Data Evaluation Report on the reproductive effects of BAS 510 F (TGAI) on avian species bobwhite quail *Colinus virginianus*

PMRA Submission Number 2001-1027 EPA MRID Number: 454049-25

Data Requirement: PMRA DATA CODE: 9.6.3.1 EPA DP
Barcode: D278418
OECD Data Point: IIA 8.1.4
EPA Guideline: 71-4

Test material: **Purity (%):** 96.3
Common name: Nicobifen
Chemical name
IUPAC: 2-chloro-N-(4'-chlororobiphenyl-2-yl) nicotinamide
CAS name: 3-Pyridinecarboxamide, 2-chloro-N_(4'-chloro[1.1'-biphenyl]-2-yl)
CAS No.: 188425-85-6
Synonyms:

Primary Reviewer: Peter Takacs **Date:** October 7/02
{PMRA}

Secondary Reviewer(s): John Ravenscroft **Date:** November 22, 2002
{EPA}

Company Code: BAZ
Active Code: CHH-BAZ-4
Use Site Category: In Canada, this fungicide is proposed for use on USC 13, 14 and 30; agricultural feed, food and turf uses. BAS 510 F is to be used 2-6 times per growing season depending on the crop, at a maximum recommended application rate of up to 875 g a.i./ha/application.
EPA PC Code:

CITATION: S. Zok, 2000. BAS 510 F - I-Generation Reproduction Study On the Bobwhite quail (Colinus virginianus) By Administration in the Diet. BASF Aktiengesellschaft Experimental Toxicology and Ecology 67056 LudwigshafedRhein, Germany, BASF study # 2000/1017245.

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EXECUTIVE SUMMARY:

The one generation reproductive toxicity of BAS F 510 F to groups of 16 pairs of 180-day-old bobwhite quail was assessed over 154 days in accordance with the Avian Reproduction Test, EPA 540/9-86- 139, July 1986 and OECD Guideline for Testing of Chemicals, 206 . BAS F 510 F was administered to the birds in the diet at 0, 100, 300 and 1000 mg ai/kg dw diet. The NOEC of BAS F 510 F to the bobwhite quail based on the reproductive parameters was 300 mg ai/kg dw diet, when compared to the control.

No mortality occurred in adult birds and no clinical signs of toxicity were noted. Statistically significant reductions in reproductive parameters occurred, for the most part, at the highest test concentration only (1000 mg/kg diet), with the exception of two endpoints, fertility rate of eggs set and viable embryos (statistically significant difference vs control at 100 mg ai/kg diet). For these two endpoints the reduction was only slight (6% or less vs. control) and no significant effects were noted at the next higher test concentration of 300 mg ai/kg diet. Therefore these two endpoints are judged to be not substance related effects at the lowest test concentration, but are substance related at the high dose level of 1000 mg ai/kg diet. The most significant reductions caused by the test material during the pre-hatch stage were: eggs laid per hen (59% of control at high dose level) and post hatch: no. of 14 day old surviving chick/hen (63% of control at high dose level).

This toxicity study is classified as acceptable and satisfies the guideline requirement for a bobwhite quail reproductive toxicity study.

Results Synopsis

Test Organism Size/Age: 6 months old

NOEC:{300 mg a.i./kg dw diet}
LOEC:{1000 mg a.i./kg dw diet}
Endpoint(s) Affected:eggs laid /hen, fertility rate of eggs, egg shell thickness, viable embryos, live 3 week embryos, no. of hatchlings /hen, no. of hatched chicks/group, no. of 14 day old surviving chicks/hen, no. of 14 day old survivors.

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I. MATERIALS AND METHODS

GUIDELINE FOLLOWED:

(U.S.) EPA-FIFRA Protocol PB 83-153908 of October 1982, § 71-4 Standard Evaluation Procedure (= SEP), Avian Reproduction Test, EPA 540/9-86-139, July 1986
OECD Guideline for Testing of Chemicals, 206 (adopted April 4, 1984)

COMPLIANCE:

This study was conducted in accordance with the GLP provisons of the Chemicals Act and with the OECD Principles of Good Laboratory Practice (Paris, 1981).

A. MATERIALS:

1. Test Material

Description: white powder
Lot No./Batch No. : N 46
Purity: 96.3%
Stability of Compound Under Test Conditions: stable for at least 7 days in feed
Storage Conditions of Test Chemicals: room temperature

Physicochemical properties of BAS 510 F.

Parameter	Values	Comments
Water solubility at 20°C	4.69 mg/L	low solubility
Vapour pressure	$7x10^{-9}$ mbar @ 20 °C	not volatile
UV absorption	UV molecular extinction: $1.53x10^3$ at 290 nm	-
pKa	does not dissociate in water	-
Kow	2.96	Not likely to bioconcentrate

2. Test organism:
Species (common and scientific names): bobwhite quail *Colinus virginianus*
Age at study initiation: 6 months
Weight at study initiation: not stated
Source: Morris Quail Farm Inc. , 18370 S.W. 232 Street, Goulds, Florida 33170 - 5399, USA

B. STUDY DESIGN:

1. Experimental Conditions

b) Definitive Study

Table 1 . Experimental Parameters

Parameter	Details	Remarks *Criteria*
Acclimation Period: Conditions (same as test or not): Feeding: Health (any mortality observed):	15 days 8 days in study pens, 7 days in communal area. Fed quail feed ad libitum. All birds were healthy, 4 additional pairs were used per treatment	acceptable *EPA recommends 2-3 week health observation period prior to selection of birds for treatment. Birds must be generally healthy without excess mortality. Sickness, injuries or mortality should be noted. Feeding should be ad libitum OECD requires acclimation of at least 2 weeks*
Test duration Pre-laying exposure: Egg-laying exposure: Withdrawal period, if used:	10 weeks each for pre- and egg laying period.	acceptable *Pre-laying exposure duration* *EPA /OECD require at least 10 weeks prior to the onset of egg-laying.* *Exposure duration with egg-laying* *EPA requires at least 10 weeks.* *Withdrawal period* *EPA requires if reduced reproduction is evident, a withdrawal period of up to 3 weeks should be added to the test phase.*

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Parameter	Details	Remarks *Criteria*
Pen (for parental and offspring) Size: Construction materials: Number:	stainless steel wire mesh cages, floor area: 59x45 cm or 0.26 m^2 16 cages per treatment	acceptable *EPA requirements:* *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)	1 male, one female	acceptable *EPA requires one male and 1 female per pen. For bobwhite, 1 male and 2 females is acceptable. For mallard, 2 males and 5 females is acceptable.*
Number of pens per group/treatment Negative control: Treated:	 16 pens + 4 additional pens 16 pens + 4 additional pens	acceptable *EPA/OECD require at least 12 pens, but considerably more if birds are kept in pairs. At least 16 is strongly recommended.*

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Parameter	Details	Remarks *Criteria*
Test concentrations (mg ai/kg diet) Nominal: Measured:	0, 100, 300, 1000 mg/kg feed 85-107% of nominal	acceptable *EPA requires at least two concentrations other than the control; three or more are recommended. The highest test concentrations should show a significant effect or be at or above the actual or expected field residue level.* *OECD requires measured concentration in diet should be at least 80% of nominal*
EEC/maximum labeled field residue anticipated and source of information:	EEC in diet of bobwhite quail: 483 mg ai/kg dw as determined by EAD spread sheet "Workbook 2" based on maximum label rate of 476 g ai/ha x 6 applications; used on bulb vegetables. Label date: March 30/2001.	acceptable *EPA requires 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:	none used	acceptable *EPA /OECD require corn oil or other appropriate vehicle and not more than 2% of diet by weight*
Was detailed description and nutrient analysis of the basal diet provided (Yes/No)	yes	acceptable *EPA requires a commercial breeder feed (or its equivalent) that is appropriate for the test species.*
Preparation of test diet	the test chemical (no carrier) was mixed in a beaker with the diet weekly	 *A premix 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.*

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Parameter	Details	Remarks *Criteria*
Indicate whether stability and homogeneity of test material in diet determined (Yes/No)	yes	acceptable
Were concentrations in diet verified by chemical analysis (Yes/No)?	Yes	acceptable
Feeding and husbandry	food was available ad libitum	acceptable
<u>Test conditions (pre-laying)</u> Temperature: Relative humidity: Photoperiod:	 21 C ° ± 1 35-70% 7hrs light, 17 hrs dark for up to week 7 by week 10, photoperiod was 17 hrs light, 7 hrs dark 10-50 lux	**humidity ranged lower than recommended** *<u>Temperature:</u> EPA: about 21°C (70°F) OECD: 22 ± 5°C <u>Relative humidity:</u> EPA: about 55% OECD: 50-75% <u>Lighting:</u> EPA/OECD: first 8 weeks: 7 h per day <u>Thereafter:</u> EPA: 16-17 h per day. At least 6 footcandles at bird level OECD: 16-18 h per day*
Egg Collection and Incubation		
<u>Egg collection and storage</u> Collection interval: Storage temperature: Storage humidity: Storage period:	 daily during egg laying period 16 C 50-80% eggs were set into incubator weekly	acceptable *EPA requires eggs to be collected daily; egg storage temperature approximately 16°C (61°F); humidity approximately 65%. Collection interval: daily*
Were eggs candled for cracks prior to setting for incubation?	Yes	acceptable *EPA requires eggs to be candled on day 0*
Were eggs set weekly?	yes	acceptable
When candling was done for fertility?	Day 11	acceptable

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Parameter	Details	Remarks *Criteria*
		EPA requires: *bobwhite: approx. day 11* *mallard: approx. day 14* *OECD requires: 6-11 day*
When the eggs were transferred to the hatcher?	21 days	acceptable *EPA requires:* *Bobwhite: day 21* *Mallard: day 23*
Hatching conditions Temperature: Humidity: Photoperiod:	 37.7-37.9 C 80-90% not stated	acceptable *Temperature:* *EPA requires: 39°C (102°F)* *OECD requires: 37°C* *Humidity* *EPA requires: 70%* *OECD requires: 70-85%*
Day the hatched eggs were removed and counted	day 25	acceptable *EPA requires Bobwhite: day 24* *Mallard: day 27*
Were egg shells washed and dried for at least 48 hrs before measuring?	Yes	acceptable
Egg shell thickness No. of eggs used: Intervals: Mode of measurement:	 all eggs laid on first day of selected weeks every second week micrometer, at 4 points	acceptable *EPA requires newly hatched eggs be collected at least once every two weeks. Thickness of the shell plus membrane should be measured to the nearest 0.01 mm; 3 - 4 measurements per shell.*
Reference chemical, if used Name: Concentration tested:	not used	

2. Observations:

Table 2: Observations

Parameter	Details	Remarks / *Criteria*
Parameters measured		
Parental: (mortality, body weight, mean feed consumption) Egg collection and subsequent development: (no. of eggs laid, no. of eggs cracked, shell thickness, no. of eggs set, no. of viable embryos, no. of live 3 week embryos, no. hatched, no. of 14-day survivors, average weight of 14-d old survivors, mortality, gross pathology, others)	mortality, body weight, mean feed consumption, palatability, post mortem examination. All birds were inspected generally at least on workdays throughout the study period. General condition, signs of toxic effects and abnormal behavior were monitored. Egg data total eggs, weights, quality, shell thickness, embryo survival, infertile eggs, chicks hatched, mortality and body wt. Of chicks, 14 day survivors.	acceptable *OECD requires that the mortality in the controls is not exceed 10% at the end of the test. The average number of 14 day-old survivors per pen in controls at least 14 and 12 for mallard and bobwhite, respectively. OECD requires average egg shell thickness for control group 0.34 and 0.19 for mallard and bobwhite, respectively* *EPA requires:* *body weight should be recorded at test initiation and a biweekly intervals up to week eight or up to the onset of egg laying and at termination.* • *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* • *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, test material was retained by birds	

Parameter	Details	Remarks *Criteria*
Observation intervals (for various parameters)	weekly for most variables	acceptable *Body weights and food consumption must be measured at least biweekly.*
were raw data included?	Yes	

II. RESULTS AND DISCUSSION:

A. MORTALITY:

Parent generation: There was no mortality that could be attributed to the test compound.

Table 3: Effect of BAS 510 F on mortality of parent bobwhite quail.

Treatment (mg a.i./kg diet, nominal conc.) **Group 1= control, Group 2 = 100 mg ai/kg, Group 3 = 300 mg ai/kg Group 4 = 1000 mg ai/kg**	
Summary table of mortalities (week 1 - 10): Males: Group 0 = 0 birds Group 1 = 0 birds Group 2 = 1 bird Group 3 = 0 birds Total = 1 bird	Females: Group 0 = 0 birds Group 1 = 0 birds Group 2 = 1 bird Group 3 = 0 birds Total = 1 bird
Summary table of mortalities (week 11 - 22): Males: Group 0 = 0 birds Group 1 = 1 bird Group 2 = 0 birds Group 3 = 0 birds Total = 1 birds	Females: Group 0 = 0 birds Group 1 = 1 bird Group 2 = 0 birds Group 3 = 1 bird Total = 2 bird

B. REPRODUCTIVE AND OTHER ENDPOINTS:

No compound-related effects in the parent generation on mortality, birds' health, palatability, feed consumption and body weight could be detected.

Clinical observations
Clinical signs attributable to the test compound were not observed.

Feed consumption
The statistical analyses revealed no evidence of any dose effect.

Palatability
No rejection of feed containing the test compound could be observed.

Body weights
There was generally no significant increase or decrease in the group mean body weights in the male and female birds compared to the control.

Number of eggs laid
The mean number of eggs laid per female quail per week was used for the statistical evaluation. The statistical analysis revealed a significant difference between control group and dose group 3 for weeks 1 - 4, weeks 5 - 8 and for the whole egg-laying period. The number of eggs laid per female in group 3 at the start of the test was clearly reduced to about 59% of the number of eggs per female in the control group and the maximum number of eggs laid per week was lower. Over the whole study period the number of eggs per female was reduced by about 13%. This is considered to be a substance related effect.

Egg weights
The statistical evaluation (Dunnett's Test) revealed no evidence of any dose effect.

Egg quality
The statistical analyses (Wilcoxon-Test) revealed no evidence of any treatment effect.

Egg shell thickness
The egg shell thickness of the treatment groups was at about the same level as in the control group. The statistical analysis revealed a significant decrease of the egg shell thickness in dose group 3 on weeks 9 and 11.

Fertility rate, infertile eggs

For the proportion of fertile eggs of eggs initially set the Wilcoxon-test revealed a statistically significant difference between control group and dose group 1 for weeks 1 - 4 and for the whole study period, and between control group and dose group 3 for weeks 5- 8 and weeks 9 - 12. The deviation of group 1 to the control was minor (only 3.5% over the whole study period). No effect was observed in the next higher dose group. Therefore the decrease in the fertility rate was not considered to be caused by the test substance.

Early embryonic deaths and viable ll-day old embryos

The rates of early embryonic deaths of fertile eggs for the total period were 0.9% (group 0 = control) 1.7% (group 1 = 100 mg/kg)

1.0% (group 2 = 300 mg/kg)
7.9% (group 3 = 1000 mg/kg diet)

There was a statistically significant increase in early embryonic mortalities in the dose group 3 compared to the control on weeks 9 -12 and over the whole study period resulting in a 6 fold higher number than in the control group. The mortalities were observed in several replicates of dose group 3 and are considered to be a substance-related effect.

The rates of viable11-day embryos of eggs initially set for the total period were:
97.3% (group 0)
93.3% (group 1)
95.4% (group 2)
85.6% (group 3).
For the proportion of eggs set at day 11(viable embryos) of eggs initially set the Wilcoxon-test revealed a significant difference between control group and dose group 1 for weeks 1 - 12, and between control group and dose group 3 for weeks 5 - 8, weeks 9 - 12 and for the whole study period.

Late embryonic deaths and live 18-day old embryos, percentage of fertile eggs

The rate of late embryonic deaths as percentage of fertile eggs was:
for group 0 (control): 1.2%
for group 1 (I00 mg/kg diet):0.1%
for group 2 (300 mg/kg diet):0.5%
for group 3 (1 000 mg/kg diet):2.3%

For the proportion of late embryonic deaths of fertile eggs the Wilcoxon-test revealed no evidence of any statistically significant dose effect. For the proportion of eggs set at day 18 (live 18-day embryos) of fertile eggs the Wilcoxon-test revealed a statistically significant effect in dose group 3 in weeks **9 - 12** and over the whole study period. For the proportion of eggs set at day 18 (live 18-day embryos) **of** eggs initially set the Wilcoxon-test revealed a statistically significant dose effect in dose group 3 for weeks **5** - 8, 9 - 12 and for the whole egg-laying period. For the proportion of eggs set at day 18 of eggs set at day 11, the Wilcoxon-test revealed no evidence of any statistically significant dose effect, indicating that the decrease in live 18 day old embryos can be mainly attributed to a decreased number of fertile eggs and an increased number **of** early embryonic mortalities.

Total embryonic deaths, percentage of fertile eggs

Corresponding to the rates of early and late embryonic deaths the total embryonic deaths of fertile eggs for the total egg-laying period were:
for group 0 (control): 2.1%
for group 1 (1 00 mg/kg diet):1.8%
for group 2 (300 mg/kg diet):1.5%
for group 3 (1 000 mg/kg diet):10.2%
These findings indicate that a compound-related impairment of embryo survival occurred in the dose group 3 in comparison to the control.

"Dead-in-shell" of fertile eggs
The statistical analyses (Wilcoxon-test) revealed no evidence of any statistically significant dose effect.

HATCHING RESULTS
The overall hatch rates (% hatched chicks of fertile eggs) over the total egg-laying period were:
83.2% (control)
80.9% (group 1 = 100 mg/kg diet)
82.7% (group 2 = 300 mg/kg diet)
70.6% (group 3 = 1000 mg/kg diet).

For the proportion of hatched chicks of fertile eggs the Wilcoxon-test revealed a statistically significant decrease in dose group 3 in weeks 9 - 12 and over the whole study period In conclusion, the hatchability (number of hatched chicks per female quail and % hatched chicks of fertile eggs) was biologically significantly impaired by feeding the test compound with the diet in test group 3 (1000 mg/kg diet). The hatch rate of viable 18-day embryos was significantly reduced.

F1-CHICKS

Clinical observations
No toxic signs and/or significant malformations exceeding the normal proportion were seen in the chicks.

14-day survivors
The mean numbers of 14-day surviving chicks per female quail and week (calculated as means of replicates for each dose group) were:
2.86 (control)
2.53 (group 1)
2.96 (group 2)
1.83 (group 3).
Regarding the mean number of the 14-day old survivors per female quail and week the Wilcoxon-test revealed a significant decrease between control group and dose group 3 for weeks 1 - 4, weeks 9 - 12 and for the whole egg-laying period.

Body weight
The initial (day zero) and 14-day body weights for the control (group 0) and the dose groups were in the same range. The mean weight for the chicks for each group at hatching was, for the total period (weeks 1 - 12), 6.1 - 6.2 g, that of the 14-day old survivors 20.4 - 21.1 g. The statistical evaluation using Dunnett's test revealed no evidence of any dose effect. In conclusion, there was no effect on chick body weight at hatch and on the body weight of the chicks 14 days post hatch.

NOAEL:
In conclusion, under the conditions of this reproduction study in bobwhite quail with BAS 510 F the "no observed adverse effect level" (NOAEL) was 300 mg ai/kg diet.

LOAEL:
The lowest observed adverse effect level (LOAEL) was 1000 mg ai/kg diet.

Table 4. Reproductive and other parameters - Results for each test group indicate the units of measurement.

Parameter	Control	100 mg/kg diet	300 mg/kg diet	1000 mg/kg diet	NOEC/ LOEC
Eggs laid/group	930	884	930	787	
Eggs laid/hen/week	2.7 (week 1-4) 5.9 (week 5-8) 6.0 (week 9-12) 4.8 (mean)	2.3(week 1-4) 5.7(week 5-8) 6.7 (week 9-12) 4.6 (mean)	2.5 (week 1-4) 6.0 (week 5-8) 6.0 (week 9-12) 4.8 (mean)	1.6* (week 1-4) 5.3* (week 5-8) 5.8 (week 9-12) 4.2* (mean)	LOEC: 1000 mg/kg NOEC: 300 mg/kg
Egg weights	9.6	9.7	9.7	9.7	NOEC: 1000 mg/kg
Eggs set	793	773	821	668	**Not Tested**
Eggs cracked	8.1	5.6	4.7	9.1	NOEC: 1000 mg/kg
Fertility rate of eggs set	780 98.2%	733* 94.8%	794 96.4%	624* 92.4%	LOEC: 100 mg/kg
Shell thickness (mm ± SD)	0.21	0.21	0.21	0.20 *	LOEC: 1000 mg/kg NOEC: 300 mg/kg
Viable embryos	97.3%	93.3%*	95.4%	85.6%*	LOEC: 100 mg/kg
Live 3-week embryos	766	720	782	569 *	LOEC: 1000 mg/kg NOEC: 300 mg/kg
No. of hatchling/hen	3.4	3.1	3.4	2.4*	LOEC: 1000 mg/kg NOEC: 300 mg/kg
No. Of hatched chicks/group	649	597	659	447*	LOEC: 1000 mg/kg NOEC: 300 mg/kg
No. of 14 day old surviving chicks/hen	2.86	2.53	2.96	1.83*	LOEC: 1000 mg/kg NOEC: 300 mg/kg
Hatchling weight	6.11	6.16	6.16	6.21	NOEC: 1000 mg/kg

Parameter	Control	100 mg/kg diet	300 mg/kg diet	1000 mg/kg diet	NOEC/ LOEC
No. of 14-day old survivors	549 81.9%	485 78.95%	568 84.7%	347 * 74.3%	LOEC: 1000 mg/kg NOEC: 300 mg/kg
14-day old survivors weight	21.05	20.38	20.69	20.41	NOEC: 1000 mg/kg
Mean food consumption	16.6	16.3	16.7	16.3	NOEC: 1000 mg/kg
Weight of females (parent) g/bird At test initiation: At onset of egg laying/other: day 56	 197.5 209.4	 195.0 211.8	 193.9 202.7	 193.6 208.3	NOEC: 1000 mg/kg
Weight of males (parent) g/bird At test initiation: at test termination:	 194.7 222.1	 195.6 221.6	 194.3 220.3	 194.0 219.7	NOEC: 1000 mg/kg

*Statistically significant vs. control ($p<0.05$).

C. REPORTED STATISTICS:

The statistical analyses used were the parametric ANOVA with Dunnett's test and non-parametric Wilcoxon rank test. The animals in the study were randomly assigned to 4 groups (0 = control group, 1 = 100 mg/kg, 2 = 300 mg/kg, 3 = 1,000 mg test compound/kg food). For the variables egg weight, egg shell thickness and chicks' body weight, a comparison of each dose group with the control group was carried out. These comparisons were performed simultaneously via Dunnett's test for the hypothesis of equal means. If the results of this test were significant, labels (* for p 5 0.05, ** for p 5 0.01) were printed together with group means in the summary tables. The test was performed two-sided.

For the body weight and food consumption of parent quails a parametric one-way ana-lysis of variance was done via the F-test (ANOVA). If the resulting p-value was equal or less than 0.05, a comparison of each dose group with the control group was carried out. These comparisons were performed simultaneously via Dunnett's test for the hypothesis of equal means. If results of this test were significant, labels (* for p 5 0.05, ** p 5 0.01) were printed together with the group means in the summary tables. Both tests were performed two-sided.

For the egg data, No. of dead-in-shell and No. of hatched chicks, a non-parametric analysis was carried out. A pair-wise comparison of each dose group with the control was performed via the Wilcoxon-test for the hypothesis of equal medians. If the results of this test were significant, labels

(* for p 5 0.05, ** for p 5 0.01) were printed in the summary tables. The test was performed one-sided. The pen is the smallest unit for the statistical analyses; consequently these values are used to generate the means, medians and the variability of the data (exception: body weight of adult quails, where the sample unit is the individual bird). For the calculation of the variability either the standard deviation or the minimal and maximal values were used.

D. VERIFICATION OF STATISTICAL RESULTS BY THE REVIEWER:

Most endpoints were not re-analyzed due to the size of this data set, however, the conclusions of the study and statistical determinations are judged to be valid. Statistical analysis conducted by US. EPA using "chicks.sas".

NOEC: 300 mg ai/kg diet (see above table for specific endpoints)
LOEC: 1000 mg ai/kg diet

E. STUDY DEFICIENCIES: The humidity during the study ranged lower than that recommended by EPA; 35-70% vs 50-75%. This is considered to be a minor deficiency.

F. REVIEWER'S COMMENTS: No further comments.

G. CONCLUSIONS: This reproduction study is acceptable. The test chemical BAS 510 F had statistically significant adverse effects on several reproductive endpoints (as outlined above) at a concentration of 1000 mg ai/kg dw diet, the highest concentration tested. There were no lethal or clinical toxicity noted in the parental generation.

NOEC:{300 mg a.i./kg diet}
LOEC:{1000 mg a.i./kg diet}
Endpoint(s) Effected:
Most Sensitive endpoint(s): Eggs laid per hen (59% of control at high dose level) and no. of 14 day old surviving chick/hen (63% of control at high dose level).

III. REFERENCES:

Approved 04/01/01 C.K.