US EPA ARCHIVE DOCUMENT

177203, 177204, 177205
RECORD NO.

110201
SHAUGHNESSY NO.

REVIEW NO.

EEB REVIEW

DATE: IN 07/22/86 OUT 09 JAN 1987

FILE OR REG. NO. 55947-UR, [redacted] 55947-UG

PETITION OR EXP. NO. ~~PENDING REGISTRATION~~ INFORMATION IS NOT INCLUDED

DATE OF SUBMISSION 07/08/86

DATE RECEIVED BY HED 07/18/86

RD REQUESTED COMPLETION DATE 11/04/86

EEB ESTIMATED COMPLETION DATE 10/28/86

RD ACTION CODE/TYPE OF REVIEW 126

TYPE PRODUCT(S): I, D, H, F, N, R, S Herbicide

DATA ACCESSION NO(S). 260681, 260682, 256456

PRODUCT MANAGER NO. R. Mountfort (23)

PRODUCT NAME(S) Technical Prodiamine (55947-UR), [redacted]

[redacted], Prodiamine 65 WDG (55947-UG)

COMPANY NAME Sandoz Crop Protection Corporation

SUBMISSION PURPOSE Proposed Registration of New Technical Chemical and End-Use Formulations for Use on Turf, Ornamentals, and Tree and Vine Crops

SHAUGHNESSY NO.	CHEMICAL & FORMULATION	% A.I.
110201	N^3,N^3-Di-n-propyl-2,4-dinitro-6-(trifluoromethyl)-m-phenylenediamine	

PENDING REGISTRATION INFORMATION IS NOT INCLUDED

EEB BRANCH REVIEW

Prodiamine

100 Submission Purpose and Label Information

100.1 Submission Purpose and Pesticide Use

The registrant (Sandoz Crop Protection Corporation) has applied for registration of prodiamine technical (formulating use) and [redacted] and Prodiamine 65 WDG herbicide for control of annual grasses and broadleaf weeds. Proposed use sites include turf, ornamentals, and tree and vine crops.

100.2 Formulation Information

(from Confidential Statement of Formula)

[redacted]

100.3 Application Methods, Directions, Rates

Please refer to appended labels.

100.4 Target Organisms

Target organisms are annual grasses and broadleaf weeds. Please refer to appended labels for lists of species.

100.5 Precautionary Labeling

Formulating-Use Product

Do not discharge into lakes, streams, ponds, or public waters unless in accordance with an NPDES permit. For guidance, contact your regional office of the Environmental Protection Agency.

COMMERCIAL/FINANCIAL INFORMATION IS NOT INCLUDED

[redacted] and Prodiamine 65 WDG

Do not apply directly to water. Do not contaminate water by cleaning of equipment or disposal of wastes. May be toxic to fish and wildlife. Do not apply where runoff is likely to occur. Do not apply when weather conditions favor drift from treated areas.

101 Hazard Assessment

101.1 Discussion

Label Information

[redacted] and Prodiamine 65 WDG are trade names for the same formulation of residual preemergence herbicide, prodiamine. The herbicide is used to control annual grasses and broadleaf weeds as they germinate. Specifically, uses are as follows:

[redacted]

Prodiamine 65 WDG: ornamental turf, ornamentals (numerous species).

General label information for all uses except turf indicates that applications should be made in 20 to 50 gal water per acre, by broadcast or band treatment, with spray being applied directly to soil surface. One-half inch or more of rainfall or sprinkler irrigation is needed to activate the herbicide. Mechanical incorporation may also be used. For turf, the options of band treatment (vs. broadcast) and mechanical incorporation (vs. irrigation) do not apply.

Application rates for tree and vine crops and ornamentals are 3 to 6 lb per acre, not to exceed 12 lb of product per acre per year. For turf, Prodiamine 65 WDG may be applied at 0.75 to 2.3 lb per acre, with one application per year.

On the basis of the use rates outlined above, the ranges of active ingredient per acre are as follows:

Turf - 0.54 - 1.66 lb ai/acre
Ornamentals, tree and vine crops -
2.17 - 4.33 lb ai/acre, not to exceed
8.66 lb ai/acre/year.

COMMERCIAL/FINANCIAL INFORMATION IS NOT INCLUDED

[redacted]

crops. See attached label for specifics. No tank mixes are indicated for Prodiamine 65 WDG.

Exposure Use Analysis

Based on the numerous proposed use sites and crops for these herbicides, potential use may involve all regions of the country and may involve extensive acreages. Major uses include [redacted] stone fruits, grapes, turf, and ornamentals.

Application of these herbicides is by ground equipment, with spray being directed to the soil or grass surface. This is followed by incorporation (rainfall, irrigation, or mechanical means). This should minimize exposure of nontarget terrestrial areas.

Due to the large number of proposed use sites, potentially involving a number of geographical areas, exposure of aquatic environments is possible. In view of the fact that substantial acreages of [redacted] and turf are located in coastal counties, exposure of estuarine environments is of special concern.

101.2 Likelihood of Adverse Effects on Nontarget Organisms

Terrestrial Organisms

Data submitted by the registrant indicate that prodiamine is practically nontoxic to birds on a dietary basis. Available data on rats indicate that the chemical has a low mammalian acute toxicity. Thus, significant hazards to populations of nontarget terrestrial organisms would not be anticipated. However, EEB will defer a final assessment pending receipt of finalized reviews of environmental fate and toxicology, and receipt of data from a valid avian single-dose oral LD_{50} test (two avian acute studies submitted with the present application for registration were reviewed by EEB and determined to be invalid).

Data on the toxicity of prodiamine to honey bees indicate that prodiamine in practically nontoxic to bees. Thus, no significant hazard to bees is expected from the proposed uses.

Aquatic Organisms

The registrant submitted data from three aquatic organism tests (acute LC_{50} tests with bluegill,

COMMERCIAL/FINANCIAL INFORMATION IS NOT INCLUDED

rainbow trout, and daphnia), to support the proposed registrations. EEB has reviewed the data and determined that none of the tests are acceptable for use in a hazard assessment. Precipitates were noted in the test chambers in all three tests, yet toxicant concentrations were not measured. All three tests must be repeated. EEB will defer the aquatic organism hazard assessment until these data and all pertinent environmental fate data and mammalian data are made available.

In addition, as noted above, substantial acreages of [redacted] and turf are located in coastal counties. This indicates a potential for hazard to estuarine/marine organisms. On that basis, EEB will require data from the following tests (§72-3): 96-hour LC_{50} for shrimp; 96-hour LC_{50} for estuarine/marine fish; and 48-hour EC_{50} (embryolarvae) or 96-hour EC_{50} shell deposition for oyster.

101.3 Endangered Species Considerations

As this product is proposed for use on a variety of use sites over a wide geographic range, it is possible that application could lead to exposure of endangered species or their habitat. This assessment will be deferred pending receipt of all pertinent environmental fate data, mammalian data, and valid ecological effects data.

101.4 Adequacy of Toxicity Data

The honey bee toxicity data have been reviewed and found acceptable to support registration. Avian dietary studies with bobwhite quail and mallard ducks were also determined to be valid. The following studies are required to support registration:

- Avian single-dose oral LD_{50} test* (§71-1);
- Acute toxicity tests on freshwater fish (one coldwater and one warmwater species) (§72-1);
- Acute toxicity test on freshwater invertebrate (§72-2);
- Acute toxicity tests on estuarine/marine organisms (§72-3).

These studies must be conducted with the technical grade of the active ingredient.

*Note - The single-dose oral test on bobwhite quail is invalid as submitted, but may be reparable with submission of raw data on time of regurgitation.

5

101.5 Adequacy of Labeling

Discussion deferred pending receipt of additional data.

102 Classification

Not applicable at this time.

103 Conclusions

EEB has reviewed the proposed registration for prodiamine on a variety of crops. EEB is unable to complete an aquatic risk assessment for these uses because pertinent ecological effects data are lacking. In order to assess the aquatic risks associated with the proposed uses, EEB requires data from the following studies:

- Acute toxicity test for freshwater fish (2 species) (§72-1);

- Acute toxicity test for freshwater aquatic invertebrates (§72-2); and

- Acute toxicity tests for estuarine/marine organisms (§72-3).

These data will be required prior to registration of the product and must be developed using the technical grade of the active ingredient. Further, EEB is unable to assess the chronic aquatic and terrestrial risks because pertinent environmental fate data and chronic mammalian data are lacking. Upon receipt of finalized EAB and Toxicology Branch (TB) reviews, plus receipt of the results of valid ecological effects studies, EEB can finalize this assessment.

Relative to mammalian and avian organisms, the available data indicate that minimal acute hazards exist for such organisms. However, EEB is unable to fully assess such acute risks or the chronic risks because pertinent ecological effects data (specifically an avian single-dose oral LD_{50}), a finalized EAB review, and a finalized TB review are lacking.

Allen W. Vaughan 1/8/87

Allen W. Vaughan, Entomologist
Ecological Effects Branch
Hazard Evaluation Division (TS-769c)

Norman Cook 1.9.87

Norman Cook, Supervisory Biologist
Ecological Effects Branch
Hazard Evaluation Division (TS-769c)

1/9/87

Michael Slimak, Chief
Ecological Effects Branch
Hazard Evaluation Division (TS-769c)

DATA EVALUATION RECORD

1. Chemical: Prodiamine

2. Test Material: Technical, 91.3% ai

3. Study Type: Freshwater fish LC_{50}

   Species tested: Rainbow trout (Salmo gairdneri)

4. Study ID: McAllister, W.A., J. Bowman, and P. Cohle (1985) Static acute toxicity report No. 32709. Acute toxicity of prodiamine technical to rainbow trout (Salmo gairdneri). Prepared by Analytical Bio-Chemistry Laboratories, Inc., Columbia, MO. Submitted by Sandoz Crop Protection Corp., Chicago, IL. EPA File Symbols 55947-UR, 55947-UE, 55947-UG. (Orig. submitted by Velsicol under EPA Reg. Nos. 876-452, 876-453, 876-454.) EPA Accession No. 260681.

5. Reviewed by: Allen W. Vaughan, Entomologist, EEB/HED — Signature: Allen W. Vaughan — Date: 1/8/87

6. Approved by: Norman Cook, Supervisory Biologist, EEB/HED — Signature: Norman Cook — Date: 1.9.87

7. Conclusions:

This study is not scientifically sound. The 96-hour LC_{50} was determined to be 6.6 mg/L. However, the authors reported a precipitate in all test solutions, and toxicant concentrations were not measured at any point during the test. Thus, actual levels of exposure cannot be determined. This study does not fulfill the Guideline requirement for an acute toxicity test on freshwater fish.

8. Recommendations: N/A.

9. Background:

This study was submitted in support of registration.

10. Discussion of Individual Studies: N/A.

11. Materials and Methods:

a. Test animals were rainbow trout, Salmo gairdneri, obtained from Spring Creek Trout Hatchery, Lewiston, Montana. At test initiation, fish had a mean weight of 0.76 g and a mean standard length of 45 mm.

b. Test system: The static fish bioassay was conducted in 5-gallon glass vessels containing 15 L of soft reconstituted water. The test vessels were kept in a water bath at 12 °C. The test fish were acclimated to the dilution water and test temperature and held without food for 48 to 96 hours prior to testing.

Fish were added to the test chambers by random assignment within 30 minutes after addition of test material. All concentrations were observed once every 24 hours for mortality and abnormal effects.

c. Dose: Acute bioassay using nominal concentrations; N,N-Dimethylformamide solvent.

d. Design: Nine nominal concentrations (1.0, 1.8, 3.2, 5.6, 10, 18, 32, 56, and 100 mg/L) plus control and solvent controls (1.5 ml DMF per test chamber); 10 fish per dose level and control.

e. Statistics: Statistical analysis of the concentration vs. effect data (generally mortality) was obtained by employing a computerized LC_{50} program developed by Stephan et al. This program calculated the LC_{50} statistic and its 95 percent confidence limits using the binomial, the moving average, and the probit tests. Three different methods of analyzing the data were used since no one method of analysis is appropriate for all possible sets of data that may be obtained. The method of calculation selected for presentation in this report was that which gave the narrowest confidence limits for the LC_{50}.

12. Reported Results:

The 24, 48, and 96-hour LC_{50} values for prodiamine technical were 55, 9.9, and 6.6 mg/L, respectively. All results were based on the nominal concentrations. The no-effect concentration after 96 hours of exposure was < 1.0 mg/L, which was the lowest concentration tested. The abnormal effects of mortality, quiescence, surfacing, loss of equilibrium, dark discoloration, distended abdomen, and/or fish on the bottom were observed in all test levels during the 96-hour exposure period.

13. Study Authors' Conclusions/QA Measures:

96-hour LC_{50} = 6.6 mg/L (CI = 4.1 - 10 mg/L) (technical material).

The study was conducted following the intent of the Good Laboratory Practice Regulations, and the final report was reviewed by ABC Laboratories' Quality Assurance Unit.

14. Reviewer's Discussion and Interpretation of the Study:

a. Test Procedures: The one major deviation from established protocol is enough to render the study invalid. That is, despite the fact the surface films and precipitates were noted and reported, concentrations were not measured at any point. The reported LC_{50} values were based on nominal concentrations only.

b. Statistical Analysis: Types of analyses conducted were appropriate for these test data. However, as data on concentration levels were not supported by measuring the actual concentrations, results of the analyses are invalid.

c. Discussion/Results: This study is not scientifically sound, due to the fact that the test material formed precipitates (surface films and bottom deposits) and actual concentrations were not measured.

d. Adequacy of Study:

1. Classification: Invalid.

2. Rationale: Actual concentrations were not measured despite reported solubility problems.

3. Reparability: None.

15. Completion of One-Liner for Study: N/A.

16. CBI Appendix: N/A.

DATA EVALUATION RECORD

1. Chemical: Prodiamine

2. Test Material: Technical, 91.3% ai

3. Study Type: Freshwater fish LC_{50}

   Species tested: Bluegill sunfish (Lepomis macrochirus)

4. Study ID: Cohle, P., and W.A. McAllister (1985) Static acute toxicity report no. 32708. Acute toxicity of prodiamine technical to bluegill sunfish (Lepomis macrochirus). Prepared by Analytical Bio-Chemistry Laboratories, Inc., Columbia, MO. Submitted by Sandoz Crop Protection Corp., Chicago, IL. EPA File Symbols 55947-UR, 55947-UE, 55947-UG. (Orig. submitted by Velsicol under EPA Reg. Nos. 876-452, 876-453, 876-454.) EPA Accession No. 260681.

5. Reviewed by: Allen W. Vaughan, Entomologist, EEB/HED — Signature: Allen W. Vaughan — Date: 1/8/87

6. Approved by: Norman Cook, Supervisory Biologist, EEB/HED — Signature: Norman Cook — Date: 1.9.87

7. Conclusions:

This study is not scientifically sound. The 96-hour LC_{50} was determined to be 68 mg/L. However, the authors reported a precipitate in all test solutions, and toxicant concentrations were not measured at any point during the test. Thus, actual levels of exposure cannot be determined. This study does not fulfill the Guideline requirement for an acute toxicity test on freshwater fish.

8. Recommendations: N/A.

9. Background:

This study was submitted in support of registration.

10. Discussion of Individual Studies: N/A.

11. Materials and Methods:

a. Test animals were bluegill sunfish, Lepomis macrochirus, obtained from Osage Catfisheries, Inc., Osage Beach, MO. At test initiation, fish had a mean weight of 0.23 g and a mean standard length of 22 mm.

b. Test system: The static fish bioassay was conducted in 5-gallon glass vessels containing 15 L of soft reconstituted water. The test vessels were kept in a water bath at 22 °C. The test fish were acclimated to the dilution water and test temperature and held without food for 48 to 96 hours prior to testing.

Fish were added to the test chambers by random assignment within 30 minutes after addition of test material. All concentrations were observed once every 24 hours for mortality and abnormal effects.

c. Dose: Acute bioassay using nominal concentrations; N,N-Dimethylformamide solvent.

d. Design: Six nominal concentrations (18, 32, 56, 100, 180, 320 mg/L) plus control and solvent control (1.5 mL DMF per test chamber); 10 fish per dose level and control.

e. Statistics: Statistical analysis of the concentration vs. effect data (generally mortality) was obtained by employing a computerized LC_{50} program developed by Stephan et al. This program calculated the LC_{50} statistic and its 95 percent confidence limits using the binomial, the moving average, and the probit tests. Three different methods of analyzing the data were used since no one method of analysis is appropriate for all possible sets of data that may be obtained. The method of calculation selected for presentation in this report was that which gave the narrowest confidence limits for the LC_{50}.

12. Reported Results:

The 24, 48, and 96-hour LC_{50} values for prodiamine technical were 130, 100, and 68 mg/L, respectively. All results were based on the nominal concentrations. The no-effect concentration after 96 hours of exposure was < 18 mg/L, which was the lowest concentration tested. There was 10 percent mortality at this level; also, remaining fish were easily excitable. The abnormal effects of mortality, surfacing, loss of equilibrium, excitability, and/or fish on the bottom were observed in all test levels during the 96-hour exposure period.

13. Study Authors' Conclusions/QA Measures:

96-hour LC_{50} = 68 mg/L (CI = 50-92 mg/L)
(technical material)

The study was conducted following the intent of the Good Laboratory Practice Regulations, and the final report was reviewed by ABC Laboratories' Quality Assurance Unit.

14. Reviewer's Discussion and Interpretation of the Study:

a. Test Procedures: The one major deviation from established protocol is enough to render the study invalid. That is, despite the fact the surface films and precipitates were noted and reported, concentrations were not measured at any point. The reported LC_{50} values were based on nominal concentrations only.

Also, it should be noted that mean weight of fish at test initiation was 0.23 g. Protocol recommends weight of 0.5 to 5.0 g.

b. Statistical Analysis: Types of analyses conducted were appropriate for these test data. However, as data on concentration levels were not supported by measuring the actual concentrations, results of the analyses are invalid.

c. Discussion/Results: This study is not scientifically sound, due to the fact that the test material formed precipitates (surface films and bottom deposits) and actual concentrations were not measured.

d. Adequacy of Study:

1. Classification: Invalid.

2. Rationale: Actual concentrations were not measured despite reported solubility problems.

3. Reparability: None.

15. Completion of One-Liner for Study: N/A.

16. CBI Appendix: N/A.

DATA EVALUATION RECORD

1. Chemical: Prodiamine

2. Test Material: USB 3153 technical, 98.4% ai (technical prodiamine)

3. Study Type: Avian dietary LC_{50}

   Species tested: Mallard duck (Anas platyrhynchos)

4. Study ID: Truslow Farms, Inc., Wildlife Research Division (1975) Eight-day dietary LC_{50} - mallard ducks. USB 3153. Final report. Submitted by Sandoz Crop Protection Crop., Chicago, IL. EPA File Symbols 55947-UR, 55947-UE, 55947-UG. (Orig. submitted by Velsicol 876-452, 876-453, 876-454.) EPA Accession No. 260681.

5. Reviewed by: Allen W. Vaughan
   Entomologist
   EEB/HED
   Signature: Allen W. Vaughan
   Date: 1/8/87

6. Approved by: Norman Cook
   Supervisory Biologist
   EEB/HED
   Signature: Norman Cook
   Date: 1.9.87

7. Conclusions:

   This study is scientifically sound, and shows the 8-day dietary LC_{50} for prodiamine technical to mallard ducks to be greater than 10,000 ppm. This study fulfills the Guideline requirement for an avian dietary LC_{50} test on mallard ducks.

8. Recommendations: N/A.

9. Background:

   This study was submitted in support of registration.

10. Discussion of Individual Studies: N/A.

11. Materials and Methods:

a. Test animals were mallard ducks, Anas platyrhynchos, from the production flock at Truslow Farms, Inc., Chestertown, MD. Birds were 14 days old at initiation of the study.

b. Test system: Mallard duck eggs were incubated in a Chick Master (Model 52E) for 26 days. The temperature during incubation was maintained between 99.1° and 99.3 °F. Upon hatching, the chicks were placed in Beacon (Model B755) battery brooders until they were 14 days of age. Battery brooder temperature was maintained at 99.0 °F from the day of hatch through completion of the study.

At 14 days of age, the birds were randomly assigned to negative control, positive control, and experimental groups, as outlined above, without regard to sex. Prior to initiation of and during the 8-day LC_{50} study, the basal diet was Truslow Farms' game bird starter ration. Starter ration and water were available ad libitum throughout the study.

The experimental material and dieldrin were dissolved in corn oil in concentrations such that the addition of two parts (by weight) of each solution to 98 parts of the standard game bird starter ration resulted in the logarithmic series of dosage levels outlined above. For the purposes of diet preparation, the experimental material was assumed to be 100 percent active material.

The birds were exposed to the appropriate dietary concentrations for 5 days, and then maintained on toxicant-free diet for an additional 3-day observation period. The negative control birds received the basal diet throughout the study.

Body weights were recorded by pen at initiation and termination of the study. Food consumption was recorded by pen during the 5-day exposure period. Food consumption was measured accurately, but is presented as an estimate due to the unavoidable wastage by the birds.

Symptoms of toxicity and mortality were recorded daily throughout the study. Mortality was analyzed statistically by the method of Litchfield, J.T., and Wilcoxon, F., J. Pharmacol. Exptl. Therap., 96, 99, 1949.

c. Dose: Dietary bioassay using measured concentrations; corn oil carrier.

d. Design: Five concentrations (464, 1000, 2150, 4640, and 10,000 ppm) plus control and dieldrin controls (68.1 to 316 ppm, five concentrations); 10 birds per dosage level.

e. Statistics: Due to lack of mortality in the test birds, with the exception of the dieldrin controls, no analyses were conducted.

12. Reported Results:

Experimental Material - USB 3153 did not cause symptoms of toxicity or behavioral abnormalities at the dosage levels tested. There was no mortality at any dosage level.

Negative Controls - There was no mortality in the negative control groups, and the birds appeared normal throughout the study.

Dieldrin Controls - There was a dose-related suppression in body weight gain and food consumption. At the 68 ppm dosage level, hyperexcitability was observed; however, no mortality occurred. The following symptoms of toxicity were observed at the 100, 147, 215, and 316 ppm dosage levels and were dose-related in severity: lack of coordination, loss of the righting reflex, rigidly extended legs and neck, and salivation.

13. Study Authors' Conclusions/QA Measures:

Eight-day dietary LC_{50} > 10,000 ppm (technical material)

QA measures were not reported.

14. Reviewer's Discussion and Interpretation of the Study:

a. Test Procedure: Procedures were in accordance with protocols recommended in the Guidelines and in the HED Standard Evaluation Procedure for the avian dietary LC_{50} test. The only significant deviation was that test birds were 14 days old at test initiation; for mallard ducks, recommended age is 5 to 10 days. Due to lack of mortality even at the highest dosage level (10,000 ppm), it is not likely that this deviation affected the outcome of the test.

b. Statistical Analysis: Analyses were conducted only on the dieldrin data. As there was no mortality in the prodiamine birds, no analysis was conducted.

c. Discussion/Results: The study is scientifically sound, and shows the dietary LC_{50} for technical prodiamine in mallard ducks to be greater than 10,000 ppm.

d. Adequacy of Study:

1. Classification: Core.

2. Rationale: SEP protocol; technical material.

3. Reparability: N/A.

15. Completion of One-Liner for Study:

One-liner completed October 14, 1986.

16. CBI Appendix: N/A.

DATA EVALUATION RECORD

1. Chemical: Prodiamine

2. Test Material: USB 3153 technical, 98.4% ai (technical prodiamine)

3. Study Type: Avian dietary LC_{50}

   Species tested: Bobwhite quail (Colinus virginianus)

4. Study ID: Truslow Farms, Inc., Wildlife Research Division (1975) Eight-day dietary LC_{50} - bobwhite quail. USB 3153. Final report. Submitted by Sandoz Crop Protection Corp., Chicago, IL. EPA File Symbols 55947-UR, 55947-UE, 55947-UG. (Orig. submitted by Velsicol under EPA Reg. Nos. 876-452, 876-453, 876-454.) EPA Accession No. 260681.

5. Reviewed by: Allen W. Vaughan, Entomologist, EEB/HED — Signature: Allen W. Vaughan — Date: 1/8/87

6. Approved by: Norman Cook, Supervisory Biologist, EEB/HED — Signature: Norman Cook — Date: 1.9.87

7. Conclusions:

This study is scientifically sound, and shows the 8-day dietary LC_{50} for prodiamine technical to bobwhite quail to be greater than 10,000 ppm. This study fulfills the Guideline requirement for an avian dietary LC_{50} test on bobwhite quail.

8. Recommendations: N/A.

9. Background:

This study was submitted in support of registration.

10. Discussion of Individual Studies: N/A.

11. Materials and Methods:

a. Test animals were bobwhite quail, Colinus virginianus, from the production flock at Truslow Farms, Inc., Chestertown, MD. Birds were 14 days old at initiation of the study.

b. Test system: Bobwhite quail eggs were incubated in a Chick Master (Model 52E) for 23 days. The temperature during incubation was maintained between 99.1° and 99.3 °F. Upon hatching, the chicks were placed in Beacon (Model B755) battery brooders until they were 14 days of age. Battery brooder temperature was maintained at 99.0 °F from the day of hatch through completion of the study.

At 14 days of age, the birds were randomly assigned to negative control, positive control, and experimental groups, as outlined above, without regard to sex. Prior to initiation of and during the 8-day LC_{50} study, the basal diet was Truslow Farms' game bird starter ration. Starter ration and water were available ad libitum throughout the study.

The experimental material and dieldrin were dissolved in corn oil in concentrations such that the addition of two parts (by weight) of each solution to 98 parts of the standard game bird starter ration resulted in the logarithmic series of dosage levels outlined above. For the purposes of diet preparation, the experimental material was assumed to be 100 percent active material.

The birds were exposed to the appropriate dietary concentrations for 5 days, and then maintained on toxicant-free diet for an additional 3-day observation period. The negative control birds received the basal diet throughout the study.

Body weights were recorded by pen at initiation and termination of the study. Food consumption was measured accurately, but is presented as an estimate due to the unavoidable wastage by the birds.

Symptoms of toxicity and mortality were recorded daily throughout the study. Mortality was analyzed statistically by the method of Litchfield, J.T., and Wilcoxon, F., J. Pharmacol. Exptl. Therap., 96, 99, 1949.

c. Dose: Dietary bioassay using measured concentrations; corn oil carrier.

d. Design: Five concentrations (464, 1000, 2150, 4640, and 10,000 ppm) plus control and dieldrin controls (10.0 to 46.4 ppm, five concentrations); 10 birds per dosage level.

e. Statistics: Due to very low mortality in the test birds, with the exception of the dieldrin controls, no analyses were conducted.

12. Reported Results:

Bobwhite quail dietary LC_{50} for technical prodiamine was determined to be greater than 10,000 ppm. With the exception of a 10 percent group mortality, wing droop, and mild depression at the 10,000 ppm dosage level, USB 3153 (prodiamine) did not cause symptoms of toxicity or behavioral abnormalities at the dosage levels tested.

There was no mortality in the negative control groups, and the birds appeared normal throughout the study.

In the dieldrin controls, hyperexcitability was noted at the 10.0 and 14.7 ppm dosage levels. Depression, loss of the righting reflex, clonic convulsions, wing droop, and salivation preceded death at the 21.5, 31.6, and 46.4 ppm dosage levels.

13. Study Authors' Conclusions/QA Measures:

Eight-day dietary LC_{50} > 10,000 ppm (technical material)

QA measures were not reported.

14. Reviewer's Discussion and Interpretation of the Study:

a. Test Procedures: Procedures were in accordance with protocols recommended in the Guidelines and in the HED Standard Evaluation Procedure for the avian dietary LC_{50} test. There were no significant problems in this regard.

b. Statistical Analysis: Analyses were conducted only on the dieldrin data. As mortality in the prodiamine birds was limited to one bird at the highest dosage level, no analysis was needed.

c. Discussion/Results: This study is scientifically sound, and shows the dietary LC_{50} for technical prodiamine in bobwhite quail to be greater than 10,000 ppm.

d. Adequacy of Study:

1. Classification: Core.

Rationale:

2. SEP protocol; technical material.

3. Reparability: N/A.

15. Completion of One-Liner for Study:

One-liner completed October 14, 1986.

16. CBI Appendix: N/A.

DATA EVALUATION RECORD

1. Chemical: Prodiamine

2. Test Material: Compound 3153 Technical, 99.6% ai

3. Study Type: Avian single-dose oral LD_{50}

   Species tested: Mallard duck (Anas platyrhynchos)

4. Study ID: Industrial Bio-Test Laboratories, Inc. (1975) Acute oral toxicity study with 3153 technical in mallard ducks. Report No. 651-06053. Prepared by IBT Laboratories, Inc., Northbrook, IL. Submitted by Sandoz Crop Protection Corp., Chicago, IL. EPA File Symbols 55947-UR, 55947-UE, 55947-UG. (Orig. submitted by Velsicol under EPA Reg. Nos. 876-452, 876-453, 876-454.) EPA Accession No. 260681. Also reviewed in conjunction with the report: Audit of Report No. 651-06053, sponsored by U.S. Borax Research Corp. (Report No. TA 79-33).

5. Reviewed by: Allen W. Vaughan
   Entomologist
   EEB/HED
   Signature: Allen W. Vaughan
   Date: 1/8/87

6. Approved by: Norman Cook
   Supervisory Biologist
   EEB/HED
   Signature: Norman Cook
   Date: 1.9.87

7. Conclusions:

This study is not scientifically sound. Although the acute oral LD_{50} was determined to be greater than 10,000 mg/kg, the report indicates that the majority of test birds "possessed symptoms" of regurgitation within 3 hours of administration. This incidence of regurgitation is also noted in the audit. This factor is sufficient to render the study invalid. This study does not fulfill the Guideline requirement for an avian acute oral LD_{50} test.

8. Recommendations:

Because regurgitation occurred so quickly following administration, the study is not reparable.

9. Background:

This study was submitted in support of registration.

10. Discussion of Individual Tests: N/A.

11. Materials and Methods:

a. Test animals were young adult mallard ducks; age and source of birds not reported.

b. Test system: The ducks were weighed individually on Test Day 0 and at sacrifice (Day 21) and by groups on Test Days 3, 7, and 14. All birds were fasted for dosing on Test Day 0. The birds were permitted a standard laboratory diet plus water at all times. Food consumption was recorded weekly during the 21-day test period. The dose for the individual test animals was administered via gelatin capsules on Test Day 0.

Observations were made daily to ascertain the presence or absence of clinical signs of toxicity indicative of test material effect.

All animals dying during the study and all animals sacrificed on Test Day 21 were subjected to a gross pathologic examination.

c. Dose: Acute oral bioassay using measured doses; test material was administered undiluted in gelatin capsules.

d. Design: One test group (10,000 mg/kg) and one control group of 5 males and 5 females each.

e. Statistics: Due to lack of mortality, no analysis was conducted.

12. Reported Results:

Mallard duck acute oral LD_{50} for technical prodiamine was determined to be greater than 10,000 mg/kg body weight. The majority of test birds possessed symptoms of regurgitation and a yellow-orange discoloration of the feces 3 hours postdosing. Gross pathological examination of all animals sacrificed at test conclusion revealed no abnormal tissue alterations. Body weight data and food consumption data were essentially the same in both the control and test groups.

13. Study Authors' Conclusions/QA Measures:

Acute oral $LD_{50} > 10,000$ mg/kg (technical material).

QA measures were not reported.

14. Reviewer's Discussion and Interpretation of the Study

a. Test Procedures: Although procedures were apparently sound, most of the birds regurgitated the test material within 3 hours of dosing.

b. Statistical Analysis: Due to lack of mortality, no analysis was conducted.

c. Discussion/Results: Data from this study cannot be used in a hazard assessment, as most of the test birds regurgitated the test material within 3 hours of dosing.

d. Adequacy of Study:

1. Classification: Invalid.

2. Rationale: Regurgitation of test substance.

3. Reparability: None

15. Completion of One-Liner for Study: N/A.

16. CBI Appendix: N/A.

DATA EVALUATION RECORD

1. Chemical: Prodiamine

2. Test Material: Compound 3153 technical, 99.6% ai

3. Study Type: Avian single-dose oral LD_{50}

   Species tested: Bobwhite quail (Colinus virginianus)

4. Study ID: Industrial Bio-Test Laboratories, Inc. (1975) Acute oral toxicity study with 3153 technical in bobwhite quail. Report No. 651-06052. Prepared by IBT Laboratories, Inc., Northbrook, IL. Submitted by Sandoz Crop Protection Corp., Chicago, IL. EPA File Symbols 55947-UR, 55947-UE, 55947-UG. (Orig. submitted by Velsicol under EPA Reg. Nos. 876-452, 876-453, 876-454.) EPA Accession No. 260681. Also reviewed in conjunction with the report: Audit of Report No. 651-06052, sponsored by U.S. Borax Research Corp. (Report No. TA 79-32).

5. Reviewed by: Allen W. Vaughan
   Entomologist
   EEB/HED
   Signature: Allen W. Vaughan
   Date: 1/8/87

6. Approved by: Norman Cook
   Supervisory Biologist
   EEB/HED
   Signature: Norman Cook
   Date: 1.9.87

7. Conclusions:

On the basis of the information provided in the IBT report, this study would appear to be scientifically sound, with the acute oral LD_{50} in bobwhite quail estimated to be greater than 10,000 mg/kg. Although several minor items were omitted in the report (e.g., age of test birds, source of test birds, description of housing conditions), these omissions would not render the study deficient in view of the lack of mortality at 10,000 mg/kg.

The major problem is indicated only in the audit of the study, which reports that the test material was regurgitated on day of treatment. The study report does not mention any incidence of regurgitation.

Data on the incidence of regurgitation (time of incidence and number of birds involved) are needed before final evaluation of the study can be made. This study, as submitted, does not fulfill the Guideline requirement for an avian acute oral LD_{50} test.

8. Recommendations:

As indicated above, information on the incidence of regurgitation is needed to allow validation of the study.

9. Background:

This study was submitted in support of registration.

10. Discussion of Individual Studies: N/A.

11. Materials and Methods:

a. Test animals were young adult bobwhite quail (Colinus virginianus; age and source of birds not reported.

b. Test system: The quail were weighed individually on Test Day 0 and at sacrifice (Day 21) and by groups on Test Days 3, 7, and 14. All birds were fasted for dosing on Test Day 0. The birds were permitted a standard laboratory diet plus water at all times. Food consumption was recorded weekly during the 21-day test period. The dose for the individual test animal was administered via gelatin capsules on Test Day 0.

Observations were made daily to ascertain the presence or absence of clinical signs of toxicity indicative of test material effect.

All animals dying during the study and all animals sacrificed on Test Day 21 were subjected to a gross pathologic examination.

c. Dose: Acute oral bioassay using measured doses; test material was administered undiluted in gelatin capsules.

d. Design: One test group (10,000 mg/kg) and one control group of 5 males and 5 females each.

e. Statistics: Due to lack of mortality, no analysis was conducted.

12. Reported Results:

Bobwhite quail acute oral LD_{50} for technical prodiamine was determined to be greater than 10,000 mg/kg body weight. No abnormal behavioral reactions were observed which could be attributed to the test material. Gross pathological examination of all animals sacrificed at test conclusion revealed no abnormal tissue alterations. Body weight data were considered normal since test group values were essentially the same when compared to the control group. Food consumption data were essentially the same in both the control and test groups.

13. Study Authors' Conclusions/QA Measures:

Acute oral $LD_{50} > 10{,}000$ mg/kg (technical material).

QA measures were not reported.

14. Reviewer's Discussion and Interpretation of the Study:

a. Test Procedures: Procedures were apparently in accordance with protocols recommended in the Guidelines. The major problem in this study was that regurgitation of the test material occurred on day of treatment, and this was not discussed in the report.

b. Statistical Analysis: Due to lack of mortality, no analysis was conducted.

c. Discussion/Results: Information provided is insufficient to assess the soundness of the study. As indicated above (#7, Conclusions), data on the incidence of regurgitation are needed to complete the evaluation.

d. Adequacy of Study:

1. Classification: Invalid as submitted.

2. Rationale: Insufficient information.

3. Repairability: May be reparable to "Core" status with submission of additional information.

15. Completion of One-Liner for Study: N/A.

16. CBI Appendix: N/A.

DATA EVALUATION RECORD

1. Chemical: Prodiamine

2. Test Material: Technical, 91.3% ai.

3. Study Type: Freshwater invertebrate acute LC_{50}

   Species tested: Daphnia magna

4. Study ID: Forbis, A.D., L. Georgie, and D. Burgess (1985) Static Acute Toxicity Report No. 32710. Acute toxicity of prodiamine technical to Daphnia magna. Prepared by Analytical Bio-Chemistry Laboratories, Inc., Columbia, MO. Submitted by Sandoz Crop Protection Corp., Chicago, IL. EPA File Symbols 55947-UR, 55947-UE, 55947-UG. (Orig. submitted by Velsicol under EPA Reg. Nos. 876-452, 876-453, 876-454.) EPA Accession No. 260681.

5. Reviewed by: Allen W. Vaughan, Entomologist, EEB/HED — Signature: Allen W. Vaughan — Date: 1/8/87

6. Approved by: Norman Cook, Supervisory Biologist, EEB/HED — Signature: Norman Cook — Date: 1.9.87

7. Conclusions:

This study is not scientifically sound. The 48-hour LC_{50} was determined to be 29 mg/L. However, the authors reported a precipitate in the test vessels at the four highest concentrations, and toxicant concentrations were not measured at any point during the test. Thus, actual levels of exposure cannot be determined.

This study does not fulfill the Guideline requirement for an acute toxicity test on freshwater invertebrates.

8. Recommendations: N/A.

9. Background:

This study was submitted in support of registration.

10. Discussion of Individual Studies: N/A.

11. Materials and Methods:

a. Test animals were Daphnia magna cultured at the ABC facilities. They were in the first instar, less than 24 hours old, at test initiation.

b. Test system: The static Daphnia bioassay was conducted in 250 mL glass beakers containing 200 mL of aged well water. Test vessels were kept at 20 °C in a temperature-controlled area. The lighting was maintained at 50 to 70 foot-candles on a 16-hour daylight photoperiod. All concentrations were observed once every 24 hours for mortality and abnormal effects such as surfacing, clumping of the daphnids together, and daphnids lying on the bottom of test chambers.

c. Dose: Acute bioassay using nominal concentrations; acetone solvent.

d. Design: Six nominal concentrations (5.6, 10, 18, 32, 56, 100 mg/L) plus control and solvent control (0.1 mL acetone per test vessel); 20 daphnids per test level and control, divided into 2 reps.

e. Statistics: The 24- and 48-hour LC_{50} values and corresponding 95 percent confidence limits were determined by an LC_{50} computer program developed by Stephan et al. This program calculated the LC_{50} statistic and its 95 percent confidence limits using the binomial, moving average angle and probit methods because no one method is appropriate for all possible sets of data. The method of calculation selected was that which gave the narrowest confidence limits for each separate analysis.

12. Reported Results:

The 24- and 48-hour LC_{50} values for prodiamine technical were > 100 and 29 mg/L. All results were based on the nominal concentrations of 5.6, 10, 18, 32, 56, and 100 mg/L. The no-effect concentration, based on the lack of mortality and abnormal effects, was < 5.6 mg/L after 48 hours. The abnormal effects of mortality, erratic movement, surfacing, and daphnids lying on the bottom were observed in the 5.6, 10, 18, 32, 56, and 100 mg/L test concentrations. A yellow precipitate formed on the bottom of the test vessels in the 18, 32, 56, and 100 mg/L concentrations. This seemed to be due to the insolubility of prodiamine technical in ABC well water at these concentrations. Also, the erratic mortality of the daphnids in these test concentrations was probably due to the test compound's insolubility in ABC well water.

13. Study Authors' Conclusions/QA Measures:

48-hour LC_{50} = 29 mg/L (CI = 20-39 mg/L) (technical material).

The study was conducted following the intent of the Good Laboratory Practice Regulations and the final report was reviewed by Analytical Bio-Chemistry Laboratories' Quality Assurance Unit. All original raw data were provided to Velsicol Chemical Corporation, with a copy retained at Analytical Bio-Chemistry Laboratories.

14. Reviewer's Discussion and Interpretation of the Study:

a. Test Procedures: The one major deviation from established protocol is enough to render the study invalid. That is, despite the fact the surface films and precipitates were noted and reported, concentrations were not measured at any point. The reported LC_{50} values were based on nominal concentrations only.

b. Statistical Analysis: Types of analyses conducted were appropriate for these test data. However, as data on concentration levels were not supported by measuring the actual concentrations, results of the analyses are invalid.

c. Discussion/Results: This study is not scientifically sound, due to the fact that the test material formed precipitates (surface films and bottom deposits) and actual concentrations were not measured.

d. Adequacy of Study:

1. Classification: Invalid.

2. Rationale: Actual concentrations were not measured despite reported solubility problems.

3. Reparability: None.

15. Completion of One-Liner for Study: N/A.

16. CBI Appendix: N/A.

Prodiamine

Page_____ is not included in this copy.

Pages 32 through 70 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

X A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

____ FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.