11-3728-2103	**Endpoint:**	Adult Emergence Rate	**CETIS Version:**	CETISv1.9.2
Analyzed:	07 May-18 0:46	**Analysis:**	Trimmed Spearman-Kärber	**Official Results:**	Yes

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Eurofins Agroscience Service GmbH**

Analysis ID:	08-5814-6348	**Endpoint:**	Day 15 Mortality	**CETIS Version:**	CETISv1.9.2
Analyzed:	07 May-18 0:47	**Analysis:**	Trimmed Spearman-Kärber	**Official Results:**	Yes
Batch ID:	01-5595-9885	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	26 Jun-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	Royal Jelly
Ending Date:	21 Sep-17	**Species:**	Apis mellifera	**Brine:**	
Duration:	87d 0h	**Source:**	Lab In-House Culture	**Age:**	
Sample ID:	07-9424-3951	**Code:**	50449801	**Client:**	CDM Smith - E. Krupka
Sample Date:	26 Jun-17	**Material:**	Difenoconazole	**Project:**	Fungicide
Receipt Date:		**Source:**	Syngenta		
Sample Age:	n/a	**Station:**			

Comments:
PC Code 044200 MRID 50218644 mean-measured concentration

Trimmed Spearman-Kärber Estimates

Threshold Option	Threshold	Trim	Mu	Sigma	LC50	95% LCL	95% UCL
Control Threshold	0.1042	48.84%	2.726	0.0505	531.7	421.4	670.9

Day 15 Mortality Summary

			Calculated Variate(A/B)								
Conc-mg ai/kg d	**Code**	**Count**	**Mean**	**Min**	**Max**	**Std Err**	**Std Dev**	**CV%**	**%Effect**	**A**	**B**
0	N	3	0.1042	0.0625	0.1250	0.0208	0.0361	34.64%	0.0%	5	48
16.8		3	0.1042	0.0625	0.1250	0.0208	0.0361	34.64%	0.0%	5	48
38.2		3	0.1458	0.0625	0.2500	0.0551	0.0955	65.47%	4.65%	7	48
98.7		3	0.1042	0.0625	0.1250	0.0208	0.0361	34.64%	0.0%	5	48
242		3	0.1250	0.0625	0.1875	0.0361	0.0625	50.00%	2.33%	6	48
542		3	0.5625	0.3750	0.6875	0.0955	0.1654	29.40%	51.16%	27	48

Day 15 Mortality Detail

Conc-mg ai/kg d	Code	Rep 1	Rep 2	Rep 3
0	N	0.1250	0.1250	0.0625
16.8		0.1250	0.0625	0.1250
38.2		0.1250	0.0625	0.2500
98.7		0.0625	0.1250	0.1250
242		0.1250	0.0625	0.1875
542		0.6875	0.3750	0.6250

Day 15 Mortality Binomials

Conc-mg ai/kg d	Code	Rep 1	Rep 2	Rep 3
0	S	1/16	1/16	0/16
0	N	0/16	0/16	0/16
16.8		0/16	1/16	0/16
38.2		0/16	0/16	0/16
98.7		0/16	0/16	0/16
242		0/16	1/16	0/16
542		8/16	4/16	6/16

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Eurofins Agroscience Service GmbH**

Analysis ID:	08-5814-6348	**Endpoint:**	Day 15 Mortality	**CETIS Version:**	CETISv1.9.2
Analyzed:	07 May-18 0:47	**Analysis:**	Trimmed Spearman-Kärber	**Official Results:**	Yes

Graphics