Data Evaluation Report on the Reproductive Effects of JAU 6476 - Desthio (Prothioconazole - Desthio) on Avian Species *Anas platyrhyncbos*
PMRA Submission Number 2004-0843 EPA MRID Number 46246045

Data Requirement:		
	PMRA DATA CODE	9.6.3.2
	EPA DP Barcode	D303488
	OECD Data Point	IIA 8.1.4
	EPA MRID	46246045
	EPA Guideline	§71-4b

Test material: JAU 6476 - Desthio **Purity:** 96.4%
Common name: Prothioconazole - Desthio
Chemical name: IUPAC: 2-(1-Chlorocyclopropyl)-1-(2-chlorophenyl)-3-(1,2,4-triazole-1-yl)-propan-2-ol
CAS name: 2-[2-(1-Chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-1,2-dihydro-3H-1,2,4-triazole
CAS No.: 120983-64-4
Synonyms: SXX 0665

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CITATION: **Frey, L.T., *et al.*** 2001. Desthio JAU-6476: A Reproduction Study with the Mallard (*Anas platyrhynchos*). Unpublished study performed by Wildlife International, Ltd., Easton, MD. Laboratory No. 149-181. Study submitted by Bayer CropScience, Research Triangle Park, NC. Study initiated August 15, 2000 and completed May 10, 2001.

The one-generation reproductive toxicity of JAU 6476 - Desthio (prothioconazole - desthio) to groups (16 pens/treatment level) of 1 male and 1 female, 20-week-old Mallard duck was assessed over approximately 20 weeks. JAU 6476 - Desthio was administered to the birds in the diet nominal concentrations of 0 (solvent control), 60, 120, and 500 ppm. Mean-measured concentrations were <6.0 (<LOD, control), 56.7, 120, and 499 ppm a.i., respectively. However, stability experiments indicated that the test substance likely degraded slightly (approximately 20-25%) during the duration of open feeder storage (7 days). Taking into account this degradation, the modified, mean-measured concentrations would be 50.2, 105, and 449 ppm a.i.

There were no significant treatment-related effects on any adult or offspring parameter. As a result, the NOAEC and LOAEC levels were 449 and >449 ppm a.i., respectively.

This toxicity study is scientifically sound. However, due to the apparent degredation of JAU 6476 - Desthio in feed, this study does not satisfy the guideline requirements for the reproductive toxicity of JAU 6476 - Desthio (prothioconazole - desthio) to Mallard duck (§71-4b). The study is, therefore, classified as SUPPLEMENTAL although it does not need to be repeated and the values may be useful for risk assessment purposes. Since the test substance likely degraded during open feeder storage, this study is not upgradable.

Results Synopsis

Test Organism Size/Age: 20 weeks old at test initiation (846-1286 g)

NOAEC: 449 ppm a.i.
LOAEC: >449 ppm a.i.
Endpoint(s) Affected: None
Most sensitive endpoints: None

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: The study protocol was based on procedures of the U.S. EPA Pesticide Assessment Guidelines, §71-4 (1982) and OECD Guideline 206 (1984); and ASTM Standard E1062-86 (1986). Deviations from §71-4 are:

1. Mortality of the ducks during acclimation was not described.

2. It was not specified if the acetone was allowed to completely evaporate from the treated feed prior to offering.

3. The test substance degraded slightly in treated feed during 7 days of open feeder storage, with recoveries of 75-80% of initial concentrations. Although slight degradation occurred, the treated feed was still offered once weekly.

4. The average egg storage temperature (prior to setting for incubation) was 13.3 ± 0.2°C, slightly lower than the recommended level of 16°C.

5. The average temperature during hatching was 37.2 ± 0.0°C, slightly lower than the recommended temperature of 39°C. The photo-period during hatching was not specified.

6. The number of normal hatchlings was not monitored, and the health of the chicks during the 14-day maintenance period was not specified.

7. Raw data pertaining to clinical effects observed in parental ducks and hatchlings were not provided.

These deviations did not affect the scientific validity of the study; however, this study does not fulfill guideline requirements.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided. This study was conducted in accordance with United States, OECD, and Japan MAFF GLP standards, with the following exception: the frequency of measurement of light intensity was not specified in the protocol.

A. MATERIALS:

1. Test Material JAU 6476 - Desthio (prothioconazole - desthio)

Description: White powder

Lot No./Batch No. : RUX76-105/8a

Purity: 96.4%

Stability of Compound Under Test Conditions: JAU 6476 - Desthio degraded slightly under actual use conditions. In feed prepared at all concentrations levels and stored under open feeder conditions for 7 days, recoveries averaged only 75-80% of initial values (Table 6 of Appendix XIII, p. 186).

Storage conditions of test chemical: Under ambient conditions in locked storage.

OECD requires water solubility, stability in water and light, pK_a, P_{ow}, and vapor pressure of the test compound. OECD requirements were not reported.

2. Test organism:

Table 1: Test organism.

Parameter	Details	Remarks *Criteria*
Species (common and scientific names):	Mallard duck (*Anas platyrhynchos*)	*EPA requires: a wild waterfowl species, preferably the mallard, Anas platyrhynchos, or an upland game species, preferably the northern bobwhite, Colinus virginianus.*
Age at Study Initiation:	20 weeks	It was stated that birds were approaching their first breeding season. *EPA requires: birds should be approaching their first breeding season.*
Body Weight: (mean and range)	Males: Overall range (n=64) 846 to 1286 g, with group means of 1104 to 1139 g. Females: Overall range (n=64) 900 to 1213 g, with group means of 1014 to 1054 g.	Individual body weights were recorded at Weeks 0, 2, 4, 6, 8 and 20 (test termination). *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.*
Source:	Whistling Wings Hanover, IL	Birds were from the same hatch, and were phenotypically indistinguishable from wild birds. *EPA requires that all birds should be from the same source.*

B. STUDY DESIGN:

1. Experimental Conditions

a. Range-finding Study - None performed. The test concentrations were selected in consultation with the Sponsor, based upon toxicity information provided by the Sponsor (p. 13).

b. Definitive Study

Table 2: Experimental Parameters.

Parameter	Details	Remarks *Criteria*
Acclimation period: Conditions (same as test or not): Feeding: Health (any mortality observed):	3 weeks Same as test Water and feed were provided *ad libitum*. Pre-test mortality was not reported.	The study author reported that at test initiation, all birds were examined for physical injuries and general health, and birds that did not appear healthy were excluded from the study. Mallard were fed a basal diet formulated by Agway Inc., to meet laboratory specifications (Appendix I, p. 40), and provided public tap water from the city of Easton. *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 ad libitum, and sickness, injuries or mortality be noted.*
Test duration pre-laying exposure: egg-laying exposure: withdrawal period, if used:	 Approximately 10 weeks Approximately 10 weeks None	 *EPA requires* ***Pre-laying exposure duration*** *At least 10 weeks prior to the onset of egg-laying.* ***Exposure duration with egg-laying*** *At least 10 weeks.* ***Withdrawal period*** *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 75 x 90 x 45 cm. Offspring (by set and group) were housed in 62 x 92 x 25.5 cm battery brooders. Parental and offspring pens were constructed of vinyl-coated wire mesh. 16 parental pens/treatment level	*Pens* *Adequate room and arranged to prevent cross contamination* *Materials* *Nontoxic material and nonbinding material, such as galvanized steel.* *Number* *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)	*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.*
Number of pens per group/treatment negative control: solvent control: treated:	N/A 16 pens 16 pens/treatment	*EPA requires at least 12 pens, but considerably more if birds are kept in pairs. At least 16 is strongly recommended.*
Test concentrations (ppm diet) nominal: measured:	0 (vehicle control), 60, 120, and 500 ppm <6.0 (<LOD, control), 56.7, 120, and 499 ppm a.i.	Mean-measured concentrations are provided in Table 7, p. 38. Concentrations were adjusted for the purity of the test material (p. 14), but were not adjusted for mean procedural recoveries (p. 18). *EPA requires at least two concentrations other than the control are required; three or more are recommended.*

Parameter	Details	Remarks *Criteria*
Maximum labeled field residue anticipated and source of information:	Not specified.	*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 & ppm), label registration no., label date, and site should be cited]*
Solvent/vehicle, if used type: amount:	Acetone and corn oil Approximately 0.08% acetone and corn oil (v:w)	Reviewer-calculated from data provided in Appendix II, p. 41. *EPA requires corn oil or other appropriate vehicle not more than 2% of diet by weight*
Was detailed description and nutrient analysis of the basal diet provided? (Yes/No)	Yes	Basal diets contained ≥27% protein, ≥2.5% fat, ≤5% fiber, and approximately 3% limestone (pp. 15-16, and Appendix I, p. 40). Offspring received basal diet without the addition of test substance or limestone. *EPA requires a commercial breeder feed (or its equivalent) that is appropriate for the test species.*

Parameter	Details	Remarks *Criteria*
Preparation of test diet	The appropriate amount of test substance was combined with acetone and corn oil, then combined with a portion of the basal ration and mixed using a Hobart mixer for approximately 15 minutes (Appendix II, p. 41). Additional feed was added, and the treated feed was mixed another 10 minutes. Separate pre-mixes were prepared for each concentration level approximately every 3-4 weeks, and were stored frozen until needed. Final diets were prepared weekly and presented to the birds on Friday of each week. The pre-mixes were combined with additional basal ration and limestone and mixed for approximately 20 minutes in a Patterson-Kelly Twin Shell blender prior to offering.	It was not specified if the acetone was allowed to completely evaporate from the treated feed prior to offering. *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.*
Indicate whether stability and homogeneity of test material in diet determined (Yes/No)	Yes	
Were concentrations in diet verified by chemical analysis?	Yes	Samples were analyzed from feed prepared during Weeks 1, 5, 10, 15, and 20 (Table 5 of Appendix XIII, p. 185).

Parameter	Details	Remarks *Criteria*
Did chemical analysis confirm that diet was stable? and homogeneous?	Yes Yes	The stability of JAU 6476 - Desthio in the treated feed was assessed at each test concentration level under actual use conditions. Samples of treated feed were collected from the feed troughs on Days 0 and 7 of Week 1 (p. 16). Recoveries were 75-80% of initial values, indicating that slight degradation occurred during the 7-day period (Table 6 of Appendix XIII, p. 186). The homogeneity of JAU 6476 - Desthio was assessed in the treated feed prepared at 60 and 500 ppm; one sample per side was collected from the top, middle, and bottom of each batch. Coefficients of Variation among the six locations were 2.34 and 3.66%, respectively (Table 4 of Appendix XIII, p. 184).
Feeding and husbandry	Feeding and husbandry conditions appeared to be adequate, given guideline recommendations.	
Test conditions (pre-laying) temperature: relative humidity: photo-period:	 22.1 ± 1.1°C 51 ± 27% 8 hr light/day up through Week 8; 17 hr light/day thereafter.	Light intensity averaged 261 lux (approximately 24 foot candles). Illumination was provided by fluorescent lights which closely approximated noon-day sunlight. *EPA Requires* *Temperature:* *About 21 °C (70 °F)* *Relative humidity:* *About 55%* *Lighting* *First 8 weeks: 7 h per day.* *Thereafter: 16-17 h per day.* *At least 6 foot candles at bird level.*

Parameter	Details	Remarks *Criteria*
Egg Collection and Incubation		
Egg collection and storage collection interval: storage temperature: storage humidity:	Daily 13.3 ± 0.2°C 72 ± 9%	To prevent pathogen contamination, the collected eggs were washed in a commercial egg washer with a chlorine-based detergent at 45°C for approximately 3 minutes (p. 20). The washed eggs were allowed to cool to approximately room temperature and rinsed with fresh water prior to storage. *EPA requires eggs to be collected daily; egg storage temperature approximately 16°C (61°F); humidity approximately 65%.*
Were eggs candled for cracks prior to setting for incubation?	Yes	*EPA requires eggs to be candled on day 0*
Were eggs set weekly?	Yes	
Incubation conditions temperature: humidity:	 37.5 ± 0.0°C Approximately 60%	
When candling was done for fertility?	Days 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 24	*EPA requires:* *Bobwhite: day 21* *Mallard: day 23*
Hatching conditions temperature: humidity: photo-period:	 37.2 ± 0.3°C Approximately 77% 16 hours light/day (hatchlings)	*EPA requires:* *temperature of 39°C (102°F)* *humidity of 70%*

Parameter	Details	Remarks *Criteria*
Day the hatched eggs were removed and counted	Days 27 or 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 at least 1 week.	
Egg shell thickness no. of eggs used:	One egg was collected (when available) from each odd numbered cage during odd numbered weeks and from each even numbered cage during the even numbered weeks.	*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.*
intervals:	Once weekly throughout the egg laying period.	
mode of measurement:	Five points around the equatorial circumference were measured to the nearest 0.002 mm.	
Reference chemical, if used	None used	

2. Observations:

Table 3: Observations.

Parameter	Details	Remarks/Criteria
Parameters measured		
Parental: (mortality, body weight, mean feed consumption)	- mortality - body weight - food consumption - signs of toxicity - necropsy	
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)	- eggs laid - eggs cracked - eggshell thickness - eggs set - viable embryos - live 3-week embryos - number of 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 were recorded at the start of acclimation, at Weeks 0, 2, 4, 6, 8 and at test termination (Week 20). Parental food consumption was determined weekly.	*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 (p. 24).

Table 4: Effect of JAU 6476 - Desthio (Prothioconazole - Desthio) on Mortality of *Anas platyrhynchos*.

Treatment, ppm a.i. measured (and nominal) concentrations	Observation Period					
	Week 7		Week 14		Week 20	
	No. Dead		No. Dead		No. Dead	
	Male	Female	Male	Female	Male	Female
Control	0	0	0	0	0	0
56.7 (60)	0	0	0	0	0	0
120 (120)	0	0	0	0	0	0
499 (500)	0	0	0	0	0	0

B. REPRODUCTIVE AND OTHER ENDPOINTS:

Abnormal Effects/Behavior: No overt signs of toxicity were observed (p. 24). Incidental clinical observations normally associated with pen wear or interactions among pen-mates were observed and included foot and head lesions, feather loss, and ocular injury. In addition, lameness was also observed. Raw data pertaining to clinical effects observed in parental Mallard were not provided.

Food Consumption: No apparent treatment-related effects on food consumption were observed (p. 24 and Table 2, p. 30). A statistically-significant increase in feed consumption was observed at the 60 ppm level during Week 16; however, the difference was not considered to be related to treatment since it was neither consistent over time nor concentration responsive. Overall feed consumption averaged 147.8 g/bird/day for the control group, and 155.0, 149.0, and 137.5 g/bird/day for the 60, 120, and 500 ppm test groups, respectively (reviewer-calculated).

Body Weight: No apparent treatment-related effects on body weight were observed (p. 24 and Table 1, p. 27).

Necropsy: All necropsy findings were considered incidental to treatment (p. 24 and Table 8, p. 39).

Reproductive Effects: No treatment-related effects were observed on egg production or quality, fertility, embryonic development, hatchability, or survival of hatchlings (Tables 3-5, pp. 32, 34, and 36).

The health of the hatchlings during the 14-day maintenance period was not addressed. No treatment-related effects on hatchling or 14-day old chick body weights were observed (Table 6, p. 37).

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

Parameter	Control	60 ppm	120ppm	500 ppm	NOAEC/ LOAEC
Eggs laid	671	709	829	773	N/A
Eggs laid/hen	42	44	52	48	N/A
Eggs laid/hen/day	0.51	0.53	0.62	0.58	N/A
Eggs laid/maximum laid (%)	63	66	78	72	500 ppm >500 ppm
Eggs cracked	12	16	12	10	N/A
Eggs cracked/eggs laid (%)	3	3	1	1	500 ppm >500 ppm
Shell thickness (mm ± SD)	0.387 ± 0.019	0.383 ± 0.022	0.375 ± 0.017	0.389 ± 0.018	500 ppm >500 ppm
Eggs set	589	626	737	695	N/A
Viable embryos	486	582	684	651	N/A
Viable embryos/eggs set (%)	82	93	93	93	500 ppm >500 ppm
Live 3-week embryos	484	576	680	640	N/A
Live 3-week embryos/viable embryos (%)	100	99	99	98	500 ppm >500 ppm
No. of hatchlings	440	495	576	525	N/A
No. of hatchlings/live 3-week embryos (%)	91	84	85	79	500 ppm >500 ppm
No. of hatchlings/eggs set (%)	74	78	79	73	500 ppm >500 ppm
Hatchling weight (g)	39	38	38	39	500 ppm >500 ppm
No. of 14-day old survivors	437	488	571	523	N/A
No. of 14-day old survivors/hen	27	31	36	33	N/A
No. of 14-day old survivors/No. of hatchlings (%)	100	98	99	100	500 ppm >500 ppm
No. of 14-day old survivors/eggs set (%)	74	77	78	73	500 ppm >500 ppm

Parameter	Control	60 ppm	120ppm	500 ppm	NOAEC/ LOAEC
14-day old survivors weight (g)	297	308	303	296	500 ppm >500 ppm
Mean adult food consumption (g/pen/day)[1]	147.8	155.0	149.0	137.5	500 ppm >500 ppm
Weight of adult males, g ± SD at start of treatment: at Week 8: at Week 20 (study termination):	 1125 ± 111 1144 ± 101 1175 ± 111	 1115 ± 71 1156 ± 90 1201 ± 102	 1139 ± 101 1154 ± 117 1196 ± 100	 1104 ± 72 1135 ± 97 1187 ± 99	500 ppm >500 ppm
Weight of adult females, g at start of treatment: at Week 8: at Week 20 (study termination):	 1054 ± 105 1058 ± 111 1183 ± 122	 1014 ± 87 1056 ± 88 1212 ± 131	 1038 ± 85 1076 ± 106 1243 ± 120	 1033 ± 83 1042 ± 94 1175 ± 98	500 ppm >500 ppm
Gross pathology (pathological incidents at study termination)	22/32	20/32	18/32	12/32	500 ppm >500 ppm

N/A = Not statistically-analyzed.
[1] Reviewer-calculated from mean weekly data provided in Table 2, p. 30.

C. REPORTED STATISTICS:

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

An analysis of variance (ANOVA) was performed to determine statistically-significant differences between groups. Dunnett's multiple comparison procedure was then used to compare the treatment means with the control group mean. Sample units were the individual pens within each experimental group, except adult body weights, where the sample unit was the individual bird. Percentage data were examined using Dunnett's method following arcsine square root transformation. Nominal concentrations were used for all estimations.

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 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 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 Jonckheere's tests. Data for dead birds were excluded from the analyses. 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 (mean-measured concentrations; reviewer-reported).

Parameter	Control	56.7ppm	120 ppm	499 ppm	NOAEC/ LOAEC
Eggs laid/pen	41.9	44.3	51.8	48.3	499 ppm >449 ppm
Eggs cracked/pen	0.75	1.00	0.75	0.63	499 ppm >449 ppm
Eggs not cracked/eggs laid (%)	96.5	97.5	98.6	98.7	499 ppm >449 ppm
Eggs set/pen	36.8	39.1	46.1	43.4	499 ppm >449 ppm
Shell thickness	0.39	0.38	0.38	0.39	499 ppm >449 ppm
Eggs set/eggs laid (%)	84.5	87.7	88.6	89.9	499 ppm >449 ppm
Viable embryo/pen	30.4	36.4	42.8	40.7	499 ppm >449 ppm
Viable embryos/eggs set (%)	82.3	93.3	93.0	93.1	499 ppm >449 ppm
Live embryos/pen	30.2	36.0	42.5	40.0	499 ppm >449 ppm
Live embryo/viable embryo (%)	99.7	99.0	99.3	98.2	499 ppm >449 ppm
No. of hatchlings/pen	27.5	30.9	36.0	32.8	499 ppm >449 ppm
No. of hatchlings/eggs laid (%)	62.1	68.2	69.6	66.0	499 ppm >449 ppm
No. of hatchlings/eggs set (%)	74.3	77.9	78.6	73.5	499 ppm >449 ppm
No. of hatchlings/live embryos (%)	90.9	84.3	84.6	79.5	499 ppm >449 ppm

Parameter	Control	56.7ppm	120 ppm	499 ppm	NOAEC/ LOAEC
Hatchling survival/pen	27.3	30.5	35.7	32.7	499 ppm >449 ppm
Hatchling survival/eggs set (%)	73.9	76.5	77.9	73.2	499 ppm >449 ppm
Hatchling survival/no. of hatchlings (%)	99.5	98.2	99.0	99.6	499 ppm >449 ppm
Hatchling weight (g)	38.9	37.9	38.4	38.9	499 ppm >449 ppm
Survivor weight (g)	296.6	307.6	303.4	295.6	499 ppm >449 ppm
Mean food consumption (g/bird/day)	147.9	155.1	149.1	169.1	499 ppm >449 ppm
Male weight gain (g)	50.5	86.4	57.2	82.7	499 ppm >449 ppm
Female weight gain (g)	128.3	197.7	205.2	141.6	499 ppm >449 ppm

E. STUDY DEFICIENCIES:

This study is considered scientifically valid, and the deficiencies listed were generally considered minor by the reviewer. However, based on storage stability data, the test material degraded slightly (20-25%) in the treated feed during 7 days of open feeder storage (the same length of time the feed remained in the trough between renewals). Therefore, this study does not fulfill guideline requirements for the reproductive toxicity of JAU 6476 - Desthio (prothioconazole - desthio) to the Mallard duck (§71-4b) and is classified SUPPLEMENTAL. The ambient stability data was used to modify the mean-measured concentrations to reflect the apparent degradation.

F. REVIEWER'S COMMENTS:

Results of the reviewer's statistical analyses were similar to those of the study authors; no statistically significant differences were detected for any measured parameters.

Mean-measured concentrations of JAU 6476 - Desthio in feed were modified to account for results seen in the ambient stability study. The mean percent of day 0 concentrations were 77, 75, and 80% for day 7 measured concentrations for the 60, 120, and 500 ppm a.i. nominal exposure concentrations, respectively. The modified, mean-measured exposure concentrations were determined by taking the mean of the day 0 exposure concentrations and the day 0 X mean percent of day 0 values. The modified, mean-measured exposure concentrations were 50.2, 105, and 449 ppm a.i., which correspond to the nominal 60, 120, and 500 ppm a.i.

Raw data pertaining to the nature and incidence of clinical effects (parental and hatchling) should have been

provided, and the incidence of effects should have been statistically analyzed.

Validation of the samples was conducted concurrently with the analytical portion of the study (Appendix XIII, pp. 179-193). Mean recoveries of JAU 6476 - Desthio from matrix spike samples fortified at 20, 100, or 600 ppm averaged 97-101% of nominal concentrations (Table 3 of Appendix XIII, pp. 182-183). The analytical LOD and LOQ were 6.0 and 20 ppm a.i., respectively (p. 17).

G. CONCLUSIONS:

This study is scientifically sound, but does not fulfill guideline requirements since stability experiments indicated that the test substance may have degraded slightly (approximately 20-25%) during the duration of open feeder storage (7 days). This study is therefore classified as SUPPLEMENTAL. As degradation of the test material likely occurred, this study is not upgradable, however, does not need to be repeated.

NOAEC: 449 ppm a.i.
LOAEC: >449 ppm a.i.
Endpoint(s) Affected: None
Most sensitive endpoints: None

III. REFERENCES:

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APPENDIX I. OUTPUT OF REVIEWER'S STATISTICAL VERIFICATION:

Mallard repro, Prothioconazole, MRID 46246045
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	41	1	97.56	34	82.93	30	88.24	30	100.00	28	68.29	82.35
2	Ctrl	13	5	61.54	4	30.77	4	100.00	4	100.00	4	30.77	100.00
3	Ctrl	28	0	100.00	23	82.14	0	0.00	0	.	0	0.00	0.00
4	Ctrl	44	0	100.00	37	84.09	34	91.89	34	100.00	28	63.64	75.68
5	Ctrl	54	0	100.00	50	92.59	47	94.00	47	100.00	42	77.78	84.00
6	Ctrl	46	1	97.83	41	89.13	38	92.68	38	100.00	32	69.57	78.05
7	Ctrl	17	0	100.00	15	88.24	13	86.67	13	100.00	10	58.82	66.67
8	Ctrl	40	0	100.00	35	87.50	31	88.57	31	100.00	26	65.00	74.29
9	Ctrl	60	0	100.00	56	93.33	55	98.21	54	98.18	51	85.00	91.07
10	Ctrl	47	1	97.87	41	87.23	40	97.56	39	97.50	36	76.60	87.80
11	Ctrl	66	1	98.48	60	90.91	14	23.33	14	100.00	14	21.21	23.33
12	Ctrl	59	0	100.00	54	91.53	46	85.19	46	100.00	44	74.58	81.48
13	Ctrl	45	2	95.56	39	86.67	36	92.31	36	100.00	33	73.33	84.62
14	Ctrl	61	0	100.00	56	91.80	55	98.21	55	100.00	49	80.33	87.50
15	Ctrl	0	0	.	0	.	0	.	0	.	0	.	.
16	Ctrl	50	1	98.00	44	88.00	43	97.73	43	100.00	43	86.00	97.73
17	Dose1	40	1	97.50	36	90.00	36	100.00	35	97.22	26	65.00	72.22
18	Dose1	47	0	100.00	42	89.36	42	100.00	42	100.00	36	76.60	85.71
19	Dose1	51	1	98.04	46	90.20	28	60.87	27	96.43	23	45.10	50.00
20	Dose1	56	1	98.21	50	89.29	47	94.00	46	97.87	44	78.57	88.00
21	Dose1	52	2	96.15	46	88.46	44	95.65	43	97.73	43	82.69	93.48
22	Dose1	49	1	97.96	43	87.76	41	95.35	41	100.00	39	79.59	90.70
23	Dose1	65	1	98.46	59	90.77	56	94.92	56	100.00	44	67.69	74.58
24	Dose1	58	4	93.10	49	84.48	46	93.88	46	100.00	46	79.31	93.88
25	Dose1	30	0	100.00	26	86.67	24	92.31	24	100.00	9	30.00	34.62
26	Dose1	26	3	88.46	20	76.92	18	90.00	18	100.00	16	61.54	80.00
27	Dose1	32	1	96.88	26	81.25	26	100.00	26	100.00	22	68.75	84.62
28	Dose1	56	0	100.00	51	91.07	49	96.08	49	100.00	47	83.93	92.16
29	Dose1	60	0	100.00	55	91.67	49	89.09	48	97.96	41	68.33	74.55
30	Dose1	43	0	100.00	38	88.37	38	100.00	38	100.00	32	74.42	84.21
31	Dose1	44	1	97.73	39	88.64	38	97.44	37	97.37	27	61.36	69.23
32	Dose1	0	0	.	0	.	0	.	0	.	0	.	.
33	Dose2	65	0	100.00	59	90.77	56	94.92	56	100.00	44	67.69	74.58
34	Dose2	67	1	98.51	60	89.55	60	100.00	60	100.00	55	82.09	91.67
35	Dose2	59	2	96.61	52	88.14	36	69.23	36	100.00	17	28.81	32.69
36	Dose2	50	0	100.00	44	88.00	43	97.73	42	97.67	36	72.00	81.82
37	Dose2	54	0	100.00	50	92.59	36	72.00	36	100.00	34	62.96	68.00
38	Dose2	40	1	97.50	34	85.00	32	94.12	31	96.88	21	52.50	61.76
39	Dose2	52	1	98.08	47	90.38	40	85.11	40	100.00	38	73.08	80.85
40	Dose2	42	0	100.00	38	90.48	37	97.37	37	100.00	31	73.81	81.58
41	Dose2	46	0	100.00	42	91.30	40	95.24	40	100.00	32	69.57	76.19
42	Dose2	62	0	100.00	57	91.94	57	100.00	57	100.00	57	91.94	100.00
43	Dose2	33	0	100.00	28	84.85	27	96.43	26	96.30	26	78.79	92.86
44	Dose2	54	1	98.15	47	87.04	46	97.87	46	100.00	45	83.33	95.74
45	Dose2	47	3	93.62	40	85.11	38	95.00	38	100.00	36	76.60	90.00
46	Dose2	53	2	96.23	46	86.79	44	95.65	43	97.73	33	62.26	71.74
47	Dose2	59	1	98.31	54	91.53	54	100.00	54	100.00	34	57.63	62.96
48	Dose2	46	0	100.00	39	84.78	38	97.44	38	100.00	37	80.43	94.87
49	Dose3	50	1	98.00	43	86.00	42	97.67	42	100.00	38	76.00	88.37
50	Dose3	60	0	100.00	55	91.67	55	100.00	55	100.00	50	83.33	90.91
51	Dose3	34	0	100.00	31	91.18	30	96.77	26	86.67	8	23.53	25.81
52	Dose3	44	1	97.73	39	88.64	39	100.00	38	97.44	36	81.82	92.31
53	Dose3	51	0	100.00	47	92.16	45	95.74	45	100.00	42	82.35	89.36
54	Dose3	53	1	98.11	47	88.68	46	97.87	42	91.30	30	56.60	63.83
55	Dose3	52	1	98.08	46	88.46	45	97.83	45	100.00	42	80.77	91.30
56	Dose3	40	0	100.00	36	90.00	33	91.67	32	96.97	30	75.00	83.33
57	Dose3	60	0	100.00	56	93.33	42	75.00	42	100.00	34	56.67	60.71
58	Dose3	50	1	98.00	45	90.00	44	97.78	44	100.00	37	74.00	82.22

59	Dose3	27	0	100.00	25	92.59	15	60.00	15	100.00	8	29.63	32.00
60	Dose3	43	1	97.67	38	88.37	37	97.37	37	100.00	32	74.42	84.21
61	Dose3	55	1	98.18	50	90.91	49	98.00	49	100.00	36	65.45	72.00
62	Dose3	52	1	98.08	47	90.38	43	91.49	43	100.00	33	63.46	70.21
63	Dose3	60	1	98.33	54	90.00	50	92.59	49	98.00	45	75.00	83.33
64	Dose3	42	1	97.62	36	85.71	36	100.00	36	100.00	24	57.14	66.67

Mallard repro, Prothioconazole, MRID 46246045
PRINTOUT OF RAW DATA (continued)

Obs	TRT	NH_LE	HS	HS_ES	HS_NH	THICK	HATWT	SURVWT	FOOD	WTGAINM	WTGAINF
1	Ctrl	93.33	28	82.35	100.00	0.39	37	291	122	-19	267
2	Ctrl	100.00	4	100.00	100.00	0.35	35	250	138	164	156
3	Ctrl	.	0	0.00	.	0.38	.	.	127	238	48
4	Ctrl	82.35	28	75.68	100.00	0.40	38	307	171	79	40
5	Ctrl	89.36	41	82.00	97.62	0.36	39	336	165	82	112
6	Ctrl	84.21	32	78.05	100.00	0.39	39	280	182	-79	109
7	Ctrl	76.92	10	66.67	100.00	0.39	39	236	93	68	172
8	Ctrl	83.87	26	74.29	100.00	0.43	41	317	166	10	180
9	Ctrl	94.44	50	89.29	98.04	0.41	42	329	225	8	125
10	Ctrl	92.31	36	87.80	100.00	0.38	38	315	140	25	195
11	Ctrl	100.00	14	23.33	100.00	0.39	41	290	146	0	85
12	Ctrl	95.65	44	81.48	100.00	0.40	38	325	130	61	240
13	Ctrl	91.67	33	84.62	100.00	0.38	38	255	123	-2	87
14	Ctrl	89.09	49	87.50	100.00	0.39	42	294	108	4	-6
15	Ctrl	.	0	.	.	.	.	.	141	62	96
16	Ctrl	100.00	42	95.45	97.67	0.36	37	328	189	107	147
17	Dose1	74.29	26	72.22	100.00	0.38	41	312	146	56	223
18	Dose1	85.71	35	83.33	97.22	0.40	35	343	145	146	63
19	Dose1	85.19	22	47.83	95.65	0.36	37	267	122	122	117
20	Dose1	95.65	44	88.00	100.00	0.35	35	300	176	-32	489
21	Dose1	100.00	42	91.30	97.67	0.38	39	294	163	-23	153
22	Dose1	95.12	39	90.70	100.00	0.39	37	336	128	57	275
23	Dose1	78.57	43	72.88	97.73	0.37	38	302	228	55	262
24	Dose1	100.00	46	93.88	100.00	0.38	40	344	185	-8	167
25	Dose1	37.50	9	34.62	100.00	0.39	34	275	198	66	189
26	Dose1	88.89	14	70.00	87.50	0.43	39	312	147	180	124
27	Dose1	84.62	22	84.62	100.00	0.34	43	314	119	89	232
28	Dose1	95.92	47	92.16	100.00	0.40	43	331	142	47	320
29	Dose1	85.42	41	74.55	100.00	0.38	34	279	143	125	69
30	Dose1	84.21	31	81.58	96.88	0.41	35	307	168	305	77
31	Dose1	72.97	27	69.23	100.00	0.38	39	298	166	189	165
32	Dose1	.	0	.	.	.	.	.	107	9	238
33	Dose2	78.57	43	72.88	97.73	0.42	39	333	125	75	106
34	Dose2	91.67	55	91.67	100.00	0.37	37	294	144	150	273
35	Dose2	47.22	17	32.69	100.00	0.36	34	243	106	22	139
36	Dose2	85.71	36	81.82	100.00	0.38	40	310	157	48	199
37	Dose2	94.44	33	66.00	97.06	0.37	41	333	195	156	251
38	Dose2	67.74	21	61.76	100.00	0.36	32	255	151	-73	243
39	Dose2	95.00	38	80.85	100.00	0.38	39	324	141	-90	320
40	Dose2	83.78	31	81.58	100.00	0.38	40	304	169	80	253
41	Dose2	80.00	31	73.81	96.88	0.36	40	273	118	81	161
42	Dose2	100.00	57	100.00	100.00	0.36	36	290	150	155	318
43	Dose2	100.00	25	89.29	96.15	0.38	40	308	140	22	93
44	Dose2	97.83	45	95.74	100.00	0.40	39	319	158	104	235
45	Dose2	94.74	36	90.00	100.00	0.36	40	306	173	150	297
46	Dose2	76.74	33	71.74	100.00	0.38	36	302	157	60	133
47	Dose2	62.96	33	61.11	97.06	0.38	38	301	159	-36	261
48	Dose2	97.37	37	94.87	100.00	0.38	44	360	143	12	2
49	Dose3	90.48	38	88.37	100.00	0.38	37	245	167	80	118
50	Dose3	90.91	50	90.91	100.00	0.39	40	345	213	28	265
51	Dose3	30.77	8	25.81	100.00	0.40	37	230	140	90	294
52	Dose3	94.74	35	89.74	97.22	0.38	41	314	245	203	215
53	Dose3	93.33	42	89.36	100.00	0.38	39	308	180	39	43

54	Dose3	71.43	29	61.70	96.67	0.37	42	290	196	190	22
55	Dose3	93.33	42	91.30	100.00	0.38	40	324	168	-73	34
56	Dose3	93.75	30	83.33	100.00	0.35	37	284	122	47	93
57	Dose3	80.95	34	60.71	100.00	0.40	40	282	142	110	190
58	Dose3	84.09	37	82.22	100.00	0.40	35	282	151	167	119
59	Dose3	53.33	8	32.00	100.00	0.39	38	287	163	76	205
60	Dose3	86.49	32	84.21	100.00	0.41	40	307	130	-9	151
61	Dose3	73.47	36	72.00	100.00	0.42	36	329	194	159	130
62	Dose3	76.74	33	70.21	100.00	0.42	41	296	150	61	176
63	Dose3	91.84	45	83.33	100.00	0.38	41	316	179	34	117
64	Dose3	66.67	24	66.67	100.00	0.39	38	291	165	121	94

Mallard repro, Prothioconazole, MRID 46246045
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
0.934	0.002	2.315	0.085	USE NON-PARAMETRIC TESTS

****
BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	16	41.94	18.70	4.67	44.58	31.98, 51.90
Dose1	16	44.31	16.21	4.05	36.59	35.67, 52.95
Dose2	16	51.81	9.33	2.33	18.01	46.84, 56.79
Dose3	16	48.31	9.42	2.36	19.50	43.29, 53.33

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	45.50	0.00	66.00	.	.
Dose1	48.00	0.00	65.00	105.66	-5.66
Dose2	52.50	33.00	67.00	123.55	-23.55
Dose3	50.50	27.00	60.00	115.20	-15.20

****
NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	2.79	0.424

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	45.50	.	.
Dose1	48.00	1.000	0.597
Dose2	52.50	1.000	0.935
Dose3	50.50	1.000	0.859

SUMMARY	NOAEC	LOAEC
MannWhit (Bonf adjust)	Dose3	>highest dose
Jonckheere	Dose3	>highest dose

Mallard repro, Prothioconazole, MRID 46246045
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
0.791	<.001	0.878	0.458	USE NON-PARAMETRIC TESTS

****
BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	16	0.75	1.29	0.32	172.13	0.06, 1.44
Dose1	16	1.00	1.15	0.29	115.47	0.38, 1.62
Dose2	16	0.75	0.93	0.23	124.13	0.25, 1.25
Dose3	16	0.63	0.50	0.13	80.00	0.36, 0.89

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	0.00	0.00	5.00	.	.
Dose1	1.00	0.00	4.00	133.33	-33.33
Dose2	0.50	0.00	3.00	100.00	0.00
Dose3	1.00	0.00	1.00	83.33	16.67

****
NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	1.13	0.770

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	0.00	.	.
Dose1	1.00	0.514	0.163
Dose2	0.50	1.000	0.352
Dose3	1.00	0.858	0.404

SUMMARY	NOAEC	LOAEC
MannWhit (Bonf adjust)	Dose3	>highest dose
Jonckheere	Dose3	>highest dose

Mallard repro, Prothioconazole, MRID 46246045
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
0.453	<.001	2.391	0.078	USE NON-PARAMETRIC TESTS

****
BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf. Interval
Ctrl	15	96.46	9.75	2.52	10.11	91.05, 100.00
Dose1	15	97.50	3.12	0.81	3.20	95.77, 99.23
Dose2	16	98.56	1.86	0.46	1.89	97.57, 99.55
Dose3	16	98.74	1.03	0.26	1.04	98.19, 99.28

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	100.00	61.54	100.00	.	.
Dose1	98.04	88.46	100.00	101.08	-1.08
Dose2	99.25	93.62	100.00	102.18	-2.18
Dose3	98.15	97.62	100.00	102.37	-2.37

****
NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	1.79	0.618

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	100.00	.	.
Dose1	98.04	0.492	0.155
Dose2	99.25	1.000	0.534
Dose3	98.15	1.000	0.586

SUMMARY	NOAEC	LOAEC
MannWhit (Bonf adjust)	Dose3	>highest dose
Jonckheere	Dose3	>highest dose

Mallard repro, Prothioconazole, MRID 46246045
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
0.946	0.007	2.481	0.070	USE NON-PARAMETRIC TESTS

****

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf. Interval
Ctrl	16	36.81	18.16	4.54	49.32	27.14, 46.49
Dose1	16	39.13	15.00	3.75	38.33	31.13, 47.12
Dose2	16	46.06	9.10	2.27	19.75	41.22, 50.91
Dose3	16	43.44	8.75	2.19	20.14	38.78, 48.10

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	40.00	0.00	60.00	.	.
Dose1	42.50	0.00	59.00	106.28	-6.28
Dose2	46.50	28.00	60.00	125.13	-25.13
Dose3	45.50	25.00	56.00	118.00	-18.00

****

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	2.79	0.425

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	40.00	.	.
Dose1	42.50	1.000	0.626
Dose2	46.50	1.000	0.937
Dose3	45.50	1.000	0.881

SUMMARY	NOAEC	LOAEC
MannWhit (Bonf adjust)	Dose3	>highest dose
Jonckheere	Dose3	>highest dose

Mallard repro, Prothioconazole, MRID 46246045
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
0.498	<.001	2.656	0.057	USE NON-PARAMETRIC TESTS

****

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.	Interval
Ctrl	15	84.46	15.24	3.93	18.04	76.02,	92.90
Dose1	15	87.66	4.00	1.03	4.57	85.44,	89.88
Dose2	16	88.64	2.77	0.69	3.13	87.16,	90.12
Dose3	16	89.88	2.17	0.54	2.41	88.73,	91.03

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	88.00	30.77	93.33	.	.
Dose1	88.64	76.92	91.67	103.79	-3.79
Dose2	88.84	84.78	92.59	104.95	-4.95
Dose3	90.00	85.71	93.33	106.42	-6.42

****

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	3.73	0.293

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	88.00	.	.
Dose1	88.64	1.000	0.582
Dose2	88.84	1.000	0.727
Dose3	90.00	1.000	0.966

SUMMARY	NOAEC	LOAEC
MannWhit (Bonf adjust)	Dose3	>highest dose
Jonckheere	Dose3	>highest dose

Mallard repro, Prothioconazole, MRID 46246045
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
0.964	0.059	3.748	0.016	USE NON-PARAMETRIC TESTS

****

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	16	30.38	18.62	4.65	61.30	20.45, 40.30
Dose1	16	36.38	14.18	3.55	38.99	28.82, 43.93
Dose2	16	42.75	9.53	2.38	22.30	37.67, 47.83
Dose3	16	40.69	9.37	2.34	23.03	35.69, 45.68

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	35.00	0.00	55.00	.	.
Dose1	39.50	0.00	56.00	119.75	-19.75
Dose2	40.00	27.00	60.00	140.74	-40.74
Dose3	42.50	15.00	55.00	133.95	-33.95

****

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	4.01	0.260

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	39.50	1.000	0.822
Dose2	40.00	1.000	0.964
Dose3	42.50	1.000	0.968

SUMMARY	NOAEC	LOAEC
MannWhit (Bonf adjust)	Dose3	>highest dose
Jonckheere	Dose3	>highest dose

Mallard repro, Prothioconazole, MRID 46246045
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
0.629	<.001	3.773	0.015	USE NON-PARAMETRIC TESTS

****

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.	Interval
Ctrl	15	82.31	29.37	7.58	35.69	66.04,	98.57
Dose1	15	93.31	9.63	2.49	10.32	87.97,	98.64
Dose2	16	93.01	9.43	2.36	10.14	87.98,	98.03
Dose3	16	93.11	10.71	2.68	11.51	87.40,	98.82

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	92.31	0.00	100.00	.	.
Dose1	95.35	60.87	100.00	113.36	-13.36
Dose2	96.04	69.23	100.00	113.00	-13.00
Dose3	97.52	60.00	100.00	113.13	-13.13

****

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	3.25	0.354

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	92.31	.	.
Dose1	95.35	1.000	0.930
Dose2	96.04	1.000	0.943
Dose3	97.52	1.000	0.963

SUMMARY	NOAEC	LOAEC
MannWhit (Bonf adjust)	Dose3	>highest dose
Jonckheere	Dose3	>highest dose

Mallard repro, Prothioconazole, MRID 46246045
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
0.966	0.078	3.510	0.021	USE NON-PARAMETRIC TESTS

****

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf. Interval
Ctrl	16	30.25	18.50	4.62	61.15	20.39, 40.11
Dose1	16	36.00	14.08	3.52	39.11	28.50, 43.50
Dose2	16	42.50	9.72	2.43	22.86	37.32, 47.68
Dose3	16	40.00	9.62	2.40	24.05	34.87, 45.13

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	35.00	0.00	55.00	.	.
Dose1	39.50	0.00	56.00	119.01	-19.01
Dose2	40.00	26.00	60.00	140.50	-40.50
Dose3	42.00	15.00	55.00	132.23	-32.23

****

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	3.82	0.281

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	39.50	1.000	0.797
Dose2	40.00	1.000	0.963
Dose3	42.00	1.000	0.963

SUMMARY	NOAEC	LOAEC
MannWhit (Bonf adjust)	Dose3	>highest dose
Jonckheere	Dose3	>highest dose

Mallard repro, Prothioconazole, MRID 46246045
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 Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
0.683	<.001	4.968	0.004	USE NON-PARAMETRIC TESTS

****
BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	14	99.69	0.80	0.21	0.80	99.23, 100.00
Dose1	15	98.97	1.35	0.35	1.36	98.23, 99.72
Dose2	16	99.29	1.31	0.33	1.32	98.59, 99.99
Dose3	16	98.15	3.81	0.95	3.89	96.12, 100.00

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	100.00	97.50	100.00	.	.
Dose1	100.00	96.43	100.00	99.28	0.72
Dose2	100.00	96.30	100.00	99.59	0.41
Dose3	100.00	86.67	100.00	98.45	1.55

****
NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	2.71	0.439

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	100.00	.	.
Dose1	100.00	1.000	0.048
Dose2	100.00	1.000	0.207
Dose3	100.00	1.000	0.172

SUMMARY	NOAEC	LOAEC
MannWhit (Bonf adjust)	Dose3	>highest dose
Jonckheere	Dose3	>highest dose

Mallard repro, Prothioconazole, MRID 46246045
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
0.962	0.049	2.243	0.092	USE PARAMETRIC TESTS

****
BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	16	27.50	17.16	4.29	62.39	18.36, 36.64
Dose1	16	30.94	14.16	3.54	45.78	23.39, 38.48
Dose2	16	36.00	10.63	2.66	29.54	30.33, 41.67
Dose3	16	32.81	11.56	2.89	35.23	26.65, 38.97

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	30.00	0.00	51.00	.	.
Dose1	34.00	0.00	47.00	112.50	-12.50
Dose2	35.00	17.00	57.00	130.91	-30.91
Dose3	35.00	8.00	50.00	119.32	-19.32

****
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
3	60	1.09	0.360

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 NOAEC or LOAEC

Level	Mean	Dunnett p-value	Isotonic mean	Williams p-value	Tukey p-values Dose1	Dose2	Dose3	Dose4	Dose5
Ctrl	27.50	.	31.81	.	0.891	0.300	0.689	.	.
Dose1	30.94	0.932	31.81	0.884	.	0.720	0.980	.	.
Dose2	36.00	0.996	31.81	0.908	.	.	0.911	.	.
Dose3	32.81	0.973	31.81	0.920	.	.	.	.	.

SUMMARY	NOAEC	LOAEC
Dunnett	Dose3	>highest dose
Williams	Dose3	>highest dose

Mallard repro, Prothioconazole, MRID 46246045
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
0.857	<.001	1.388	0.255	USE NON-PARAMETRIC TESTS

****

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf. Interval
Ctrl	15	62.06	25.06	6.47	40.38	48.18, 75.94
Dose1	15	68.19	14.69	3.79	21.55	60.06, 76.33
Dose2	16	69.59	14.90	3.73	21.41	61.65, 77.53
Dose3	16	65.95	17.93	4.48	27.18	56.40, 75.50

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	69.57	0.00	86.00	.	.
Dose1	68.75	30.00	83.93	109.88	-9.88
Dose2	72.54	28.81	91.94	112.14	-12.14
Dose3	74.21	23.53	83.33	106.27	-6.27

****

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	0.24	0.970

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	69.57	.	.
Dose1	68.75	1.000	0.622
Dose2	72.54	1.000	0.682
Dose3	74.21	1.000	0.557

SUMMARY	NOAEC	LOAEC
MannWhit (Bonf adjust)	Dose3	>highest dose
Jonckheere	Dose3	>highest dose

Mallard repro, Prothioconazole, MRID 46246045
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
0.828	<.001	0.498	0.685	USE NON-PARAMETRIC TESTS

****
BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.	Interval
Ctrl	15	74.30	27.20	7.02	36.60	59.24,	89.37
Dose1	15	77.86	16.69	4.31	21.43	68.62,	87.10
Dose2	16	78.58	17.05	4.26	21.70	69.50,	87.67
Dose3	16	73.54	20.24	5.06	27.52	62.75,	84.32

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	82.35	0.00	100.00	.	.
Dose1	84.21	34.62	93.88	104.79	-4.79
Dose2	81.22	32.69	100.00	105.76	-5.76
Dose3	82.78	25.81	92.31	98.97	1.03

****
NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	0.62	0.892

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	82.35	.	.
Dose1	84.21	1.000	0.550
Dose2	81.22	1.000	0.540
Dose3	82.78	1.000	0.294

SUMMARY	NOAEC	LOAEC
MannWhit (Bonf adjust)	Dose3	>highest dose
Jonckheere	Dose3	>highest dose

Mallard repro, Prothioconazole, MRID 46246045
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
0.853	<.001	1.715	0.174	USE NON-PARAMETRIC TESTS

****

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	14	90.94	7.13	1.90	7.84	86.83, 95.06
Dose1	15	84.27	15.47	3.99	18.36	75.70, 92.84
Dose2	16	84.61	15.15	3.79	17.90	76.54, 92.68
Dose3	16	79.52	17.56	4.39	22.08	70.16, 88.88

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	91.99	76.92	100.00	.	.
Dose1	85.42	37.50	100.00	92.66	7.34
Dose2	88.69	47.22	100.00	93.04	6.96
Dose3	85.29	30.77	94.74	87.44	12.56

****

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	4.26	0.234

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	91.99	.	.
Dose1	85.42	0.469	0.147
Dose2	88.69	0.600	0.174
Dose3	85.29	0.079	0.026

SUMMARY	NOAEC	LOAEC
MannWhit (Bonf adjust)	Dose3	>highest dose
Jonckheere	**Dose2**	**Dose3**

Mallard repro, Prothioconazole, MRID 46246045
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
0.962	0.046	2.093	0.111	USE PARAMETRIC TESTS

****

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.	Interval
Ctrl	16	27.31	16.95	4.24	62.07	18.28,	36.35
Dose1	16	30.50	14.21	3.55	46.58	22.93,	38.07
Dose2	16	35.69	10.71	2.68	30.00	29.98,	41.39
Dose3	16	32.69	11.56	2.89	35.37	26.53,	38.85

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	30.00	0.00	50.00	.	.
Dose1	33.00	0.00	47.00	111.67	-11.67
Dose2	34.50	17.00	57.00	130.66	-30.66
Dose3	34.50	8.00	50.00	119.68	-19.68

****

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
3	60	1.08	0.363

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 NOAEC or LOAEC

Level	Mean	Dunnett p-value	Isotonic mean	Williams p-value	Tukey p-values Dose1	Dose2	Dose3	Dose4	Dose5
Ctrl	27.31	.	31.55	.	0.910	0.310	0.679	.	.
Dose1	30.50	0.924	31.55	0.881	.	0.703	0.968	.	.
Dose2	35.69	0.996	31.55	0.905	.	.	0.924	.	.
Dose3	32.69	0.974	31.55	0.918	.	.	.	.	.

SUMMARY	NOAEC	LOAEC
Dunnett	Dose3	>highest dose
Williams	Dose3	>highest dose

Mallard repro, Prothioconazole, MRID 46246045
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
0.833	<.001	0.424	0.737	USE NON-PARAMETRIC TESTS

****

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.	Interval
Ctrl	15	73.90	26.94	6.96	36.46	58.98,	88.82
Dose1	15	76.46	16.79	4.33	21.96	67.16,	85.76
Dose2	16	77.86	17.14	4.28	22.01	68.73,	87.00
Dose3	16	73.24	20.16	5.04	27.53	62.50,	83.99

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	82.00	0.00	100.00	.	.
Dose1	81.58	34.62	93.88	103.46	-3.46
Dose2	81.22	32.69	100.00	105.36	-5.36
Dose3	82.78	25.81	91.30	99.11	0.89

****

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	0.32	0.955

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	82.00	.	.
Dose1	81.58	1.000	0.450
Dose2	81.22	1.000	0.484
Dose3	82.78	1.000	0.321

SUMMARY	NOAEC	LOAEC
MannWhit (Bonf adjust)	Dose3	>highest dose
Jonckheere	Dose3	>highest dose

Mallard repro, Prothioconazole, MRID 46246045
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
0.686	<.001	4.186	0.010	USE NON-PARAMETRIC TESTS

****

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.	Interval
Ctrl	14	99.52	0.95	0.25	0.96	98.97,	100.00
Dose1	15	98.18	3.31	0.85	3.37	96.34,	100.00
Dose2	16	99.05	1.48	0.37	1.49	98.27,	99.84
Dose3	16	99.62	1.05	0.26	1.05	99.06,	100.00

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	100.00	97.62	100.00	.	.
Dose1	100.00	87.50	100.00	98.65	1.35
Dose2	100.00	96.15	100.00	99.53	0.47
Dose3	100.00	96.67	100.00	100.09	-0.09

****

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	3.75	0.290

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	100.00	.	.
Dose1	100.00	1.000	0.092
Dose2	100.00	1.000	0.223
Dose3	100.00	1.000	0.712

SUMMARY	NOAEC	LOAEC
MannWhit (Bonf adjust)	Dose3	>highest dose
Jonckheere	Dose3	>highest dose

Mallard repro, Prothioconazole, MRID 46246045
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
0.970	0.133	0.201	0.895	USE PARAMETRIC TESTS

****
BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.	Interval
Ctrl	15	0.39	0.02	0.00	4.97	0.38,	0.40
Dose1	15	0.38	0.02	0.01	5.64	0.37,	0.39
Dose2	16	0.38	0.02	0.00	4.46	0.37,	0.38
Dose3	16	0.39	0.02	0.00	4.67	0.38,	0.40

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	0.39	0.35	0.43	.	.
Dose1	0.38	0.34	0.43	98.95	1.05
Dose2	0.38	0.36	0.42	97.05	2.95
Dose3	0.39	0.35	0.42	100.62	-0.62

****
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
3	58	1.62	0.195

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 NOAEC or LOAEC

Level	Mean	Dunnett p-value	Isotonic mean	Williams p-value	Tukey p-values Dose1	Dose2	Dose3	Dose4	Dose5
Ctrl	0.39	.	0.39	.	0.936	0.345	0.985	.	.
Dose1	0.38	0.500	0.38	0.334	.	0.703	0.780	.	.
Dose2	0.38	0.116	0.38	0.326	.	.	0.179	.	.
Dose3	0.39	0.856	0.38	0.338	.	.	.	.	.

SUMMARY	NOAEC	LOAEC
Dunnett	Dose3	>highest dose
Williams	Dose3	>highest dose

Mallard repro, Prothioconazole, MRID 46246045
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 Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
0.985	0.649	1.211	0.314	USE PARAMETRIC TESTS

****
BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	14	38.86	2.03	0.54	5.23	37.68, 40.03
Dose1	15	37.93	3.01	0.78	7.94	36.27, 39.60
Dose2	16	38.44	2.90	0.72	7.54	36.89, 39.98
Dose3	16	38.88	2.06	0.52	5.30	37.78, 39.97

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	38.50	35.00	42.00	.	.
Dose1	38.00	34.00	43.00	97.62	2.38
Dose2	39.00	32.00	44.00	98.92	1.08
Dose3	39.50	35.00	42.00	100.05	-0.05

****
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
3	57	0.46	0.714

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 NOAEC or LOAEC

Level	Mean	Dunnett p-value	Isotonic mean	Williams p-value	Tukey p-values Dose1	Dose2	Dose3	Dose4	Dose5
Ctrl	38.86	.	38.86	.	0.764	0.969	1.000	.	.
Dose1	37.93	0.329	38.43	0.387	.	0.946	0.734	.	.
Dose2	38.44	0.557	38.43	0.410	.	.	0.962	.	.
Dose3	38.88	0.749	38.43	0.425	.	.	.	.	.

SUMMARY	NOAEC	LOAEC
Dunnett	Dose3	>highest dose
Williams	Dose3	>highest dose

Mallard repro, Prothioconazole, MRID 46246045
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
0.968	0.110	0.423	0.737	USE PARAMETRIC TESTS

****
BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	14	296.64	31.85	8.51	10.74	278.25, 315.03
Dose1	15	307.60	23.77	6.14	7.73	294.44, 320.76
Dose2	16	303.44	29.31	7.33	9.66	287.82, 319.06
Dose3	16	295.63	29.32	7.33	9.92	280.00, 311.25

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	300.50	236.00	336.00	.	.
Dose1	307.00	267.00	344.00	103.69	-3.69
Dose2	305.00	243.00	360.00	102.29	-2.29
Dose3	293.50	230.00	345.00	99.66	0.34

****
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
3	57	0.60	0.619

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 NOAEC or LOAEC

Level	Mean	Dunnett p-value	Isotonic mean	Williams p-value	Tukey p-values Dose1	Dose2	Dose3	Dose4	Dose5
Ctrl	296.64	.	302.71	.	0.734	0.916	1.000	.	.
Dose1	307.60	0.965	302.71	0.799	.	0.978	0.653	.	.
Dose2	303.44	0.916	302.71	0.832	.	.	0.867	.	.
Dose3	295.63	0.706	295.63	0.593	.	.	.	.	.

SUMMARY	NOAEC	LOAEC
Dunnett	Dose3	>highest dose
Williams	Dose3	>highest dose

Mallard repro, Prothioconazole, MRID 46246045
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
0.968	0.096	1.062	0.372	USE PARAMETRIC TESTS

****
BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.	Interval
Ctrl	16	147.89	33.47	8.37	22.63	130.06,	165.73
Dose1	16	155.14	31.49	7.87	20.30	138.36,	171.92
Dose2	16	149.11	21.63	5.41	14.51	137.58,	160.63
Dose3	16	169.06	31.97	7.99	18.91	152.03,	186.10

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	140.50	93.00	225.00	.	.
Dose1	146.25	107.00	228.00	104.90	-4.90
Dose2	150.50	106.00	195.00	100.82	-0.82
Dose3	166.00	122.00	245.00	114.32	-14.32

****
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
3	60	1.67	0.182

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 NOAEC or LOAEC

Level	Mean	Dunnett p-value	Isotonic mean	Williams p-value	Tukey p-values Dose1	Dose2	Dose3	Dose4	Dose5
Ctrl	147.89	.	155.30	.	0.903	0.999	0.201	.	.
Dose1	155.14	0.927	155.30	0.836	.	0.941	0.559	.	.
Dose2	149.11	0.790	155.30	0.865	.	.	0.247	.	.
Dose3	169.06	0.998	155.30	0.879	.	.	.	.	.

SUMMARY	NOAEC	LOAEC
Dunnett	Dose3	>highest dose
Williams	Dose3	>highest dose

Mallard repro, Prothioconazole, MRID 46246045
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
0.981	0.443	0.205	0.893	USE PARAMETRIC TESTS

****
BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	16	50.50	76.05	19.01	150.59	9.98, 91.02
Dose1	16	86.44	89.08	22.27	103.05	38.97, 133.90
Dose2	16	57.25	78.34	19.59	136.84	15.50, 99.00
Dose3	16	82.69	74.34	18.59	89.91	43.07, 122.30

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	43.00	-79.00	238.00	.	.
Dose1	61.50	-32.00	305.00	171.16	-71.16
Dose2	67.50	-90.00	156.00	113.37	-13.37
Dose3	78.00	-73.00	203.00	163.74	-63.74

****
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
3	60	0.82	0.490

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 NOAEC or LOAEC

Level	Mean	Dunnett p-value	Isotonic mean	Williams p-value	Tukey p-values Dose1	Dose2	Dose3	Dose4	Dose5
Ctrl	50.50	.	69.22	.	0.582	0.995	0.665	.	.
Dose1	86.44	0.983	69.22	0.827	.	0.729	0.999	.	.
Dose2	57.25	0.828	69.22	0.856	.	.	0.803	.	.
Dose3	82.69	0.976	69.22	0.871	.	.	.	.	.

SUMMARY	NOAEC	LOAEC
Dunnett	Dose3	>highest dose
Williams	Dose3	>highest dose

Mallard repro, Prothioconazole, MRID 46246045
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
0.980	0.379	0.752	0.525	USE PARAMETRIC TESTS

****
BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	16	128.31	72.76	18.19	56.71	89.54, 167.09
Dose1	16	197.69	109.14	27.28	55.21	139.53, 255.84
Dose2	16	205.25	90.94	22.73	44.31	156.79, 253.71
Dose3	16	141.63	78.96	19.74	55.75	99.55, 183.70

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	118.50	-6.00	267.00	.	.
Dose1	178.00	63.00	489.00	154.07	-54.07
Dose2	239.00	2.00	320.00	159.96	-59.96
Dose3	124.50	22.00	294.00	110.38	-10.38

****
PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
Analysis of Variance (ANOVA) - overall F-test

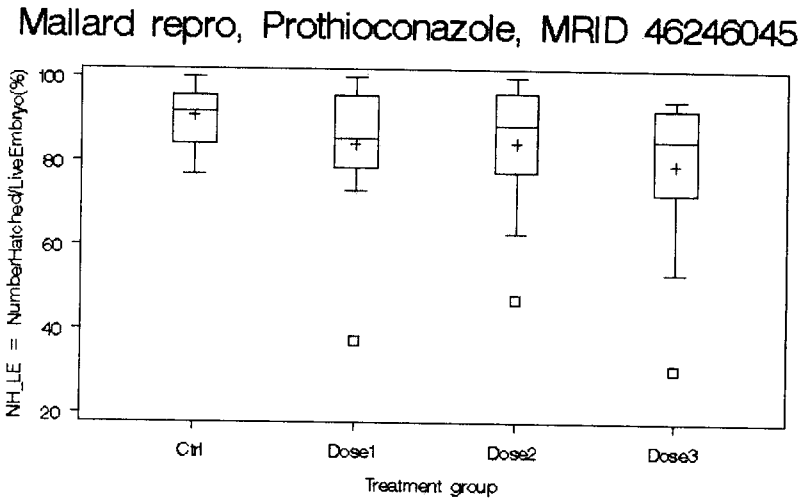
Numerator df	Denominator df	F-stat	P-value
3	60	3.05	0.035

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 NOAEC or LOAEC

Level	Mean	Dunnett p-value	Isotonic mean	Williams p-value	Tukey p-values Dose1	Dose2	Dose3	Dose4	Dose5
Ctrl	128.31	.	177.08	.	0.134	0.080	0.974	.	.
Dose1	197.69	0.999	177.08	0.972	.	0.995	0.292	.	.
Dose2	205.25	1.000	177.08	0.981	.	.	0.192	.	.
Dose3	141.63	0.876	141.63	0.801	.	.	.	.	.

SUMMARY	NOAEC	LOAEC
Dunnett	Dose3	>highest dose
Williams	Dose3	>highest dose

Box Plots:


Mallard repro, Prothioconazole, MRID 46246045
NH_LE = NumberHatched/LiveEmbryo(%)
100
80
60
40
20
Ctrl
Dose1
Dose2
Dose3
Treatment group

EAD Assessment of USEPA DER

Reviewer: Émilie Larivière (#1269); PMRA Date: October 18, 2005

PMRA Submission Number: 2004-0843

Study Type: Avian Reproduction - Bobwhite Quail

Frey, L.T., K. H. Martin, J.B. Beavers and M. Jaber. 2001. Desthio JAU-6476: A Reproduction Study with the Mallard (*Anas platyrhynchos*). Unpublished study performed by Wildlife International, Ltd., Easton, MD. Laboratory No. 149-181. Study submitted by Bayer CropScience, Research Triangle Park, NC. Study initiated August 15, 2000 and completed May 10, 2001.

PMRA DATA CODE: 9.6.3.2
EPA DP Barcode: D303488
OECD Data Point: IIA 8.1.4
EPA MRID: 46246045
EPA Guideline: §71-4b

Reviewing Agency: US EPA

EAD Executive Summary:

The one-generation reproductive toxicity of JAU 6476-desthio (prothioconazole - desthio; purity 96.4%) to groups (16 pens/treatment level) of 1 male and 1 female, 20-week-old mallard duck was assessed over approximately 20 weeks. This study was conducted following procedures of the U.S. EPA Pesticide Assessment Guidelines, §71-4 (1982) and OECD Guideline 206 (1984); and ASTM Standard E1062-86 (1986), and was in compliance with United States, OECD, and Japan MAFF GLP standards, with the following exception: the frequency of measurement of light intensity was not specified in the protocol. JAU 6476-desthio was administered to the birds in the diet nominal concentrations of 0 (solvent control), 60, 120, and 500 ppm. Mean measured concentrations were <6.0 (<LOD, control), 56.7, 120, and 499 mg JAU6476-desthio/kg, respectively. However, stability experiments indicated that the test substance likely degraded slightly (approximately 20-25%) during the duration of open feeder storage (7 days). Taking into account this degradation, the modified, mean-measured concentrations would be 50.2, 105, and 449 mg JAU6476-desthio/kg.

There were no significant treatment-related effects on any adult or offspring parameter. As a result, the NOEC and LOEC levels were 105 and 449 mg JAU6476-desthio/kg, respectively.

Results Synopsis

Test Organism Size/Age: 20 weeks old at test initiation (846-1286 g)

NOEC: 449 mg JAU6476-desthio/kg
LOEC: >449 mg JAU6476-desthio/kg
Endpoint(s) Affected: None
Most sensitive endpoints: None

Evaluator Comments:

1. The appropriate PMRA information (PMRA Submission Number, PMRA Data Code, PMRA company code, PMRA active ingredient code, PMRA use site category, OECD data point, name of PMRA secondary reviewer) was added to the EPA-DER as well as information on the chemical (CAS number) available from other sources.

2. The validity criteria according to OECD Guideline 206 and U.S. EPA OPPTS 850.2300 are met. Mortality in the controls was less than 10%; the average number of 14-day old survivors per hen in the controls was 42, greater than the criteria of 14 of the OECD and 10 of the U.S. EPA guidelines; the average eggshell thickness for the control group was greater than 0.34 mm.

3. The average temperature of egg storage was slightly lower than recommended by the OECD, while the average temperature during hatching was acceptable. OECD Guideline 206 recommends a storage temperature of 14-16°C and a hatching temperature of 37.5°C.

4. The EAD reviewer verified the statistical analyses for the number of hatchings of live three-week embryos. The data were arcsin square root transformed prior to statistical analysis, as they are proportions. An ANOVA was run and no significant differences were detected between treatments ($F=1.750$; $p=0.167$). Assumptions of normality and homogeneity of variances were met. The box plot provided by the EPA reviewer clearly shows that there is significant overlap between all the treatment levels. The EAD reviewer agrees with the study author that the NOEC for this endpoint should be the highest treatment level, 449 mg JAU6476-desthio/kg.

5. The EAD reviewed the other data and results of both the study author and the EPA reviewer and did not feel that redoing other statistical analyses was warranted.

6. The EAD reviewer agrees with modified mean-measured concentrations calculated by the EPA reviewer. No effects were observed at the highest treatment level, therefore which values (449 or 499 mg JAU6476-desthio/kg) are used is likely of little consequence.

Study Acceptability: This toxicity study is scientifically sound and is considered acceptable despite the degredation of JAU 6476 - desthio in feed. The results may be used for future risk assessment purposes.

Verification of statistical analyses by the EAD reviewer:

Arcsin square root transformed data
Number of hatchlings/number of live 3-week embryos (%)

One Way Analysis of Variance Tuesday, October 18, 2005, 09:48:34

Data source: Data 1 in Notebook

Normality Test: Passed (P > 0.200)

Equal Variance Test: Passed (P = 0.620)

Group Name	N	Missing	Mean	Std Dev	SEM
control	16	2	74.823	9.427	2.519
60 mg/kg	16	1	69.245	12.958	3.346
120 mg/kg	16	0	69.874	13.207	3.302
500 mg/kg	16	0	64.702	12.165	3.041

Source of Variation	DF	SS	MS	F	P
Between Groups	3	768.157	256.052	1.750	0.167
Residual	57	8342.013	146.351		
Total	60	9110.170			

The differences in the mean values among the treatment groups are not great enough to exclude the possibility that the difference is due to random sampling variability; there is not a statistically significant difference (P = 0.167).

Power of performed test with alpha = 0.050: 0.194

The power of the performed test (0.194) is below the desired power of 0.800.
You should interpret the negative findings cautiously.