

ERB31

**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***

PMRA Submission Number

EPA MRID Number 001345-02

<b>Data Requirement:</b>	PMRA DATA CODE	
	EPA DP Barcode	D312346
	OECD Data Point	
	EPA MRID	001345-02
	EPA Guideline	§71-4b

<b>Test material:</b>	CGA-64250	<b>Purity:</b> Technical-grade, not otherwise specified
<b>Common name:</b>	<del>Metaldehyde</del> Propiconazole	
<b>Chemical name:</b>	IUPAC: 1-[2-(2',4'-Dichlorophenyl)-4-propyl-1,3-dioxalan-2-yl-methyl]-1H-1,2,4-triazole	
	CAS name: Not reported	
	CAS No.: 9002-91-2	
	Synonyms: None reported	

**Primary Reviewer:** Christie E. Padova  
Staff Scientist, Dynamac Corporation

**Signature:** *C. E. Padova*  
**Date:** 5/23/05

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**Signature:** *Teri Myers*  
**Date:** 5/27/05

**Primary Reviewer:** William Evans, Biologist  
OPP/EFED/ERB - I

**Date:** *William Evans*  
7/23/05

**Secondary Reviewer(s):**  
{EPA/OECD/PMRA}

**Date:**

**Reference/Submission No.:**

**Company Code:**  
**Active Code:**  
**EPA PC Code:** 122101

**Date Evaluation Completed:**

**CITATION:** Fink, R., J.B. Beavers, G. Joiner, *et al.* 1982. One-Generation Reproduction Study - Mallard Duck, CGA-64250 Technical, Final Report. Unpublished study performed by Wildlife International Ltd., St. Michaels, MD. Laboratory Project No. 108-203. Study sponsored by Ciba-Geigy Corporation, Greensboro, NC. Experimental start date August 4, 1981 and experimental termination date February 11, 1982. Final report issued April 5, 1982.



**EXECUTIVE SUMMARY:**

The one-generation reproductive toxicity of CGA-64250 Technical (propiconazole) to groups (12 pens/treatment level) of 1 male and 1 female, 6-month old mallard duck was assessed over approximately 20 weeks. CGA-64250 Technical was administered to the birds in the diet at nominal concentrations of 0 (control), 25, 100, 300, and 1000 ppm. Mean-measured concentrations were not determined.

There were no treatment-related effects on adult mortality, body weight, or feed consumption at any test level. In addition, all birds in the control and treatment groups appeared normal throughout the study.

At the 1000 ppm level, a treatment-related effect on egg viability was observed, as reflected in the percentage of viable embryos of eggs set (57 versus 75% for the control). The percentage of viable embryos of eggs set at the 1000 ppm level was 24% less than the control group, and at least 18% less than any other treatment group. Although the difference was not statistically-significant, it was considered to be a result of treatment, and thus biologically-significant. No other treatment-related effect on any reproductive parameter was observed. No overt signs of toxicity in the offspring were reported and no treatment-related effect on offspring body weights were observed at any treatment level (offspring body weights were assessed for effects by week lot by the study authors only).

This study is scientifically unsound, as the treated feed was not analyzed to verify test concentrations, homogeneity of the mixing procedure, and stability under actual use conditions. The study does not satisfy the guideline requirements for the reproductive toxicity of CGA-64250 Technical (propiconazole) to mallard duck (§71-4b) because replicate data for hatchling and survivor weight were not provided, so results for these endpoints could not be statistically verified by the reviewer. Furthermore, adult body weight data were not discriminated by sex. This study is classified as INVALID. This study is not upgradable.

**Results Synopsis**

Test Organism Size/Age: 6-Months old at test initiation. Individual body weights were not provided. Mean pair (pen) weights (1 male and 1 female) ranged from 1004 to 1326 g.

NOEC: Not determined (Invalid study)

LOEC: Not determined (Invalid study)

Endpoint(s) Affected: Not determined (Invalid study)

**I. MATERIALS AND METHODS**

**GUIDELINE FOLLOWED:** Not reported. This study was conducted at the time the Pesticide Assessment Guidelines (1982) were being finalized. Deviations from U.S. EPA FIFRA Guideline §71-4 are:

1. The precise purity and storage conditions of CGA-64250 Technical were not reported.
2. Individual body weights were not provided, thus any differences observed between genders could not be assessed. In addition, the mean pair weight for the 100 ppm level was statistically-lower at study initiation than the control group (1116 versus 1146 g).
3. Acclimation of the ducks were not reported, including length of acclimation, conditions, feeding, and pre-test mortality.
4. The exposure period during egg-laying was only 9 weeks, whereas guidance requires at least 10 weeks.
5. Since effects on reproduction were observed, a withdrawal period should have been conducted.

6. It was reported that hatchlings were housed in Beacon (Model B735) battery brooders. No other information regarding the size or construction materials was provided.
  7. As the birds were housed in pairs of one male and one female, considerably more than 12 replicates should have been tested. EPA strongly recommends at least 16 replicates when pairs are maintained.
  8. It was not reported if the control feed contained corn oil (carrier for the test substance).
  9. The treated feed was not analyzed to verify test concentrations, homogeneity of the mixing procedure, and stability under actual use conditions.
  10. The expected field residue level was not reported.
  11. The average egg storage temperature (prior to setting for incubation) was 56°F, slightly lower than the recommended level of 61°F.
  12. The average hatching temperature was 99.0°F, slightly lower than the recommended level of 102°F.
  13. The percentage of 14-day old survivors of eggs set averaged only 47% in the control group.
- Analysis of the treated feed was not performed, which affects the scientific validity of this study.

**COMPLIANCE:**

Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were not provided. This study likely preceded such requirements.

**A. MATERIALS:**

**1. Test Material**

CGA-64250 Technical

**Description:**

Viscous, light amber liquid

**Lot No./Batch No.:**

FL-810175

**Purity:**

Not reported

**Stability of Compound Under Test Conditions:**

The stability of CGA-64250 Technical in the treated feed was not assessed.

**Storage conditions of test chemical:**

Not reported

*OECD requires water solubility, stability in water and light,  $pK_a$ ,  $P_{ow}$  and vapor pressure of the test compound. The following OECD requirements were reported:*

**Water solubility:**

110 ppm for amorphous form

**Vapor pressure:**

$\leq 3 \times 10^{-6}$  Torr (20°C)

2. Test organism:

Table 1: Test organism.

Parameter	Details	Remarks
		Criteria
Species (common and scientific names):	Mallard duck ( <i>Anas platyrhynchos</i> )	<i>EPA requires: a wild waterfowl species, preferably the mallard, Anas platyrhynchos, or an upland game species, preferably the northern bobwhite, Colinus virginianus.</i>
Age at Study Initiation:	6 months (approx. 24 months)	It was stated that birds were approaching their first breeding season.  <i>EPA requires: birds should be approaching their first breeding season.</i>
Body Weight: (mean and range)	Mean pair (pen) weights (1 male and 1 female) ranged from 1004 to 1326 g. With group mean pair weights ranging from 1116 to 1146 g. The mean pair weight for the 100 ppm level was statistically-lower at study initiation than the control group (1116 versus 1146 g).	Mean pair (pen) body weights were recorded at Weeks 0, 2, 4, 6, 8 and 20 (test termination).  <i>EPA requires that body weights should be recorded at test initiation and at biweekly intervals up to week eight or up to the onset of egg laying and at termination.</i>
Source:	Production flock, Wildlife International, Ltd., St. Michaels, MD Blood-tested U.S. Pullorum-Typhoid clean.	Birds were from the same hatch, and were phenotypically indistinguishable from wild birds.  Representative ducks were submitted to the MD Department of Agriculture (Salisbury, MD) for examination, and following a gross necropsy and bacteriological and serologic examination, were determined to be healthy.  <i>EPA requires that all birds should be from the same source.</i>

**B. STUDY DESIGN:**

**1. Experimental Conditions**

- a. Range-finding Study - None reported.
- b. Definitive Study

**Table 2: Experimental Parameters.**

Parameter	Details	Remarks
		Criteria
Acclimation period: Conditions (same as test or not): Feeding: Health (any mortality observed):	Acclimation of the ducks was not described.	EPA recommends a 2-3 week health observation period prior to selection of birds for treatment. Birds must be generally healthy without excess mortality. Feeding should be <u>ad libitum</u> , and sickness, injuries or mortality be noted.
Test duration pre-laying exposure: egg-laying exposure: withdrawal period, if used:	Approximately 11 weeks Approximately 9 weeks None	Effects on reproduction were observed, and a withdrawal period should have been conducted. EPA requires <u>Pre-laying exposure duration</u> At least 10 weeks prior to the onset of egg-laying. <u>Exposure duration with egg-laying</u> At least 10 weeks. <u>Withdrawal period</u> If reduced reproduction is evident, a withdrawal period of up to 3 weeks should be added to the test phase.

Parameter	Details	Remarks
		Criteria
Pen (for parental and offspring) size:  construction materials:  number:	Parents (one pair) were housed in battery breeding cages measuring 72 x 90 x 33 cm. Offspring (by set and group) were housed in battery brooders of an unspecified size.  Parental pens were constructed of wire grid (external walls), galvanized sheeting (ceilings and common walls), and plastic-coated mesh grid (floors). Offspring pens were of an unspecified material.  12 parental pens/treatment level	  <hr/> <u>Pens</u> Adequate room and arranged to prevent cross contamination <u>Materials</u> Nontoxic material and nonbinding material, such as galvanized steel. <u>Number</u> At least 5 replicate pens are required for mallards housed in groups of 7. For other arrangements, at least 12 pens are required, but considerably more may be needed if birds are kept in pairs. Chicks are to be housed according to parental grouping.
Number of birds per pen (male:female)	2 birds/pen (1 male:1 female)	<hr/> EPA requires one male and 1 female per pen. For quail, 1 male and 2 females is acceptable. For ducks, 2 males and 5 females is acceptable.

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Parameter	Details	Remarks
		Criteria
Number of pens per group/treatment control: treated:	12 pens 12 pens/treatment	<i>EPA requires at least 12 pens, but considerably more if birds are kept in pairs. At least 16 is strongly recommended.</i>
Test concentrations (ppm diet) nominal:  measured:	0 (control), 25, 100, 300, and 1000 ppm  Not measured	<i>EPA requires at least two concentrations other than the control are required; three or more are recommended.</i>
Maximum labeled field residue anticipated and source of information:	Not specified	<i>EPA requires that the highest test concentrations should show a significant effect or be at or above the actual or expected field residue level. The source [i.e., maximum label rate (in lb ai/A &amp; ppm), label registration no., label date, and site should be cited]</i>
Solvent/vehicle, if used type:  amount:	Corn oil  Approx. 0.024% (v:w)	Percent of corn oil in the final test diets were calculated by the reviewer in the following manner (same for all test levels): $\{[(130 \text{ mL corn oil}/5880 \text{ total g premix weight}) \times 500 \text{ g subsample of premix}] / 45859 \text{ total g final diet}\} \times 100.$  <i>EPA requires corn oil or other appropriate vehicle not more than 2% of diet by weight</i>

Parameter	Details	Remarks
		<i>Criteria</i>
Was detailed description and nutrient analysis of the basal diet provided? (Yes/No)	Yes	Wildlife International, Ltd.'s game bird breeder ration contained 19.4% protein, 6.7% fat, and 3.8% fiber.  Offspring received Wildlife International, Ltd.'s game bird starter ration.  <i>EPA requires a commercial breeder feed (or its equivalent) that is appropriate for the test species.</i>
Preparation of test diet	The appropriate amount of test substance was mixed with corn oil, combined with a portion of basal diet, and mixed for 20 minutes in a Hobart mixer. The premixes were divided into weekly aliquots and frozen. Separate premixes were prepared for each concentration level  Once weekly, final diets were prepared by combining a portion of the premix with additional basal feed and mixing for 15 minutes in a Patterson-Kelley twin shell dry blender.	<i>A premixed containing the test substance should be mechanically mixed with basal diet. If an evaporative vehicle is used, it must be completely evaporated prior to feeding.</i>
Indicate whether stability and homogeneity of test material in diet determined (Yes/No)	No	
Were concentrations in diet verified by chemical analysis?	No	
Did chemical analysis confirm that diet was stable?  and homogeneous?	N/A  N/A	
Feeding and husbandry	Feeding and husbandry conditions appeared to be adequate, given guideline recommendations.	



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Parameter	Details	Remarks
		Criteria
Test conditions (pre-laying) temperature: relative humidity: photo-period:	68 ± 8°F  Average of 80%  8 hr light/day up through Week 7; 17 hr light/day thereafter.	Light intensity averaged 12 foot-candles. Illumination was provided by fluorescent lights which closely approximated noon-day sunlight.  <i>EPA Requires</i> <i>Temperature:</i> <i>About 21°C (70°F)</i> <i>Relative humidity:</i> <i>About 55%</i> <i>Lighting</i> <i>First 8 weeks: 7 h per day.</i> <i>Thereafter: 16-17 h per day.</i> <i>At least 6 foot candles at bird level.</i>
<b>Egg Collection and Incubation</b>		
Egg collection and storage collection interval: storage temperature: storage humidity:	Daily  56 ± 1°F  Average of 88%	To prevent pathogen contamination, the collected eggs were washed in a commercial egg washer with a chlorine-based detergent at 115°F for approximately 3 minutes.  <i>EPA requires eggs to be collected daily; egg storage temperature approximately 16°C (61°F); humidity approximately 65%.</i>
Were eggs candled for cracks prior to setting for incubation?	Yes	<i>EPA requires eggs to be candled on day 0</i>
Were eggs set weekly?	Yes	
Incubation conditions temperature: humidity:	99.5 ± 0.1°F  Wet bulb humidity index of 85 ± 0.1°F	

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Parameter	Details	Remarks
		Criteria
When candling was done for fertility?	Day 14 for embryo viability and Day 21 for embryo survival.	EPA requires: Quail: approx. day 11 Ducks: approx. day 14
When the eggs were transferred to the hatcher?	Day 25	EPA requires: Bobwhite: day 21 Mallard: day 23
Hatching conditions temperature: humidity: photo-period:	99.0 ± 0.1°F Wet bulb humidity index of 92 ± 0.1°F Not reported	EPA requires: temperature of 39°C (102°F) humidity of 70%
Day the hatched eggs were removed and counted	Day 28	EPA requires Bobwhite: day 24 Mallard: day 27
Were egg shells washed and dried for at least 48 hrs before measuring?	Yes, shells were washed and air-dried for 1 week.	
Egg shell thickness no. of eggs used: intervals: mode of measurement:	One egg was collected (when available) from every other pen at all levels. Once weekly throughout the egg laying period. Five points around the equatorial circumference were measured to the nearest 0.01 mm.	EPA requires newly hatched eggs be collected at least once every two weeks. Thickness of the shell plus membrane should be measured to the nearest 0.01 mm; 3 - 4 measurements per shell.
Reference chemical, if used	None used	

2. Observations:

Table 3: Observations.

Parameter	Details	Remarks/Criteria
<b>Parameters measured</b>		
Parental: (mortality, body weight, mean feed consumption)  Egg collection and subsequent development: (no. of eggs laid, no. of eggs cracked, shell thickness, no. of eggs set, no. of viable embryos, no. of live 3 week embryos, no. hatched, no. of 14-day survivors, average weight of 14-day-old survivors, mortality, gross pathology, others)	- mortality - body weight - food consumption - signs of toxicity  - eggs laid - eggs cracked - egg weight - eggshell thickness - eggs set - viable embryos - live 3-week embryos - number of normal hatchlings - hatchling body weight - number of 14-day-old survivors - 14-day-old survivor body weight	EPA requires: • Eggs laid/pen • Eggs cracked/pen • Eggs set/pen • Viable embryos/pen • Live 3-week embryos/pen • Normal hatchlings/pen • 14-day-old survivors/pen • 14-day-old survivors/pen • Weights of 14-day-old survivors (mean per pen) • Egg shell thickness • Food consumption (mean per pen) • Initial and final body weight (mean per pen)
Indicate if the test material was regurgitated	No indications of dietary regurgitation.	
Observation intervals (for various parameters)	Parental and hatchling mortality and signs of toxicity were recorded once daily. Parental body weights, determined as the mean of each pair, were recorded at Weeks 0, 2, 4, 6, 8 and at test termination (Week 20). Parental food consumption was determined every 2 weeks.	Body weights and food consumption must be measured at least biweekly.
Were raw data included?	Yes, sufficient.	

**I. RESULTS AND DISCUSSION:**

**A. MORTALITY:**

No mortality was observed during the study. The NOEC and LOEC for mortality was 1000 and >1000 ppm, respectively.

**Table 4: Effect of CGA-64250 Technical (Propiconazole) on Mortality of *Anas platyrhynchos*.**

Treatment, ppm nominal concentrations	Observation Period					
	Week 7		Week 14		Week 22	
	No. Dead Male	No. Dead Female	No. Dead Male	No. Dead Female	No. Dead Male	No. Dead Female
Control	0	0	0	0	0	0
25	0	0	0	0	0	0
100	0	0	0	0	0	0
300	0	0	0	0	0	0
1000	0	0	0	0	0	0

**B. REPRODUCTIVE AND OTHER ENDPOINTS:**

Abnormal Effects/Behavior: All birds in the control and treatment groups appeared normal throughout the study. The NOEC and LOEC for clinical signs of toxicity in adult birds was 1000 and >1000 ppm, respectively.

Food Consumption: No statistically-significant differences in food consumption were observed between the control and treatment groups. For all groups, consumption increased from an average 35-48 g/bird/day at Week 0 to 72-84 g/bird/day at Week 10, to 153-175 g/bird/day at Week 20. The NOEC and LOEC for food consumption was 1000 and >1000 ppm, respectively.

Body Weight: Statistically-significant differences in body weights from the control group were observed at Weeks 4, 6, and 8 at the 25 ppm level, and at all intervals at the 100 ppm level. The study author reported that the differences observed do not appear to be biologically meaningful. The reviewer agrees with this conclusion for the following reasons: initial body weights for the 100 ppm group were statistically-lower than the controls; no statistical differences in body weights were observed at the 300 and 1000 ppm levels for any interval; and reviewer-calculated percent body weight changes from Weeks 0-8 and Weeks 0-20 were comparable for all treatment and control groups, ranging from -6 to 0.5% and 14-16%, respectively. The NOEC and LOEC for adult body weight was 1000 and >1000 ppm, respectively.

Necropsy: Necropsies were not performed (and are not required).

Reproductive Effects: No treatment-related effects were observed on egg production or quality, embryonic development, hatchability, or survival of hatchlings at all test levels. At the 1000 ppm level, a treatment-related effect on egg viability was observed, as reflected in the percentage of viable embryos of eggs set (55 versus 76% for the control; study author calculations most likely differ from reviewer calculations for this endpoint due to rounding). The percentage of viable embryos of eggs set at the 1000 ppm level was 28% less than the control group, and at least 18% less than any other treatment group. Although the difference was not statistically-significant, it was considered to be a result of treatment, and thus biologically significant.

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No overt signs of toxicity in the offspring were reported and no treatment-related effect on offspring body weights were observed at any treatment level. The NOEC and LOEC for effects on reproduction was 300 and 1000 ppm, respectively.

**Table 5: Reproductive and other parameters (nominal concentrations; study author-reported).**

Parameter	Control	25 ppm	100 ppm	300 ppm	1000 ppm	NOEC/ LOEC
Eggs laid	424	308	461	475	392	1000 ppm >1000 ppm
Eggs laid/hen	35	26	38	40	33	N/A
Eggs laid/hens in production <sup>1</sup>	35	39	46	40	33	N/A
Eggs laid/maximum laid (%)	56	41	61	63	52	1000 ppm >1000 ppm
Eggs cracked	16	9	8	10	7	N/A
Eggs cracked/eggs laid (%)	4	3	2	2	2	1000 ppm >1000 ppm
Egg weight (g)	54.8	57.6	58.0	57.8	60.7	1000 ppm >1000 ppm
Shell thickness (mm ± SD) <sup>2</sup>	0.376	0.381	0.377	0.373	0.373	1000 ppm >1000 ppm
Eggs set	369	272	410	421	347	N/A
Viable embryos	279	181	386	333	190	N/A
Viable embryos/eggs set (%)	76	67	94	79	55*	300 ppm 1000 ppm
Live 3-week embryos	258	166	363	305	186	N/A
Live 3-week embryos/viable embryos (%)	92	92	94	92	98	1000 ppm >1000 ppm
No. of normal hatchlings	184	121	263	204	132	N/A
No. of normal hatchlings/live 3-week embryos (%)	71	73	72	67	71	1000 ppm >1000 ppm
Hatchling weight (g ± SD) <sup>2</sup>	35	36	36	38	38	1000 ppm >1000 ppm
No. of 14-day old survivors	175	121	256	195	131	N/A
No. of 14-day old survivors/hen	15	10	21	16	11	N/A
No. of 14-day old survivors/hens in production <sup>1</sup>	15	15	26	16	11	N/A

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Parameter	Control	25 ppm	100 ppm	300 ppm	1000 ppm	NOEC/ LOEC
No. of 14-day old survivors/No. of hatchlings (%)	95	100	97	96	99	1000 ppm >1000 ppm
No. of 14-day old survivors/eggs set (%)	47	44	62	46	38	1000 ppm >1000 ppm
14-day old survivors weight (g ± SD) <sup>2</sup>	226	245	226	229	213	1000 ppm >1000 ppm
Mean adult food consumption (g/pen/day) <sup>3</sup>	103.9	100.8	104.7	101.1	96.8	1000 ppm >1000 ppm
Weight of adult pair, g at start of treatment:	1146	1146	1116**	1143	1146	1000 ppm
at Week 8:	1124	1083**	1074**	1149	1139	>1000 ppm
at Week 20 (study termination):	1325	1303	1271**	1330	1306	
Gross pathology (pathological incidents at study termination)	Not assessed.					

N/A = Not statistically-analyzed.

\* Not statistically-significant, but considered biologically significant.

\*\* Significantly different from the control at p<0.05; however, no differences are considered to be biologically significant.

<sup>1</sup> Four hens from the 25 ppm group, two hens from the 100 ppm group, and 1 hen from the 300 ppm group did not produce eggs. This parameter was recalculated excluding the number of non-laying hens.

<sup>2</sup> Standard deviations were not determined.

<sup>3</sup> Reviewer-calculated from mean data collected every 2 weeks.

**C. REPORTED STATISTICS:**

The following variables were statistically analyzed: adult body weight, adult feed consumption, eggs laid of theoretical maximum (%), eggs cracked of eggs laid (%), viable embryos of eggs set (%), live 3-week embryos of viable embryos (%), normal hatchlings of 3-week embryos (%), 14-day old survivors of normal hatchlings (%), 14-day old survivors of eggs set (%), normal hatchlings of theoretical maximum (%), 14-day old survivors of theoretical maximum (%), egg shell thickness, and offspring's body weight.

Body weights, egg weights, feed consumption, and egg shell thickness ("measurement variables") were analyzed using traditional analysis of variance (ANOVA). The remaining endpoints pertaining to reproduction ("count variables") were analyzed using Cochran's concept of extraneous variability for the binomial distribution. Sample units were the individual pens within each experimental group.

**D. VERIFICATION OF STATISTICAL RESULTS:**

Statistical Method: Analysis was conducted using "chicks.sas" (Ver. 3; March 2002), a SAS program provided by EFED/OPP/USEPA. Data for each endpoint were tested to determine if their distributions were normal and if their variances were homogeneous using Shapiro-Wilk's and Levene's tests, respectively. Data that satisfied these assumptions were subjected to Dunnett's and William's tests and data that did not satisfy these assumptions were subjected to the non-parametric MannWhitney-U (with a Bonferroni adjustment) and

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Jonckheere's tests. Data for all endpoints were examined graphically using box plots to determine if they exhibited a dose-dependent response, which was ultimately used to select the multiple comparison test to detect LOAEC and NOAEC. Data for dead birds were excluded from the analyses. Data for hatchling and survivor weight were not provided for replicate birds, but by week lot so they could not be included in the statistical analysis. Furthermore, adult body weight data were not discriminated by sex. Pair body weight data were entered in the initial and final "male body weight" fields for the purpose of this analysis. See Appendix I for output of reviewer's statistical verification and graphs for affected endpoints to support any reviewer-generated conclusions that may differ from those reported in the study.

**Table 6. Reproductive and other parameters (nominal concentrations; reviewer-reported).**

Parameter	Control	25 ppm	100 ppm	300 ppm	1000 ppm	NOEC/LOEC
Eggs laid/pen	35.3	25.7	38.4	39.6	32.7	1000 >1000
Eggs cracked/pen	1.36	0.75	0.67	0.83	0.58	1000 >1000
Eggs not cracked/eggs laid (%)	96.3	99.0	97.9	98.1	100.0	1000 >1000
Eggs set/pen	30.8	22.7	34.2	35.1	28.9	1000 >1000
Shell thickness	0.38	0.39	0.38	0.37	0.38	1000 >1000
Eggs set/eggs laid (%)	85.7	88.5	88.3	88.0	88.0	1000 >1000
Viable embryo/pen	23.2	15.1	32.2	27.8	15.8	1000 >1000
Viable embryos/eggs set (%)	75.0	69.0	93.0	75.3	56.7*	300 1000
Live embryos/pen	21.5	13.8	30.2	25.4	15.5	1000 >1000
Live embryo/viable embryo (%)	80.6	80.6	94.4	89.5	97.0	1000 >1000
No. of hatchlings/pen	15.3	10.1	21.9	17.0	11.0	1000 >1000
No. of hatchlings/eggs laid (%)	40.0	40.0	55.9	38.5	31.1	1000 >1000
No. of hatchlings/eggs set (%)	45.4	45.1	63.3	43.2	35.2	1000 >1000
No. of hatchlings/live embryos (%)	58.6	70.9	71.6	58.9	68.2	1000 >1000

Parameter	Control	25 ppm	100 ppm	300 ppm	1000 ppm	NOEC/LOEC
Hatchling survival/pen	14.6	10.1	21.3	16.3	10.9	1000 >1000
Hatchling survival/eggs set (%)	43.2	45.1	61.7	41.2	34.9	1000 >1000
Hatchling survival/no. of hatchlings (%)	95.9	100.0	67.7	95.7	99.6	1000 >1000
Hatchling weight (g)	ND	ND	ND	ND	ND	ND
Survivor weight (g)	ND	ND	ND	ND	ND	ND
Mean food consumption (g/bird/day)	102.5	100.8	104.2	101.3	96.5	1000 >1000
Male weight gain (g)	179.0	157.0	155.2	186.0	159.7	1000 >1000
Female weight gain (g)	ND	ND	ND	ND	ND	ND

\*The NOAEC and LOAEC for this endpoint were visually determined; statistical tests revealed no differences, but the reduction at the highest level was considered to be biologically-significant.  
 ND=not determined; appropriate replicate data for these endpoints were not provided for analysis.

**E. STUDY DEFICIENCIES:**

The treated feed was not analyzed to verify test concentrations, homogeneity of the mixing procedure, and stability under actual use conditions. This deviation is significant, and affects the scientific validity of the study. In addition, unusually low overall survival of offspring was observed in the control group (percentage of 14-day old survivors of eggs set averaged 47%); as this study was conducted in 1982 (which pre-dates the 1986 US EPA SEP guidance document for an avian reproduction test §71-4), the significance of this deviation was not clear.

**F. REVIEWER'S COMMENTS:**

Results of the reviewer's statistical analyses agreed with those of the study authors. There was no statistically-significant effect of treatment on adult bird or reproductive response detected. There was, however, a biologically-significant reduction (24%) of viable embryos to eggs set at the highest treatment level. There were several deviations from the US EPA SEP guideline (§71-4) which resulted in the INVALID classification of this study. As a result, the reviewer/study author-determined NOAEC and LOAEC values are not reported in the Executive Summary and Conclusions sections of this DER.

A high level of mortality was observed in the offspring from the control group, specifically pertaining to the percentage of 14-day old survivors of eggs set, which averaged only 47%. The losses primary occurred as early embryo viability and hatchability, as demonstrated by the percentage of viable embryos to eggs set (76%) and normal hatchlings of live 3-week embryos (71%). Losses were not unique to the control group, as the percentage of 14-day old survivors of eggs set ranged from 38-62% for the treatment groups. As this study was conducted in 1982, this level of hatchling success may have been normal for studies conducted at that time; however, compared to more recent avian reproduction studies using mallard, typical percentages of 14-day old survivors of eggs set average  $\geq 70\%$  for controls.



**G. CONCLUSIONS:**

This study is not scientifically sound, does not fulfill U.S. EPA guideline §71-4(b), and is classified as INVALID.

NOEC: Not determined (Invalid study)

LOEC: Not determined (Invalid study)

Endpoint(s) Affected: Not determined (Invalid study)

**III. REFERENCES:**

A reference list was not provided.

**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
 PMRA Submission Number

EPA MRID Number 001345-02

**APPENDIX I. OUTPUT OF REVIEWER'S STATISTICAL VERIFICATION:**

Mallard repro, Propiconazole, MRID 00134502  
 PRINTOUT OF RAW DATA

Obs	TRT	EL	EC	ENC	EL	ES	ES	EL	VE	VE	ES	LE	LE	VE	NH	NH	EL	NH	ES
1	Ctrl	45	1	97.78	39	86.67	38	97.44	35	92.11	30	66.67	76.92						
2	Ctrl	42	1	97.62	37	88.10	32	86.49	33	103.13	21	50.00	56.76						
3	Ctrl	42	2	95.24	36	85.71	34	94.44	30	88.24	22	52.38	61.11						
4	Ctrl	21	0	100.00	19	90.48	10	52.63	8	80.00	1	4.76	5.26						
5	Ctrl	33	1	96.97	29	87.88	27	93.10	25	92.59	20	60.61	68.97						
6	Ctrl	51	2	96.08	45	88.24	43	95.56	42	97.67	35	68.63	77.78						
7	Ctrl	25	4	84.00	19	76.00	14	73.68	12	85.71	4	16.00	21.05						
8	Ctrl	26	0	100.00	24	92.31	23	95.83	21	91.30	15	57.69	62.50						
9	Ctrl	9	0	100.00	6	66.67	2	33.33	1	50.00	0	0.00	0.00						
10	Ctrl	33	.	.	30	90.91	29	96.67	26	89.66	18	54.55	60.00						
11	Ctrl	37	1	97.30	33	89.19	26	78.79	25	96.15	18	48.65	54.55						
12	Ctrl	60	3	95.00	52	86.67	1	1.92	0	0.00	0	0.00	0.00						
13	Dose1	40	0	100.00	37	92.50	37	100.00	35	94.59	27	67.50	72.97						
14	Dose1	49	1	97.96	43	87.76	42	97.67	38	90.48	28	57.14	65.12						
15	Dose1	0	0	.	0	.	0	.	0	.	0	.	.						
16	Dose1	10	0	100.00	9	90.00	8	88.89	7	87.50	4	40.00	44.44						
17	Dose1	28	0	100.00	25	89.29	20	80.00	18	90.00	15	53.57	60.00						
18	Dose1	0	0	.	0	.	0	.	0	.	0	.	.						
19	Dose1	49	1	97.96	44	89.80	2	4.55	0	0.00	0	0.00	0.00						
20	Dose1	0	0	.	0	.	0	.	0	.	0	.	.						
21	Dose1	45	6	86.67	35	77.78	19	54.29	18	94.74	15	33.33	42.86						
22	Dose1	51	0	100.00	47	92.16	39	82.98	37	94.87	25	49.02	53.19						
23	Dose1	36	1	97.22	32	88.89	14	43.75	13	92.86	7	19.44	21.88						
24	Dose1	0	0	.	0	.	0	.	0	.	0	.	.						
25	Dose2	46	1	97.83	41	89.13	40	97.56	39	97.50	25	54.35	60.98						
26	Dose2	58	0	100.00	53	91.38	51	96.23	49	96.08	34	58.62	64.15						
27	Dose2	45	0	100.00	41	91.11	40	97.56	36	90.00	27	60.00	65.85						
28	Dose2	58	0	100.00	53	91.38	52	98.11	44	84.62	28	48.28	52.83						
29	Dose2	22	0	100.00	18	81.82	15	83.33	14	93.33	9	40.91	50.00						
30	Dose2	45	1	97.78	40	88.89	40	100.00	37	92.50	26	57.78	65.00						
31	Dose2	0	0	.	0	.	0	.	0	.	0	.	.						
32	Dose2	0	0	.	0	.	0	.	0	.	0	.	.						
33	Dose2	39	1	97.44	34	87.18	24	70.59	23	95.83	13	33.33	38.24						
34	Dose2	37	2	94.59	31	83.78	29	93.55	29	100.00	27	72.97	87.10						
35	Dose2	49	1	97.96	44	89.80	44	100.00	43	97.73	32	65.31	72.73						
36	Dose2	62	2	96.77	55	88.71	51	92.73	49	96.08	42	67.74	76.36						
37	Dose3	50	0	100.00	46	92.00	43	93.48	43	100.00	41	82.00	89.13						
38	Dose3	48	1	97.92	42	87.50	40	95.24	38	95.00	16	33.33	38.10						
39	Dose3	49	0	100.00	45	91.84	0	0.00	0	.	0	0.00	0.00						
40	Dose3	44	1	97.73	39	88.64	36	92.31	31	86.11	18	40.91	46.15						
41	Dose3	57	1	98.25	52	91.23	52	100.00	50	96.15	34	59.65	65.38						
42	Dose3	44	2	95.45	38	86.36	38	100.00	37	97.37	33	75.00	86.84						
43	Dose3	30	1	96.67	26	86.67	21	80.77	17	80.95	4	13.33	15.38						
44	Dose3	37	2	94.59	31	83.78	30	96.77	26	86.67	15	40.54	48.39						
45	Dose3	35	0	100.00	32	91.43	31	96.88	27	87.10	26	74.29	81.25						
46	Dose3	40	0	100.00	36	90.00	33	91.67	29	87.88	17	42.50	47.22						
47	Dose3	22	2	90.91	18	81.82	0	0.00	0	.	0	0.00	0.00						
48	Dose3	19	0	100.00	16	84.21	9	56.25	7	77.78	0	0.00	0.00						
49	Dose4	26	0	100.00	23	88.46	20	86.96	20	100.00	15	57.69	65.22						
50	Dose4	35	0	100.00	31	88.57	28	90.32	27	96.43	16	45.71	51.61						
51	Dose4	50	2	96.00	44	88.00	0	0.00	0	.	0	0.00	0.00						
52	Dose4	11	1	90.91	7	63.64	6	85.71	5	83.33	1	9.09	14.29						
53	Dose4	30	0	100.00	27	90.00	0	0.00	0	.	0	0.00	0.00						
54	Dose4	32	0	100.00	30	93.75	27	90.00	26	96.30	17	53.13	56.67						
55	Dose4	45	0	100.00	41	91.11	27	65.85	27	100.00	22	48.89	53.66						
56	Dose4	42	2	95.24	36	85.71	36	100.00	35	97.22	28	66.67	77.78						
57	Dose4	48	1	97.92	43	89.58	28	65.12	28	100.00	24	50.00	55.81						
58	Dose4	49	1	97.96	43	87.76	1	2.33	1	100.00	1	2.04	2.33						

**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
 PMRA Submission Number

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59 Dose4 20 0 100.00 18 90.00 17 94.44 17 100.00 8 40.00 44.44  
 60 Dose4 4 0 100.00 4 100.00 0 0.00 0 0 0 0.00 0.00

Mallard repro, Propiconazole, MRID 00134502

PRINTOUT OF RAW DATA (continued)

Obs	TRT	NH	LE	HS	HS	ES	HS	NH	THICK	HATWT	SURVWT	FOOD	WTGAINM	WTGAINF
1	Ctrl	85.71	29	74.36	96.67	0.37	.	.	.	.	.	86	286	.
2	Ctrl	63.64	20	54.05	95.24	0.39	.	.	.	.	.	114	116	.
3	Ctrl	73.33	21	58.33	95.45	0.36	.	.	.	.	.	123	160	.
4	Ctrl	12.50	1	5.26	100.00	0.42	.	.	.	.	.	85	-18	.
5	Ctrl	80.00	19	65.52	95.00	0.41	.	.	.	.	.	88	334	.
6	Ctrl	83.33	33	73.33	94.29	0.38	.	.	.	.	.	139	238	.
7	Ctrl	33.33	4	21.05	100.00	0.36	.	.	.	.	.	89	49	.
8	Ctrl	71.43	14	58.33	93.33	0.34	.	.	.	.	.	105	117	.
9	Ctrl	0.00	0	0.00	.	0.36	.	.	.	.	.	81	305	.
10	Ctrl	69.23	17	56.67	94.44	0.38	.	.	.	.	.	130	225	.
11	Ctrl	72.00	17	51.52	94.44	0.40	.	.	.	.	.	97	122	.
12	Ctrl	.	0	0.00	.	0.36	.	.	.	.	.	94	214	.
13	Dose1	77.14	27	72.97	100.00	0.38	.	.	.	.	.	111	130	.
14	Dose1	73.68	28	65.12	100.00	0.40	.	.	.	.	.	94	178	.
15	Dose1	.	0	.	.	.	.	.	.	.	.	97	-25	.
16	Dose1	57.14	4	44.44	100.00	0.41	.	.	.	.	.	85	103	.
17	Dose1	83.33	15	60.00	100.00	0.42	.	.	.	.	.	92	285	.
18	Dose1	.	0	.	.	.	.	.	.	.	.	79	85	.
19	Dose1	.	0	0.00	.	0.35	.	.	.	.	.	115	341	.
20	Dose1	.	0	.	.	.	.	.	.	.	.	96	137	.
21	Dose1	83.33	15	42.86	100.00	0.35	.	.	.	.	.	112	338	.
22	Dose1	67.57	25	53.19	100.00	0.39	.	.	.	.	.	107	181	.
23	Dose1	53.85	7	21.88	100.00	0.36	.	.	.	.	.	125	125	.
24	Dose1	.	0	.	.	.	.	.	.	.	.	96	6	.
25	Dose2	64.10	25	60.98	100.00	0.39	.	.	.	.	.	114	287	.
26	Dose2	69.39	33	62.26	97.06	0.39	.	.	.	.	.	116	217	.
27	Dose2	75.00	26	63.41	96.30	0.38	.	.	.	.	.	139	214	.
28	Dose2	63.64	27	50.94	96.43	0.39	.	.	.	.	.	117	125	.
29	Dose2	64.29	9	50.00	100.00	0.36	.	.	.	.	.	100	-79	.
30	Dose2	70.27	25	62.50	96.15	0.34	.	.	.	.	.	82	141	.
31	Dose2	.	0	.	.	.	.	.	.	.	.	69	146	.
32	Dose2	.	0	.	.	.	.	.	.	.	.	82	75	.
33	Dose2	56.52	13	38.24	100.00	0.36	.	.	.	.	.	99	236	.
34	Dose2	93.10	26	83.87	96.30	0.35	.	.	.	.	.	119	198	.
35	Dose2	74.42	31	70.45	96.88	0.41	.	.	.	.	.	114	65	.
36	Dose2	85.71	41	74.55	97.62	0.40	.	.	.	.	.	100	238	.
37	Dose3	95.35	39	84.78	95.12	0.38	.	.	.	.	.	135	205	.
38	Dose3	42.11	15	35.71	93.75	0.39	.	.	.	.	.	98	182	.
39	Dose3	.	0	0.00	.	0.36	.	.	.	.	.	96	153	.
40	Dose3	58.06	17	43.59	94.44	0.38	.	.	.	.	.	109	171	.
41	Dose3	68.00	33	63.46	97.06	0.39	.	.	.	.	.	88	125	.
42	Dose3	89.19	32	84.21	96.97	0.37	.	.	.	.	.	119	227	.
43	Dose3	23.53	4	15.38	100.00	0.39	.	.	.	.	.	100	178	.
44	Dose3	57.69	14	45.16	93.33	0.34	.	.	.	.	.	106	134	.
45	Dose3	96.30	25	78.13	96.15	0.36	.	.	.	.	.	88	161	.
46	Dose3	58.62	16	44.44	94.12	0.38	.	.	.	.	.	105	366	.
47	Dose3	.	0	0.00	.	0.34	.	.	.	.	.	84	182	.
48	Dose3	0.00	0	0.00	.	0.36	.	.	.	.	.	89	148	.
49	Dose4	75.00	15	65.22	100.00	0.36	.	.	.	.	.	94	253	.
50	Dose4	59.26	16	51.61	100.00	0.39	.	.	.	.	.	109	304	.
51	Dose4	.	0	0.00	.	0.38	.	.	.	.	.	106	215	.
52	Dose4	20.00	1	14.29	100.00	0.39	.	.	.	.	.	84	156	.
53	Dose4	.	0	0.00	.	0.33	.	.	.	.	.	87	194	.
54	Dose4	65.38	17	56.67	100.00	0.38	.	.	.	.	.	89	238	.
55	Dose4	81.48	22	53.66	100.00	0.38	.	.	.	.	.	86	-25	.
56	Dose4	80.00	27	75.00	96.43	0.36	.	.	.	.	.	90	47	.
57	Dose4	85.71	24	55.81	100.00	0.38	.	.	.	.	.	101	100	.

**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***

EPA MRID Number 001345-02

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58	Dose4	100.00	1	2.33	100.00	0.35	.	.	109	160	.
59	Dose4	47.06	8	44.44	100.00	0.44	.	.	110	112	.
60	Dose4	.	0	0.00	.	.	.	.	92	162	.

**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
 PMRA Submission Number

EPA MRID Number 001345-02

Mallard repro, Propiconazole, MRID 00134502  
 ANALYSIS RESULTS FOR VARIABLE EL ( Eggs Laid )

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01  
 Levenes test for homogeneity of variance (absolute residuals) -- alpha-level=0.05  
 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
0.954	0.024	2.678	0.041	USE NON-PARAMETRIC TESTS

\*\*\*\*\*

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval	
Ctrl	12	35.33	13.96	4.03	39.50	26.47,	44.20
Dose1	12	25.67	21.96	6.34	85.54	11.72,	39.62
Dose2	12	38.42	20.90	6.03	54.39	25.14,	51.69
Dose3	12	39.58	11.53	3.33	29.13	32.26,	46.91
Dose4	12	32.67	15.23	4.40	46.62	22.99,	42.34

Level	Median	Min	Max	%of Control (means)	%Reduction (means)
Ctrl	35.00	9.00	60.00	.	.
Dose1	32.00	0.00	51.00	72.64	27.36
Dose2	45.00	0.00	62.00	108.73	-8.73
Dose3	42.00	9.00	57.00	112.03	-12.03
Dose4	33.50	4.00	50.00	92.45	7.55

\*\*\*\*\*

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
4	3.37	0.498

MannWhit(Bon) - testing each trt median signif. less than control

Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	35.00	.	.
Dose1	32.00	0.884	0.209
Dose2	45.00	1.000	0.771
Dose3	42.00	1.000	0.836
Dose4	33.50	1.000	0.626

SUMMARY

	NOEC	LOEC
MannWhit (Bonf adjust)	Dose4	>highest dose
Jonckheere	Dose4	>highest dose

**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
 PMRA Submission Number

EPA MRID Number 001345-02

Mallard repro, Propiconazole, MRID 00134502  
 ANALYSIS RESULTS FOR VARIABLE NEG\_EC ( Eggs Cracked )

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01  
 Levenes test for homogeneity of variance (absolute residuals) -- alpha-level=0.05  
 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
0.796	<.001	0.659	0.623	USE NON-PARAMETRIC TESTS

\*\*\*\*\*

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval	
Ctrl	11	1.36	1.29	0.39	94.33	0.50,	2.23
Dose1	12	0.75	1.71	0.49	228.30	0.00,	1.84
Dose2	12	0.67	0.78	0.22	116.77	0.17,	1.16
Dose3	12	0.83	0.83	0.24	100.18	0.30,	1.36
Dose4	12	0.58	0.79	0.23	135.94	0.08,	1.09

Level	Median	Min	Max	%of Control (means)	%Reduction (means)
Ctrl	1.00	0.00	4.00	.	
Dose1	0.00	0.00	6.00	55.00	45.00
Dose2	0.50	0.00	2.00	48.89	51.11
Dose3	1.00	0.00	2.00	61.11	38.89
Dose4	0.00	0.00	2.00	42.78	57.22

\*\*\*\*\*

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
4	4.91	0.297

MannWhit (Bon) - testing each trt median signif. greater than control

Jonckheere - test assumes dose-response relationship, testing positive trend

Level	Median	MannWhit (Bon adjust) p-value	Jonckheere p-value
Ctrl	1.00		
Dose1	0.00	1.000	0.968
Dose2	0.50	1.000	0.888
Dose3	1.00	1.000	0.692
Dose4	0.00	1.000	0.808

SUMMARY

	NOEC	LOEC
MannWhit (Bonf adjust)	Dose4	>highest dose
Jonckheere	Dose4	>highest dose

**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
 PMRA Submission Number

EPA MRID Number 001345-02

Mallard repro, Propiconazole, MRID 00134502  
 ANALYSIS RESULTS FOR VARIABLE ENC\_EL ( (EL-EC)/EL (%) )

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS  
 Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01  
 Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05  
 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
0.784	<.001	0.530	0.715	USE NON-PARAMETRIC TESTS

\*\*\*\*\*  
 BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval	
Ctrl	11	96.36	4.48	1.35	4.65	93.35,	99.37
Dose1	8	97.48	4.52	1.60	4.63	93.70,	100.00
Dose2	10	98.24	1.79	0.57	1.83	96.95,	99.52
Dose3	12	97.63	2.84	0.82	2.91	95.82,	99.43
Dose4	12	98.17	2.85	0.82	2.91	96.36,	99.98

Level	Median	Min	Max	%of Control (means)	%Reduction(means)
Ctrl	97.30	84.00	100.00	.	.
Dose1	98.98	86.67	100.00	101.16	-1.16
Dose2	97.89	94.59	100.00	101.95	-1.95
Dose3	98.08	90.91	100.00	101.31	-1.31
Dose4	100.00	90.91	100.00	101.87	-1.87

\*\*\*\*\*  
 NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups  
 Degrees of Freedom TestStat P-value  
 4 3.21 0.523

MannWhit(Bon) - testing each trt median signif. less than control  
 Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	97.30		
Dose1	98.98	1.000	0.912
Dose2	97.89	1.000	0.880
Dose3	98.08	1.000	0.783
Dose4	100.00	1.000	0.898

SUMMARY  
 MannWhit (Bonf adjust) NOEC Dose4 >highest dose  
 Jonckheere NOEC Dose4 >highest dose

**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
 PMRA Submission Number

EPA MRID Number 001345-02

Mallard repro, Propiconazole, MRID 00134502  
 ANALYSIS RESULTS FOR VARIABLE ES ( Eggs Set )

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS  
 Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01  
 Levenes test for homogeneity of variance (absolute residuals) -- alpha-level=0.05  
 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
0.954	0.025	2.422	0.059	USE PARAMETRIC TESTS

\*\*\*\*\*  
 BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval	
Ctrl	12	30.75	12.55	3.62	40.81	22.78,	38.72
Dose1	12	22.67	19.43	5.61	85.72	10.32,	35.01
Dose2	12	34.17	19.01	5.49	55.63	22.09,	46.24
Dose3	12	35.08	11.04	3.19	31.47	28.07,	42.10
Dose4	12	28.92	13.77	3.97	47.61	20.17,	37.66

Level	Median	Min	Max	%of Control (means)	%Reduction (means)
Ctrl	31.50	6.00	52.00	.	.
Dose1	28.50	0.00	47.00	73.71	26.29
Dose2	40.50	0.00	55.00	111.11	-11.11
Dose3	37.00	16.00	52.00	114.09	-14.09
Dose4	30.50	4.00	44.00	94.04	5.96

\*\*\*\*\*  
 PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Analysis of Variance (ANOVA) - overall F-test

Numerator df	Denominator df	F-stat	P-value
4	55	1.22	0.313

Dunnett - testing each trt mean signif. less than control  
 Williams - test assumes dose-response relationship, testing negative trend  
 Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC

Level	Mean	Dunnett p-value	Isotonic mean	Williams p-value	Tukey p-values				
					Dose1	Dose2	Dose3	Dose4	Dose5
Ctrl	30.75	.	30.75	.	0.708	0.983	0.959	0.998	.
Dose1	22.67	0.266	30.64	0.576	.	0.377	0.301	0.861	.
Dose2	34.17	0.929	30.64	0.610	.	.	1.000	0.921	.
Dose3	35.08	0.949	30.64	0.629	.	.	.	0.867	.
Dose4	28.92	0.693	28.92	0.515	.	.	.	.	.

SUMMARY	NOEC	LOEC
Dunnett	Dose4	>highest dose
Williams	Dose4	>highest dose



**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
 PMRA Submission Number

EPA MRID Number 001345-02

Mallard repro, Propiconazole, MRID 00134502  
 ANALYSIS RESULTS FOR VARIABLE ES\_EL ( EggsSet/EggsLaid (%) )

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS  
 Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01  
 Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05  
 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
0.785	<.001	0.622	0.649	USE NON-PARAMETRIC TESTS

\*\*\*\*\*

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval	
Ctrl	12	85.73	7.27	2.10	8.48	81.12,	90.35
Dose1	8	88.52	4.62	1.63	5.22	84.66,	92.38
Dose2	10	88.32	3.23	1.02	3.66	86.01,	90.63
Dose3	12	87.96	3.47	1.00	3.94	85.75,	90.16
Dose4	12	88.05	8.51	2.46	9.67	82.64,	93.46

  

Level	Median	Min	Max	%of Control (means)	%Reduction (means)
Ctrl	87.99	66.67	92.31	.	.
Dose1	89.54	77.78	92.50	103.25	-3.25
Dose2	89.01	81.82	91.38	103.01	-3.01
Dose3	88.07	81.82	92.00	102.59	-2.59
Dose4	89.08	63.64	100.00	102.70	-2.70

\*\*\*\*\*

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups  
 Degrees of Freedom TestStat P-value  
 4 2.18 0.702

MannWhit(Bon) - testing each trt median signif. less than control  
 Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	87.99		
Dose1	89.54	1.000	0.905
Dose2	89.01	1.000	0.830
Dcse3	88.07	1.000	0.678
Dose4	89.08	1.000	0.768

SUMMARY  
 MannWhit (Bonf adjust) NOEC Dose4 >highest dose  
 Jonckheere NOEC Dose4 >highest dose

**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
 PMRA Submission Number

EPA MRID Number 001345-02

Mallard repro, Propiconazole, MRID 00134502  
 ANALYSIS RESULTS FOR VARIABLE VE ( Viable Embryo(d14) )

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS  
 Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01  
 Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05  
 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
0.960	0.049	0.528	0.715	USE PARAMETRIC TESTS

\*\*\*\*\*

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval	
Ctrl	12	23.25	13.69	3.95	58.89	14.55,	31.95
Dose1	12	15.08	16.37	4.73	108.55	4.68,	25.49
Dose2	12	32.17	18.75	5.41	58.29	20.25,	44.08
Dose3	12	27.75	16.85	4.87	60.73	17.04,	38.46
Dose4	12	15.83	13.62	3.93	86.00	7.18,	24.49

Level	Median	Min	Max	%of Control (means)	%Reduction (means)
Ctrl	26.50	1.00	43.00	.	.
Dose1	11.00	0.00	42.00	64.87	35.13
Dose2	40.00	0.00	52.00	138.35	-38.35
Dose3	32.00	0.00	52.00	119.35	-19.35
Dose4	18.50	0.00	36.00	68.10	31.90

\*\*\*\*\*

PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Analysis of Variance (ANOVA) - overall F-test

Numerator df	Denominator df	F-stat	P-value
4	55	2.59	0.046

Dunnnett - testing each trt mean signif. less than control

Williams - test assumes dose-response relationship, testing negative trend

Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC

Level	Mean	Dunnnett p-value	Isotonic mean	Williams p-value	Tukey p-values				
					Dose1	Dose2	Dose3	Dose4	Dose5
Ctrl	23.25	.	24.56	.	0.721	0.651	0.958	0.786	.
Dose1	15.08	0.274	24.56	0.667	.	0.081	0.308	1.000	.
Dose2	32.17	0.992	24.56	0.702	.	.	0.961	0.105	.
Dose3	27.75	0.950	24.56	0.721	.	.	.	0.369	.
Dose4	15.83	0.319	15.83	0.174	.	.	.	.	.

SUMMARY

	NOEC	LOEC
Dunnnett	Dose4	>highest dose
Williams	Dose4	>highest dose

**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
 PMRA Submission Number

EPA MRID Number 001345-02

Mallard repro, Propiconazole, MRID 00134502  
 ANALYSIS RESULTS FOR VARIABLE VE\_ES ( ViableEmbryo/EggsSet (%) )

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS  
 Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01  
 Levenes test for homogeneity of variance (absolute residuals) -- alpha-level=0.05  
 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
0.855	<.001	4.443	0.004	USE NON-PARAMETRIC TESTS

\*\*\*\*\*  
 BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval	
Ctrl	12	74.99	30.54	8.82	40.73	55.59,	94.39
Dose1	8	69.02	32.74	11.58	47.44	41.64,	96.39
Dose2	10	92.97	9.26	2.93	9.96	86.34,	99.59
Dose3	12	75.28	37.13	10.72	49.32	51.69,	98.87
Dose4	12	56.73	42.70	12.33	75.26	29.60,	83.86

Level	Median	Min	Max	%of Control (means)	%Reduction (means)
Ctrl	89.79	1.92	97.44	.	.
Dose1	81.49	4.55	100.00	92.03	7.97
Dose2	96.89	70.59	100.00	123.97	-23.97
Dose3	92.89	0.00	100.00	100.39	-0.39
Dose4	75.78	0.00	100.00	75.65	24.35

\*\*\*\*\*  
 NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups  
 Degrees of Freedom TestStat P-value  
 4 8.58 0.072

MannWhit(Bon) - testing each trt median signif. less than control  
 Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	89.79	.	.
Dose1	81.49	1.000	0.439
Dose2	96.89	1.000	0.970
Dose3	92.89	1.000	0.860
Dose4	75.78	0.432	0.236

SUMMARY  
 MannWhit (Bonf adjust) NOEC Dose4 >highest dose  
 Jonckheere LOEC Dose4 >highest dose

**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
 PMRA Submission Number

EPA MRID Number 001345-02

Mallard repro, Propiconazole, MRID 00134502  
 ANALYSIS RESULTS FOR VARIABLE LE ( Live Embryo(d21) )

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS  
 Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01  
 Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05  
 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
0.958	0.040	0.296	0.879	USE PARAMETRIC TESTS

\*\*\*\*\*  
 BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval	
Ctrl	12	21.50	13.51	3.90	62.83	12.92,	30.08
Dose1	12	13.83	15.40	4.44	111.30	4.05,	23.62
Dose2	12	30.25	17.47	5.04	57.76	19.15,	41.35
Dose3	12	25.42	16.39	4.73	64.48	15.00,	35.83
Dose4	12	15.50	13.40	3.87	86.45	6.99,	24.01

  

Level	Median	Min	Max	%of Control (means)	%Reduction (means)
Ctrl	25.00	0.00	42.00	.	35.66
Dose1	10.00	0.00	38.00	64.34	-40.70
Dose2	36.50	0.00	49.00	140.70	-18.22
Dose3	28.00	0.00	50.00	118.22	27.91
Dose4	18.50	0.00	35.00	72.09	

\*\*\*\*\*  
 PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Analysis of Variance (ANOVA) - overall F-test

Numerator df	Denominator df	F-stat	P-value
4	55	2.38	0.062

Dunnnett - testing each trt mean signif. less than control  
 Williams - test assumes dose-response relationship, testing negative trend  
 Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC

Level	Mean	Dunnnett p-value	Isotonic mean	Williams p-value	Dose1	Dose2	Tukey p-values		
							Dose3	Dose4	Dose5
Ctrl	21.50	.	22.75	.	0.736	0.631	0.970	0.872	.
Dose1	13.83	0.284	22.75	0.666	.	0.080	0.355	0.999	.
Dose2	30.25	0.993	22.75	0.701	.	.	0.937	0.142	.
Dose3	25.42	0.942	22.75	0.720	.	.	.	0.513	.
Dose4	15.50	0.394	15.50	0.230	.	.	.	.	.

SUMMARY

	NOEC	LOEC
Dunnnett	Dose4	>highest dose
Williams	Dose4	>highest dose

**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
 PMRA Submission Number

EPA MRID Number 001345-02

Mallard repro, Propiconazole, MRID 00134502  
 ANALYSIS RESULTS FOR VARIABLE LE\_VE ( LiveEmbryo/ViableEmbryo (%) )

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS  
 Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01  
 Levenes test for homogeneity of variance (absolute residuals) -- alpha-level=0.05  
 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.  
 Shapiro-Wilks Shapiro-Wilks Levenes Levenes Conclusion  
 Test Stat P-value Test Stat P-value  
 0.627 <.001 3.146 0.023 USE NON-PARAMETRIC TESTS

\*\*\*\*\*  
 BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval	
Ctrl	12	80.55	28.65	8.27	35.57	62.34,	98.75
Dose1	8	80.63	32.69	11.56	40.54	53.30,	100.00
Dose2	10	94.37	4.47	1.41	4.73	91.17,	97.56
Dose3	10	89.50	7.34	2.32	8.20	84.25,	94.75
Dose4	9	97.03	5.39	1.80	5.56	92.89,	100.00

Level	Median	Min	Max	%of Control (means)	%Reduction (means)
Ctrl	90.48	0.00	103.13	.	
Dose1	91.67	0.00	94.87	100.10	-0.10
Dose2	95.96	84.62	100.00	117.16	-17.16
Dose3	87.49	77.78	100.00	111.12	-11.12
Dose4	100.00	83.33	100.00	120.47	-20.47

\*\*\*\*\*  
 NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups  
 Degrees of Freedom TestStat P-value  
 4 12.00 0.017

MannWhit(Bon) - testing each trt median signif. less than control  
 Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	90.48		
Dose1	91.67	1.000	0.636
Dose2	95.96	1.000	0.972
Dose3	87.49	1.000	0.773
Dose4	100.00	1.000	0.995

SUMMARY  
 MannWhit (Bonf adjust) NOEC Dose4 >highest dose  
 Jonckheere NOEC Dose4 >highest dose

**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
 PMRA Submission Number

EPA MRID Number 001345-02

Mallard repro, Propiconazole, MRID 00134502  
 ANALYSIS RESULTS FOR VARIABLE NH ( Number Hatched )

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS  
 Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01  
 Levenes test for homogeneity of variance (absolute residuals) -- alpha-level=0.05  
 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
0.960	0.049	0.219	0.927	USE PARAMETRIC TESTS

\*\*\*\*\*  
 BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval	
Ctrl	12	15.33	11.75	3.39	76.63	7.87,	22.80
Dose1	12	10.08	11.41	3.29	113.19	2.83,	17.34
Dose2	12	21.92	13.39	3.87	61.11	13.41,	30.43
Dose3	12	17.00	14.28	4.12	84.02	7.93,	26.07
Dose4	12	11.00	10.57	3.05	96.05	4.29,	17.71

  

Level	Median	Min	Max	%of Control (means)	%Reduction (means)
Ctrl	18.00	0.00	35.00	.	.
Dose1	5.50	0.00	28.00	65.76	34.24
Dose2	26.50	0.00	42.00	142.93	-42.93
Dose3	16.50	0.00	41.00	110.87	-10.87
Dose4	11.50	0.00	28.00	71.74	28.26

\*\*\*\*\*  
 PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Analysis of Variance (ANOVA) - overall F-test

Numerator df	Denominator df	F-stat	P-value
4	55	1.81	0.140

Dunnett - testing each trt mean signif. less than control  
 Williams - test assumes dose-response relationship, testing negative trend  
 Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC

Level	Mean	Dunnett p-value	Isotonic mean	Williams p-value	Tukey p-values				
					Dose1	Dose2	Dose3	Dose4	Dose5
Ctrl	15.33	.	16.08	.	0.835	0.689	0.997	0.910	.
Dose1	10.08	0.359	16.08	0.646	.	0.146	0.648	1.000	.
Dose2	21.92	0.991	16.08	0.681	.	.	0.865	0.209	.
Dose3	17.00	0.890	16.08	0.700	.	.	.	0.757	.
Dose4	11.00	0.438	11.00	0.267	.	.	.	.	.

SUMMARY	NOEC	LOEC
Dunnett	Dose4	>highest dose
Williams	Dose4	>highest dose

**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
 PMRA Submission Number

EPA MRID Number 001345-02

Mallard repro, Propiconazole, MRID 00134502  
 ANALYSIS RESULTS FOR VARIABLE NH\_EL ( NumberHatched/EggsLaid (%) )

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01  
 Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05  
 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
0.937	0.007	3.215	0.020	USE NON-PARAMETRIC TESTS

\*\*\*\*\*  
 BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval	
Ctrl	12	39.99	26.67	7.70	66.69	23.05,	56.94
Dose1	8	40.00	21.98	7.77	54.95	21.62,	58.38
Dose2	10	55.93	12.21	3.86	21.84	47.19,	64.67
Dose3	12	38.46	30.28	8.74	78.72	19.22,	57.70
Dose4	12	31.10	26.38	7.61	84.81	14.34,	47.86

Level	Median	Min	Max	%of Control (means)	%Reduction (means)
Ctrl	51.19	0.00	68.63	.	.
Dose1	44.51	0.00	67.50	100.02	-0.02
Dose2	58.20	33.33	72.97	139.84	-39.84
Dose3	40.72	0.00	82.00	96.17	3.83
Dose4	42.86	0.00	66.67	77.77	22.23

\*\*\*\*\*  
 NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups  
 Degrees of Freedom TestStat P-value  
 4 5.62 0.229

MannWhit(Bon) - testing each trt median signif. less than control  
 Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	51.19	.	.
Dose1	44.51	1.000	0.379
Dose2	58.20	1.000	0.913
Dose3	40.72	1.000	0.602
Dose4	42.86	0.563	0.177

SUMMARY	NOEC	LOEC
MannWhit (Bonf adjust)	Dose4	>highest dose
Jonckheere	Dose4	>highest dose

**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
 PMRA Submission Number

EPA MRID Number 001345-02

Mallard repro, Propiconazole, MRID 00134502  
 ANALYSIS RESULTS FOR VARIABLE NH\_ES ( NumberHatched/EggsSet (%) )

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01  
 Levenes test for homogeneity of variance (absolute residuals) -- alpha-level=0.05  
 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
0.940	0.009	3.144	0.022	USE NON-PARAMETRIC TESTS

\*\*\*\*\*

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval	
Ctrl	12	45.41	29.98	8.66	66.03	26.36,	64.46
Dose1	8	45.06	24.04	8.50	53.34	24.96,	65.15
Dose2	10	63.32	13.97	4.42	22.06	53.33,	73.32
Dose3	12	43.15	33.58	9.69	77.82	21.82,	64.49
Dose4	12	35.15	29.43	8.50	83.74	16.45,	53.85

Level	Median	Min	Max	%of Control (means)	%Reduction (means)
Ctrl	58.38	0.00	77.78	.	.
Dose1	48.82	0.00	72.97	99.23	0.77
Dose2	64.58	38.24	87.10	139.45	-39.45
Dose3	46.69	0.00	89.13	95.04	4.96
Dose4	48.03	0.00	77.78	77.41	22.59

\*\*\*\*\*

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
4	5.39	0.249

MannWhit(Bonf) - testing each trt median signif. less than control

Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bonf adjust)p-value	Jonckheere p-value
Ctrl	58.38	.	.
Dose1	48.82	1.000	0.335
Dose2	64.58	1.000	0.878
Dose3	46.69	1.000	0.518
Dose4	48.03	0.471	0.152

SUMMARY

	NOEC	LOEC
MannWhit (Bonf adjust)	Dose4	>highest dose
Jonckheere	Dose4	>highest dose



**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
**PMRA Submission Number**

EPA MRID Number 001345-02

Mallard repro, Propiconazole, MRID 00134502  
 ANALYSIS RESULTS FOR VARIABLE NH\_LE ( NumberHatched/LiveEmbryo (%) )

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01  
 Levenes test for homogeneity of variance (absolute residuals) -- alpha-level=0.05  
 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
0.937	0.013	2.433	0.062	USE PARAMETRIC TESTS

\*\*\*\*\*  
 BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval	
Ctrl	11	58.59	29.50	8.89	50.35	38.77,	78.41
Dose1	7	70.86	11.88	4.49	16.77	59.88,	81.85
Dose2	10	71.64	11.00	3.48	15.35	63.78,	79.51
Dose3	10	58.88	31.15	9.85	52.90	36.60,	81.17
Dose4	9	68.21	23.82	7.94	34.92	49.90,	86.52

  

Level	Median	Min	Max	%of Control (means)	%Reduction (means)
Ctrl	71.43	0.00	85.71	.	.
Dose1	73.68	53.85	83.33	120.95	-20.95
Dose2	69.83	56.52	93.10	122.28	-22.28
Dose3	58.34	0.00	96.30	100.50	-0.50
Dose4	75.00	20.00	100.00	116.42	-16.42

\*\*\*\*\*  
 PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Analysis of Variance (ANOVA) - overall F-test

Numerator df	Denominator df	F-stat	P-value
4	42	0.70	0.594

Dunnett - testing each trt mean signif. less than control  
 Williams - test assumes dose-response relationship, testing negative trend  
 Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC

Level	Mean	Dunnett p-value	Isotonic mean	Williams p-value	Tukey p-values				
					Dose1	Dose2	Dose3	Dose4	Dose5
Ctrl	58.59	.	66.32	.	0.824	0.721	1.000	0.896	.
Dose1	70.86	0.985	66.32	0.828	.	1.000	0.845	0.999	.
Dose2	71.64	0.991	66.32	0.875	.	.	0.754	0.998	.
Dose3	58.88	0.825	63.30	0.810	.	.	.	0.913	.
Dose4	68.21	0.976	63.30	0.817	.	.	.	.	.

SUMMARY	NOEC	LOEC
Dunnett	Dose4	>highest dose
Williams	Dose4	>highest dose

**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
 PMRA Submission Number

EPA MRID Number 001345-02

Mallard repro, Propiconazole, MRID 00134502  
 ANALYSIS RESULTS FOR VARIABLE HS ( Hatching Survival(d14) )

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01  
 Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05  
 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
0.957	0.035	0.204	0.935	USE PARAMETRIC TESTS

\*\*\*\*\*  
 BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval	
Ctrl	12	14.58	11.16	3.22	76.55	7.49,	21.68
Dose1	12	10.08	11.41	3.29	113.19	2.83,	17.34
Dose2	12	21.33	12.97	3.74	60.80	13.09,	29.57
Dose3	12	16.25	13.73	3.96	84.46	7.53,	24.97
Dose4	12	10.92	10.42	3.01	95.47	4.29,	17.54

Level	Median	Min	Max	%of Control (means)	%Reduction (means)
Ctrl	17.00	0.00	33.00	.	.
Dose1	5.50	0.00	28.00	69.14	30.86
Dose2	25.50	0.00	41.00	146.29	-46.29
Dose3	15.50	0.00	39.00	111.43	-11.43
Dose4	11.50	0.00	27.00	74.86	25.14

\*\*\*\*\*  
 PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Analysis of Variance (ANOVA) - overall F-test

Numerator df	Denominator df	F-stat	P-value
4	55	1.71	0.161

Dunnett - testing each trt mean signif. less than control  
 Williams - test assumes dose-response relationship, testing negative trend  
 Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC

Level	Mean	Dunnett p-value	Isotonic mean	Williams p-value	Dose1	Dose2	Dose3	Dose4	Dose5
Ctrl	14.58	.	15.56	.	0.889	0.644	0.997	0.944	.
Dose1	10.08	0.412	15.56	0.666	.	0.162	0.717	1.000	.
Dose2	21.33	0.993	15.56	0.701	.	.	0.837	0.224	.
Dose3	16.25	0.892	15.56	0.720	.	.	.	0.812	.
Dose4	10.92	0.489	10.92	0.310	.	.	.	.	.

SUMMARY	NOEC	LOEC
Dunnett	Dose4	>highest dose
Williams	Dose4	>highest dose

**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
 PMRA Submission Number

EPA MRID Number 001345-02

Mallard repro, Propiconazole, MRID 00134502  
 ANALYSIS RESULTS FOR VARIABLE HS\_ES ( HatchingSurvival/EggsSet (%) )

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS  
 Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01  
 Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05  
 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
0.940	0.009	3.247	0.019	USE NON-PARAMETRIC TESTS

\*\*\*\*\*

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval	
Ctrl	12	43.20	28.39	8.20	65.71	25.16,	61.24
Dose1	8	45.06	24.04	8.50	53.34	24.96,	65.15
Dose2	10	61.72	13.08	4.14	21.20	52.36,	71.08
Dose3	12	41.24	32.23	9.31	78.16	20.76,	61.72
Dose4	12	34.92	29.08	8.39	83.27	16.44,	53.39

Level	Median	Min	Max	%of Control (means)	%Reduction (means)
Ctrl	55.36	0.00	74.36	.	.
Dose1	48.82	0.00	72.97	104.29	-4.29
Dose2	62.38	38.24	83.87	142.86	-42.86
Dose3	44.02	0.00	84.78	95.46	4.54
Dose4	48.03	0.00	75.00	80.83	19.17

\*\*\*\*\*

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
4	4.80	0.309

MannWhit(Bonf) - testing each trt median signif. less than control  
 Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bonf adjust)p-value	Jonckheere p-value
Ctrl	55.36	.	.
Dose1	48.82	1.000	0.439
Dose2	62.38	1.000	0.921
Dose3	44.02	1.000	0.572
Dose4	48.03	0.726	0.215

SUMMARY	NOEC	LOEC
MannWhit (Bonf adjust)	Dose4	>highest dose
Jonckheere	Dose4	>highest dose

**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
 PMRA Submission Number

EPA MRID Number 001345-02

Mallard repro, Propiconazole, MRID 00134502  
 ANALYSIS RESULTS FOR VARIABLE HS\_NH ( HatchingSurvival/NumberHatched (%) )

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS  
 Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01  
 Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05  
 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
0.926	0.007	4.621	0.004	USE NON-PARAMETRIC TESTS

\*\*\*\*\*

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval	
Ctrl	10	95.89	2.34	0.74	2.44	94.22,	97.56
Dose1	7	100.00	0.00	0.00	0.00		
Dose2	10	97.67	1.66	0.53	1.70	96.48,	98.86
Dose3	9	95.66	2.12	0.71	2.22	94.03,	97.29
Dose4	9	99.60	1.19	0.40	1.20	98.69,	100.00

Level	Median	Min	Max	%of Control (means)	%Reduction (means)
Ctrl	95.12	93.33	100.00		
Dose1	100.00	100.00	100.00	104.29	-4.29
Dose2	96.97	96.15	100.00	101.86	-1.86
Dose3	95.12	93.33	100.00	99.76	0.24
Dose4	100.00	96.43	100.00	103.88	-3.88

\*\*\*\*\*

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
4	23.19	<.001

MannWhit(Bon) - testing each trt median signif. less than control

Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	95.12		
Dose1	100.00	1.000	0.998
Dose2	96.97	1.000	0.936
Dose3	95.12	1.000	0.248
Dose4	100.00	1.000	0.922

SUMMARY

	NOEC	LOEC
MannWhit (Bonf adjust)	Dose4	>highest dose
Jonckheere	Dose4	>highest dose

**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
 PMRA Submission Number

EPA MRID Number 001345-02

Mallard repro, Propiconazole, MRID 00134502  
 ANALYSIS RESULTS FOR VARIABLE THICK ( Eggshell thickness )

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01  
 Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05  
 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
0.986	0.801	0.604	0.662	USE PARAMETRIC TESTS

\*\*\*\*\*  
 BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval	
Ctrl	12	0.38	0.02	0.01	6.53	0.36,	0.39
Dose1	8	0.38	0.03	0.01	7.03	0.36,	0.41
Dose2	10	0.38	0.02	0.01	6.34	0.36,	0.39
Dose3	12	0.37	0.02	0.01	4.71	0.36,	0.38
Dose4	11	0.38	0.03	0.01	7.11	0.36,	0.39

  

Level	Median	Min	Max	%of Control (means)	%Reduction (means)
Ctrl	0.38	0.34	0.42	.	.
Dose1	0.39	0.35	0.42	102.01	-2.01
Dose2	0.38	0.34	0.41	100.12	-0.12
Dose3	0.37	0.34	0.39	98.54	1.46
Dose4	0.38	0.33	0.44	99.97	0.03

\*\*\*\*\*  
 PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Analysis of Variance (ANOVA) - overall F-test

Numerator df	Denominator df	F-stat	P-value
4	48	0.36	0.836

Dunnett - testing each trt mean signif. less than control  
 Williams - test assumes dose-response relationship, testing negative trend  
 Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC

Level	Mean	Dunnett p-value	Isotonic mean	Williams p-value	Tukey p-values				
					Dose1	Dose2	Dose3	Dose4	Dose5
Ctrl	0.38	.	0.38	.	0.957	1.000	0.980	1.000	.
Dose1	0.38	0.957	0.38	0.697	.	0.970	0.753	0.958	.
Dose2	0.38	0.828	0.38	0.637	.	.	0.977	1.000	.
Dose3	0.37	0.588	0.37	0.500	.	.	.	0.982	.
Dose4	0.38	0.810	0.37	0.513	.	.	.	.	.

SUMMARY	NOEC	LOEC
Dunnett	Dose4	>highest dose
Williams	Dose4	>highest dose

**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
 PMRA Submission Number EPA MRID Number 001345-02

Mallard repro, Propiconazole, MRID 00134502  
 ANALYSIS RESULTS FOR VARIABLE HATWT ( Hatchling Weight )

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS  
 Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01  
 Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05  
 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.  

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion
Test Stat	P-value	Test Stat	P-value	
				NO DATA FOR TEST

\*\*\*\*\*  
 BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	0	.	.	.	.	.
Dose1	0	.	.	.	.	.
Dose2	0	.	.	.	.	.
Dose3	0	.	.	.	.	.
Dose4	0	.	.	.	.	.

  

Level	Median	Min	Max	%of Control (means)	%Reduction (means)
Ctrl	.	.	.	.	.
Dose1	.	.	.	.	.
Dose2	.	.	.	.	.
Dose3	.	.	.	.	.
Dose4	.	.	.	.	.

**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
 PMRA Submission Number

EPA MRID Number 001345-02

Mallard repro, Propiconazole, MRID 00134502  
 ANALYSIS RESULTS FOR VARIABLE SURVWT ( Survivor Wt (d14) )

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01  
 Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05  
 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
.	.	.	.	NO DATA FOR TEST

\*\*\*\*\*

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	0	.	.	.	.	.
Dose1	0	.	.	.	.	.
Dose2	0	.	.	.	.	.
Dose3	0	.	.	.	.	.
Dose4	0	.	.	.	.	.

Level	Median	Min	Max	%of Control (means)	%Reduction (means)
Ctrl	.	.	.	.	.
Dose1	.	.	.	.	.
Dose2	.	.	.	.	.
Dose3	.	.	.	.	.
Dose4	.	.	.	.	.

**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
**PMRA Submission Number** **EPA MRID Number 001345-02**

Mallard repro, Propiconazole, MRID 00134502  
 ANALYSIS RESULTS FOR VARIABLE FOOD ( Food Consumption )

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS  
 Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01  
 Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05  
 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
0.974	0.236	1.801	0.142	USE PARAMETRIC TESTS

\*\*\*\*\*  
 BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval	
Ctrl	12	102.51	19.30	5.57	18.83	90.25	114.77
Dose1	12	100.83	13.38	3.86	13.27	92.33	109.33
Dose2	12	104.25	19.68	5.68	18.88	91.74	116.76
Dose3	12	101.28	14.65	4.23	14.46	91.98	110.59
Dose4	12	96.50	9.71	2.80	10.07	90.33	102.67

  

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	95.25	81.10	138.90	.	.
Dose1	96.45	78.60	125.20	98.37	1.63
Dose2	106.80	68.70	139.40	101.70	-1.70
Dose3	98.80	83.70	134.50	98.80	1.20
Dose4	93.10	84.00	109.60	94.14	5.86

\*\*\*\*\*  
 PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Analysis of Variance (ANOVA) - overall F-test

Numerator df	Denominator df	F-stat	P-value
4	55	0.40	0.809

Dunnett - testing each trt mean signif. less than control  
 Williams - test assumes dose-response relationship, testing negative trend  
 Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC

Level	Mean	Dunnett p-value	Isotonic mean	Williams p-value	Tukey p-values				
					Dose1	Dose2	Dose3	Dose4	Dose5
Ctrl	102.51	.	102.53	.	0.999	0.999	1.000	0.883	.
Dose1	100.83	0.705	102.53	0.585	.	0.984	1.000	0.962	.
Dose2	104.25	0.876	102.53	0.619	.	.	0.991	0.750	.
Dose3	101.28	0.732	101.28	0.551	.	.	.	0.946	.
Dose4	96.50	0.406	96.50	0.240	.	.	.	.	.

SUMMARY

	NOEC	LOEC
Dunnett	Dose4	>highest dose
Williams	Dose4	>highest dose



**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
 PMRA Submission Number

EPA MRID Number 001345-02

Mallard repro, Propiconazole, MRID 00134502  
 ANALYSIS RESULTS FOR VARIABLE WTGAINM ( Male wt gain )

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS  
 Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01  
 Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05  
 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
0.980	0.437	1.423	0.239	USE PARAMETRIC TESTS

\*\*\*\*\*  
 BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	12	179.00	106.73	30.81	59.63	111.19, 246.81
Dose1	12	157.00	116.85	33.73	74.43	82.76, 231.24
Dose2	12	155.25	100.22	28.93	64.55	91.57, 218.93
Dose3	12	186.00	63.49	18.33	34.14	145.66, 226.34
Dose4	12	159.67	91.73	26.48	57.45	101.38, 217.95

  

Level	Median	Min	Max	%of Control (means)	%Reduction (means)
Ctrl	187.00	-18.00	334.00	.	.
Dose1	133.50	-25.00	341.00	87.71	12.29
Dose2	172.00	-79.00	287.00	86.73	13.27
Dose3	174.50	125.00	366.00	103.91	-3.91
Dose4	161.00	-25.00	304.00	89.20	10.80

\*\*\*\*\*  
 PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Analysis of Variance (ANOVA) - overall F-test

Numerator df	Denominator df	F-stat	P-value
4	55	0.25	0.908

Dunnett - testing each trt mean signif. less than control  
 Williams - test assumes dose-response relationship, testing negative trend  
 Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC

Level	Mean	Dunnett p-value	Isotonic mean	Williams p-value	Dose1	Dose2	Dose3	Dose4	Dose5
Ctrl	179.00	.	179.00	.	0.981	0.975	1.000	0.988	.
Dose1	157.00	0.578	166.08	0.443	.	1.000	0.949	1.000	.
Dose2	155.25	0.558	166.08	0.472	.	.	0.937	1.000	.
Dose3	186.00	0.853	166.08	0.488	.	.	.	0.964	.
Dose4	159.67	0.609	159.67	0.424	.	.	.	.	.

SUMMARY	NOEC	LOEC
Dunnett	Dose4	>highest dose
Williams	Dose4	>highest dose

**Data Evaluation Report on the Reproductive Effects of CGA-64250 Technical (Propiconazole) on Mallard Duck, *Anas platyrhynchos***  
 PMRA Submission Number

EPA MRID Number 001345-02

Mallard repro, Propiconazole, MRID 00134502  
 ANALYSIS RESULTS FOR VARIABLE WTGAINF ( Female wt gain )

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01  
 Levenes test for homogeneity of variance (absolute residuals) -- alpha-level=0.05  
 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
				NO DATA FOR TEST

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BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	0	.	.	.	.	.
Dose1	0	.	.	.	.	.
Dose2	0	.	.	.	.	.
Dose3	0	.	.	.	.	.
Dose4	0	.	.	.	.	.

  

Level	Median	Min	Max	%of Control (means)	%Reduction (means)
Ctrl	.	.	.	.	.
Dose1	.	.	.	.	.
Dose2	.	.	.	.	.
Dose3	.	.	.	.	.
Dose4	.	.	.	.	.