UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

February 11, 2020

PC Code: 555555
DP Barcode: 452040

MEMORANDUM

SUBJECT: **Pyrifluquinazon:** Transmittal of Data Evaluation Records (DERs) for Ecological Effects Studies

FROM: N.E. Federoff, Wildlife Biologist
Environmental Risk Branch 2
Environmental Fate and Effects Division
Office of Pesticide Programs (7507P)

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THRU: Amy Blankinship, Branch Chief
Elyssa Arnold, Risk Assessment Process Leader
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TO: Debra Rate, Risk Manager
Shanta Adeeb, Product Manager
Marion Johnson, Branch Chief
Invertebrate Vertebrate Branch 2
Registration Division (7505P)

This memorandum is to inform you that 2 ecological effects study DERs have been finalized for pyrifluquinazon. These studies were submitted under FIFRA 6(a)(2). Studies and their classifications are listed in **Table 1** below. Study summaries are also included.

Table 1: Ecological Toxicity Data for Pyrifluquinazon

MRID	Guideline	Study Type	Study Classification	Comments	CETIS
50735801	OECD 239	Chronic 22-day Larval Honey bee *(Apis mellifera)* 97.45%	Acceptable	Endpoints: Larval and pupal mortality Mean Measured Dietary concentration: EC_{50} = 81 ug ai/kg diet NOAEC = 42 ug ai/kg diet LOAEC = 79 ug ai/kg diet Dietary dose: ED_{50} = 3.3 ug ai/larva/day NOAEC = 1.7 ug ai/larva/day LOAEC = 3.3 ug ai/larva/day	CO
50735802	OECD 245	Oral 10-day Adult Honey bee *(Apis mellifera)* 97.45%	Acceptable	Dietary concentration: LC_{50} = 118 mg ai/kg diet NOAEC = 45 mg ai/kg diet LOAEC = 140 mg ai/kg diet Dietary dose: LD_{50} = 3.1 ug ai/larva/day NOAEC = 1.2 ug ai/larva/day LOAEC = 3.1 ug ai/larva/day	CO

"CO" for studies with unaltered contractor CETIS analyses

MRID 50735801
Pyrifluquinazon: Honey Bee (*Apis mellifera* L.) Larval Toxicity Test, Repeated Exposure.
Guideline: OECD 239

Larval mortality, pupal mortality, adult emergence, and weight were all affected endpoints in this study. Effects on larval and pupal mortality were dose responsive. The NOAEC and LOAEC were 42 and 79 µg ai/g diet, respectively (corresponding to a NOAEL and LOAEC of 1.7 and 3.3 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.

MRID 50735802
Pyrifluquinazon: 10-Day Oral Toxicity Test with the Adult Honey Bee (*Apis Mellifera*).
Guideline: OECD 245

The 10-day mortality NOAEC and LC_{50} were 45 and 118 mg ai/kg diet, respectively (corresponding to a NOAEL and LD_{50} of 1.2 and 3.1 µg ai/bee/day, respectively). There were no effects on food consumption. This study is scientifically sound and is classified as acceptable.

DATA EVALUATION RECORD
CHRONIC (REPEATED DOSE) TOXICITY TEST WITH THE HONEY BEE
NON-GUIDELINE

1. **CHEMICAL:** Pyrifluquinazon PC Code No.: 555555

2. **TEST MATERIAL: Pyrifluquinazon Technical Grade** Purity: 97.45%

3. **CITATION**

Authors:	Patnaude, M.R.
Title:	Pyrifluquinazon: Honey Bee (*Apis mellifera*) Larval Toxicity Test, Repeat Exposure
Study Completion Date:	September 27, 2017
Laboratory:	Smithers Viscient
Sponsor:	Nichino America, Inc.
Study No.:	14078.6105
MRID:	50735801
DP Barcode:	452040

4. **REVIEWED BY:** Julie Burns, Environmental Scientist, CDM/CSS-Dynamac JV

Signature: Julie Burns **Date:** 6/24/2019

APPROVED BY: Moncie V. Wright, Ph.D., Environmental Scientist, CDM/CSS-Dynamac JV

Signature: Moncie V Wright **Date:** 6/26/2019

(Stats and DER update completed 11/18/2019)

5. **APPROVED BY:** N.E. Federoff, OPP/EFED/ERB-2

Signature: **Date:** 1/23/2020

This Data Evaluation Record may have been altered by the Environmental Fate and Effects Division subsequent to signing by CDM/CSS-Dynamac JV personnel. The CDM/CSS-

Dynamac Joint Venture role does not include establishing Agency policies.

6. STUDY PARAMETERS:

Test Species and strain: Larval honey bees, (*Apis mellifera ligustica*)
Age of Test Organisms at Test Initiation: First instar larvae (≤ 24-hour old)
Exposure Duration: 22 days

7. CONCLUSIONS:

Individual synchronized honey bee (*Apis mellifera ligustica*) larvae (first instar) were exposed *in vitro* to **Pyrifluquinazon Technical Grade** on Day 3 (D3) through Day 6 (D6) of the study at the nominal diet concentrations and nominal daily doses, adjusted for purity, reported in the table below. The study author calculated the mean-measured concentrations and cumulative dietary doses based on the analyzed concentrations of test substance in the stock solutions on D3 through D6. The reviewer converted the nominal and measured cumulative doses to daily dietary doses by dividing the cumulative doses by the number of days of exposure (4). The diet concentrations and dietary doses are summarized in the table below.

Nominal Concentration (µg ai/g diet)	Mean-Measured Concentration (µg ai/g diet)	Nominal Daily Dietary dose (µg ai/larva/day)	Measured Daily Dietary dose (µg ai/larva/day)
39	42	1.6	1.7
79	79	3.3	3.3
160	160	6.3	6.3
320	320	13	13
630	610	25	24

Larvae used in the study were provided by Wood's Beekeeping Supply, Lincoln, Rhode Island. Dimethoate was tested as the reference toxicant at a nominal dose of 7.4 µg ai/larva. All groups consisted of 36 larvae per treatment group (each larva was considered a replicate), placed within 48-well cell culture plates.

On Day 8, cumulative larval mortality was 6% and 8% in the negative and solvent control, respectively, as compared to mortality ranged from 3% to 100% in the treatment groups. By Day 15, mortality averaged 11 and 8% in the negative and solvent control, respectively, as compared to mortality ranged from 3% to 100% in the groups exposed to the test material. On Day 22, adult emergence averaged 86% and 92% in the negative and solvent controls, respectively, as compared to emergence that ranged from 0% to 94% in the treatment groups. There was no unconsumed diet in any control or treatment group by Day 8. Emerged bee weight averaged 0.1015 and 0.0998 in the negative and solvent control, respectively, as compared to

weight ranging from 0.0917 to 0.0949 g in the groups exposed to the test material, with no clear dose response.

Larval mortality, pupal mortality, adult emergence, and weight were all affected endpoints in this study. Effects on larval and pupal mortality were dose responsive. The NOAEC and LOAEC were 42 and 79 µg ai/g diet, respectively (corresponding to a NOAEL and LOAEC of 1.7 and 3.3 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**	**Adult Weight**
Diet Concentration µg ai/g diet	LC_{50}: 133 95% CI: 114-156 Slope: 4.0 (C.I.: 3.0-4.9) NOAEC: 42 LOAEC: 79	LC_{50}: 92 95% CI: 80-106 Slope: 5.0 (C.I.: 3.7-6.4) NOAEC: 42 LOAEC: 79	EC_{50}: 81 95% CI: 71-92 Slope: 6.0 (C.I.: 4.2-7.8) NOAEC: 42 LOAEC: 79	EC_{50}: >160 95% CI: N/A Slope: N/A NOAEC: 42 LOAEC: 79
Dietary Dose µg ai/larva/day	LD_{50}: 5.4 95% CI: 4.6-6.3 Slope: 4.1 (C.I.: 3.1-5.1) NOAEL: 1.7 LOAEL: 3.3	LD_{50}: 3.8 95% CI: 3.3-4.3 Slope: 5.2 (C.I.: 3.8-6.7) NOAEL: 1.7 LOAEL: 3.3	ED_{50}: 3.3 95% CI: 2.9-3.8 Slope: 6.1 (C.I.: 4.3-7.9) NOAEL: 1.7 LOAEL: 3.3	ED_{50}: >6.3 95% CI: N/A Slope: N/A NOAEL: 1.7 LOAEL: 3.3

8. ADEQUACY OF THE STUDY:

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

B. Rationale:

C. Reparability:

9. GUIDELINE DEVIATIONS

The procedures used in this study are based on OECD Guidance Document No. 239 dated July 15, 2016 and Schmehl et al. The following deviations from OECD 239 were noted by the reviewer:

1. Physicochemical properties of Pyrifluquinazon were not reported.
2. The test temperature ranged from 33 to 34°C during the larval and pupal phase and ranged from 32-34°C during the emergence phase. The temperature should range from 34 to 35°C.
3. The relative humidity ranged from 46 to 72% during the pupal phase and from 41 to 71% during the emergence phase. Relative humidity should be 80 ± 5% during the pupal phase and range from 50 to 80% during the emergence phase.

4. The % composition of Diets A, B, and C deviated from OECD guidance.
5. The shape of the grafted larvae at transfer was not reported. OECD recommends that newly hatched larvae are selected that have not yet formed a "C" shape.
6. It was not reported whether bees were kept in conditions conforming to proper cultural practices.
7. It was not reported if bees were randomly assigned to treatment groups.
8. Emerged bee weight and day 22 emergence were not reported individually on a per larva basis as the previous endpoints had been.

These deviations do not affect the study.

10. SUBMISSION PURPOSE: This study was conducted to determine the effects of Pyrifluquinazon on honey bee (*Apis mellifera* L.) larva following chronic oral exposure for the purpose of pesticide registration.

11. MATERIALS AND METHODS:

A. Test Material:	Pyrifluquinazon Technical Grade
Description:	Not reported
Lot No./Batch No.:	TY0401
Purity:	97.45%
CAS Number:	337458-27-2
Stability of compound under test conditions:	Analytical quality control sample measurements of Pyrifluquinazon in the royal jelly diet demonstrated that the mean test item concentrations were recovered at rates ranging from 87% to 112% of nominal.
Storage conditions of test chemical:	Room temperature; dark, ventilated cabinet

Range finding test yes/no (if yes, describe): Yes, a non-GLP preliminary study was initiated on June 23, 2015. Methodologies and procedures were similar to those described in the definitive testing. Nominal cumulative doses tested were control (0), solvent control (0), 0.10, 1.0, 10, and 100 µg a.i./larva, with 22-day emergence at 91, 92, 73, 90, 82, and 0%, respectively.

Physicochemical properties of Pyrifluquinazon used in solubility/homogeneity study.

Parameter	Values	Comments
Molecular Weight	Not reported	
Water solubility at 20°C (mg/L)	Not reported	
Vapor pressure (torr, at 25°C)	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

Guideline Criteria	Reported Information	Comments
Species	Honey bee (*Apis mellifera ligustica*)	*OECD recommends European honey bee (Apis mellifera)*
Age at beginning of test Worker bees of uniform age.	First instar larvae, ≤24-hr	*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	Wood's Beekeeping Supply, Lincoln, Rhode Island. Larvae were from three or more different colonies.	*OECD recommends larvae are collected from three different colonies.*
Were bees from disease-free colonies?	Not reported. The larvae were obtained from hives not previously exposed to any chemical treatments within 4 weeks of 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?	Not reported.	

C. Test System

Guideline Criteria	Reported Information	Comments
Test Chambers	Larvae were reared in sterile, 48-well cell culture plates (1.6 mL/well, Corning Costar 3548) containing a plastic queen cup grafting cell (Mann Lake) in 32 wells during acclimation and in 12 wells during exposure. The perimeter wells within each plate were partially filled with deionized water to maintain relative humidity. Larvae that completely consumed the diet on days 7 and 8 were transferred to sterile, 24-well cell pupal plates (3.4 mL/well, Corning Costar 3526) containing two layers of sterile Kimwipes.	*OECD recommends 48-well plate with each well containing a crystal polystyrene grafting cell.*
Temperature during exposure	The larvae, in their cell plates, were kept inside a plastic container in the incubator and monitored continuously. Upon transfer to pupal plates, the plates were maintained in the incubator. Days 1-7: 33-34°C Days 8-15: 33-34°C Days 16-22: 32-34°C	*OECD recommends incubator at 34 – 35°C. Deviations may occur but temperature should not be lower than 23°C or higher than 40°C; deviations not last more than 15 minutes once every 24 hrs.*
Relative humidity during exposure	The perimeter wells within each cell culture plate were partially filled with deionized water to assist in maintaining relative humidity. Larval plates and pupal plates were kept in an incubator. Days 1-7: 96-98% Days 8-15: 46-72% Days 16-22: 41-71%	Fluctuations (≤60 minutes) in relative humidity are shown in Table 1 p. 35 of the MRID. *OECD recommends use of K_2SO_4 to maintain water saturated atmosphere.*

Guideline Criteria	Reported Information	Comments

Guideline Criteria	Reported Information	Comments
Lighting	Near darkness, except approximately 30 minutes a day during assessments and renewal of the diet.	_____ *OECD recommends that plates should be maintained in darkness.*
Feeding	Each larva was fed for 6 days (except on Day 2) with a standardized amount of an artificial diet of 20 µL untreated **Diet A** on Day 1, not fed on Day 2, and fed 20 µL of treated **Diet B** on Day 3. On Days 4, 5, and 6, larvae were fed 30, 40, and 50 µL, respectively, of treated **Diet C**. The diet was warmed to test temperature in the incubator before being added to the plate wells. Diet A[a]: 50% weight of royal jelly + 50% weight of an aqueous solution containing 2% weight of yeast extract, 10% weight of glucose + 10% weight of fructose. Diet B[a]: 50% weight of royal jelly + 50% weight of an aqueous solution containing 2% weight of yeast extract, 11% weight of glucose + 11% weight of fructose. Diet C[a]: 62.5% weight of royal jelly + 37.5% weight of an aqueous solution containing 4% weight of yeast extract, 18% weight of glucose + 18% weight of fructose. [a] Calculated by the reviewer based on diet components provided on p. 15 of the MRID.	_____ *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 of 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.*

D. Test Design

Guideline Criteria	Reported Information	Comments
Nominal test applications	Diet Concentrations: 0 (negative and solvent controls), 39, 79, 160, 320, and 630 µg ai/g diet Daily Dietary Doses[a]: 0 (negative and solvent controls) 1.6, 3.3, 6.3, 13, and 25 µg ai/larva/day [a] Calculated by the reviewer based on cumulative doses.	*OECD recommends 5 treatments of increasing test concentrations. Alternatively, when a limit test is performed, a single dose of 100 µg ai/larva or the maximum achievable solubility (whichever is lower).*
Measured test applications	Diet Concentrations: <3.3 (<LOQ, controls), 42, 79, 160, 320, and 610 µg ai/g diet Daily Dietary Doses[a]: 1.7, 3.3, 6.3, 13, and 24 µg ai/larva/day [a] Calculated by the reviewer based on cumulative doses.	
Number of bees exposed per dosage level	36 larvae Each larva was considered to be a replicate. Larvae were from 3 or more different colonies.	*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	The queen was isolated on a single frame for one day to provide known-aged eggs and subsequent larvae. Frames with brood cells containing newly hatched larvae were placed in a grafting chamber at approximately 28°C. Larvae were removed from the brood cells using a sterile grafting tool. Larvae were acclimated for two days and were fed 20 µL of untreated Diet A on the day of transfer into cell plates.	*OECD recommends that newly hatched larvae are selected that have not yet formed a "C" shape and randomizing the allocation of larvae into the plates for each colony. On Day 1, larva is deposited in cell containing 20 µL diet.*

	The shape of the grafted larvae at transfer was not reported. Untreated artificial royal jelly diets A, B, and C were prepared prior to test initiation and stored frozen until use. On feeding days, unused, untreated, and thawed diet were stored in a refrigerator. A 150 mg ai/mL primary stock solution was prepared by bringing 7.3272 g of the test material to a volume of 50 mL with acetone and mixed using a magnetic stir plate for 5 minutes and 20 seconds. The solution was observed to be clear and amber. Dosing stock solutions were made by dilution of the primary solution and mixed using a magnetic stir plate. Dilutions were observed to be clear and light yellow to light amber in color, with no visible undissolved test substance. Treated royal jelly diets were mixed with the dosing solution for 1 to 2 hours on days 3, 4, and 6, and for 4 hours on day 5, and appeared opaque. Treated diets were prepared daily. A sample of each treated diet and control were collected after sonification on days 3, 4, 5, and 6, and analyzed for Pyrifluquinazon concentration. Stock solution samples were collected for analysis on day 3.	
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. 36 negative control larvae.	_____ *OECD recommends 12 larvae x 3 colonies=36 larvae minimum and that control mortality from D4 to D7 should be ≤15%.*
Solvent control	Acetone.	_____ *OECD recommends maximum of 5%.*
Reference Toxicant	Dimethoate, tested at a nominal dose and concentration of 7.4 µg ai/larva and 46 µg ai/g, respectively. 36 reference larvae per toxicant.	_____ *OECD recommends technical grade dimethoate at dose of 8.8 ± 0.5 µg a.i./larva. Mortality should be ≥50% at D7 for toxic reference.*
Total observation period and frequency of interim observations	Mortality and health were observed and recorded from D3-D8, D15, and D22. Death of a larva was defined by lack of movement. Diet in the wells and number of larvae transferred to pupal plates was observed on D7 and D8. Survival of pupae was checked on D15 and D22. Larvae that failed to develop into pupae by D15 were classified as dead. At the time of emergence, each adult bee was removed from the well plate and individually weighed. The test was terminated on D22, and pupae that had not emerged as adults were considered dead.	_____ *OECD recommends that following chemical exposure on D4, mortalities are checked at time of feeding on D5, D6 and D7 (test termination). Other observations including presence of uneaten food on D7 should be qualitatively reported.*

12. REPORTED RESULTS:

Guideline Criteria	Reported Information
Quality assurance and GLP compliance statements were included in the report?	Yes. The data and report were produced and compiled in accordance with the Good Laboratory Practice Standards as specified in 40 CFR Part 160 with the following exceptions: 1. Routine water and royal jelly diet contaminant screening analyses for pesticides, PCBs, toxic metals, and antibiotics were conducted using standard U.S. EPA procedures by GeoLabs, Inc., Braintree, Massachusetts and the U.S. Department of Agriculture, Gastonia, North Carolina, and are considered facility records under Smithers Viscient's Standard Operating Procedures. Since the analyses were conducted following standard validated methods, this exception had no impact on the study results. 2. The reference toxicant, dimethoate, was purchased from a commercial supplier and was not characterized under Good Laboratory Practices (GLP).
Observed adverse effects on bees at respective dosages	Unconsumed diet was qualitatively recorded on D7 and D8. Biological observations and bee development were recorded on D3-D8, D15, and D22. On Day 22, emerged bees were assessed for health and normal development.

Guideline Criteria	Reported Information
Control and Solvent Control Mortality	D8 Cumulative Mortality Negative control: 6% Solvent control: 8% D15 Cumulative Mortality Negative control: 11% Solvent control: 8% D22 Cumulative Mortality Negative control: 14% Solvent control: 8%
Were raw data included?	Yes.
Analytical Analysis?	Yes, conducted in-house at Smithers Viscient with Liquid Chromatography-Mass Spectrometry/ Mass Spectrometry (LC-MS/MS)

Mortality and Observations:

On Day 8, cumulative larval mortality was 6% and 8% in the negative and solvent control, respectively, as compared to mortality ranged from 3% to 100% in the treatment groups (Table 1). By Day 15, mortality averaged 11 and 8% in the negative and solvent control, respectively, as compared to mortality ranged from 3% to 100% in the groups exposed to the test material. On Day 22, adult emergence averaged 86% and 92% in the negative and solvent controls, respectively, as compared to emergence that ranged from 0% to 94% in the treatment groups (Table 2).

There was no unconsumed diet in any control or treatment group by Day 8. Emerged bee weight averaged 0.1015 and 0.0998 in the negative and solvent control, respectively, as compared to weights ranging from 0.0917 to 0.0949 g in the groups exposed to the test material (Table 2).

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

Mean-Measured Concentration (Measured Daily Dietary Dose)	Number Exposed	Day 4 % Mortality	Day 5 % Mortality	Day 6 % Mortality	Day 7 % Mortality	Day 8 % Mortality
Negative Control	36	0	0	3	3	6
Solvent Control	36	0	0	6	6	8
42 µg ai/g diet (1.7 µg ai/larva/day)	36	3	3	3	3	3
79 µg ai/g diet (3.3 µg ai/larva/day)	36	0	0	0	11	19
160 µg ai/g diet (6.3 µg ai/larva/day)	36	0	0	31	39	58
320 µg ai/g diet (13 µg ai/larva/day)	36	6	6	83	92	94
610 µg ai/g diet (24 µg ai/larva/day)	36	0	0	75	94	100
Nominal Dose Dimethoate 7.4 µg ai/larva	36	6	25	67	72	89

[a] Daily mortality data obtained from p. 38 and Appendix 6: Study Data, pp. 116 – 122 in the MRID.

Table 2. Cumulative honey bee pupal mortality, adult emergence, and weight at emergence data after repeated dietary exposure (dose) of Pyrifluquinazon[ab].

Mean-Measured Concentration (Measured Daily Dietary Dose)	Number Exposed	Day 15 % Mortality	Day 22 Adult % Emergence	Mean Adult Weight at Emergence (g) Mean (SD)
Negative Control	36	11	86	0.1015 (0.0093)
Solvent Control	36	8	92	0.0998 (0.0117)
42 µg ai/g diet (1.7 µg ai/larva/day)	36	3	94	0.0949 (0.0175)
79 µg ai/g diet (3.3 µg ai/larva/day)	36	42	56	0.0917 (0.0108)
160 µg ai/g diet (6.3 µg ai/larva/day)	36	86	3	0.0931 (N/A)
320 µg ai/g diet (13 µg ai/larva/day)	36	100	0	N/A
610 µg ai/g diet (24 µg ai/larva/day)	36	100	0	N/A
Nominal Dose Dimethoate 7.4 µg ai/larva	36	--	--	N/A

[a] Daily mortality data obtained from p. 31 and Appendix 6: Study Data, pp. 116 – 122 in the MRID.
[b] Mean adult weight at emergence data obtained from Table 6 p. 40 in the MRID.

Reported Statistics:

CETIS software (version 1.8) was used to perform all statistical analyses. The negative and solvent control groups were compared using Fisher's Exact Test or an Equal Variance t-test. There were no statistically significant effects in these groups, and subsequent data were compared to the negative control group. The NOAEL/LOAEL values ($p \leq 0.05$) for Day 8 survival, pupal survival (Day 8-22), and adult emergence (Day 22) were determined using Fisher's Exact Test with Bonferroni-Holm's Adjustment. The highest test treatment level data were excluded from analysis for pupal survival and adult emergence due to 100% mortality at Day 8. Emergence weight was analyzed using Wilcoxon's Test with Bonferroni-Holm's Adjustment. LD_{50}/ED_{50} values were determined using an appropriate statistical model within CETIS when ≥50% effect levels occurred. Emergence weight did not exceed 50% effect levels in any test item concentration, therefore the ID_{50} value was empirically estimated to be greater than the highest adjusted cumulative dose. The study author reported the following, based on the measured diet concentrations and measured cumulative doses:

	Mortality (Day 3-8)	Mortality (Day 8-22)	Adult Emergence	Weight
Diet Concentration µg ai/g diet	LC_{50}: 140 95% CI: 120-170 NOAEC: 79 LOAEC: 160	LC_{50}: 99 95% CI: 86-110 NOAEC: 42 LOAEC: 79	EC_{50}: 89 95% CI: 79-100 NOAEC: 42 LOAEC: 79	IC_{50}: >160 95% CI: N/A NOAEC: 42 LOAEC: 79
Dietary Dose µg ai/larva	LD_{50}: 23 95% CI: 20-27 NOAEL: 13 LOAEL: 25	LD_{50}: 16 95% CI: 14-18 NOAEL: 6.7 LOAEL: 13	ED_{50}: 14 95% CI: 13-16 NOAEL: 13 LOAEL: 6.7	ID_{50}: >25 95% CI: N/A NOAEL: 6.7 LOAEL: 13

*Data obtained from pp. 10-11 in the MRID.

Reviewer's Statistical Analysis:
Mortality and emergence data were analyzed using CETIS statistical software version 1.9.5.3 with database backend settings implemented by EFED on 7/25/17. The study author-calculated measured diet concentrations and measured daily dietary doses were used for the analyses. Data were represented in CETIS as two separate test records (acronyms "dc" = diet concentration, "dd" = dietary dose.

Negative and solvent control data were compared using an Equal Variance t Two-Sample test (weight) or Fisher's Exact Test (mortality and emergence), with no statistically significant differences noted. All subsequent analyses were completed comparing treatment data to negative control data only.

The emergence data were analyzed using Fisher's Exact Test with a Bonferroni-Holm Adjustment due to a lack of monotonicity. The larval and pupal mortality data were analyzed using the Cochran-Armitage (N) Trend Test, because the data exhibited a dose response. The LC/LD_{50} and ED/EC_{50} values were determined using linear regression.

Emerged bee weight data were analyzed using a Mann-Whitney U Two-Sample test. The reviewer attempted to extrapolate the ID/IC_{50} values using nonlinear regression, but the data were not suitable due to a low effect size and valid 95% confidence limits could not be obtained.

All analyses were conducted at $\alpha = 0.05$ unless specified otherwise.

	Mortality (Day 8)	Mortality (Day 15)	Adult Emergence	Adult Weight
Diet Concentration µg ai/g diet	LC_{50}: 133 95% CI: 114-156 Slope: 4.0 (C.I.: 3.0-4.9) NOAEC: 42 LOAEC: 79	LC_{50}: 92 95% CI: 80-106 Slope: 5.0 (C.I.: 3.7-6.4) NOAEC: 42 LOAEC: 79	EC_{50}: 81 95% CI: 71-92 Slope: 6.0 (C.I.: 4.2-7.8) NOAEC: 42 LOAEC: 79	EC_{50}: >160 95% CI: N/A Slope: N/A NOAEC: 42 LOAEC: 79
Dietary Dose µg ai/larva/day	LD_{50}: 5.4 95% CI: 4.6-6.3 Slope: 4.1 (C.I.: 3.1-5.1) NOAEL: 1.7 LOAEL: 3.3	LD_{50}: 3.8 95% CI: 3.3-4.3 Slope: 5.2 (C.I.: 3.8-6.7) NOAEL: 1.7 LOAEL: 3.3	ED_{50}: 3.3 95% CI: 2.9-3.8 Slope: 6.1 (C.I.: 4.3-7.9) NOAEL: 1.7 LOAEL: 3.3	ED_{50}: >6.3 95% CI: N/A Slope: N/A NOAEL: 1.7 LOAEL: 3.3

13. REVIEWER'S COMMENTS:

The reviewer's and the study author's results for emergence were in agreement with regard to the NOAEC. The reviewer's LC_{50} and EC_{50} were lower than the study author's, but the reviewer could not determine the reason because the study author did not report how the values were calculated. The pupal data weren't comparable because the study author considered the pupal stage to range from day 8 to 22 whereas the reviewer considered the pupal stage to range from day 8 to 15. The reviewer's and the study author's NOAEC values for larval mortality were not in agreement, because the reviewer used the Cochran-Armitage (N) Trend Test while the study author used Fisher's Exact Test with a Bonferroni-Holm Adjustment. The reviewer's results are presented in the Conclusions and Reviewer's Conclusions sections of this DER.

Emerged bee weight and day 22 emergence were not reported individually on a per larva basis as the previous endpoints had been.

All three validity criteria were met for the OECD draft guidance followed:

1. Cumulative larval mortality across all control replicates from D3 to D8 was ≤15%.
2. Adult emergence across all control replicates on D22 was ≥ 70%.
3. Cumulative larval mortality in the positive control of Dimethoate on D8 was ≥ 50%.

The in-life phase of this study was conducted from May 17 to June 7, 2017.

14. REVIEWER'S CONCLUSIONS:

Larval mortality, pupal mortality, adult emergence, and weight were all affected endpoints in this study. Effects on larval and pupal mortality were dose responsive. The NOAEC and LOAEC were 42 and 79 µg ai/g diet, respectively (corresponding to a NOAEL and LOAEC of 1.7 and 3.3 µg ai/larva/day, respectively).

15. REFERENCES:

1. ASTM, 2007. Standard practice for conducting acute toxicity tests with fishes, macroinvertebrates and amphibians. Standard E729-96. American Society for Testing and Materials, 100 Barr Harbor Drive, West Conshohocken, Pennsylvania.

2. Ives, Michael, 2013. CETIS, Comprehensive Environmental Toxicity Information SystemTM, User's Guide. Tidepool Scientific Software, McKinleyville, California.

3. Schmehl. D.R., H.V.V. Tomé, A. N. Morttensen, G. Ferreira Martins and J. D. Ellis, 2016. Protocol for the in vitro rearing of honey bee (*Apis mellifera* L.) workers. Journal of Apicultural Research. Volume 55, No. 2. 113 – 129 pp.

4. U.S. EPA, 1997. Office of Waste. Test Methods for Evaluating Solid Waste, Physical/Chemical Methods (SW-846). Update IV January 2008. U.S. Environmental Protection Agency,Washington, D.C.

All other references are standard guidance or methodologies.

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

Batch ID:	08-6406-6952	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

Sample ID:	16-1352-2653	**Code:**	50735801 dc	**Project:**	Insecticide
Sample Date:	19 May-17	**Material:**	Pyrifluquinazon	**Source:**	Nichino America, Inc
Receipt Date:	20 Jun-19 14:12	**CAS (PC):**		**Station:**	
Sample Age:	n/a	**Client:**	CDM Smith		

555555 50735801 measured diet concentrations; Record created by: J. Burns

SIngle Comparison Summary

Analysis ID	Endpoint	Comparison Method	P-Value	Comparison Result	S
10-1788-4191	Adult Emergence Rate	Fisher Exact Test	0.7101	Solvent Blank passed adult emergence rat	1
08-7913-8333	Day 15 Mortality	Fisher Exact Test	1.0000	Solvent Blank passed day 15 mortality	1
05-0050-6975	Emerged Bee Weight	Equal Variance t Two-Sample Test	0.5335	Solvent Blank passed emerged bee weight	1
21-0887-0967	Larval Mortality	Fisher Exact Test	1.0000	Solvent Blank passed larval mortality	1

Multiple Comparison Summary

Analysis ID	Endpoint	Comparison Method	✓	NOEL	LOEL	TOEL	TU	PMSD	S
05-0518-9561	Adult Emergence Rate	Cochran-Armitage (N) Trend Test	✓	42	79	57.6		n/a	1
04-0761-0309	Adult Emergence Rate	Fisher Exact/Bonferroni-Holm Test	✓	42	79	57.6		n/a	1
09-1777-7536	Day 15 Mortality	Cochran-Armitage (N) Trend Test	✓	42	79	57.6		n/a	1
11-4288-9860	Day 15 Mortality	Fisher Exact/Bonferroni-Holm Test	✓	42	79	57.6		n/a	1
13-3753-8305	Emerged Bee Weight	Jonckheere-Terpstra Step-Down Test	✓	42	79	57.6		n/a	1
12-2978-5450	Emerged Bee Weight	Mann-Whitney U Two-Sample Test	✓	42	79	57.6		22.9%	1
07-7905-2321	Larval Mortality	Cochran-Armitage (N) Trend Test	✓	42	79	57.6		n/a	1
13-3732-4230	Larval Mortality	Fisher Exact/Bonferroni-Holm Test		79	160	112.4		n/a	1

Point Estimate Summary

Analysis ID	Endpoint	Point Estimate Method	✓	Level	µg ai/g	95% LCL	95% UCL	TU	S
09-9607-2375	Adult Emergence Rate	GLM: Log-Normal (Probit)		EC5	43.1	32	51.5		1
			✓	EC10	49.5	38.7	57.8		
			✓	EC25	62.5	52.5	71		
			✓	EC50	80.9	71.2	92.2		
06-4178-7772	Adult Emergence Rate	Spearman-Kärber		EC50	88.8	79.1	99.7		1
03-9472-2292	Day 15 Mortality	GLM: Log-Normal (Probit)		LC5	43.3	31.4	53		1
				LC10	51.2	39.1	60.9		
				LC25	67.5	55.8	77.8		
				LC50	91.9	79.9	106		
14-8566-3445	Day 15 Mortality	Spearman-Kärber		LC50	97.2	84.9	111		1
00-6549-3542	Emerged Bee Weight	NLR: 3P Cum Log-Normal (Probit)	✓	EC5	23.1	n/a	147		1
				EC10	97.4	7.69	372		
				EC25	1080	n/a	1480000		
				EC50	15700	n/a	n/a		
06-2360-3547	Larval Mortality	GLM: Log-Normal (Probit)		LC5	51.5	36.3	64.9		1
				LC10	63.5	47.4	77.7		
				LC25	90.3	73.1	106		
				LC50	133	114	156		
10-8918-3919	Larval Mortality	Spearman-Kärber		LC50	142	122	166		1

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

Adult Emergence Rate Summary

Conc-µg ai/g	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	%Effect
0	S	1	0.917			0.917	0.917	0.000	0.000	0.00%	0.00%
0	N	1	0.861			0.861	0.861	0.000	0.000	0.00%	6.06%
42		1	0.944			0.944	0.944	0.000	0.000	0.00%	-3.03%
79		1	0.556			0.556	0.556	0.000	0.000	0.00%	39.39%
160		1	0.028			0.028	0.028	0.000	0.000	0.00%	96.97%
320		1	0.000			0.000	0.000	0.000	0.000		100.00%
610		1	0.000			0.000	0.000	0.000	0.000		100.00%

Day 15 Mortality Summary

Conc-µg ai/g	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	%Effect
0	S	1	0.083			0.083	0.083	0.000	0.000	0.00%	0.00%
0	N	1	0.111			0.111	0.111	0.000	0.000	0.00%	3.03%
42		1	0.028			0.028	0.028	0.000	0.000	0.00%	-6.06%
79		1	0.417			0.417	0.417	0.000	0.000	0.00%	36.36%
160		1	0.861			0.861	0.861	0.000	0.000	0.00%	84.85%
320		1	1.000			1.000	1.000	0.000	0.000	0.00%	100.00%
610		1	1.000			1.000	1.000	0.000	0.000	0.00%	100.00%

Emerged Bee Weight Summary

Conc-µg ai/g	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	%Effect
0	S	33	0.0998	0.0957	0.104	0.0779	0.119	0.00204	0.0117	11.71%	0.00%
0	N	31	0.102	0.0981	0.105	0.0797	0.122	0.00168	0.00935	9.21%	-1.67%
42		34	0.0949	0.0888	0.101	0.027	0.122	0.00299	0.0175	18.41%	4.98%
79		20	0.0917	0.0867	0.0968	0.0732	0.111	0.00242	0.0108	11.78%	8.13%
160		1	0.0931			0.0931	0.0931	0	0	0.00%	6.75%

Larval Mortality Summary

Conc-µg ai/g	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	%Effect
0	S	1	0.083			0.083	0.083	0.000	0.000	0.00%	0.00%
0	N	1	0.056			0.056	0.056	0.000	0.000	0.00%	-3.03%
42		1	0.028			0.028	0.028	0.000	0.000	0.00%	-6.06%
79		1	0.194			0.194	0.194	0.000	0.000	0.00%	12.12%
160		1	0.583			0.583	0.583	0.000	0.000	0.00%	54.55%
320		1	0.944			0.944	0.944	0.000	0.000	0.00%	93.94%
610		1	1.000			1.000	1.000	0.000	0.000	0.00%	100.00%

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

Adult Emergence Rate Detail

Conc-µg ai/g	Code	Rep 1	Rep 2	Rep 3	Rep 4	Rep 5	Rep 6	Rep 7	Rep 8	Rep 9	Rep 10
0	S	0.917									
0	N	0.861									
42		0.944									
79		0.556									
160		0.028									
320		0.000									
610		0.000									

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

Day 15 Mortality Detail

Conc-µg ai/g	Code	Rep 1	Rep 2	Rep 3	Rep 4	Rep 5	Rep 6	Rep 7	Rep 8	Rep 9	Rep 10
0	S	0.083									
0	N	0.111									
42		0.028									
79		0.417									
160		0.861									
320		1.000									
610		1.000									

Emerged Bee Weight Detail

Conc-µg ai/g	Code	Rep 1	Rep 2	Rep 3	Rep 4	Rep 5	Rep 6	Rep 7	Rep 8	Rep 9	Rep 10
0	S	0.0919	0.105	0.102	0.104	0.108	0.105	0.1	0.114	0.109	0.101
		0.105	0.0915	0.08	0.0996	0.0974	0.0845	0.0779	0.0885	0.11	0.111
		0.109	0.0847	0.0937	0.119	0.118	0.103	0.0826	0.106	0.103	0.114
		0.111	0.079	0.0871							
0	N	0.0985	0.107	0.0955	0.106	0.0984	0.103	0.107	0.106	0.114	0.0956
		0.0889	0.0862	0.0965	0.0926	0.0984	0.107	0.109	0.0911	0.122	0.0969
		0.0907	0.114	0.0797	0.107	0.117	0.102	0.103	0.11	0.097	0.102
		0.104									
42		0.108	0.0934	0.0973	0.0847	0.0949	0.112	0.108	0.1	0.122	0.0555
		0.102	0.102	0.0986	0.106	0.0638	0.0852	0.027	0.101	0.0999	0.0866
		0.105	0.0974	0.0906	0.107	0.0917	0.111	0.0998	0.0968	0.11	0.0953
		0.0851	0.101	0.0922	0.0935						
79		0.0889	0.0756	0.102	0.0908	0.0908	0.0908	0.0885	0.0852	0.1	0.0732
		0.0798	0.102	0.0757	0.0948	0.101	0.107	0.0853	0.0894	0.102	0.111
160		0.0931									
320											
610											

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

Larval Mortality Detail

Conc-µg ai/g	Code	Rep 1	Rep 2	Rep 3	Rep 4	Rep 5	Rep 6	Rep 7	Rep 8	Rep 9	Rep 10
0	S	0.083									
0	N	0.056									
42		0.028									
79		0.194									
160		0.583									
320		0.944									
610		1.000									

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

Batch ID:	13-9126-3717	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

Sample ID:	08-1687-1013	**Code:**	50735801 dd	**Project:**	Insecticide
Sample Date:	19 May-17	**Material:**	Pyrifluquinazon	**Source:**	Nichino America, Inc
Receipt Date:		**CAS (PC):**		**Station:**	
Sample Age:	n/a	**Client:**	CDM Smith		

555555 50735801 measured dietary doses; Record Created by: J. Burns

Point Estimate Summary

Analysis ID	Endpoint	Point Estimate Method	✓	Level	µg/bee/da	95% LCL	95% UCL	TU	S
09-3740-9337	Adult Emergence Rate	GLM: Log-Normal (Probit)		EC5	1.78	1.32	2.13		1
			✓	EC10	2.05	1.59	2.39		
			✓	EC25	2.57	2.15	2.92		
			✓	EC50	3.32	2.92	3.77		
09-1624-8963	Adult Emergence Rate	Spearman-Kärber		EC50	3.62	3.23	4.05		1
10-6591-2726	Day 15 Mortality	GLM: Log-Normal (Probit)		LC5	1.81	1.31	2.21		1
				LC10	2.13	1.63	2.53		
				LC25	2.78	2.3	3.2		
				LC50	3.75	3.27	4.3		
00-0948-4834	Day 15 Mortality	Spearman-Kärber		LC50	3.96	3.46	4.52		1
06-1762-7517	Emerged Bee Weight	NLR: 3P Cum Log-Normal (Probit)	✓	EC5	0.943	n/a	5.95		1
				EC10	4	0.336	15.1		
				EC25	44.8	n/a	50400		
				EC50	655	n/a	n/a		
08-8492-1464	Larval Mortality	GLM: Log-Normal (Probit)		LC5	2.12	1.5	2.67		1
				LC10	2.61	1.95	3.18		
				LC25	3.68	2.99	4.31		
				LC50	5.39	4.62	6.29		
03-1512-9139	Larval Mortality	Spearman-Kärber		LC50	5.75	4.96	6.67		1

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

Adult Emergence Rate Summary

Conc-µg/bee/day	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	%Effect
0	S	1	0.917			0.917	0.917	0.000	0.000	0.00%	0.00%
0	N	1	0.861			0.861	0.861	0.000	0.000	0.00%	6.06%
1.7		1	0.944			0.944	0.944	0.000	0.000	0.00%	-3.03%
3.3		1	0.556			0.556	0.556	0.000	0.000	0.00%	39.39%
6.3		1	0.028			0.028	0.028	0.000	0.000	0.00%	96.97%
13		1	0.000			0.000	0.000	0.000	0.000		100.00%
24		1	0.000			0.000	0.000	0.000	0.000		100.00%

Day 15 Mortality Summary

Conc-µg/bee/day	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	%Effect
0	S	1	0.083			0.083	0.083	0.000	0.000	0.00%	0.00%
0	N	1	0.111			0.111	0.111	0.000	0.000	0.00%	3.03%
1.7		1	0.028			0.028	0.028	0.000	0.000	0.00%	-6.06%
3.3		1	0.417			0.417	0.417	0.000	0.000	0.00%	36.36%
6.3		1	0.861			0.861	0.861	0.000	0.000	0.00%	84.85%
13		1	1.000			1.000	1.000	0.000	0.000	0.00%	100.00%
24		1	1.000			1.000	1.000	0.000	0.000	0.00%	100.00%

Emerged Bee Weight Summary

Conc-µg/bee/day	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	%Effect
0	S	33	0.0998	0.0957	0.104	0.0779	0.119	0.00204	0.0117	11.71%	0.00%
0	N	31	0.102	0.0981	0.105	0.0797	0.122	0.00168	0.00935	9.21%	-1.67%
1.7		34	0.0949	0.0888	0.101	0.027	0.122	0.00299	0.0175	18.41%	4.98%
3.3		20	0.0917	0.0867	0.0968	0.0732	0.111	0.00242	0.0108	11.78%	8.13%
6.3		1	0.0931			0.0931	0.0931	0	0	0.00%	6.75%

Larval Mortality Summary

Conc-µg/bee/day	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	%Effect
0	S	1	0.083			0.083	0.083	0.000	0.000	0.00%	0.00%
0	N	1	0.056			0.056	0.056	0.000	0.000	0.00%	-3.03%
1.7		1	0.028			0.028	0.028	0.000	0.000	0.00%	-6.06%
3.3		1	0.194			0.194	0.194	0.000	0.000	0.00%	12.12%
6.3		1	0.583			0.583	0.583	0.000	0.000	0.00%	54.55%
13		1	0.944			0.944	0.944	0.000	0.000	0.00%	93.94%
24		1	1.000			1.000	1.000	0.000	0.000	0.00%	100.00%

Adult Emergence Rate Detail

Conc-µg/bee/day	Code	Rep 1	Rep 2	Rep 3	Rep 4	Rep 5	Rep 6	Rep 7	Rep 8	Rep 9	Rep 10
0	S	0.917									
0	N	0.861									
1.7		0.944									
3.3		0.556									
6.3		0.028									
13		0.000									
24		0.000									

Day 15 Mortality Detail

Conc-µg/bee/day	Code	Rep 1	Rep 2	Rep 3	Rep 4	Rep 5	Rep 6	Rep 7	Rep 8	Rep 9	Rep 10
0	S	0.083									
0	N	0.111									
1.7		0.028									
3.3		0.417									
6.3		0.861									
13		1.000									
24		1.000									

Emerged Bee Weight Detail

Conc-µg/bee/day	Code	Rep 1	Rep 2	Rep 3	Rep 4	Rep 5	Rep 6	Rep 7	Rep 8	Rep 9	Rep 10
0	S	0.0919	0.105	0.102	0.104	0.108	0.105	0.1	0.114	0.109	0.101
		0.105	0.0915	0.08	0.0996	0.0974	0.0845	0.0779	0.0885	0.11	0.111
		0.109	0.0847	0.0937	0.119	0.118	0.103	0.0826	0.106	0.103	0.114
		0.111	0.079	0.0871							
0	N	0.0985	0.107	0.0955	0.106	0.0984	0.103	0.107	0.106	0.114	0.0956
		0.0889	0.0862	0.0965	0.0926	0.0984	0.107	0.109	0.0911	0.122	0.0969
		0.0907	0.114	0.0797	0.107	0.117	0.102	0.103	0.11	0.097	0.102
		0.104									
1.7		0.108	0.0934	0.0973	0.0847	0.0949	0.112	0.108	0.1	0.122	0.0555
		0.102	0.102	0.0986	0.106	0.0638	0.0852	0.027	0.101	0.0999	0.0866
		0.105	0.0974	0.0906	0.107	0.0917	0.111	0.0998	0.0968	0.11	0.0953
		0.0851	0.101	0.0922	0.0935						
3.3		0.0889	0.0756	0.102	0.0908	0.0908	0.0908	0.0885	0.0852	0.1	0.0732
		0.0798	0.102	0.0757	0.0948	0.101	0.107	0.0853	0.0894	0.102	0.111
6.3		0.0931									
13											
24											

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

Larval Mortality Detail

Conc-µg/bee/day	Code	Rep 1	Rep 2	Rep 3	Rep 4	Rep 5	Rep 6	Rep 7	Rep 8	Rep 9	Rep 10
0	S	0.083									
0	N	0.056									
1.7		0.028									
3.3		0.194									
6.3		0.583									
13		0.944									
24		1.000									

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

Analysis ID:	04-0761-0309	**Endpoint:**	Adult Emergence Rate	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:32	**Analysis:**	STP 2xK Contingency Tables	**Status Level:**	1

Batch ID:	08-6406-6952	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

Data Transform	Alt Hyp	NOEL	LOEL	TOEL	TU
Untransformed	C > T	42	79	57.6	

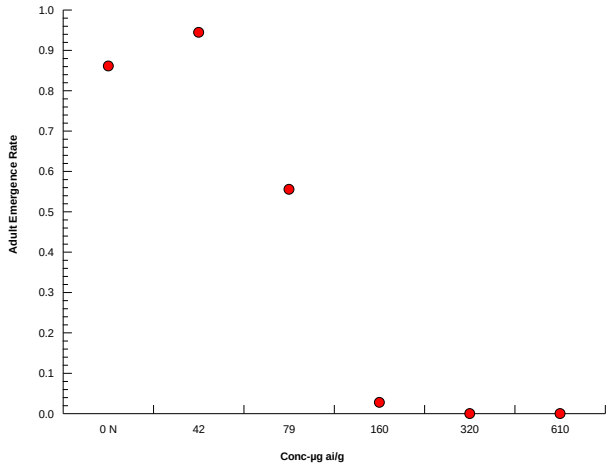
Fisher Exact/Bonferroni-Holm Test

Control vs	Group	Test Stat	P-Type	P-Value	Decision(α:5%)
Negative Control	42	0.947	Exact	0.9467	Non-Significant Effect
	79*	0.004	Exact	0.0086	Significant Effect
	160*	0.000	Exact	1.4E-13	Significant Effect
	320*	0.000	Exact	8.5E-15	Significant Effect
	610*	0.000	Exact	8.5E-15	Significant Effect

Data Summary

Conc-µg ai/g	Code	NR	R	NR + R	Prop NR	Prop R	%Effect
0	N	31	5	36	0.861	0.139	0.0%
42		34	2	36	0.944	0.0556	-9.68%
79		20	16	36	0.556	0.444	35.5%
160		1	35	36	0.0278	0.972	96.8%
320		0	36	36	0	1	100.0%
610		0	36	36	0	1	100.0%

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

Analysis ID:	05-0518-9561	**Endpoint:**	Adult Emergence Rate	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:32	**Analysis:**	STP 2xK Contingency Tables-Numerical Sc	**Status Level:**	1

Batch ID:	08-6406-6952	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

Data Transform	Alt Hyp	NOEL	LOEL	TOEL	TU
Untransformed	C > T	42	79	57.6	

Cochran-Armitage (N) Trend Test

Control	vs	Group	Test Stat	P-Type	P-Value	Decision(α:5%)
Negative Control		42	-1.193	Asymp	0.8836	Non-Significant Effect
		79*	3.061	Asymp	0.0011	Significant Effect
		160*	8.293	Asymp	<1.0E-37	Significant Effect
		320*	9.473	Asymp	<1.0E-37	Significant Effect
		610*	9.408	Asymp	<1.0E-37	Significant Effect

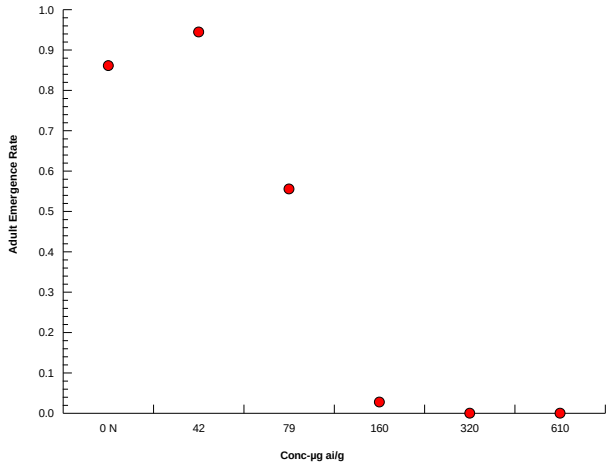
Auxiliary Tests

Attribute	Test	Test Stat	Critical	P-Value	Decision(α:5%)
Overall Effect	Pearson Chi-Square Test	149	11.1	1.3E-07	Significant Overall Effect
Nonlinearity	Chi-Square Lack of Fit Test	60.5	9.49	<1.0E-37	Significant Lack of Linearity

Data Summary

Conc-µg ai/g	Code	NR	R	NR + R	Prop NR	Prop R	%Effect
0	N	31	5	36	0.861	0.139	0.0%
42		34	2	36	0.944	0.0556	-9.68%
79		20	16	36	0.556	0.444	35.5%
160		1	35	36	0.0278	0.972	96.8%
320		0	36	36	0	1	100.0%
610		0	36	36	0	1	100.0%

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

Analysis ID:	10-1788-4191	**Endpoint:**	Adult Emergence Rate	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:35	**Analysis:**	Single 2x2 Contingency Table	**Status Level:**	1

Batch ID:	08-6406-6952	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

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

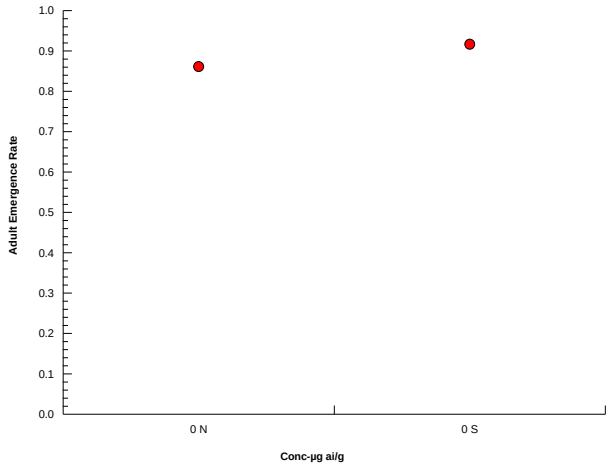
Fisher Exact Test

Control	vs	Control	Test Stat	P-Type	P-Value	Decision(α:5%)
Negative Control		Solvent Blank	0.710	Exact	0.7101	Non-Significant Effect

Data Summary

Conc-µg ai/g	Code	NR	R	NR + R	Prop NR	Prop R	%Effect
0	S	33	3	36	0.917	0.0833	-6.45%
0	N	31	5	36	0.861	0.139	0.0%

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

Analysis ID:	11-4288-9860	**Endpoint:**	Day 15 Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:31	**Analysis:**	STP 2xK Contingency Tables	**Status Level:**	1

Batch ID:	08-6406-6952	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

Data Transform	Alt Hyp	NOEL	LOEL	TOEL	TU
Untransformed	C < T	42	79	57.6	

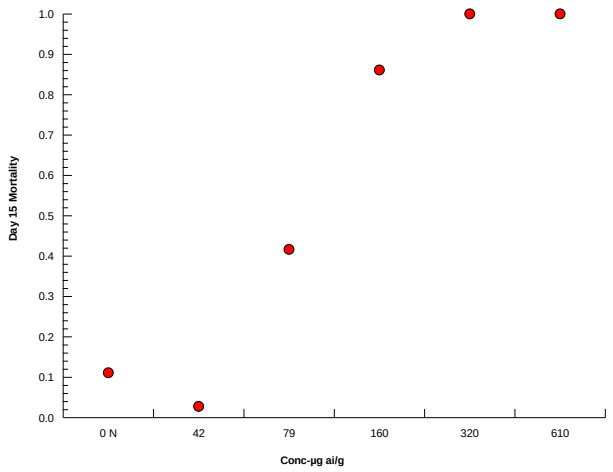
Fisher Exact/Bonferroni-Holm Test

Control vs	Group	Test Stat	P-Type	P-Value	Decision(α:5%)
Negative Control	42	0.973	Exact	0.9731	Non-Significant Effect
	79*	0.003	Exact	0.0066	Significant Effect
	160*	0.000	Exact	1.6E-10	Significant Effect
	320*	0.000	Exact	1.0E-15	Significant Effect
	610*	0.000	Exact	1.0E-15	Significant Effect

Data Summary

Conc-µg ai/g	Code	NR	R	NR + R	Prop NR	Prop R	%Effect
0	N	32	4	36	0.889	0.111	0.0%
42		35	1	36	0.972	0.0278	75.0%
79		21	15	36	0.583	0.417	-275.0%
160		5	31	36	0.139	0.861	-675.0%
320		0	36	36	0	1	-800.0%
610		0	36	36	0	1	-800.0%

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Smithers Viscient**

Analysis ID:	09-1777-7536	**Endpoint:**	Day 15 Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:32	**Analysis:**	STP 2xK Contingency Tables-Numerical Sc	**Status Level:**	1

Batch ID:	08-6406-6952	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

Data Transform	Alt Hyp	NOEL	LOEL	TOEL	TU
Untransformed	C < T	42	79	57.6	

Cochran-Armitage (N) Trend Test

Control vs	Group	Test Stat	P-Type	P-Value	Decision(α:5%)
Negative Control	42	-1.391	Asymp	0.9179	Non-Significant Effect
	79*	3.226	Asymp	6.3E-04	Significant Effect
	160*	7.707	Asymp	<1.0E-37	Significant Effect
	320*	9.575	Asymp	<1.0E-37	Significant Effect
	610*	9.728	Asymp	<1.0E-37	Significant Effect

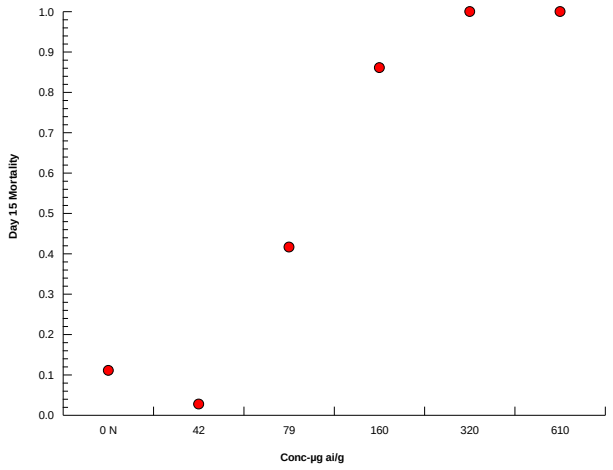
Auxiliary Tests

Attribute	Test	Test Stat	Critical	P-Value	Decision(α:5%)
Overall Effect	Pearson Chi-Square Test	144	11.1	1.3E-07	Significant Overall Effect
Nonlinearity	Chi-Square Lack of Fit Test	49.6	9.49	<1.0E-37	Significant Lack of Linearity

Data Summary

Conc-µg ai/g	Code	NR	R	NR + R	Prop NR	Prop R	%Effect
0	N	32	4	36	0.889	0.111	0.0%
42		35	1	36	0.972	0.0278	75.0%
79		21	15	36	0.583	0.417	-275.0%
160		5	31	36	0.139	0.861	-675.0%
320		0	36	36	0	1	-800.0%
610		0	36	36	0	1	-800.0%

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

Analysis ID:	08-7913-8333	**Endpoint:**	Day 15 Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:35	**Analysis:**	Single 2x2 Contingency Table	**Status Level:**	1

Batch ID:	08-6406-6952	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

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

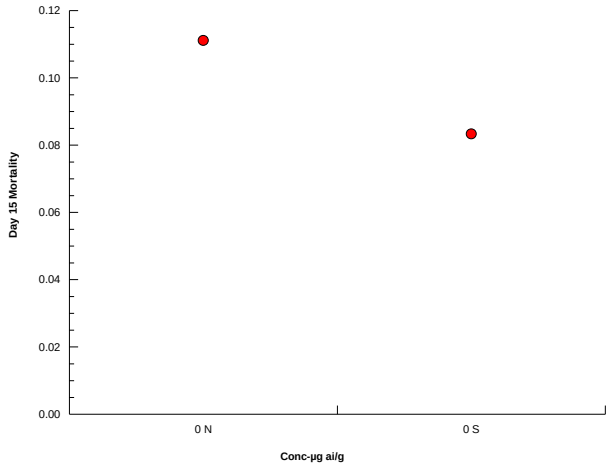
Fisher Exact Test

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-µg ai/g	Code	NR	R	NR + R	Prop NR	Prop R	%Effect
0	S	33	3	36	0.917	0.0833	25.0%
0	N	32	4	36	0.889	0.111	0.0%

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

Analysis ID:	13-3732-4230	**Endpoint:**	Larval Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:31	**Analysis:**	STP 2xK Contingency Tables	**Status Level:**	1

Batch ID:	08-6406-6952	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

Data Transform	Alt Hyp	NOEL	LOEL	TOEL	TU
Untransformed	C < T	79	160	112.4	

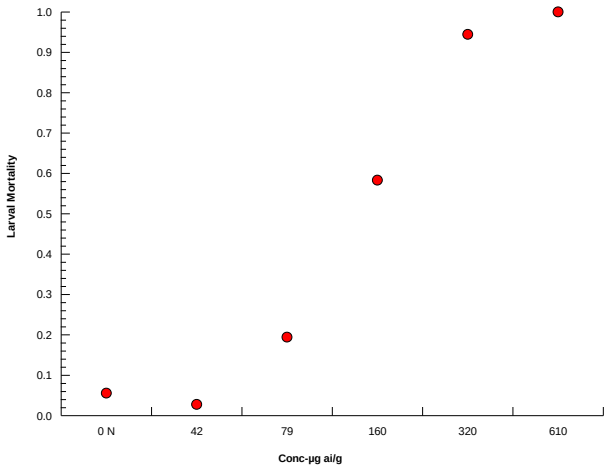
Fisher Exact/Bonferroni-Holm Test

Control vs	Group	Test Stat	P-Type	P-Value	Decision(α:5%)
Negative Control	42	0.880	Exact	0.8803	Non-Significant Effect
	79	0.076	Exact	0.1514	Non-Significant Effect
	160*	0.000	Exact	2.8E-06	Significant Effect
	320*	0.000	Exact	3.6E-15	Significant Effect
	610*	0.000	Exact	7.9E-18	Significant Effect

Data Summary

Conc-µg ai/g	Code	NR	R	NR + R	Prop NR	Prop R	%Effect
0	N	34	2	36	0.944	0.0556	0.0%
42		35	1	36	0.972	0.0278	50.0%
79		29	7	36	0.806	0.194	-250.0%
160		15	21	36	0.417	0.583	-950.0%
320		2	34	36	0.0556	0.944	-1600.0%
610		0	36	36	0	1	-1700.0%

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

Analysis ID:	07-7905-2321	**Endpoint:**	Larval Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:32	**Analysis:**	STP 2xK Contingency Tables-Numerical Sc	**Status Level:**	1

Batch ID:	08-6406-6952	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

Data Transform	Alt Hyp	NOEL	LOEL	TOEL	TU
Untransformed	C < T	42	79	57.6	

Cochran-Armitage (N) Trend Test

Control vs	Group	Test Stat	P-Type	P-Value	Decision(α:5%)
Negative Control	42	-0.590	Asymp	0.7223	Non-Significant Effect
	79*	1.972	Asymp	0.0243	Significant Effect
	160*	6.120	Asymp	<1.0E-37	Significant Effect
	320*	9.649	Asymp	<1.0E-37	Significant Effect
	610*	10.675	Asymp	<1.0E-37	Significant Effect

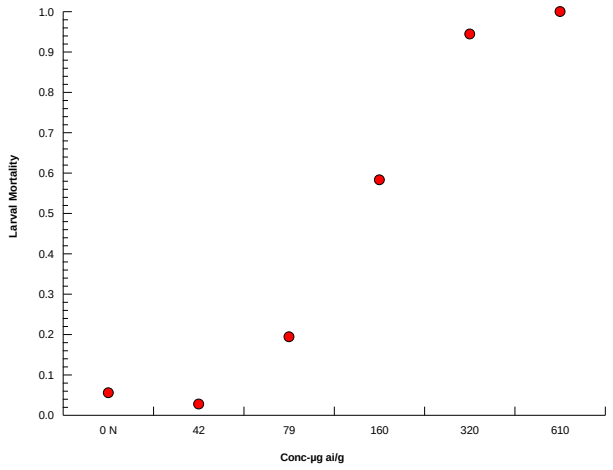
Auxiliary Tests

Attribute	Test	Test Stat	Critical	P-Value	Decision(α:5%)
Overall Effect	Pearson Chi-Square Test	139	11.1	<1.0E-37	Significant Overall Effect
Nonlinearity	Chi-Square Lack of Fit Test	25.2	9.49	4.6E-05	Significant Lack of Linearity

Data Summary

Conc-µg ai/g	Code	NR	R	NR + R	Prop NR	Prop R	%Effect
0	N	34	2	36	0.944	0.0556	0.0%
42		35	1	36	0.972	0.0278	50.0%
79		29	7	36	0.806	0.194	-250.0%
160		15	21	36	0.417	0.583	-950.0%
320		2	34	36	0.0556	0.944	-1600.0%
610		0	36	36	0	1	-1700.0%

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Smithers Viscient**

Analysis ID:	21-0887-0967	**Endpoint:**	Larval Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:35	**Analysis:**	Single 2x2 Contingency Table	**Status Level:**	1

Batch ID:	08-6406-6952	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

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

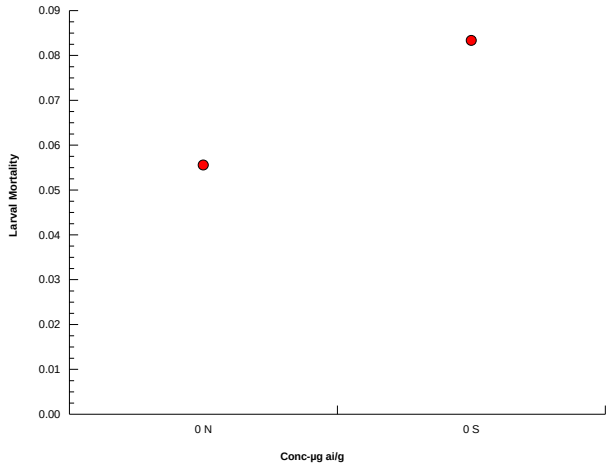
Fisher Exact Test

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

Data Summary

Conc-µg ai/g	Code	NR	R	NR + R	Prop NR	Prop R	%Effect
0	S	33	3	36	0.917	0.0833	-50.0%
0	N	34	2	36	0.944	0.0556	0.0%

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Smithers Viscient**

Analysis ID:	12-2978-5450	**Endpoint:**	Emerged Bee Weight	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:33	**Analysis:**	Nonparametric-Two Sample	**Status Level:**	1

Batch ID:	08-6406-6952	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

Data Transform	Alt Hyp	NOEL	LOEL	TOEL	TU	PMSD
Untransformed	C > T	42	79	57.6		22.90%

Mann-Whitney U Two-Sample Test

Control	vs	Conc-µg ai/g	Test Stat	Critical	Ties	DF	P-Type	P-Value	Decision(α:5%)
Negative Control		42	1.52	1.64	2	63	Asymp	0.0646	Non-Significant Effect
		79*	3.03	1.64	1	49	Asymp	0.0012	Significant Effect
		160	0.975	1.64	0	30	Asymp	0.1648	Non-Significant Effect

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision(α:5%)
Between	0.0013342	0.0004447	3	2.45	0.0696	Non-Significant Effect
Error	0.0149014	0.0001817	82			
Total	0.0162356		85			

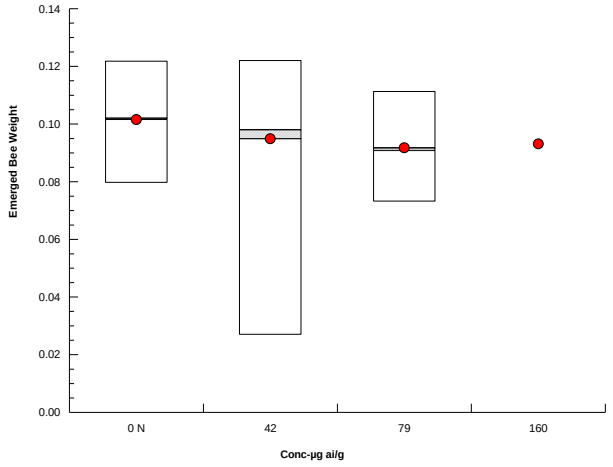
ANOVA Assumptions Tests

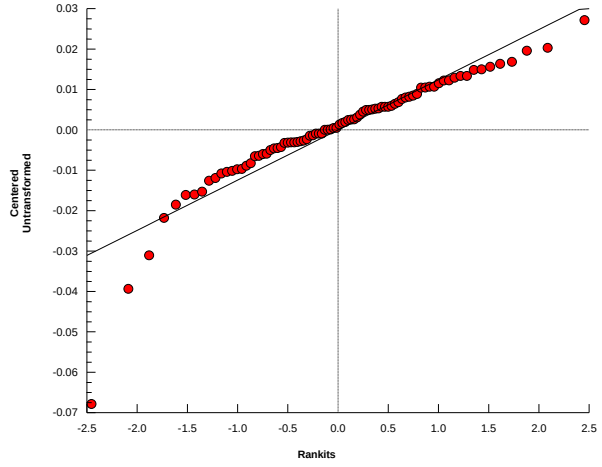
Attribute	Test	Test Stat	Critical	P-Value	Decision(α:1%)
Variance	Levene Equality of Variance Test	1.14	4.03	0.3369	Equal Variances
Distribution	Shapiro-Wilk W Normality Test	0.875	0.96	6.1E-07	Non-Normal Distribution

Emerged Bee Weight Summary

Conc-µg ai/g	Code	Count	Mean	95% LCL	95% UCL	Median	Min	Max	Std Err	CV%	%Effect
0	N	31	0.102	0.0981	0.105	0.102	0.0797	0.122	0.00168	9.21%	0.00%
42		34	0.0949	0.0888	0.101	0.098	0.027	0.122	0.00299	18.41%	6.54%
79		20	0.0917	0.0867	0.0968	0.0908	0.0732	0.111	0.00242	11.78%	9.63%
160		1	0.0931			0.0931	0.0931	0.0931	0	0.00%	8.28%

Graphics





Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Smithers Viscient**

Analysis ID:	13-3753-8305	**Endpoint:**	Emerged Bee Weight	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:34	**Analysis:**	Nonparametric-Control vs Ord. Treatments	**Status Level:**	1

Batch ID:	08-6406-6952	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

Data Transform	Alt Hyp	NOEL	LOEL	TOEL	TU
Untransformed	C > T	42	79	57.6	

Jonckheere-Terpstra Step-Down Test

Control	vs	Conc-µg ai/g	Test Stat	Critical	Ties	P-Type	P-Value	Decision(α:5%)
Negative Control		42	1.52	1.64	5	Asymp	0.0638	Non-Significant Effect
		79*	2.93	1.64	9	Asymp	0.0017	Significant Effect
		160*	2.99	1.64	9	Asymp	0.0014	Significant Effect

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision(α:5%)
Between	0.0013342	0.0004447	3	2.45	0.0696	Non-Significant Effect
Error	0.0149014	0.0001817	82			
Total	0.0162356		85			

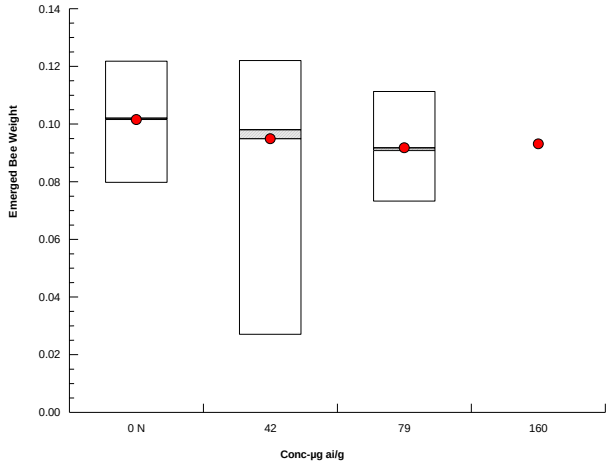
ANOVA Assumptions Tests

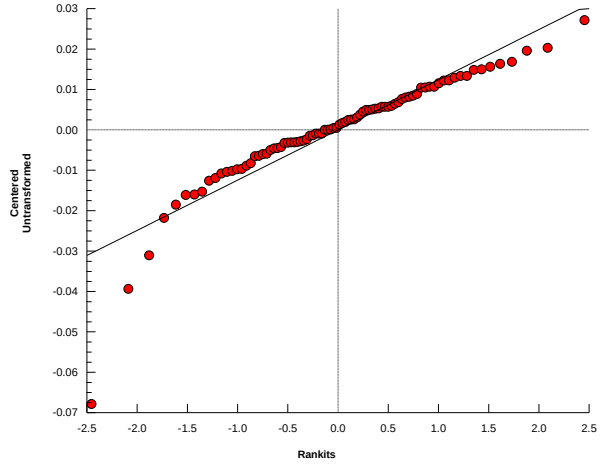
Attribute	Test	Test Stat	Critical	P-Value	Decision(α:1%)
Variance	Levene Equality of Variance Test	1.14	4.03	0.3369	Equal Variances
Distribution	Shapiro-Wilk W Normality Test	0.875	0.96	6.1E-07	Non-Normal Distribution

Emerged Bee Weight Summary

Conc-µg ai/g	Code	Count	Mean	95% LCL	95% UCL	Median	Min	Max	Std Err	CV%	%Effect
0	N	31	0.102	0.0981	0.105	0.102	0.0797	0.122	0.00168	9.21%	0.00%
42		34	0.0949	0.0888	0.101	0.098	0.027	0.122	0.00299	18.41%	6.54%
79		20	0.0917	0.0867	0.0968	0.0908	0.0732	0.111	0.00242	11.78%	9.63%
160		1	0.0931			0.0931	0.0931	0.0931	0	0.00%	8.28%

Graphics





Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Smithers Viscient**

Analysis ID:	05-0050-6975	**Endpoint:**	Emerged Bee Weight	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:34	**Analysis:**	Parametric-Two Sample	**Status Level:**	1

Batch ID:	08-6406-6952	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

Data Transform	Alt Hyp	Comparison Result	PMSD
Untransformed	C <> T	Solvent Blank passed emerged bee weight	5.23%

Equal Variance t Two-Sample Test

Control	vs	Control II	Test Stat	Critical	MSD	DF	P-Type	P-Value	Decision(α:5%)
Negative Control		Solvent Blank	0.626	2	0.005	62	CDF	0.5335	Non-Significant Effect

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision(α:5%)
Between	4.426E-05	4.426E-05	1	0.392	0.5335	Non-Significant Effect
Error	0.0069982	0.0001129	62			
Total	0.0070425		63			

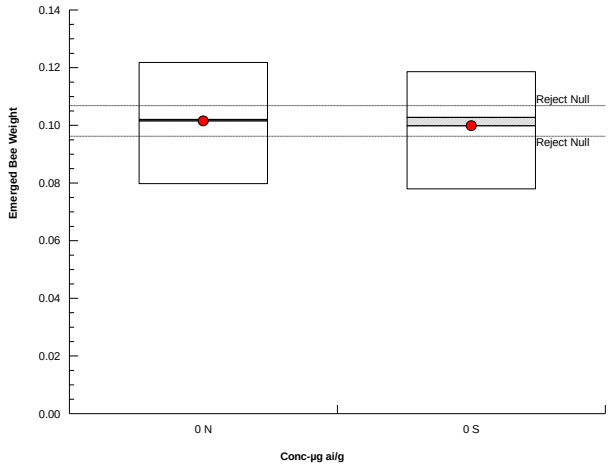
ANOVA Assumptions Tests

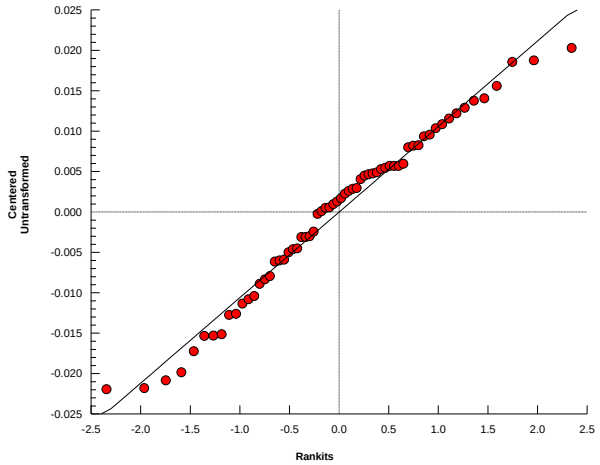
Attribute	Test	Test Stat	Critical	P-Value	Decision(α:1%)
Variance	Variance Ratio F Test	1.57	2.6	0.2203	Equal Variances
Distribution	Shapiro-Wilk W Normality Test	0.977	0.949	0.2634	Normal Distribution

Emerged Bee Weight Summary

Conc-µg ai/g	Code	Count	Mean	95% LCL	95% UCL	Median	Min	Max	Std Err	CV%	%Effect
0	S	33	0.0998	0.0957	0.104	0.103	0.0779	0.119	0.00204	11.71%	0.00%
0	N	31	0.102	0.0981	0.105	0.102	0.0797	0.122	0.00168	9.21%	-1.67%

Graphics





Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Smithers Viscient**

Analysis ID:	09-9607-2375	**Endpoint:**	Adult Emergence Rate	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:33	**Analysis:**	Linear Regression (GLM)	**Status Level:**	1

Batch ID:	08-6406-6952	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

Linear Regression Options

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

Regression Summary

Iters	LL	AICc	BIC	Mu	Sigma	Adj R2	PMSD	F Stat	P-Value	Decision(α:5%)
4	-4.47	18.9	12.2	1.91	0.167	0.999				Lack of Fit Not Tested

Point Estimates

Level	µg ai/g	95% LCL	95% UCL
EC5	43.1	32	51.5
EC10	49.5	38.7	57.8
EC25	62.5	52.5	71
EC50	80.9	71.2	92.2

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision(α:5%)
Intercept	-11.5	1.73	-14.9	-8.07	-6.62	0.0070	Significant Parameter
Slope	6.01	0.907	4.23	7.78	6.62	0.0070	Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision(α:5%)
Model	565	565	1	4680	6.9E-06	Significant
Residual	0.362	0.121	3			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision(α:5%)
Model Fit	Likelihood Ratio GOF Test	0.368	7.81	0.9467	Non-Significant Heterogeneity
	Pearson Chi-Sq GOF Test	0.362	7.81	0.9479	Non-Significant Heterogeneity
Distribution	Shapiro-Wilk W Normality Test	0.912	0.34	0.4788	Normal Distribution

Adult Emergence Rate Summary

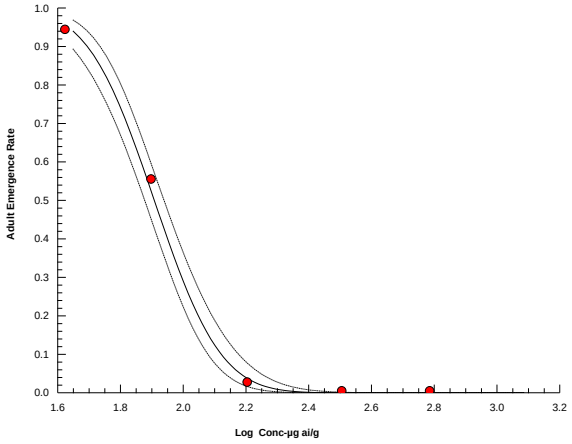
			Calculated Variate(A/B)								
Conc-µg ai/g	**Code**	**Count**	**Mean**	**Min**	**Max**	**Std Err**	**Std Dev**	**CV%**	**%Effect**	**A**	**B**
42		1	0.944	0.944	0.944	0.000	0.000	0.00%	0.0%	34	36
79		1	0.556	0.556	0.556	0.000	0.000	0.00%	41.2%	20	36
160		1	0.028	0.028	0.028	0.000	0.000	0.00%	97.1%	1	36
320		1	0.000	0.000	0.000	0.000	0.000		100.0%	0	36
610		1	0.000	0.000	0.000	0.000	0.000		100.0%	0	36

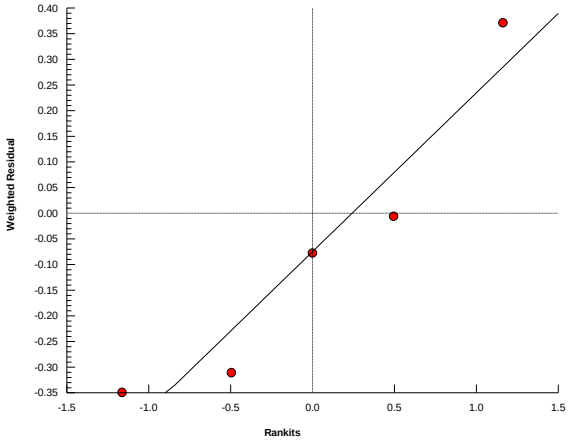
Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

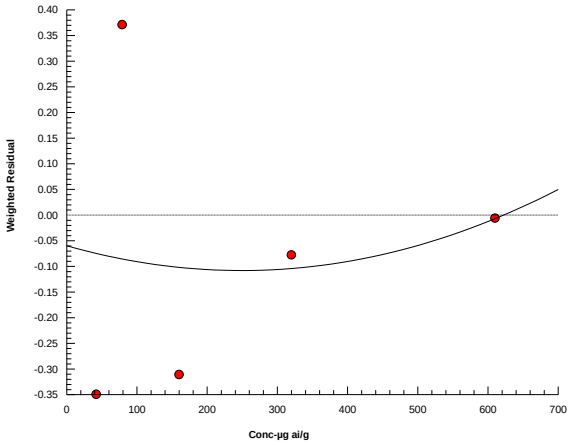
Analysis ID:	09-9607-2375	**Endpoint:**	Adult Emergence Rate	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:33	**Analysis:**	Linear Regression (GLM)	**Status Level:**	1

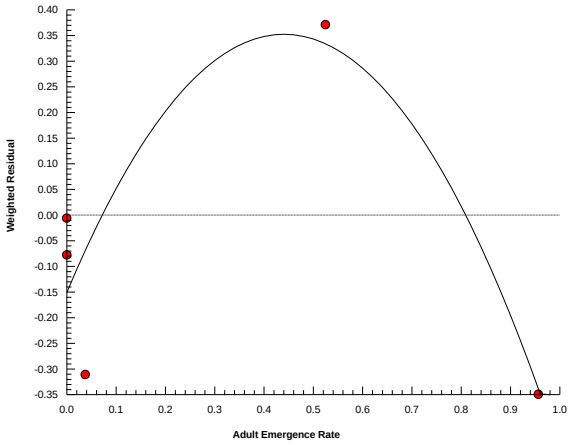
Graphics

Log-Normal: inv Φ[π]=α+β·log[x]









Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

Analysis ID:	03-9472-2292	**Endpoint:**	Day 15 Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:32	**Analysis:**	Linear Regression (GLM)	**Status Level:**	1

Batch ID:	08-6406-6952	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

Linear Regression Options

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

Regression Summary

Iters	LL	AICc	BIC	Mu	Sigma	Adj R2	PMSD	F Stat	P-Value	Decision(α:5%)
5	-5.18	20.4	13.6	1.96	0.199	0.998				Lack of Fit Not Tested

Point Estimates

Level	µg ai/g	95% LCL	95% UCL
LC5	43.3	31.4	53
LC10	51.2	39.1	60.9
LC25	67.5	55.8	77.8
LC50	91.9	79.9	106

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision(α:5%)
Intercept	-9.89	1.38	-12.6	-7.17	-7.14	0.0057	Significant Parameter
Slope	5.04	0.703	3.66	6.41	7.17	0.0056	Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision(α:5%)
Model	582	582	1	1930	2.6E-05	Significant
Residual	0.906	0.302	3			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision(α:5%)
Model Fit	Likelihood Ratio GOF Test	1.03	7.81	0.7940	Non-Significant Heterogeneity
	Pearson Chi-Sq GOF Test	0.906	7.81	0.8239	Non-Significant Heterogeneity
Distribution	Shapiro-Wilk W Normality Test	0.907	0.34	0.4517	Normal Distribution

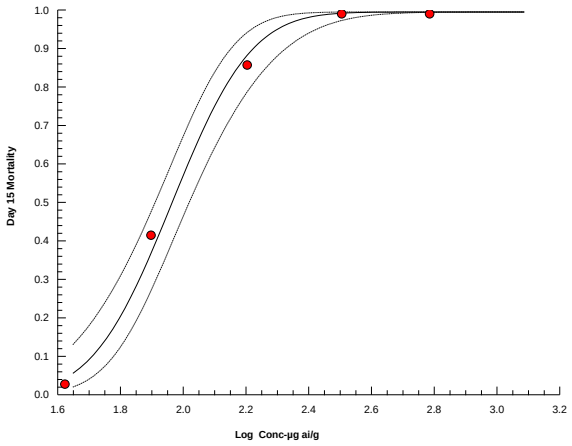
Day 15 Mortality Summary

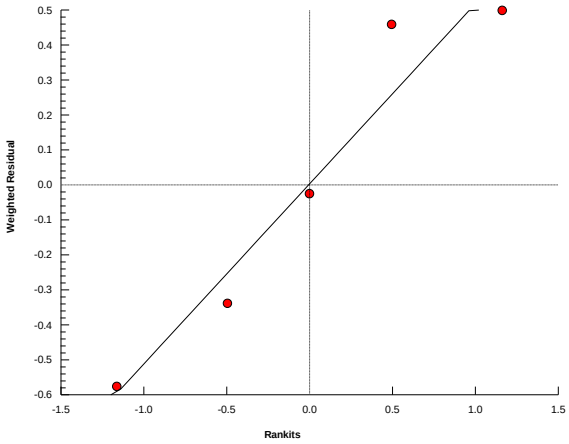
			Calculated Variate(A/B)								
Conc-µg ai/g	Code	Count	Mean	Min	Max	Std Err	Std Dev	CV%	%Effect	A	B
42		1	0.028	0.028	0.028	0.000	0.000	0.00%	0.0%	1	36
79		1	0.417	0.417	0.417	0.000	0.000	0.00%	40.0%	15	36
160		1	0.861	0.861	0.861	0.000	0.000	0.00%	85.7%	31	36
320		1	1.000	1.000	1.000	0.000	0.000	0.00%	100.0%	36	36
610		1	1.000	1.000	1.000	0.000	0.000	0.00%	100.0%	36	36

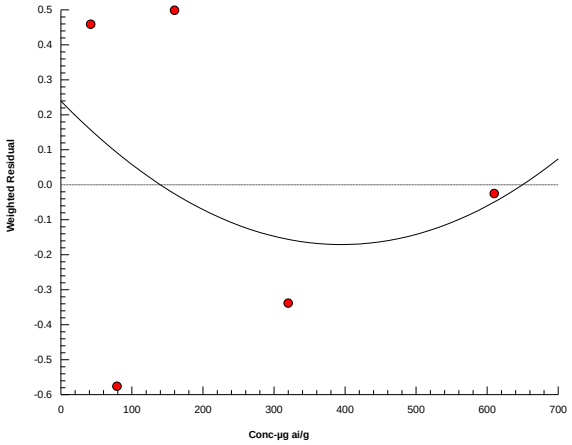
Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

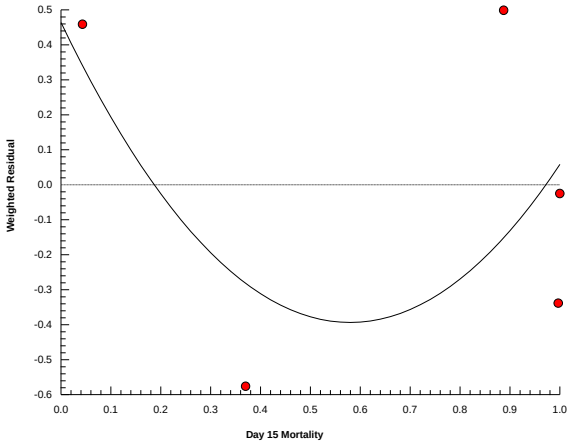
Analysis ID:	03-9472-2292	**Endpoint:**	Day 15 Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:32	**Analysis:**	Linear Regression (GLM)	**Status Level:**	1

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









Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Smithers Viscient**

Analysis ID:	06-2360-3547	**Endpoint:**	Larval Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:32	**Analysis:**	Linear Regression (GLM)	**Status Level:**	1

Batch ID:	08-6406-6952	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

Linear Regression Options

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

Regression Summary

Iters	LL	AICc	BIC	Mu	Sigma	Adj R2	PMSD	F Stat	P-Value	Decision(α:5%)
4	-6.41	22.8	16	2.12	0.251	0.999				Lack of Fit Not Tested

Point Estimates

Level	µg ai/g	95% LCL	95% UCL
LC5	51.5	36.3	64.9
LC10	63.5	47.4	77.7
LC25	90.3	73.1	106
LC50	133	114	156

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision(α:5%)
Intercept	-8.46	1.05	-10.5	-6.4	-8.06	0.0040	Significant Parameter
Slope	3.98	0.49	3.02	4.94	8.13	0.0039	Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision(α:5%)
Model	1030	1030	1	5850	4.9E-06	Significant
Residual	0.53	0.177	3			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision(α:5%)
Model Fit	Likelihood Ratio GOF Test	0.679	7.81	0.8780	Non-Significant Heterogeneity
	Pearson Chi-Sq GOF Test	0.53	7.81	0.9124	Non-Significant Heterogeneity
Distribution	Shapiro-Wilk W Normality Test	0.765	0.34	0.0404	Non-Normal Distribution

Larval Mortality Summary

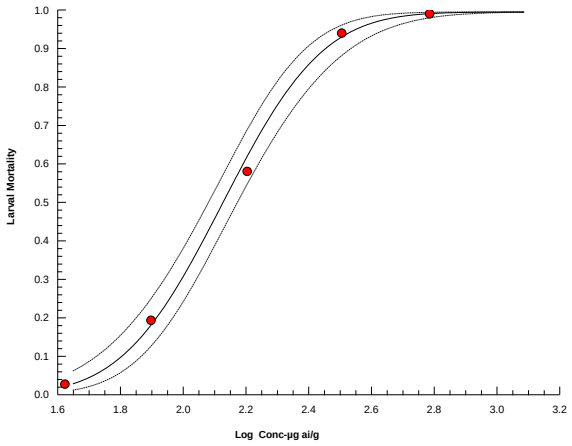
			Calculated Variate(A/B)								
Conc-µg ai/g	**Code**	**Count**	**Mean**	**Min**	**Max**	**Std Err**	**Std Dev**	**CV%**	**%Effect**	**A**	**B**
42		1	0.028	0.028	0.028	0.000	0.000	0.00%	0.0%	1	36
79		1	0.194	0.194	0.194	0.000	0.000	0.00%	17.1%	7	36
160		1	0.583	0.583	0.583	0.000	0.000	0.00%	57.1%	21	36
320		1	0.944	0.944	0.944	0.000	0.000	0.00%	94.3%	34	36
610		1	1.000	1.000	1.000	0.000	0.000	0.00%	100.0%	36	36

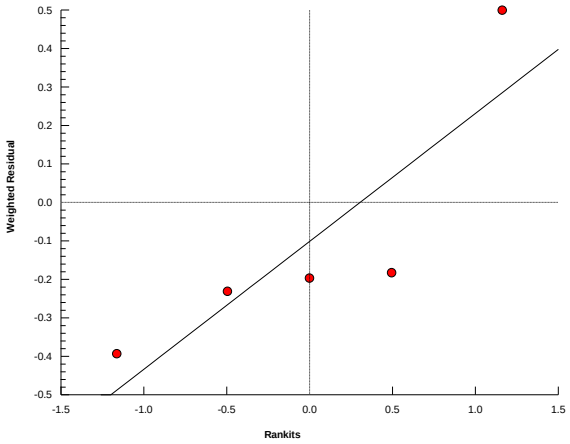
Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

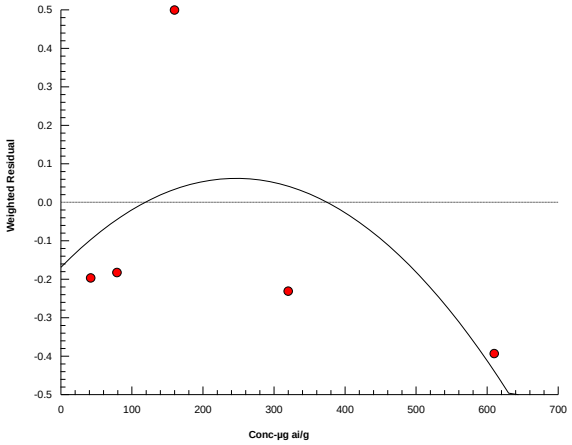
Analysis ID:	06-2360-3547	**Endpoint:**	Larval Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:32	**Analysis:**	Linear Regression (GLM)	**Status Level:**	1

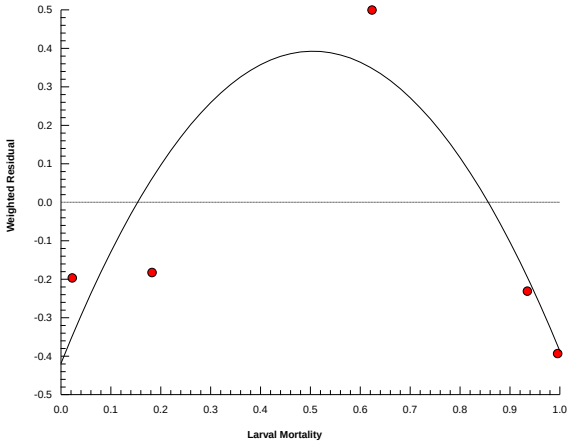
Graphics

Log-Normal: inv Φ[π]=α+β·log[x]









Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Smithers Viscient**

Analysis ID:	06-4178-7772	**Endpoint:**	Adult Emergence Rate	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:33	**Analysis:**	Untrimmed Spearman-Kärber	**Status Level:**	1

Batch ID:	08-6406-6952	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

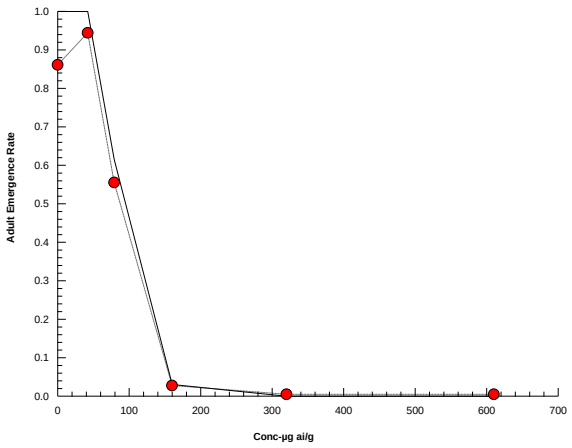
Spearman-Kärber Estimates

Threshold Option	Threshold	Trim	Mu	Sigma	EC50	95% LCL	95% UCL
Control Threshold	0.139	0.00%	1.95	0.0251	88.8	79.1	99.7

Adult Emergence Rate Summary

			Calculated Variate(A/B)							Isotonic Variate	
Conc-µg ai/g	**Code**	**Count**	**Mean**	**Min**	**Max**	**Std Dev**	**CV%**	**%Effect**	**A/B**	**Mean**	**%Effect**
0	N	1	0.861	0.861	0.861	0.000	0.00%	0.0%	31/36	0.903	0.0%
42		1	0.944	0.944	0.944	0.000	0.00%	-9.68%	34/36	0.903	0.0%
79		1	0.556	0.556	0.556	0.000	0.00%	35.5%	20/36	0.556	38.5%
160		1	0.028	0.028	0.028	0.000	0.00%	96.8%	1/36	0.0278	96.9%
320		1	0.000	0.000	0.000	0.000		100.0%	0/36	0	100.0%
610		1	0.000	0.000	0.000	0.000		100.0%	0/36	0	100.0%

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Smithers Viscient**

Analysis ID:	14-8566-3445	**Endpoint:**	Day 15 Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:32	**Analysis:**	Untrimmed Spearman-Kärber	**Status Level:**	1

Batch ID:	08-6406-6952	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

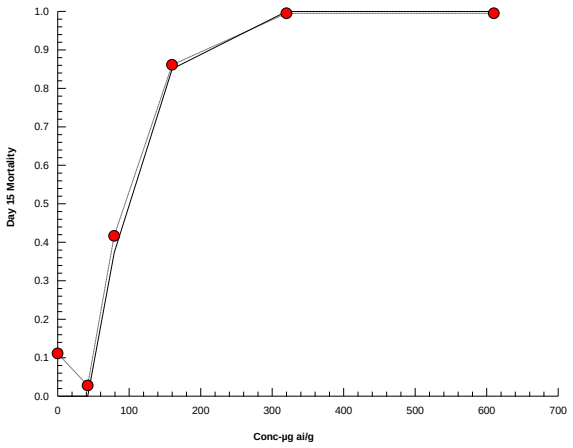
Spearman-Kärber Estimates

Threshold Option	Threshold	Trim	Mu	Sigma	LC50	95% LCL	95% UCL
Control Threshold	0.111	0.00%	1.99	0.0296	97.2	84.9	111

Day 15 Mortality Summary

			Calculated Variate(A/B)							Isotonic Variate	
Conc-µg ai/g	**Code**	**Count**	**Mean**	**Min**	**Max**	**Std Dev**	**CV%**	**%Effect**	**A/B**	**Mean**	**%Effect**
0	N	1	0.111	0.111	0.111	0.000	0.00%	0.0%	4/36	0.0694	0.0%
42		1	0.028	0.028	0.028	0.000	0.00%	-9.38%	1/36	0.0694	0.0%
79		1	0.417	0.417	0.417	0.000	0.00%	34.4%	15/36	0.417	37.3%
160		1	0.861	0.861	0.861	0.000	0.00%	84.4%	31/36	0.861	85.1%
320		1	1.000	1.000	1.000	0.000	0.00%	100.0%	36/36	1	100.0%
610		1	1.000	1.000	1.000	0.000	0.00%	100.0%	36/36	1	100.0%

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Smithers Viscient**

Analysis ID:	10-8918-3919	**Endpoint:**	Larval Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:32	**Analysis:**	Untrimmed Spearman-Kärber	**Status Level:**	1

Batch ID:	08-6406-6952	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

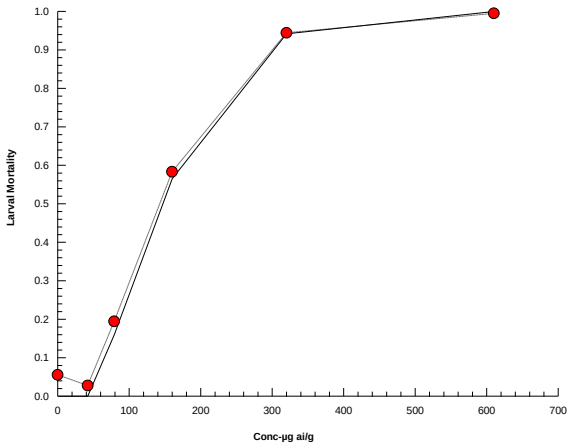
Spearman-Kärber Estimates

Threshold Option	Threshold	Trim	Mu	Sigma	LC50	95% LCL	95% UCL
Control Threshold	0.0556	0.00%	2.15	0.0327	142	122	166

Larval Mortality Summary

			Calculated Variate(A/B)							Isotonic Variate	
Conc-µg ai/g	**Code**	**Count**	**Mean**	**Min**	**Max**	**Std Dev**	**CV%**	**%Effect**	**A/B**	**Mean**	**%Effect**
0	N	1	0.056	0.056	0.056	0.000	0.00%	0.0%	2/36	0.0417	0.0%
42		1	0.028	0.028	0.028	0.000	0.00%	-2.94%	1/36	0.0417	0.0%
79		1	0.194	0.194	0.194	0.000	0.00%	14.7%	7/36	0.194	15.9%
160		1	0.583	0.583	0.583	0.000	0.00%	55.9%	21/36	0.583	56.5%
320		1	0.944	0.944	0.944	0.000	0.00%	94.1%	34/36	0.944	94.2%
610		1	1.000	1.000	1.000	0.000	0.00%	100.0%	36/36	1	100.0%

Graphics



CETIS Analytical Report

Report Date:	18 Nov-19 20:37 (p 1 of 2)
Test Code/ID:	50735801 dc / 13-3158-4771

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Smithers Viscient**

Analysis ID:	00-6549-3542	**Endpoint:**	Emerged Bee Weight	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:34	**Analysis:**	Nonlinear Regression (NLR)	**Status Level:**	1

Batch ID:	08-6406-6952	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

Non-Linear Regression Options

Model Name and Function	Weighting Function	PTBS Function	X Trans	Y Trans
3P Cum Log-Normal (Probit): μ=α·[1- Φ[log[x/δ]/γ]]	Normal [ω=1]	Off [μ*=μ]	None	None

Regression Summary

Iters	Log LL	AICc	BIC	Adj R2	PMSD	Thresh	Optimize	F Stat	P-Value	Decision(α:5%)
14	372	-737	-730	0.0585	4.72%	0.102	Yes			Lack of Fit Not Tested

Point Estimates

Level	μg ai/g	95% LCL	95% UCL
EC5	23.1	n/a	147
EC10	97.4	7.69	372
EC25	1080	n/a	1480000
EC50	15700	n/a	n/a

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision(α:5%)
α	0.102	0.00241	0.0967	0.106	42.2	<1.0E-37	Significant Parameter
γ	3.96	5.36	-6.69	14.6	0.74	0.4613	Non-Significant Parameter
δ	15700	117000	-218000	249000	0.134	0.8940	Non-Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision(α:5%)
Model	0.802	0.267	3	1490	<1.0E-37	Significant
Residual	0.0149	0.00018	83			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision(α:5%)
Distribution	Anderson-Darling A2 Normality Te	1.77	2.49	<1.0E-37	Non-Normal Distribution
	Shapiro-Wilk W Normality Test	0.878	0.971	7.4E-07	Non-Normal Distribution

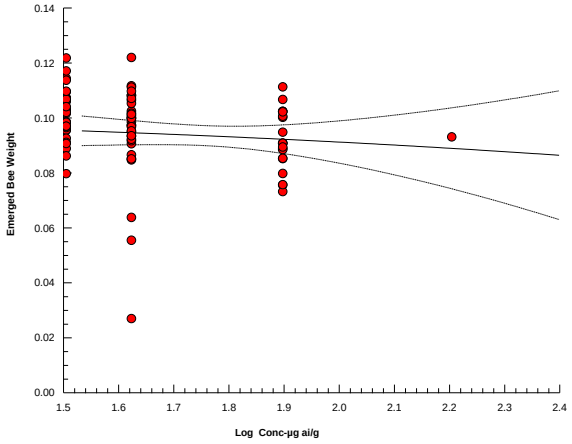
Emerged Bee Weight Summary

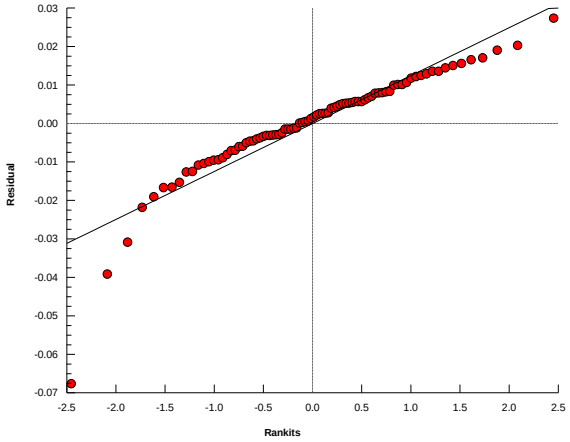
			Calculated Variate						
Conc-μg ai/g	Code	Count	Mean	Min	Max	Std Err	Std Dev	CV%	%Effect
0	N	31	0.102	0.0797	0.122	0.00168	0.00935	9.21%	0.0%
42		34	0.0949	0.027	0.122	0.00299	0.0175	18.40%	6.54%
79		20	0.0917	0.0732	0.111	0.00242	0.0108	11.80%	9.63%
160		1	0.0931	0.0931	0.0931	0	0	0.00%	8.28%

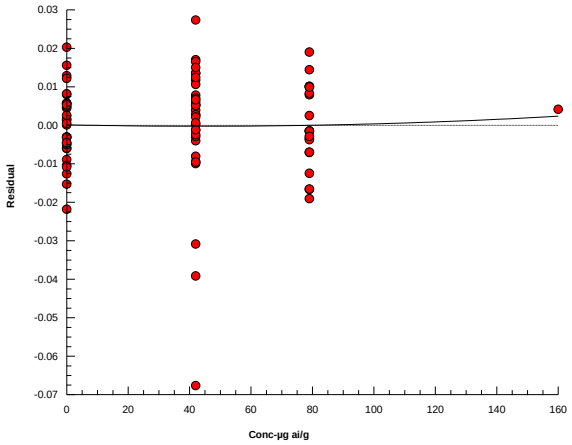
Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

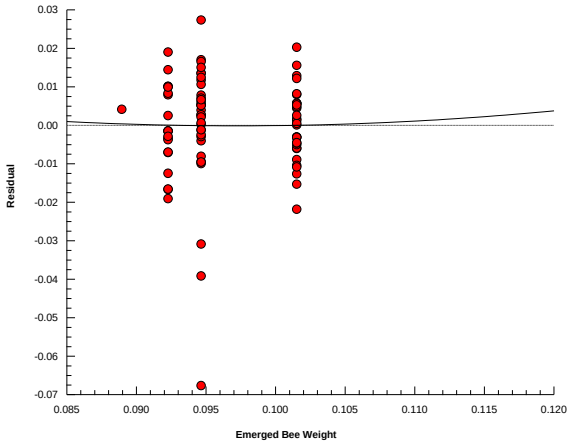
Analysis ID:	00-6549-3542	**Endpoint:**	Emerged Bee Weight	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:34	**Analysis:**	Nonlinear Regression (NLR)	**Status Level:**	1

Graphics Model: 3P Cum Log-Normal (Probit): μ=α·[1- Φ[log[x/δ]/γ]] Distribution: Normal [ω=1]









Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Smithers Viscient**

Analysis ID:	09-3740-9337	**Endpoint:**	Adult Emergence Rate	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:48	**Analysis:**	Linear Regression (GLM)	**Status Level:**	1

Batch ID:	13-9126-3717	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

Linear Regression Options

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

Regression Summary

Iters	LL	AICc	BIC	Mu	Sigma	Adj R2	PMSD	F Stat	P-Value	Decision(α:5%)
5	-4.74	19.5	12.7	0.521	0.164	0.998				Lack of Fit Not Tested

Point Estimates

Level	µg/bee/da	95% LCL	95% UCL
EC5	1.78	1.32	2.13
EC10	2.05	1.59	2.39
EC25	2.57	2.15	2.92
EC50	3.32	2.92	3.77

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision(α:5%)
Intercept	-3.17	0.509	-4.17	-2.18	-6.24	0.0083	Significant Parameter
Slope	6.09	0.918	4.29	7.89	6.63	0.0070	Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision(α:5%)
Model	641	641	1	2150	2.2E-05	Significant
Residual	0.893	0.298	3			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision(α:5%)
Model Fit	Likelihood Ratio GOF Test	0.904	7.81	0.8244	Non-Significant Heterogeneity
	Pearson Chi-Sq GOF Test	0.893	7.81	0.8271	Non-Significant Heterogeneity
Distribution	Shapiro-Wilk W Normality Test	0.9	0.34	0.4107	Normal Distribution

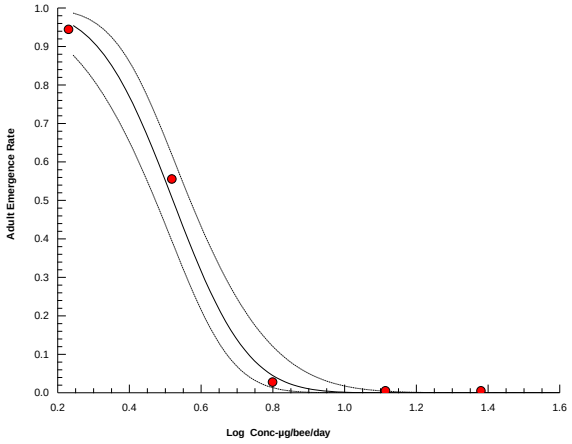
Adult Emergence Rate Summary

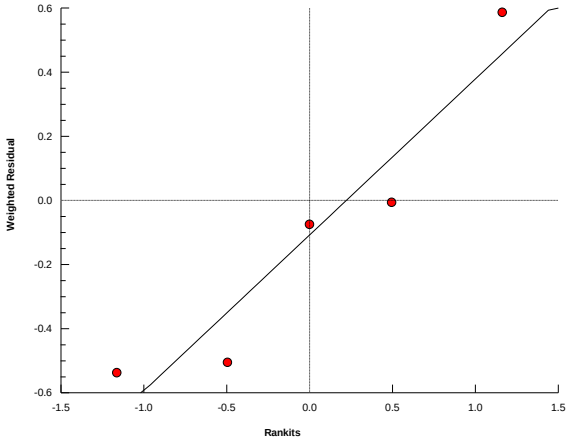
			Calculated Variate(A/B)								
Conc-µg/bee/day	**Code**	**Count**	**Mean**	**Min**	**Max**	**Std Err**	**Std Dev**	**CV%**	**%Effect**	**A**	**B**
1.7		1	0.944	0.944	0.944	0.000	0.000	0.00%	0.0%	34	36
3.3		1	0.556	0.556	0.556	0.000	0.000	0.00%	41.2%	20	36
6.3		1	0.028	0.028	0.028	0.000	0.000	0.00%	97.1%	1	36
13		1	0.000	0.000	0.000	0.000	0.000		100.0%	0	36
24		1	0.000	0.000	0.000	0.000	0.000		100.0%	0	36

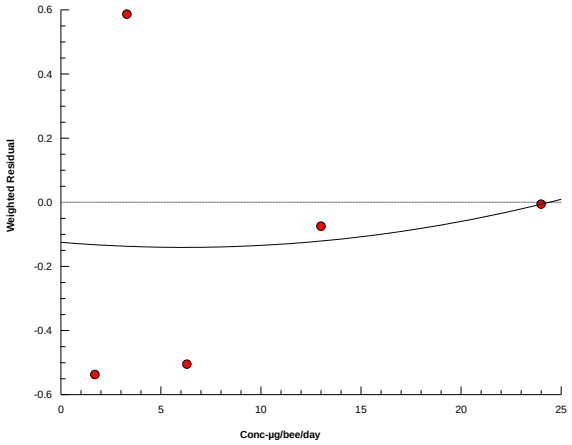
Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

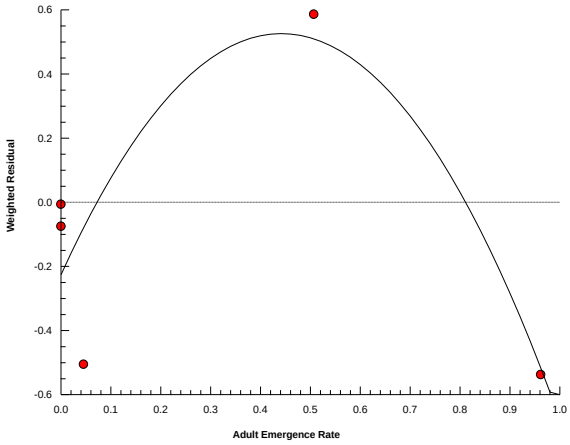
Analysis ID:	09-3740-9337	**Endpoint:**	Adult Emergence Rate	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:48	**Analysis:**	Linear Regression (GLM)	**Status Level:**	1

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









Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Smithers Viscient**

Analysis ID:	10-6591-2726	**Endpoint:**	Day 15 Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:48	**Analysis:**	Linear Regression (GLM)	**Status Level:**	1

Batch ID:	13-9126-3717	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

Linear Regression Options

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

Regression Summary

Iters	LL	AICc	BIC	Mu	Sigma	Adj R2	PMSD	F Stat	P-Value	Decision(α:5%)
4	-4.92	19.8	13.1	0.574	0.192	0.999				Lack of Fit Not Tested

Point Estimates

Level	µg/bee/da	95% LCL	95% UCL
LC5	1.81	1.31	2.21
LC10	2.13	1.63	2.53
LC25	2.78	2.3	3.2
LC50	3.75	3.27	4.3

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision(α:5%)
Intercept	-3	0.457	-3.89	-2.1	-6.56	0.0072	Significant Parameter
Slope	5.22	0.748	3.75	6.69	6.97	0.0061	Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision(α:5%)
Model	691	691	1	4790	6.6E-06	Significant
Residual	0.432	0.144	3			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision(α:5%)
Model Fit	Likelihood Ratio GOF Test	0.519	7.81	0.9147	Non-Significant Heterogeneity
	Pearson Chi-Sq GOF Test	0.432	7.81	0.9335	Non-Significant Heterogeneity
Distribution	Shapiro-Wilk W Normality Test	0.901	0.34	0.4178	Normal Distribution

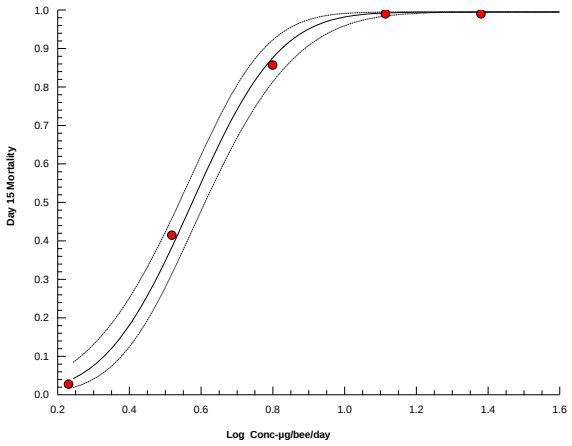
Day 15 Mortality Summary

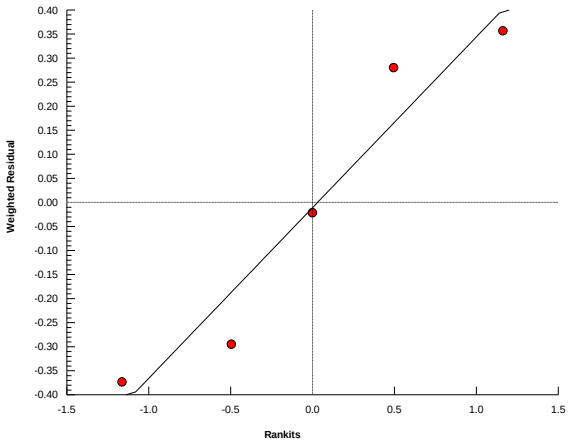
			Calculated Variate(A/B)								
Conc-µg/bee/day	**Code**	**Count**	**Mean**	**Min**	**Max**	**Std Err**	**Std Dev**	**CV%**	**%Effect**	**A**	**B**
1.7		1	0.028	0.028	0.028	0.000	0.000	0.00%	0.0%	1	36
3.3		1	0.417	0.417	0.417	0.000	0.000	0.00%	40.0%	15	36
6.3		1	0.861	0.861	0.861	0.000	0.000	0.00%	85.7%	31	36
13		1	1.000	1.000	1.000	0.000	0.000	0.00%	100.0%	36	36
24		1	1.000	1.000	1.000	0.000	0.000	0.00%	100.0%	36	36

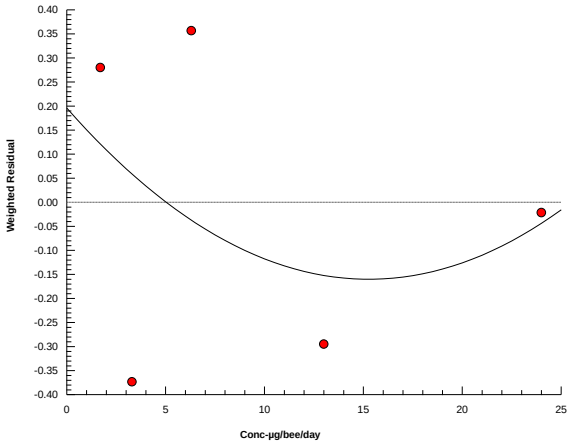
Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

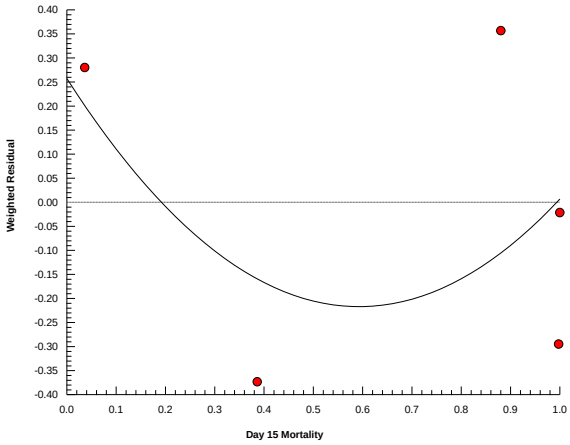
Analysis ID:	10-6591-2726	**Endpoint:**	Day 15 Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:48	**Analysis:**	Linear Regression (GLM)	**Status Level:**	1

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









Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

Analysis ID:	08-8492-1464	**Endpoint:**	Larval Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:48	**Analysis:**	Linear Regression (GLM)	**Status Level:**	1

Batch ID:	13-9126-3717	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

Linear Regression Options

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

Regression Summary

Iters	LL	AICc	BIC	Mu	Sigma	Adj R2	PMSD	F Stat	P-Value	Decision(α:5%)
4	-6.32	22.6	15.8	0.731	0.246	1				Lack of Fit Not Tested

Point Estimates

Level	µg/bee/da	95% LCL	95% UCL
LC5	2.12	1.5	2.67
LC10	2.61	1.95	3.18
LC25	3.68	2.99	4.31
LC50	5.39	4.62	6.29

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision(α:5%)
Intercept	-2.97	0.394	-3.75	-2.2	-7.54	0.0048	Significant Parameter
Slope	4.06	0.507	3.07	5.06	8.01	0.0041	Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision(α:5%)
Model	1130	1130	1	9840	2.3E-06	Significant
Residual	0.346	0.115	3			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision(α:5%)
Model Fit	Likelihood Ratio GOF Test	0.488	7.81	0.9216	Non-Significant Heterogeneity
	Pearson Chi-Sq GOF Test	0.346	7.81	0.9513	Non-Significant Heterogeneity
Distribution	Shapiro-Wilk W Normality Test	0.955	0.34	0.7695	Normal Distribution

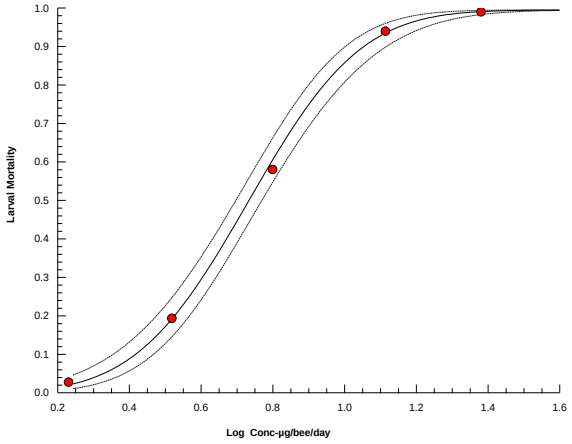
Larval Mortality Summary

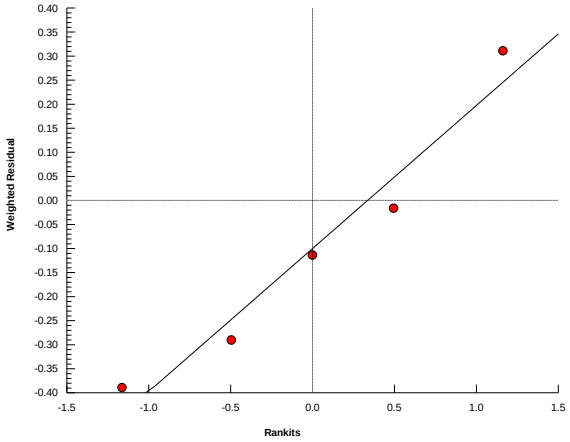
			Calculated Variate(A/B)								
Conc-µg/bee/day	**Code**	**Count**	**Mean**	**Min**	**Max**	**Std Err**	**Std Dev**	**CV%**	**%Effect**	**A**	**B**
1.7		1	0.028	0.028	0.028	0.000	0.000	0.00%	0.0%	1	36
3.3		1	0.194	0.194	0.194	0.000	0.000	0.00%	17.1%	7	36
6.3		1	0.583	0.583	0.583	0.000	0.000	0.00%	57.1%	21	36
13		1	0.944	0.944	0.944	0.000	0.000	0.00%	94.3%	34	36
24		1	1.000	1.000	1.000	0.000	0.000	0.00%	100.0%	36	36

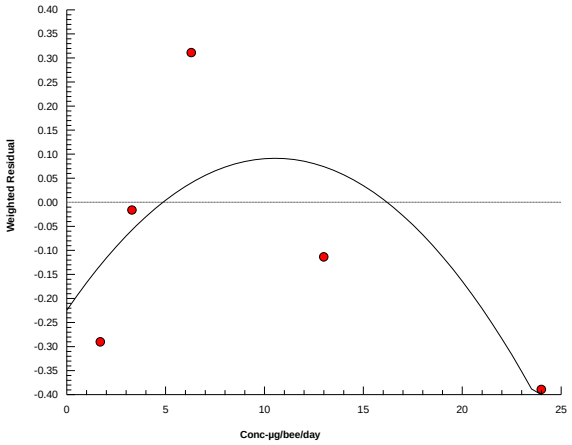
Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

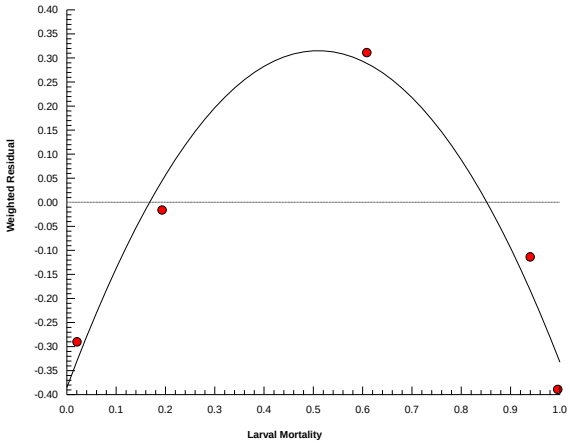
Analysis ID:	08-8492-1464	**Endpoint:**	Larval Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:48	**Analysis:**	Linear Regression (GLM)	**Status Level:**	1

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









Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Smithers Viscient**

Analysis ID:	09-1624-8963	**Endpoint:**	Adult Emergence Rate	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:49	**Analysis:**	Untrimmed Spearman-Kärber	**Status Level:**	1

Batch ID:	13-9126-3717	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

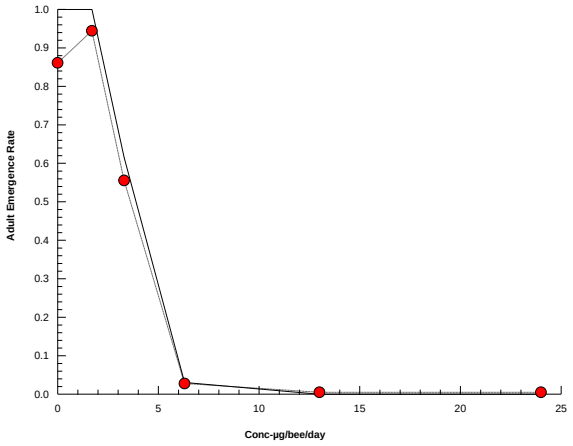
Spearman-Kärber Estimates

Threshold Option	Threshold	Trim	Mu	Sigma	EC50	95% LCL	95% UCL
Control Threshold	0.139	0.00%	0.559	0.0246	3.62	3.23	4.05

Adult Emergence Rate Summary

			Calculated Variate(A/B)							Isotonic Variate	
Conc-µg/bee/day	**Code**	**Count**	**Mean**	**Min**	**Max**	**Std Dev**	**CV%**	**%Effect**	**A/B**	**Mean**	**%Effect**
0	N	1	0.861	0.861	0.861	0.000	0.00%	0.0%	31/36	0.903	0.0%
1.7		1	0.944	0.944	0.944	0.000	0.00%	-9.68%	34/36	0.903	0.0%
3.3		1	0.556	0.556	0.556	0.000	0.00%	35.5%	20/36	0.556	38.5%
6.3		1	0.028	0.028	0.028	0.000	0.00%	96.8%	1/36	0.0278	96.9%
13		1	0.000	0.000	0.000	0.000		100.0%	0/36	0	100.0%
24		1	0.000	0.000	0.000	0.000		100.0%	0/36	0	100.0%

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Smithers Viscient**

Analysis ID:	00-0948-4834	**Endpoint:**	Day 15 Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:48	**Analysis:**	Untrimmed Spearman-Kärber	**Status Level:**	1

Batch ID:	13-9126-3717	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

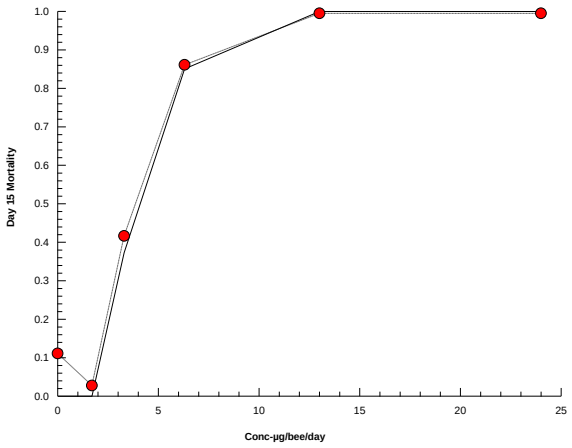
Spearman-Kärber Estimates

Threshold Option	Threshold	Trim	Mu	Sigma	LC50	95% LCL	95% UCL
Control Threshold	0.111	0.00%	0.597	0.029	3.96	3.46	4.52

Day 15 Mortality Summary

			Calculated Variate(A/B)							Isotonic Variate	
Conc-µg/bee/day	**Code**	**Count**	**Mean**	**Min**	**Max**	**Std Dev**	**CV%**	**%Effect**	**A/B**	**Mean**	**%Effect**
0	N	1	0.111	0.111	0.111	0.000	0.00%	0.0%	4/36	0.0694	0.0%
1.7		1	0.028	0.028	0.028	0.000	0.00%	-9.38%	1/36	0.0694	0.0%
3.3		1	0.417	0.417	0.417	0.000	0.00%	34.4%	15/36	0.417	37.3%
6.3		1	0.861	0.861	0.861	0.000	0.00%	84.4%	31/36	0.861	85.1%
13		1	1.000	1.000	1.000	0.000	0.00%	100.0%	36/36	1	100.0%
24		1	1.000	1.000	1.000	0.000	0.00%	100.0%	36/36	1	100.0%

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Smithers Viscient**

Analysis ID:	03-1512-9139	**Endpoint:**	Larval Mortality	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:48	**Analysis:**	Untrimmed Spearman-Kärber	**Status Level:**	1

Batch ID:	13-9126-3717	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

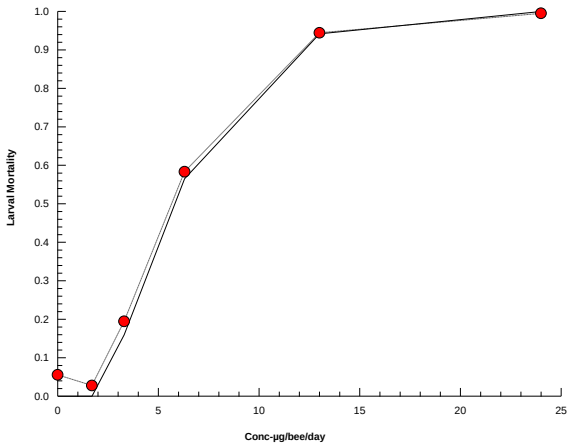
Spearman-Kärber Estimates

Threshold Option	Threshold	Trim	Mu	Sigma	LC50	95% LCL	95% UCL
Control Threshold	0.0556	0.00%	0.76	0.0322	5.75	4.96	6.67

Larval Mortality Summary

			Calculated Variate(A/B)							Isotonic Variate	
Conc-µg/bee/day	**Code**	**Count**	**Mean**	**Min**	**Max**	**Std Dev**	**CV%**	**%Effect**	**A/B**	**Mean**	**%Effect**
0	N	1	0.056	0.056	0.056	0.000	0.00%	0.0%	2/36	0.0417	0.0%
1.7		1	0.028	0.028	0.028	0.000	0.00%	-2.94%	1/36	0.0417	0.0%
3.3		1	0.194	0.194	0.194	0.000	0.00%	14.7%	7/36	0.194	15.9%
6.3		1	0.583	0.583	0.583	0.000	0.00%	55.9%	21/36	0.583	56.5%
13		1	0.944	0.944	0.944	0.000	0.00%	94.1%	34/36	0.944	94.2%
24		1	1.000	1.000	1.000	0.000	0.00%	100.0%	36/36	1	100.0%

Graphics



CETIS Analytical Report

Report Date:	18 Nov-19 20:50 (p 1 of 2)
Test Code/ID:	50735801 dd / 17-4452-3480

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study — **Smithers Viscient**

Analysis ID:	06-1762-7517	**Endpoint:**	Emerged Bee Weight	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:49	**Analysis:**	Nonlinear Regression (NLR)	**Status Level:**	1

Batch ID:	13-9126-3717	**Test Type:**	OECD 2014 HB Larval Repeat Exp	**Analyst:**	
Start Date:	19 May-17	**Protocol:**	Larval Chronic Oral Toxicity, 21-day Study	**Diluent:**	
Ending Date:	07 Jun-17	**Species:**	Apis mellifera	**Brine:**	
Test Length:	19d 0h	**Taxon:**		**Source:**	Wood's Beekeeping Supply, **Age:**

Non-Linear Regression Options

Model Name and Function	Weighting Function	PTBS Function	X Trans	Y Trans
3P Cum Log-Normal (Probit): μ=α·[1- Φ[log[x/δ]/γ]]	Normal [ω=1]	Off [μ*=μ]	None	None

Regression Summary

Iters	Log LL	AICc	BIC	Adj R2	PMSD	Thresh	Optimize	F Stat	P-Value	Decision(α:5%)
12	372	-737	-730	0.0587	4.72%	0.102	Yes			Lack of Fit Not Tested

Point Estimates

Level	μg/bee/da	95% LCL	95% UCL
EC5	0.943	n/a	5.95
EC10	4	0.336	15.1
EC25	44.8	n/a	50400
EC50	655	n/a	n/a

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision(α:5%)
α	0.102	0.00241	0.0967	0.106	42.2	<1.0E-37	Significant Parameter
γ	3.98	5.28	-6.53	14.5	0.753	0.4534	Non-Significant Parameter
δ	655	4830	-8950	10300	0.136	0.8924	Non-Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision(α:5%)
Model	0.802	0.267	3	1490	<1.0E-37	Significant
Residual	0.0149	0.00018	83			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision(α:5%)
Distribution	Anderson-Darling A2 Normality Te	1.78	2.49	<1.0E-37	Non-Normal Distribution
	Shapiro-Wilk W Normality Test	0.877	0.971	7.2E-07	Non-Normal Distribution

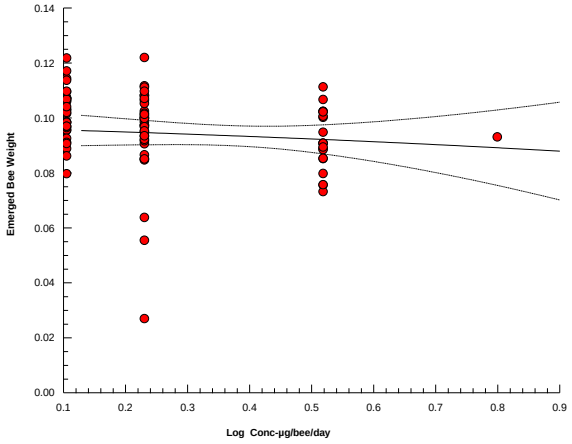
Emerged Bee Weight Summary

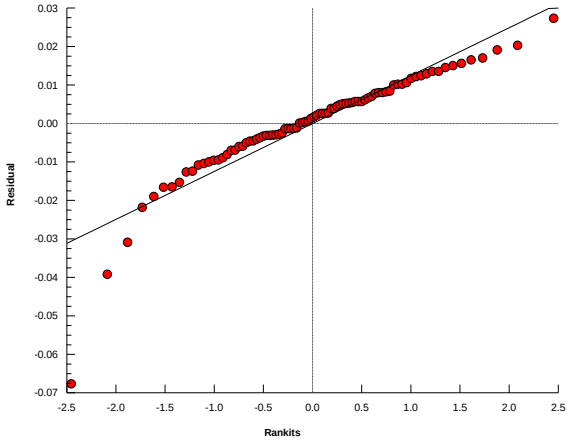
			Calculated Variate						
Conc-μg/bee/day	Code	Count	Mean	Min	Max	Std Err	Std Dev	CV%	%Effect
0	N	31	0.102	0.0797	0.122	0.00168	0.00935	9.21%	0.0%
1.7		34	0.0949	0.027	0.122	0.00299	0.0175	18.40%	6.54%
3.3		20	0.0917	0.0732	0.111	0.00242	0.0108	11.80%	9.63%
6.3		1	0.0931	0.0931	0.0931	0	0	0.00%	8.28%

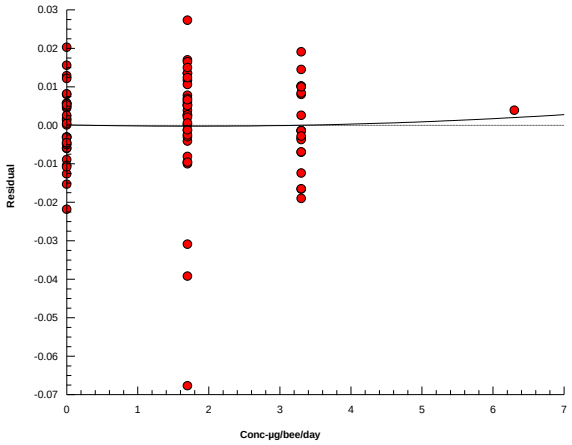
Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study **Smithers Viscient**

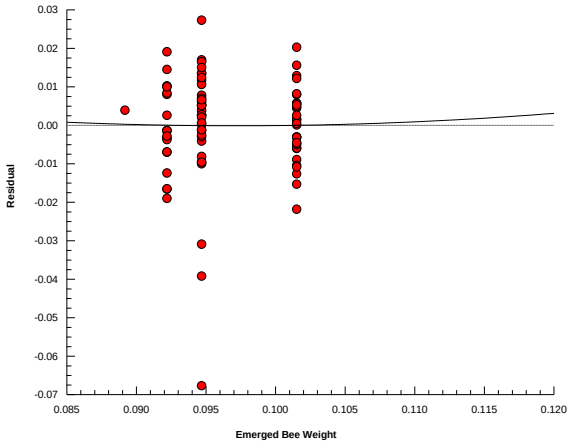
Analysis ID:	06-1762-7517	**Endpoint:**	Emerged Bee Weight	**CETIS Version:**	CETISv1.9.5
Analyzed:	18 Nov-19 20:49	**Analysis:**	Nonlinear Regression (NLR)	**Status Level:**	1

Graphics Model: 3P Cum Log-Normal (Probit): μ=α·[1- Φ[log[x/δ]/γ]] Distribution: Normal [ω=1]









DATA EVALUATION RECORD
CHRONIC TOXICITY TEST WITH THE HONEY BEE
Non-Guideline Chronic Feeding Study

1. **CHEMICAL:** Pyrifluquinazon PC Code No.: 555555

2. **TEST MATERIAL:** Pyrifluquinazon Technical Grade Purity: 97.45%

3. **CITATION**

Author: Patnaude, M.R.

Title: Pyrifluquinazon – 10-Day Oral Toxicity Test with the Adult Honey Bee (*Apis mellifera*)

Study Completion Date: October 31, 2018

Laboratory: Smithers Viscient

Sponsors: Nichino America, Inc.

Laboratory Report ID: 14078.6106
DP Barcode: 452040
MRID No.: 50735802

4. **REVIEWED BY:** Julie Burns, Environmental Scientist, CDM/CSS-Dynamac JV

Signature: Julie Burns **Date:** 6/25/2019

APPROVED BY: Moncie V. Wright, Ph.D., Environmental Scientist, CDM/CSS-Dynamac JV

Signature: Moncie V Wright **Date:** 6/26/2019

5. **APPROVED BY:** N.E. Federoff, Wildlife Biologist, OPP/EFED/ERB-2

Signature: **Date:** 11/7/19

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

7. STUDY PARAMETERS:

Test Species: *Apis mellifera* L.
Age of Test Organisms at Test Initiation: ≤2 days
Exposure Duration: 10 days

8. CONCLUSIONS: The honey bee, *Apis mellifera* L., was exposed to **Pyrifluquinazon Technical Grade** for 10 days in a feeding study at the nominal and measured concentrations/actual intake dietary doses shown in the tables below. The mean-measured concentrations were calculated by the study author and were analytically corrected for purity. The measured actual intake doses were also calculated by the study author, and were corrected for evaporative loss, daily diet consumption, and bee mortality.

Nominal Concentration (mg ai/kg diet)	Mean-Measured Concentration (mg ai/kg diet)	Nominal Dietary Dose (µg ai/bee/day)	Measured Actual Intake Dietary Dose (µg ai/bee/day)
0.20	0.20	0.0050	0.0039
0.56	0.56	0.014	0.016
1.7	1.7	0.042	0.045
4.9	4.8	0.12	0.13
15	15	0.38	0.44
45	45	1.1	1.2
140	140	3.4	3.1
410	400	10	6.9

After 10 days, mortality averaged 0% in the negative control and 10% in the solvent control as compared to mortality ranging from 3 to 87% in the groups exposed to the test material. Mortality in the positive control (Dimethoate) was 100% after 10 days of exposure. Behavioral abnormalities were recorded daily for each test group, with the number of observed affected bees quickly increasing as the concentration of the test substance increased. Daily food consumption averaged 18 and 20 mg/bee/day in the negative and solvent controls, respectively, and averaged 20, 29, 27, 28, 29, 27, 23, and 18 mg/bee/day in the measured 0.0039, 0.016, 0.045, 0.13, 0.44, 1.2, 3.1, and 6.9 µg ai/bee/day groups, respectively.

The 10-day mortality NOAEC and LC_{50} were 45 and 118 mg ai/kg diet, respectively (corresponding to a NOAEL and LD_{50} of 1.2 and 3.1 µg ai/bee/day, respectively). There were no effects on food consumption.

Endpoint	Mortality	Food Consumption
Diet Concentration (mg ai/kg diet)	LC_{50}: 118 95% CI: 23-18500 Slope: 0.53 (0.17-0.89)	IC_{50}: >400 95% CI: N/A Slope: N/A

	NOAEC: 45 LOAEC: 140	NOAEC: 400 LOAEC: >400
Dietary Dose (µg ai/bee/day)	LD_{50}: 3.1 95% CI: 0.56-2710 Slope: 0.51 (0.13-0.89) NOAEL: 1.2 LOAEL: 3.1	ID_{50}: >6.9 95% CI: N/A Slope: N/A NOAEL: 6.9 LOAEL: >6.9

9. ADEQUACY OF THE STUDY:

This study is scientifically sound and is classified as acceptable.

10. GUIDELINE DEVIATIONS: This study was conducted following the proposed OECD Guideline for the Testing of Chemicals: Honey bees *(Apis mellifera* L.), chronic oral toxicity test (10 day feeding test in the laboratory). Deviations were noted:

1. The study author did not report if bees were kept in conditions conforming to proper cultural practices.

This deviation does not impact the acceptability of this study.

11. SUBMISSION PURPOSE: Classification unknown for the submission of this study.

12. MATERIALS AND METHODS:

A. Test Organisms

Guideline Criteria	Reported Information
Species Honey Bee (*Apis mellifera L.*)	Honey bee Italian hybrids (*Apis mellifera lingustica* and unidentified subspecies).
Age at beginning of test Worker bees of uniform age.	≤ 2-day old emerged adult bees.
Source	Wood's Beekeeping Supply, Lincoln, Rhode Island
Were bees from diseased-free colonies?	Unknown. Honey bees were from hives not exposed to chemical application for at least 1 month prior to testing.

Guideline Criteria	Reported Information
Were bees kept in conditions conforming to proper cultural practices?	Not reported. Capped brood frames containing adults were received and incubated at test temperature three days prior to acclimation.
<u>Acclimation conditions</u>	1 day prior to test start, newly emerged bees were manually transferred to test vessels, containing 10 bees each. The vessels were then placed in an environmental chamber and test organisms were supplied with 2.0 mL of 50% (w/w) untreated sucrose solution diet.

B. Test System

Guideline Criteria	Reported Information
Test Chambers	Glass jars (120 mL) with screw top lid (having ventilation holes and a larger hole for the feeding syringe).
Temperature during exposure	32-34°C
Relative humidity during exposure	62-69%
Lighting	Near darkness, except approximately 30 minutes a day when bees were exposed to laboratory lighting for observations and renewal of diet.
Feeding	Bees were fed treated 50% sucrose solution in acetone (exposed groups), untreated 50% sucrose solution (negative control), or untreated sucrose solution prepared with 0.50 mL acetone per 24.5 mL sucrose solution (solvent control). Bees were fed *ad libitum* with syringes that were renewed daily.

C. Test Design

Guideline Criteria	Reported Information
Test material	Identity: Pyrifluquinazon Technical Grade Synonyms: R-40598 technical grade, NNI-0101 technical grade, Pyrifluquinazon IUPAC name: 1-acetyl-3,4-dihydro-3-[(3-pyridinylmethyl)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]-2(1*H)*-quinazolinone CAS No.: 337458-27-2 Lot No.: TY0401 Purity: 97.45% Storage: Room temperature; dark, ventilated cabinet
Nominal application rates The test material should be applied at the maximum proposed label rate.	Diet concentrations: 0 (negative and solvent controls), 0.20, 0.56, 1.7, 4.9, 15, 45, 140, and 410 mg ai/kg diet Dietary doses: 0 (negative and solvent controls), 0.0050, 0.014, 0.042, 0.12, 0.38, 1.1, 3.4, and 10 µg ai/bee/day
Dose Preparation	A 25 mg ai/mL primary stock solution was prepared by bringing 1.252 g active ingredient to a volume of 50 mL with acetone. This solution was then diluted with acetone and 50% sucrose solution to prepare each dose. Diet solutions were prepared daily and observed to be amber in color and cloudy in proportion to the test diet concentration.
Number of bees exposed	Each treatment (including untreated control, vehicle control, and toxic reference item) had 3 replicates, with 10 bees per replicate (30 bees total)

Guideline Criteria	Reported Information
Application methods	The test sucrose feeding solutions were provided *ad libitum* with syringe feeders (3.0 mL plastic syringes containing ~2.0 mL diet). Feeders were renewed daily. Feeders were weighed before and after they were offered. The food consumed per vessel was determined by comparing the initial and remaining weights.
Other experimental design information	Syringes in three additional test vessels filled with untreated diet without honey bees were weighed daily for evaporative loss. Individual daily consumption was corrected for daily diet consumption, evaporative loss, and mortality. A sample of each stock solution used to dose the sucrose solution diets was collected on day one. Samples of each treated, control, and solvent control diets were collected on days 1, 3, 7, and 8. These samples were analyzed for test substance concentration.
Were bees randomly or impartially assigned to test groups?	Yes, each replicate vessel ID randomly assigned using a random number generator prior to exposure.
Control(s)	Negative control: untreated 50% sucrose solution Solvent Control: 0.50 mL of acetone per 24.5 mL of untreated sucrose solution
Exposure period	10 days
Positive Control, (if any)	Toxic reference item: Dimethoate (1.0 mg ai/kg diet)

13. REPORTED RESULTS:

Guideline Criteria	Reported Information
Quality assurance and GLP compliance statements were included in the report?	Yes. This study was conducted in compliance with the EPA GLP Standards specified under FIFRA and as accepted by the OECD Principles of Good Laboratory Practice with the following exceptions: 1. Routine sucrose solution (comprised of water and sucrose) contaminant screening analyses were conducted at Eurofins Lancaster Laboratories Environmental, Lancaster, Pennsylvania and U.S. Department of Agriculture, Gastonia, North Carolina, using standard U.S. EPA procedures and are considered facility records under Smithers Viscient's Standard Operating Procedures. Since the analyses were conducted following standard validated methods, this exception has no impact on the study results. 2. The reference toxicant, dimethoate, was purchased from a commercial supplier and was not characterized in accordance with GLP standards.
Control mortality	0% mortality was observed in the negative control, and 10% mortality was observed in the solvent control at test termination.
Were raw data included?	Yes.
Were signs of toxicity (if any) described?	Affected bees were observed daily at all treatment levels for abnormalities such as apathy, affected, cramps, vomiting, etc.

Mortality and Observations:

Measured Diet Concentrations, mg ai/kg diet (Actual Intake Doses, µg ai/bee/day)		Number Exposed	Mortality at 10 days (%)	Behavioral Abnormalities[a]
10-day Chronic Feeding Toxicity Test				
Negative control		30	0	None
Solvent control		30	10	Few affected
Pyrifluquinazon	0.20 (0.0039)	30	23	More than half affected after day 3
	0.56 (0.016)	30	3	All affected by day 4
	1.7 (0.045)	30	10	More than half affected by day 1
	4.8 (0.13)	30	30	All affected by day 1
	15 (0.44)	30	23	All but one bee affected by day 1
	45 (1.2)	30	10	All affected by day 1
	140 (3.1)	30	53	All affected by day 1
	400 (6.9)	30	87	All affected by day 1

[a] Behavioral abnormality and mortality data obtained from Appendix 6 pp. 116-121 in the MRID.

After 10 days, mortality averaged 0% in the negative control and 10% in the solvent control, as compared to mortality ranging from 3 to 87% in the groups exposed to the test material. Mortality in the positive control (Dimethoate) was 100% at ten days.

Daily food consumption averaged 18 and 20 mg/bee/day in the negative and solvent controls, respectively, and averaged 20, 29, 27, 28, 29, 27, 23, and 18 mg/bee/day in the measured 0.0039, 0.016, 0.045, 0.13, 0.44, 1.2, 3.1, and 6.9 µg ai/bee/day groups, respectively.

Behavioral abnormalities were recorded daily. There were no abnormalities observed in the negative control, and very few abnormalities observed in the solvent control. The number of bees affected increased as the concentration of test substance increased, with most bees affected after the third lowest test concentration throughout the entire duration of the study.

Study Author's Statistical Analysis

Solvent and negative control survival data were compared using Fisher's Exact Test. Adult weight data for the controls were compared using an Equal Variance Two Sample t-Test. NOAEC/LOAEC values for 10-day mortality were determined using Fisher's Exact Test with Bonferroni Holm's Adjustment. The 10-day LC/LD_{50} values were calculated using the Trimmed Spearman-Kärber method. The study author evaluated body weight of bees exposed to treatment as an endpoint, using Dunnett's Multiple Comparison Test to determine NOAEC/LOAEC values, and empirically estimated the ED/EC_{50} values. All statistical analyses were performed using CETIS statistical software and the measured diet concentrations and measured actual intake dietary doses.

Endpoint	**Mortality**	**Live Adult Weight**
Diet Concentration (mg ai/kg diet)	LC_{50}: 91 95% CI: 56-150 Slope: N/A NOAEC: 1.7 LOAEC: 4.8	EC_{50}: >400 95% CI: N/A Slope: N/A NOAEC: 400 LOAEC: >400
Dietary Dose (µg ai/bee/day)	LD_{50}: 2.1 95% CI: 1.3-3.2 Slope: N/A NOAEL: 0.045 LOAEL: 0.13	ED_{50}: >6.9 95% CI: N/A Slope: N/A NOAEL: 6.9 LOAEL: >6.9

Reviewer's Statistical Verification:

The reviewer analyzed mortality and mean daily food consumption using CETIS statistical software version 1.9.5.3 with database backend settings implemented by EFED on 7/25/17. The test codes were designated the MRID number, followed by the acronyms "dc" for diet concentration and "dd" for dietary dose. The study author-calculated measured actual intake dietary doses and measured diet concentrations were used for the analyses.

The negative and solvent control data were compared using an Equal Variance t Two-Sample test ($\alpha = 0.05$) and no significant differences were noted. All subsequent test item data were compared to the negative control data.

Data were tested for normality using Shapiro-Wilk's test ($\alpha = 0.01$) and for homogeneity of

variance using Bartlett's ($\alpha = 0.01$) or Levene's test ($\alpha = 0.01$). Mortality and food consumption data fit the normal distribution and were homoscedastic, so were subsequently analyzed using ANOVA and Dunnett's Multiple Comparison Test ($\alpha = 0.05$). The LC/LD_{50} values were determined using linear regression. The IC/ID_{50} values were empirically estimated to be higher than the highest measured concentration/dose as there were no significant effects in the data.

Endpoint	Mortality	Food Consumption
Diet Concentration (mg ai/kg diet)	LC_{50}: 118 95% CI: 23-18500 Slope: 0.53 (0.17-0.89) NOAEC: 45 LOAEC: 140	IC_{50}: >400 95% CI: N/A Slope: N/A NOAEC: 400 LOAEC: >400
Dietary Dose (µg ai/bee/day)	LD_{50}: 3.1 95% CI: 0.56-2710 Slope: 0.51 (0.13-0.89) NOAEL: 1.2 LOAEL: 3.1	ID_{50}: >6.9 95% CI: N/A Slope: N/A NOAEL: 6.9 LOAEL: >6.9

14. REVIEWER'S COMMENTS:

The reviewer's LC/LD_{50} values were higher than the study author's due to the reviewer using linear regression and the study author using the Trimmed Spearman Kärber method. The reviewer also obtained higher NOAEC/NOAEL values for mortality because the reviewer used Dunnett's test for comparisons while the study author used Fisher's Exact Test with Bonferroni-Holm's Adjustment. Additionally, the study author did not analyze food consumption. The reviewer's results are reported in the Conclusions sections of this DER.

According to OECD Draft Guidance, the test was considered to be valid if:

1. The average control mortality was ≤15% by test termination; and
2. The average reference item mortality was ≥50% by test termination.

Both validity criteria were met.

The experimental portion of this study was conducted from June 5 to June 15, 2018.

15. REFERENCES:

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USDA, 1981. Sucrose Conversion Table. 135-A-50. United States Department of Agriculture, Agricultural Marketing Service, Fruit and Vegetable Division, Processed Products Branch: Washington, D.C.

U.S. EPA, 1997. Office of Waste. Test Methods for Evaluating Solid Waste, Physical/Chemical Methods (SW-846). Update IV January 2008. U.S. Environmental Protection Agency, Washington, D.C.

All other references are standard guidance or methodologies