Joint Exhibit 55

EPA OALJ Docket No. FIFRA-HQ-2022-0002

Data Evaluation Record on the Acute Oral Toxicity of DCPA (Chlorthal Dimethyl) to Zebra Finch (*Taeniopygia guttata*)

PMRA Submission Number {.....} EPA MRID Number 49477601

Data Requirement:	PMRA Data Code	{.....}
	EPA DP Barcode	423300
	OECD Data Point	{.....}
	EPA MRID	49477601
	EPA Guideline	850.2100

Test material: Chlorthal Dimethyl **Purity:** 99.3%
Common name DCPA
Chemical name: IUPAC: Not reported
CAS name: Not reported
CAS No.: 1861-32-1
Synonyms: Dacthal Technical

Primary Reviewer: Kindra L. Bozicevich **Signature:** Kindra Bozicevich
Staff Scientist, CDM Smith/CSS-Dynamac JV **Date:** 12/10/2016

Secondary Reviewer: Teri S. Myers **Signature:** Teri S Myers
Staff Scientist, CDM Smith/CSS-Dynamac JV **Date:** 12/16/2016

Primary Reviewer: Christina M. Wendel **Signature:**
EPA/OPP/EFED/ERB2/Biologist **Date:** 12/02/2021

Secondary Reviewer(s): Michael Wagman **Signature:**
EPA/OPP/EFED/ERB2/Senior Scientist **Date:** 12/02/2021

Reference/Submission No.: {.....}

Company Code	{.....}	[For PMRA]
Active Code	{.....}	[For PMRA]
Use Site Category	{.....}	[For PMRA]
EPA PC Code	078701	

Date Evaluation Completed: 02-12-2021

CITATION: Bull, A.D. 2014. DCPA (Chlorthal Dimethyl): Acute Oral Toxicity (LD_{50}) to the Zebra Finch. Unpublished study performed by Huntingdon Life Sciences Ltd, Cambridgeshire, England. Project ID BDG0198. Study sponsored by AMVAC Chemical Corporation, Newport Beach, California. Study initiated April 10, 2014 and completed September 16, 2014.

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

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EXECUTIVE SUMMARY:

The acute oral toxicity of **DCPA (Chlorthal Dimethyl) technical** to zebra finch (*Taeniopygia guttata*) (minimum of 16 weeks old) was assessed over 14 days. DCPA was administered to the birds by oral intubation at nominal levels of 0 (vehicle control) and 2000 mg a.i./kg bw. The observed 14-day acute oral LD_{50} was >2000 mg a.i./kg bw.

No mortalities were observed in the control or any of the treatment groups. Wiping of the beak was observed in both the control and treatment group on the day of dosing but had resolved by 3-hours post-dosing. There were no apparent treatment-related effects on food consumption or on body weight at any dosage level tested. Based upon the lack of treatment-related mortalities and sublethal effects, the observational NOAEL was 2000 mg a.i./kg bw. The acute-oral LD_{50} was >2000 mg a.i./kg bw.

According to the U.S. EPA classification system, DCPA would be classified as *practically non-toxic* to zebra finch on an acute oral basis.

This study **is scientifically sound** and is classified as **supplemental and may be used to calculate risk quotients.** If application rates result in higher estimated exposure concentrations on dietary items than the concentration tested in this study, additional data may be required.

Results Synopsis

Test Organism Size/Age (Mean Weight): Minimum 16 weeks old; group means 14.7 to 25.5 g (combined sexes)

LD_{50}: >2000 mg a.i./kg bw 95% C.I.: N/A
Probit slope: N/A 95% C.I.: N/A

Endpoint(s) Affected: None

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: U.S. EPA Ecological Effects Test Guideline, OCSPP 850.2100 (2012)

Deviations from OCSPP 850.2100 guidance included:

1. The stability of the compound under the test conditions was not verified. However, prior to the main test a homogeneity and stability trail was undertaken, to assess the suitability of the formulation methods and storage. Results showed that the formulation procedures and storage at ambient temperature (nominally +21°C) and refrigerated (nominally +4°C) for 48 hours were satisfactory at the nominal concentration of 400 mg/mL. Full details are available in the study report in Annex 2. This is considered a minor deviation.

These deviations *do not* affect the scientific soundness of this study.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided. This study was conducted in compliance with UK GLP regulations, OECD Principles of GLP, and EC Commission Directive 2004/10/EC.

A. MATERIALS:

1. Test material DCPA (Chlorthal Dimethyl) technical

Description: Yellowish white crystalline solid

Lot No./Batch No. : 120904-1

Purity: 99.3%

Stability of compound under test conditions: Not assessed.

Storage conditions of test chemicals: Ambient temperature under dry conditions.

Physicochemical properties of DCPA.

Parameter	Values	Comments
Water solubility at 20°C	Not reported	
Vapor pressure	Not reported	
UV absorption	Not reported	
pKa	Not reported	
Kow	Not reported	

(OECD recommends water solubility, stability in water and light, pKa, Pow, and vapor pressure of test compound)

2. Test Organism:

Species (common and scientific names): Zebra finch (*Taeniopygia guttata*)
Age at study initiation: minimum of 16 weeks old
Weight at study initiation (mean and range): range 14.7 to 25.5 g (14.0-23.3 g males, 15.8-23.9 g females)
Source: Originally from a commercial supplier (not specified); allocated from the Huntington Life Sciences stock, phenotypically indistinguishable from wild type.

(EPA recommends using either bobwhite quail or mallard duck. Birds should be at

least 16 weeks old at test initiation and should be uniform in size and weight as well as phenotypically indistinguishable from wild birds).

B. STUDY DESIGN:

1. Experimental Conditions

a. Range-finding study: An initial range-finding test was carried out using two birds (1 male, 1 female). The birds were held under similar environmental conditions that were used in the definitive test. Food, dose preparation and dosing procedures were also similar to those used in the definitive test, the same vehicle material, 1% methylcellulose was used. Birds were observed for fourteen days following dosing of 2000 mg/kg at 400 mg/mL dose concentration (10 mL/kg dose volume). There were no signs of toxicity observed during the range finding phase of this study. However, wiping of the beak (on perches or other cage surfaces) was noted in both male and female birds approximately 3 hours after dosing. This observation had resolved approximately 4 hours after dosing. On the basis of these results, it was considered appropriate to select the dose level 2000 mg/kg for the main study.

b. Definitive study

Table 1: Experimental Parameters

Parameter	Details	Remarks
		Criteria
Acclimation Period:	14 days	The diet mixture nominally contained no added antibiotic or other non-nutritional feed additive and was not anticipated to contain contaminants capable of interfering with the integrity of the study. However, no general contaminant analyses were performed. The test diet contained not less than 15% crude protein, not less than 5% crude fat, and not less than 3% crude fiber.
Conditions: (same as test or not)	Same as test	
Feeding:	Proprietary pelleted diet formulated for finches, mixture and potable water (Anglian Water) were available *ad libitum* with the exception of the time food was withheld prior to dosing. Water was available at all times.	*The recommended acclimation period is a minimum of 15 days. OECD recommends a minimum of 7 days.*
Health: (any mortality observed)	All birds appeared in good health, and no mortality was reported.	
Pen size and construction materials	Powder-coated wire mesh cages measuring 75 x 45.5 x 46 cm.	The floor space was *ca*. 341 cm^2 per bird.
		Pen size and construction should conform to good husbandry practices and should not create crowding stress. *OECD recommends that pens be suitable for the captive rearing of that species.*
Test duration	14 days	
		Recommended test duration is one day for dosing and at least 14 days observation.

Parameter	Details	Remarks ***Criteria***
Dose preparation [Indicate method of confirmation of dose]	Although the dosages were not adjusted for purity and the concentration of DCPA in the test formulation was analyzed during the study.	The mean concentrations of DCPA in test formulations analyzed for the study was within ±2% of nominal concentrations. The analytical work was completed between May 7 and June 22, 2014. Full details are available in the study report in Annex 2.
Mode of dose administration	Gavage	A single dose was orally intubated directly into the crop of each bird using a plastic syringe and a flexible catheter. *Gavage or gelatin capsule is recommended*
Dose levels nominal: measured:	0 (vehicle control) and 2000 mg a.i./kg bw Not reported.	Dose volume was 5 mL/kg bw *Dose levels should be a minimum of 5 treatment levels unless LD_{50} is demonstrated to be greater than 2000 mg ai/kg*
Solvent/vehicle, if used type: amount/bw:	1% Methylcellulose	 *The test material should be administered without a vehicle if possible. Maximum vehicle should not exceed 0.1 to 1.0% of body weight.*
Number of birds per groups/treatment for negative control: for solvent/vehicle control: for treated:	 N/A N/A 5 males:5 females 5 males:5 females	Twenty healthy birds were randomly allocated. *Recommended number of birds in a treatment group is 10 and 10 birds for each control and vehicle group.*
No. of feed withholding days before dosing	3-4 hours	 *Food should be withheld for at least 15 hours prior to dosing.*
Test conditions Temperature: Relative humidity: Photoperiod:	 18-25°C 45-70% 10 hours light:14 hours dark (fluorescent tube lighting with an emission spectrum approximating to natural daylight)	Ventilation fans were adjusted as necessary. *The recommended photoperiod is 10 hours of light and 14 hours of dark.*
Reference chemical, if used name: concentrations tested:	None tested	

2. Observations:

Table 2: Observations

Criteria	Details	Remarks ***Criteria***
Parameters measured (mortality/individual body weight at test initiation and termination/ mean feed consumption/ others)	-Mortality -Clinical signs of toxicity -Body weight -Feed consumption -Necropsy	*Body weight should be measured at test initiation, on day 14 and at the end of the test if the test is extended beyond 14 days. Mortality should not be more than 10% in controls.* *Feed consumption should be measured as average daily food consumption.*
Indicate if the test material was regurgitated	None.	*Regurgitation is an indication that the dose was rejected. If this problem persists, the test should be repeated.*
Groups on which necropsies were performed	All birds that survived until study termination.	Tissues examined included digestive tract, liver, kidneys, heart, spleen, muscle, and subcutaneous fat. *Gross necropsies should be performed with inspections of the GI tract, liver, kidneys, heart, and spleen.*
Observation intervals	Birds were observed at least twice daily during the study and continuously for a minimum of one hour immediately after dosing. Mean feed consumption was determined on Days -14 to -8, -7 to -1, 1 to 7, and 8 to 14. Body weights were measured individually on Days -14, -7, 0 (prior to dosing), 7, and 14.	
Were raw data included?	Yes.	

II. RESULTS AND DISCUSSION:

A. MORTALITY:

There were no mortalities in the control group or in the 2000 mg a.i./kg bw treatment group. The 14-day LD_{50} was >2000 mg a.i./kg bw.

Table 3: Effect of DCPA on Mortality of Zebra Finch.

Treatment (mg a.i./kg bw)		No. of Birds	Cumulative Mortality				
			day 0	day 2	day 6	day 10	day 14
Vehicle control		10 (5♂, 5♀)	0	0	0	0	0
2000		10 (5♂, 5♀)	0	0	0	0	0
NOAEL		2000 mg a.i./kg bw					
LD_{50}		>2000 mg a.i./kg bw					
Reference chemical	mortality	N/A					
	LD_{50}	N/A					
	NOAEL	N/A					

B. SUBLETHAL TOXICITY ENDPOINTS:

No clinical signs of toxicity were seen in the control group, however wiping of the beak (on perches or other cage surfaces) was noted by the study author in 2 females. This observation was made between 26-40 minutes after dose administration. The study author considered to be a response to residual traces of vehicle present in the mouth following removal of the dosing catheter. This observation had resolved between 1-2 hours after dosing. In the 2000 mg a.i./kg bw treatment group, wiping of the beak was noted by the study author in 3 males and 1 female between 22-39 minutes after dosing. In addition, ruffled feathers were noted in three (3) females between 14-40 minutes after dosing and underactivity in three (3) female birds between 15-56 minutes after dosing. These signs had resolved 2-3 hours after dosing.

No emesis or regurgitation was observed in any birds after dosing.

There were no treatment-related trends in mean body weight or food consumption throughout the study.

No macroscopic abnormalities were found at necropsy in any birds examined.

Table 4: Sub-lethal Effects of DCPA on Zebra Finch.

Mean Body Weights (and Changes), g										
Treatment (mg a.i./kg bw)	**Males**					**Females**				
	Day -14	**Day -7**	**Day 0**	**Day 7**	**Day 14**	**Day -14**	**Day -7**	**Day 0**	**Day 7**	**Day 14**
Vehicle control	20.1	20.6 (0.5)	19.6 (-1.0)	21.5 (1.9)	20.7 (-0.8)	17.0 (0.4)	17.4 (-1.1)	16.3 (1.4)	17.7 (1.4)	17.8 (0.1)
2000	16.9	16.9 (0.0)	15.5 (-1.4)	16.6 (1.1)	16.7 (0.1)	19.5	19.3 (-0.2)	17.8 (-1.5)	19.7 (1.9)	19.6 (-0.1)
NOAEL	Not reported					Not reported				
EC_{50}	Not reported					Not reported				

Mean Feed Consumption, g/bird/day								
Treatment (mg a.i./kg bw)	**Males**				**Females**			
	Days -14 to -8	**Days -7 to 1**	**Days 1 to 7**	**Days 8 to 14**	**Days -14 to -8**	**Days -7 to 1**	**Days 1 to 7**	**Days 8 to 14**
Vehicle control	3.7	4.4	4.9	4.5	6.7	4.4	4.7	4.0
2000	6.6	4.5	5.2	5.6	5.7	4.3	4.8	4.6
NOAEL	Not reported							
EC_{50}	Not reported							
Reference chemical	effect NOAEL LD_{50}	N/A						

C. REPORTED STATISTICS:

LD_{50} values were determined using SAFEStat.

D. VERIFICATION OF STATISTICAL RESULTS:

Statistical Method: Data were entered into CETIS statistical software version 1.8.7.12 with database backend settings implemented by EFED on 10/20/15. The LD_{50} value was visually estimated to be greater than the single treatment level based on a complete lack of mortality.

LD_{50}: >2000 mg a.i./kg bw 95% C.I.: N/A
Probit slope: N/A 95% C.I.: N/A

Endpoint(s) affected: None

E. STUDY DEFICIENCIES:

1. The stability of the compound under the test conditions was not verified. However, prior to the main test a homogeneity and stability trail was undertaken, to assess the suitability of the formulation methods and storage. Results showed that the formulation procedures and storage at ambient temperature (nominally +21°C) and refrigerated (nominally +4°C) for 48 hours were satisfactory at the

nominal concentration of 400 mg/mL. Full details are available in the study report in Annex 2. This is considered a minor deviation.

F. REVIEWER'S COMMENTS:

The reviewer's conclusions agreed with the study author's.

The observation of beak wiping may potentially be related to the vehicle carrier that was used, 1% methylcellulose. Although this specific vehicle carrier may be different than recommended in OCSPP guideline, it does not appear to have had a toxic effect on the test birds nor does it appear to have affected the dose amount entering the birds. The dose volume of per bird was 5 mL/kg bw per bird as recommended in OCSPP guideline, and dosing precision was to the nearest 0.01 mL. The dose volumes administered to individual birds are listed in Appendix 3. This is considered a minor deviation.

In-life study dates were 20 May to 03 June 2014.

G. CONCLUSIONS:

This study is **scientifically sound** and classified as **supplemental and may be used to calculate risk quotients**. No mortalities were observed in the control or any of the treatment groups. Wiping of the beak was observed in all treatment groups on the day of dosing but had resolved by 3-hours post-dosing. There were no treatment-related effects on food consumption or on body weight at any dosage level tested. Based upon the lack of treatment-related mortalities and sublethal effects, the observational NOAEL was 2000 mg a.i./kg bw. The acute-oral LD_{50} was >2000 mg a.i./kg bw.

LD_{50}: >2000 mg a.i./kg bw 95% C.I.: N/A
Probit slope: N/A 95% C.I.: N/A

Endpoint(s) Affected: None

III. REFERENCES:

None reported.