DATA EVALUATION RECORD

1. CHEMICAL: Paclobutrazol

2. FORMULATION: Technical (PP 333); 92.4% a.i.

3. CITATION: Roberts, N.L., C. Fairley, and R. Almond. 1982. The subacute dietary toxicity (LC_{50}) of PP 333 to the Bobwhite quail. Prepared by the Huntingdon Research Center (HRC), Huntingdon, England; submitted by ICI Americas, Inc., Wilmington, Del.; under Reg. No. 10182-TT; Acc. No. 248689.

4. REVIEWED BY: John J. Bascietto
Wildlife Biologist
EEB/HED

5. DATE REVIEWED: 1-18-83

6. TEST TYPE: Avian subacute (dietary) LC_{50}

A.) Test species: Bobwhite quail, Colinus virginianus

7. REPORTED RESULTS: "It was not possible to determine a meaningful LC_{50} value for PP 333. However, the low mortality observed in the high dose group would indicate that the LC_{50} was probably in excess of 20,000 ppm."

8. REVIEWER'S CONCLUSIONS: The study is scientifically sound but the author's conclusions are too broad and tentative. The study reasonably shows that the LC_{50} is in excess of 5,000 ppm. PP 333 is therefore considered "practically non-toxic" to Bobwhite quail when administered in the diet. The study fulfills the requirement for an avian LC_{50} on an upland game species, and an exact determination of the LC_{50} will not be necessary.

9. Materials/Methods

A. Test Procedures:

1. Range Finder – 42 quail of mixed sex, 15 days of age were tested by dietary inclusion at: 0. (control), 100, 500 1000, 5000, 10,000, 20000 ppm – each level tested 6 birds. No mortalities occurred.

2. Definitive study – 220 one-day old quail (mixed sex) obtained from commercial breeders. 155 birds used in study. At 10 days of age birds were randomly assigned to groups (below); at 13 days of age birds were placed on test diets for 5 days; followed by 6 days of observation during which no test compounds were administered.

Groups # 1-3 (–) Control groups – 10 birds each group (0 ppm).

4-8 (+) Dieldrin controls – 10 birds per group; tested at: 15, 24, 38, 61 and 98 ppm Dieldrin.

9 (10 birds) at 554 ppm of PP 333

10 (" ") " 1007 " " "
11 (" ") " 1830 " " "
12 (" ") " 3328 " " "
13 (" ") " 6050 " " "
14 (" ") " 11,000 " " "
15 (" ") " 20,000 " " "

Management – birds housed in groups of 10 in wooden pens 80 x 50 x 60 cm. Each pen fitted with wire mesh cover, feeder, and drinker. Wood shavings used for bedding. Temperature range was 24°C – 33°C. R.H. range =43 – 59%. Ventilation fans used plus a low light intensity to reduce fighting.

N.B. – During pre – treatment period, birds dying were replaced with new birds.

Feeding – all had standard HRC chick diet until age 13 days. Over the test period of 5 days birds were offered diet only or diet + Dieldrin or diet + PP 333, depending on Group. Chick diet only was offered over the 6 day post-treatment observation period. No artibiotic or growth promoters were used. Water and Food offered ad libitum.

Diet Preparation

Dieldrin – homogenization with corn oil into final chick diet. Level of oil was 0.392% by weight.

PP 333 — "not practicable" to mix with corn oil. Premixes where made using basal diet prior to incorporation in the final diet.

All diets stored in plastic bags at room temperature.

All test diets were analyzed for PP 333 homogeneity and stability by HRC Dept. of Analytical Chemistry. Results were given in an appendix to report, and proved to be satisfactory with values within 10-11% of "nominal".

Observations —

Mortalities — Daily
Bird health — Daily
Group mean body weight — Days −3, 0 (prior to introduction of test material), 5, 8 and 11
Group mean food consumption — Days −3 to −1
1 to 5 daily
6 to 8
9 to 11

Gross post morten exam — birds examined macraccopically at death or termination of study.

B. Statistics — Finney probit analysis was used to determine LC_{50} and 95% and c.i. when appropriate dose - mortality reponses were obtained.

10. RESULTS

MORTALITIES

The distribution of mortalities which occurred is given in Table 1.

TABLE 1

Distribution of mortalities

Group	Treatment	No. of birds	Days of study													Including birds bullied		Excluding birds bullied	
			-3	-2	-1	1	2	3	4	5	6	7	8	9	10	11	Total Days 1 to 11	% Days 1 to 11	Total Days 1 to 11	% Days 1 to 11
1	Control 0	10															0	0	0	0
2	Control 0	10			1+								1				1	10	1	10
3	Control 0	10											1	1*			2	20	1	10
4	Dieldrin 15	10																		
5	Dieldrin 24	10	1+					1					1				1	10	1	10
6	Dieldrin 38	10								2	1	1	1*				2	20	1	10
7	Dieldrin 61	10					2	2	5								4	40	4	40
8	Dieldrin 98	10		1+		2	3	1		2							9	90	9	90
9	PP333 554	10		1+													8	80	8	80
10	PP333 1007	10																		
11	PP333 1830	10									1*	1	1				0	0	0	0
12	PP333 3328	10							2	1		2		1	1		3	30	2	20
13	PP333 6050	10															7	70	7	70
14	PP333 11000	10			1*						1*			1	2*		0	0	0	0
15	PP333 20000	10		1+		1											5	50	1	10
							1							1			1	10	1	10
																	2	20	2	20

\+ Birds replaced by new birds

* Birds showed evidence of bullying

Range — Finder: No mortalities occurred with PP 333 up to 20,000 ppm.

LC_{50} values: PP. 333 — not possible to determine "meaningful" LC_{50} for PP 333. Authors state that the low mortality in the high dose groups indicate "that the LC_{50} was probably in excess of 20,000 ppm".

Dieldrin

LC_{50} = 46 ppm (31-65 ppm); all birds

or

47 ppm (33-64 ppm); excluding the bird which was bullied.

See results table.

Bird health: Several birds died as a result of "bulling". The authors state this is "a common problem with this species". Groups affected were Groups # 3, 5, 10 and 13.

In addition there was "loss of balance" and birds appearing "quiet" in Groups # 5, 7 and 8 (Dieldrin) and Group #10, 11 and 15 (PP 333). Two "unsteady" birds in PP 333 groups # 11 and 15 were later found dead on Day 4 and Day 9.

Body weight: Group #7 (dieldrin 61 ppm) had mean decrease form Day 0 to 5. Some evidence of lower mean bodyweight increases in groups experiencing "bullying". Other changes were variable but normal.

Food Consumption: These data were variable though there was evidence of a reduced food consumption in 24 and 98 ppm dieldrin groups on Day 3. No other treatment-related trends detected.

Gross post mortem exam: "No treatment — related abnormalities observed."
PP 333 1830 ppm — one with spotted liver.
" " 1100 ppm — was "comparatively the in".

Dietary analysis: Levels of PP. 333 discussed were validated by the fact that chemical analysis showed the PP 333 diets to be within 10-11 % of nominal values.

11. Reviewer's Evaluation

A. Procedure: acceptable under the proposed guidelines.

B. Statistics: acceptable for dieldrin; none performed for PP 333.

C. Results:

The results have to be viewed in terms of several factors in order to interpret the erratic mortality. First, at 1830 ppm of PP 333 there was an unexpected and unexplainable (author's comment) 70% mortality. No "bullying" was observed for this group. 70% may not be indicative of the actual toxicity considering: a) the control mortality (Day 1-11) was excessive (10% or 3 out of 30 birds), but nonetheless, borderline acceptable; b) dosing in the range-finder and at the highest dose levels of 11,000 and 20,000 ppm indicate much lower toxicity; c) the results of a related study on mallard ducks indicates very low toxicity of PP 333 to birds.

Also to be considered is the fact that the investigators extended the observation period from the required 3 days to 6 days. In this way (2) "additional" mortalities were observed in the 70% figure (1830 ppm). "Additional" mortalities were also observed for the 1007 ppm group the 6050 ppm group and the 20,000 ppm group. However, due to the unusual amount of control mortality and "bullying" EEB would have expected the investigators to extend the observation period, as they correctly did.

It should noted however that the required lack of mortality for undertermined LC_{50}'s (i.e., LC_{50} >5000 ppm) as perscribed by the guidelines, has not been conclusively demonstrated. By this we refer to mortalities (0% and 50%) observed at 3328 and 6050 ppm respectively. The guideline is to demonstrate that "less than 1/2" of the birds died in a test of at least 10 birds dosed at 5000 ppm or more. No test was conducted between 3328 and 6850 ppm.

The authors overstated their case by saying "the LC_{50} is probably greater than 20,000 ppm". Considering that this is a tentative statement at best, and that the required guideline was not met, but that there are also several mitigating factors (discussed above), EEB concludes that the LC_{50} is greater than 5000 ppm, and that no precise demonstration of a bobwhite LC_{50} will be necesary in this case for PP 333.

D. Conclusions:

1. Category: Core
2. Rationale: See "C" above
3. Repair: N/A