Section A7.5.3.1.1 Acute oral toxicity on birds

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			Official use only
		1 REFERENCE	
1.1	**Reference**	[redacted], 1986, Acute Oral LD50 of Preventol A4-S to Bobwhite Quail, [redacted], Toxicology Report No. [redacted] 1986-09-04.	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Bayer Chemicals AG	
1.2.2	Companies with letter of access	-	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I/IA	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	Yes; according to US-EPA, FIFRA Guideline, Section 163, 71-1 (1984) as well as the US-EPA Toxic Substances Control Act (TSCA) and the ASTM Standard Practice (Draft 6) "Standard Practice for Conducting Acute Oral LD_{50} Tests with Avian Species"	
2.2	**GLP**	Yes	
2.3	**Deviations**	Yes; The mixture of the test substance with the carrier was not analyzed for concentration, homogeneity, and stability of the test substance.	X
		3 MATERIALS AND METHODS	
3.1	**Test material**	Dichlofluanid	
3.1.1	Lot/Batch number	Batch No. [redacted]; Source: Mobay Corp., Organic and Rubber Chemicals Division	
3.1.2	Specification	As given in section 2 of dossier	
3.1.3	Purity	[redacted]	X
3.1.4	Composition of Product	-	
3.1.5	Further relevant properties	low water solubility: 1.3 mg/l	
3.1.6	Method of analysis in the diet	Methods not mentioned, results of feed analysis conducted by Hazleton Lab., Inc., USA (Study No. 86-015-04). Analysis of protein, moisture, fat, ash, crude fiber, carbohydrates, calories, several heavy metals, several aflatoxins, several organophosphates/organochlorine insecticides and PCB.	X
3.2	**Administration of the test substance**	See table A7_5_3_1_1-1	
3.3	**Reference substance**	No	

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3.3.1	Method of analysis for reference substance	-
3.4	**Testing procedure**	
3.4.1	Test organisms	See table A7_5_3_1_1-2
3.4.2	Test system	See table A7_5_3_1_1-3
3.4.3	Diet	See table A7_5_3_1_1-4
3.4.4	Test conditions	See table A7_5_3_1_1-4
3.4.5	Duration of the test	14 days
3.4.6	Test parameter	Mortality, toxic signs, body weight changes, feed consumption, necropsy examinations
3.4.7	Examination/ Observation	See table A7_5_3_1_1-3
3.4.8	Statistics	Body weight and feed consumption: The control group mean data was compared using t-test with $P \leq 0.05$ (Sokal, R.R. & F.J. Rohlf (1969): Biometry. Freeman & Co, San Fransisco, USA) and all treatment groups data were subjected to analysis of variance (ANOVA) with $P \leq 0.05$ (Sokal, R.R. & F.J. Rohlf (1969)). If ANOVA indicated significant differences, the mean of treated group was compared to the control group using the Williams test (Williams, D.A.: A test for differences between treatment means when several dose levels are compared with a zero dose control. Biometrics, 27, 103-117. Williams, D.A.: The comparison of several dose levels with a zero dose control. Biometrics, 28, 519-531). When a parameter mean was significantly different from the controls, that treatment was considered a toxicant effect. All statistical analysis were conducted using software supplied by SAS Institute Inc., Cary, North Carolina, USA.
		4 RESULTS
4.1	**Limit Test / Range finding test**	Limit test was performed
4.1.1	Concentration	See data given below
4.1.2	Number/ percentage of animals showing adverse effects	See data given below
4.1.3	Nature of adverse effects	See data given below
4.2	**Results test substance**	
4.2.1	Applied concentrations	2226 mg test substance/kg bw
4.2.2	Effect data (Mortality)	No mortality was observed during 14-day observation period.

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4.2.3	Body weight	See table A7_5_3_1_1-5
4.2.4	Feed consumption	See table A7_5_3_1_1-5
4.2.5	Concentration / response curve	Not applicable
4.2.6	Other effects	No overt clinical signs of toxicity were noted in treated birds. No compound-related lesions were noted in postmortem examination of birds at study termination. No test substance-related effects: 6 males and 6 females showed gross lesions, 1 male showed thickened white gizzard mucosal zone, 1 female showed bilaterally enlarged thyroid glands.
4.3	**Results of controls**	See table A7_5_3_1_1-5
4.3.1	Number/ percentage of animals showing adverse effects	1 male and 2 females showed gross lesions, 1 female showed gizzard erosion, 1 female showed thickend nodular proventriculus, 1 male showed thickened white gizzard mucosal zone
4.3.2	Nature of adverse effects	See data given above
4.4	**Test with reference substance**	Not performed
4.4.1	Concentrations	-
4.4.2	Results	-

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	An avian single dose LD_{50} limit test was conducted to estimate the toxicity of Preventol A4-S to Bobwhite quail (*Colinus virginianus*). The test complies with US-EPA FIFRA Guideline, Section 163.71-1 (1984) as well as those of the US-EPA Toxic Substances Control Act (TSCA) and the ASTM Standard Practice (Draft 6) "Standard Practice for Conducting Acute Oral LD_{50} Tests with Avian Species". One group of 10 birds, 5 per sex, was given a single oral dose of 2226 mg/kg bw Preventol A4-S in corn oil. Two different groups of 10 birds, 5 per sex, were similarly dosed with corn oil only and maintained as concomitant controls. Following dosing all groups were held for a 14-day observation period.
5.2	**Results and discussion**	No mortalities were observed during the course of the study. No overt clinical signs of toxicity were noted in treated birds. Statistically significant decreases in body weight were observed between the 2226 mg/kg bw group, and the control group at day 7. No such differences were noted at test termination, suggesting recovery from toxic effects. Feed consumption data support these findings. No compound-related lesions were noted in postmortem examination of birds at study termination.
5.2.1	LD_{50}	> 2226 mg test substance/kg bw

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5.2.2	NOEC	< 2226 mg test substance/kg bw
5.3	**Conclusion**	The mortality rate in the control was below 10%. Therefore the validity criteria for avian acute oral toxicity test according to EPA OPPTS 850.2100 are fulfilled.
5.3.1	Reliability	1
5.3.2	Deficiencies	No

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Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	13/12/04
Materials and Methods	Accept applicant's version, the UK CA notes that: **2.3** Concentration of test substance was not analysed, as identified by the applicant in this section. **3.1.3** Purity was only [redacted] dichlofluanid **3.1.6** Methods not mentioned for the analysis of diet which was performed. Malathion at trace level in diet.
Results and discussion	Accept applicant's version
Conclusion	Accept applicant's version
Reliability	Reliability = 1
Acceptability	Acceptable
Remarks	All endpoints and data presented in the summary and tables have been checked against the original summary and are correct.
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table A7_5_3_1_1-1: Method of administration of the test substance

Carrier/Vehicle	Details
Water	No
Organic carrier	Yes; corn oil
concentration of the carrier [% v/v]	Total solution volume: 30 ml
Other vehicle	No
Function of the carrier / vehicle	Solvent for test substance

Table A7_5_3_1_1-*2*: Test animals

Criteria	Details
Species/Strain	Bobwhite quail (Colinus virginianus)
Source	[redacted]
Age (in weeks), sex and initial body weight (bw)	Age: adult animals, 22-24 weeks old; Sex: males and females; Mean body weights: 211 ±13 g (control group), 214 ± 9 g (dose group)
Breeding population	no data
Amount of food	Food and water were available ad libitum, prior to and throughout the study with the exception of the 21 hours immediately prior to dosing, during which the birds were fasted.
Age at time of first dosing	Age: adult animals, 22-24 weeks old
Health condition / medication	No prophylactic medication.

Table A7_5_3_1_1-3: Test system

Criteria	Details
Test location	Indoor, in steel brooders
Holding pens	galvanized steel brooders (90 x 70 x 23 cm), pelletized wood was used as cage bedding und cages were not changed during the course of the study
Number of animals	30 (15 males and 15 females)
Number of animals per pen [cm²/bird]	5 birds of a single sex (1260 cm²/bird)
Number of animals per dose	Two control groups, each with 5 males + 5 females, One dose group with 5 males + 5 females
Pre-treatment / acclimatisation	Food (Agway Gamebird Ration) and water were available ad libitum, prior to and throughout the study with the exception of the 21 hours immediately prior to dosing, during which the birds were fasted. No data about length of acclimatisation period
Diet during test	Food (Agway Gamebird Ration) and water were available ad libitum throughout the study.
Dosage levels (of test substance)	One single oral dose of 2226 mg/kg bw; total volume of test solution: 30 ml
Replicate/dosage level	One dose group with 5 males and 5 females; gang housed in two separate breeders
Feed dosing method	Orally by gavage
Dosing volume per application	Total solution volume: 30 ml; The test solutions were administered at a rate equal to 1% of the bird body weight.
Frequency, duration and method of animal monitoring after dosing	Observations for mortality and toxic signs were made twice daily for 14 days post-dosing except on weekends when only one observation per day was made; feed consumption for each group was recorded daily. At the end of the study, all surviving birds were sacrificed by CO_2 asphyxiation. Necropsy examinations were conducted on all surviving birds.
Time and intervals of body weight determination	Body weights were recorded on day 0, 7 and 14

Table A7_5_3_1_1-4: Test conditions (housing)

Criteria	Details
Test temperature	21.1 ± 2.2 °C.
Shielding of the animals	No data
Ventilation	No data
Relative huminity	40-60%
Photoperiod and lighting	8/16 hour light/dark cycle

Table A7_5_3_1_1-5: Average body weight change and feed consumption of animals during study

		CONTROL 1		CONTROL 2		DOSE GROUP	
		males	females	males	females	males	females
Mean body weight [g]	Day 0	215	206	209	215	211	217
	Day 7	229	213	217	220	198	194
	Day 14	231	214	221	222	218	209
Daily food consumption [g/bird/day]	Day 1	17.0				5.4	
	Day 2	22.8				7.9	
	Day 3	8.1				1.2	
	Day 4	17.4				8.0	
	Day 5	18.7				16.4	
	Day 6	24.6				26.2	
	Day 7	15.4				16.0	
	Day 8	13.1				13.4	
	Day 9	11.1				11.5	
	Day 10	11.5				12.1	
	Day 11	17.4				19.0	
	Day 12	19.3				20.4	
	Day 13	15.4				16.4	
	Day 14	10.4				11.7	
	Mean	15.9 ± 4.7				13.3 ± 6.5	