DP Barcode : D217045
PC Code No : 111801
EEB Out : 8/18 RS

To:
Product Manager
Special Review and Reregistration Division (7508W)

From: Anthony F. Maciorowski, Chief
Ecological Effects Branch/EFED (7507C)

Attached, please find the EEB review of...

Reg./File # :
Chemical Name : PHMB
Type Product : biocide
Product Name :
Company Name :
Purpose : Review waiver request.

Action Code: Date Due: 8/7/95
Reviewer: ~~David Bays~~
Harry Craven

EEB Guideline/MRID Summary Table: The review in this package contains an evaluation of the following:

GDLN NO	MRID NO	CAT	GDLN NO	MRID NO	CAT	GDLN NO	MRID NO	CAT
71-1(A)			72-2(A)			72-7(A)		
71-1(B)			72-2(B)			72-7(B)		
71-2(A)			72-3(A)			122-1(A)		
71-2(B)			72-3(B)			122-1(B)		
71-3			72-3(C)			122-2		
71-4(A)			72-3(D)			123-1(A)		
71-4(B)			72-3(E)			123-1(B)		
71-5(A)			72-3(F)			123-2		
71-5(B)			72-4(A)			124-1		
72-1(A)			72-4(B)			124-2		
72-1(B)			72-5			141-1		
72-1(C)			72-6			141-2		
72-1(D)						141-5		

Y=Acceptable (Study satisfied Guideline)/Concur
P=Partial (Study partially fulfilled Guideline but additional information is needed
S=Supplemental (Study provided useful information but Guideline was not satisfied)
N=Unacceptable (Study was rejected)/Nonconcur

(1)

DP BARCODE: D217045

DATA PACKAGE RECORD
BEAN SHEET

DATE: 07/06/9
Page 1 of 1

* * * FREE STANDING DATA PACKAGE * * *

THERE IS NO CASE OR SUBMISSION DATA

* * * DATA PACKAGE INFORMATION * * *

DP BARCODE: 217045 EXPEDITE: Y DATE SENT: 07/06/95 DATE RET.: / /
CHEMICAL: 111801 Poly(iminoimidocarbonyliminoimidocarbonyliminohexamethylene
DP TYPE: 001 Submission Related Data Package
CSF: N LABEL: N

ASSIGNED TO	DATE IN	DATE OUT
DIV : EFED	7/6/95	/ /
BRAN: EEB	7/6/95	8/18/95
SECT: RS4	8/18/95	8/18/95
REVR :Craven	8/18/95	8/18/95
CONTR:	/ /	/ /

ADMIN DUE DATE: 08/07/95
NEGOT DATE: / /
PROJ DATE: / /

* * * DATA REVIEW INSTRUCTIONS * * *

Harry Craven:
Please review the attached Greybeard Data Waiver/Time-Extension for PHMB. Thanks in advance for your time and cooperation!!

Rachelle

* * * DATA PACKAGE EVALUATION * * *

No evaluation is written for this data package

THERE ARE NO ADDITIONAL DATA PACKAGES

— GREYBEARD —

8/18/95

The waiver for the requirement 72-1d is granted. The registrant need only conduct one study on each of the 3 freshwater species: rainbow trout, bluegill sunfish and daphnia magna. The test material can be any of the 3 products (10182-95, 1280-19)

(2)

PHMB (Poly(hexamethylenebiguanide))
Case # 3122
Chemical # 111801
May 1, 1995

To Greybeard Reviewers:

Attached is a letter from Zeneca Biocides, dated.April 7, 1995, written in an effort to eliminate unnecessary data requirements concerning guidelines 72-1(a)- (d) Fish Toxicity for PHMB.

In this letter, Zeneca indicates that their manufacturing use product (MUP) is essentially the same as their typical end use products (TEP) for PHMB. They attach Confidential Statements of Formula in an effort to prove this.

It seems that 72-1(a) and (b) Fish Toxicity Bluegill (and TEP) have been consolidated-- as indicated in the 2/15/95 report card; however, I have not found any other records supporting this. Furthermore, despite the consolidation of the Bluegill studies, both 72-1(c) and (d) Fish Toxicity Rainbow Trout (and TEP) still require separate sets of data. This appears to be contradictory to the registrant who is required to submit two sets of data for trout but only one set for bluegill.

Please verify the interchangeability of data between 72-1(a) and (b), and determine whether the same can be done to 72-1(c) and (d).

Thank you for your assistance. If you have any questions please call Marie Boucher at 308-8178.

Marie A Boucher

08/17/94

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

AUG 17 1994

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM:

SUBJECT: Freshwater Fish Flow-Through Toxicity Test for Vantocil P (20%) to the rainbow trout (MRID # 93191003/ 74296)

TO: Bruce Sidwell, Product Manager 53
Special Review and Reregistration Division

FROM: Anthony F. Maciorowski, Chief
Ecological Effects Branch
Environmental Fate and Effects Division (H7507C) 8/17/94

The EEB has completed a Data Evaluation Report (DER) for a freshwater fish flow-through toxicity test for Vantocil P 20% to the rainbow trout. Because the concentration of test material in each test chamber was not measured, the study was found to "Invalid" and does not meet the 72-1 (d) guideline requirement.

If you have any further questions, please contact Dick Felthousen (305-5829).

Invalid

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DP BARCODE: D205133 REREG CASE # 3122

CASE: 816384 DATA PACKAGE RECORD DATE: 07/08/94
SUBMISSION: S469350 BEAN SHEET Page 1 of 1

* * * CASE/SUBMISSION INFORMATION * * *

CASE TYPE: REREGISTRATION ACTION: 606 GENERIC DATA
CHEMICALS: 111801 Poly(iminoimidocarbonyliminoimidocarbonyliminohexa %

ID#: 111801-010182
COMPANY: 010182 ZENECA INC
PRODUCT MANAGER: 53 BRUCE SIDWELL 703-308-8078 ROOM: CS1 3J2
PM TEAM REVIEWER: BRUCE SIDWELL 703-308-8078 ROOM: CS1 3J2
RECEIVED DATE: 07/08/94 DUE OUT DATE: 11/05/94

* * * DATA PACKAGE INFORMATION * * *

DP BARCODE: 205133 EXPEDITE: N DATE SENT: 07/08/94 DATE RET.: / /
CHEMICAL: 111801 Poly(iminoimidocarbonyliminoimidocarbonyliminohexamethylene
DP TYPE: 100 Phase II Review
CSF: N LABEL: N

ASSIGNED TO	DATE IN	DATE OUT
DIV : EFED	/ /	/ /
BRAN: EEB	7/8/94	/ /
SECT: RS1	/ /	/ /
REVR :	/ /	/ /
CONTR:	/ /	/ /

ADMIN DUE DATE: 11/05/94
NEGOT DATE: / /
PROJ DATE: / /

* * * DATA REVIEW INSTRUCTIONS * * *

Please review submitted data for gdln 72-1(a), MRIDs 74296 and 9319003. If you have any questions, please call Kathryn Scanlon on 308-8178.

* * * DATA PACKAGE EVALUATION * * *

No evaluation is written for this data package

* * * ADDITIONAL DATA PACKAGES FOR THIS SUBMISSION * * *

DP BC	BRANCH/SECTION	DATE OUT	DUE BACK	INS	CSF	LABEL
205132	EEB/RS1	07/08/94	11/05/94	Y	N	N

X

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DATA EVALUATION RECORD

1. **CHEMICAL:** Poly(iminoimidocarbonyliminoimidocarbonylimino-hexamethylene hydrochloride). Shaughnessey Number: 111801.

2. **TEST MATERIAL:** Vantocil P; 20% w/v aqueous solution of Poly(iminoimidocarbonyliminoimidocarbonyliminohexamethylene hydrochloride); CAS No. (32289-58-0) (A-2); a water-white liquid.

3. **STUDY TYPE:** Freshwater Fish Flow-Through Toxicity Test. Species Tested: Rainbow Trout (*Salmo gairdneri*).

4. **CITATION:** Brown, D. and B.G. Maddock. 1981. Determination of the Acute Toxicity of "Vantocil P" to Rainbow Trout (*Salmo gairdneri*). Study No. G 184/G. Report No. BL/B/2081. Study performed by Imperial Chemical Industries Limited, Brixham Laboratory, Freshwater Quarry, Brixham, Devon, U.K. Submitted by ICI Americas, Inc., Wilmington, Delaware. EPA MRID No. 74296 and EPA MRID No. 93191-003 for the Summary Report.

5. **REVIEWED BY:**

Rosemary Graham Mora, M.S.
Associate Scientist
KBN Engineering and
Applied Sciences, Inc.

Signature: Rosemary Graham Mora
Date: 14 November 91

6. **APPROVED BY:**

Pim Kosalwat, Ph.D.
Senior Scientist
KBN Engineering and
Applied Sciences, Inc.

Signature: Richard McCutheon Sr. P. Kosalwat 9/28/
Date: 11/14/91

LES TOUART
[redacted]
Supervisor, EEB/EFED
USEPA

Signature: Denise McLane for Les Touart
Date: 8-16-94

7. **CONCLUSIONS:** This study is not scientifically sound and does not meet the guideline requirements for a flow-through acute toxicity study using freshwater fish. The concentration of test material in each test chamber was not measured. Therefore, the actual concentrations to which the test organisms were exposed are unknown. The 96-hour LC_{50} of Vantocil P for *Salmo gairdneri* was 0.88 mg a.i./l nominal test concentration which classifies Vantocil P as highly

INVALID 1 6 hrs 3 6

toxic to *Salmo gairdneri*. The NOEC was 0.36 mg a.i./l nominal test concentration.

8. **RECOMMENDATIONS:** The study should be repeated with the concentration of test material measured in all test solutions.

9. **BACKGROUND:**

10. **DISCUSSION OF INDIVIDUAL TESTS:** N/A

11. **MATERIALS AND METHODS:**

A. **Test Animals:** Juvenile rainbow trout (*Salmo gairdneri*) were obtained from Zeals Fisheries, Zeals, Wiltshire and held for approximately 2 months at ambient temperature in the laboratory. The fish were acclimated in the test vessels to the test temperature (12 ±1°C) for a period of 3 days before the test. The fish were last treated with malachite green approximately 18 days prior to test initiation. The fish were reported to be in good conditions.

The fish had a mean weight of 3.9 g (range of 1.64-7.05 g) and a mean length of 64 mm (range of 49-79 mm).

B. **Test System:** The test chambers were spherical glass vessels (37 cm in diameter and height) with a nominal capacity of 20 l. The test system was a continuous flow-through system. Concentrated stock solutions (prepared in distilled water) and freshwater (dilution water) were delivered by a series of peristaltic pumps to glass splash heads. The ratio of stock solution to dilution water was 1:100. The solutions were mixed before entering into the test vessels. The flow rate to each test chamber was 200 ml/minute.

The dilution water was freshwater supplied from a 20,000 gallon reservoir and the total hardness was measured daily.

C. **Dosage:** Ninety-six-hour flow-through acute test. Eight nominal concentrations were chosen for this study (1.8, 2.4, 3.2, 4.2, 5.6, 7.5, 10.0, and 13.5 mg/l). In addition, a dilution water control was also used. Concentrations were not adjusted for the percentage of active ingredient.

D. **Design:** Twenty fish were randomly distributed to each test concentration and control (one vessel/treatment

and control). The fish loading rate was 78 g/288 l/day or 0.27 g/l/day.

Mortality and symptoms of stress were noted every 24 hours during the study.

Dissolved oxygen concentration, pH, temperature, and hardness were measured daily.

The concentration of test material of each stock solution was determined daily. Vantocil P has a characteristic absorption in the ultra-violet spectrum. Absorption was determined using a spectrophotometer at 236 nm. "The analytical method available for "Vantocil P" in freshwater had a detection limit of approximately 5 mg/l; in view of this the nominal test exposure concentrations were used in the calculation of the LC_{50} values."

E. **Statistics:** The LC_{50} values were calculated with the probit method (Finney, 1971).

12. **REPORTED RESULTS:** In addition to the 1981 report, a summary was included (Adams, D.S. 1990. Phase 3 Summary of MRID 74296, "Vantocil P": Determination of the Acute Toxicity to Rainbow Trout *Salmo gairdneri*) which presented information from historical records which was not presented in the original report.

Measured concentrations of the test material in the stock solutions were 181, 246.8, 333.5, 430.5, 550, 777, 1003, and 1344 mg/l (Tables 1 and 2, attached). The mean measurements represent 98.2-104.2% of nominal stock solution concentrations. "The dilution ratios were calculated daily for each test vessel from the ratio of the measured flow rate of the dilution water to that of the concentrated stock solution. In all cases, this ratio was within 20% of the nominal 100:1 ratio."

No mortality was observed in the control or the three lowest test concentrations (1.8-3.2 mg/l nominal test concentrations) (Table I, attached). Thirty-five-percent mortality was observed at the 4.2 mg/l nominal test concentration and total mortality was observed at the remaining test concentrations (5.6-13.5 mg/l nominal test concentrations). The 96-hour LC_{50} value and 95% confidence interval for rainbow trout exposed to Vantocil P were 4.4 mg/l and 4.1-4.6 mg/l nominal test concentrations, respectively. Sublethal effects were demonstrated in the

seven highest test concentrations (2.4-13.5 mg/l). Therefore, the NOEC is 1.8 mg/l nominal test concentration.

During the study, the pH was 7.1-7.8, the temperature was 11.5-12.6°C, and the dissolved oxygen concentration was 9.3-11.6 mg/l. Total hardness of the dilution water was 26-30 mg/l as $CaCO_3$.

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:** The authors made no conclusions in the report.

A Statement of GLP Compliance, signed by the study director and representatives of the sponsor company, was included in the summary indicating that the study was conducted prior to the effective date of 40 CFR Part 160. A Quality Assurance Statement was included in the report and was signed by a representative of the performing laboratory's Quality Assurance Unit.

14. **REVIEWER'S DISCUSSION AND INTERPRETATION OF STUDY RESULTS:**

A. **Test Procedure:** The test procedures were generally in accordance with the protocols recommended by the guidelines, except for the following deviations:

The concentration of test material in each test chamber was not measured; only the levels of test material in the stock solutions were measured and the dilution ratio determined. For a flow-through system, the guidelines state that the concentration of test material in each test chamber must be determined.

Test fish were acclimated to test conditions for only 3 days; a minimum of 2 weeks is recommended.

Pre-test mortality was not reported; not greater than 3% mortality during the 48 hours prior to test initiation is required.

The weight range of the fish (1.64-7.05 g) was larger than recommended (0.1-5.0 g) in the SEP.

The age of the test organisms was not reported.

The report did not mention whether feeding of the test organisms was limited to just prior to testing.

The authors did not report how the test temperature was maintained (i.e. by a water bath or by air).

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The actual test solution volume and depth were not reported. The summary stated the test vessels were "spherical glass vessels 37 cm in height and diameter and of nominal capacity 20 litres."

The original source of the dilution water was not stated. It is not known whether the water had been analyzed for inorganic and organic pollutants before use.

The conductivity and alkalinity of the dilution water were not reported.

The recommended photoperiod for a freshwater fish acute toxicity study is 16-hour light/8-hour dark with 15- to 30-minute transitions. The report did not mention the use of transition periods.

The light intensity during the study was not measured.

The test temperature was not continuously monitored.

B. **Statistical Analysis:** EPA's Toxanal computer program was used to verify the LC_{50} value and 95% confidence interval presented by the authors. The reviewer's LC_{50} (4.4 mg/l nominal test concentration) and 95% confidence interval (3.2-5.6 mg/l) are similar to those of the authors (printout, attached). The LC_{50} adjusted for the active ingredient of the test material is 0.88 mg a.i./l.

C. **Discussion/Results:** Most of the deviations listed above probably did not affect the results of this test. However, the concentration of test material in each test chamber was not measured as required by the guidelines. Therefore, the actual concentrations to which the test organisms were exposed are unknown.

This study is not scientifically sound and does not meet the guideline requirements for a flow-through toxicity study using freshwater fish. The 96-hour LC_{50} of Vantocil P to *Salmo gairdneri* was 0.88 mg a.i./l nominal concentration. Based on the results of this study, Vantocil P is highly toxic to *Salmo gairdneri*. The NOEC was 0.36 mg a.i./l nominal test concentration.

D. **Adequacy of the Study:**

(1) **Classification:** Invalid.

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(2) **Rationale:** The concentration of test material in each test chamber was not measured. Therefore, the actual concentrations to which the test organisms were exposed are unknown.

(3) **Repairability:** No.

15. **COMPLETION OF ONE-LINER FOR STUDY:** Yes, November 11, 1991.

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Page _____ is not included in this copy.

Pages 12 through 14 are not included in this copy.

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.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action.

X 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 confi by product registrants. If you have any questions, please the individual who prepared the response to your request.

Rosemary Graham Mora Vantocil P Salmo gairdneri 9-25-91

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
13.5	20	20	100	9.536742E-05
10	20	20	100	9.536742E-05
7.5	20	20	100	9.536742E-05
5.6	20	20	100	9.536742E-05
4.2	20	7	35	13.1588
3.2	20	0	0	9.536742E-05
2.4	20	0	0	9.536742E-05
1.8	20	0	0	9.536742E-05

THE BINOMIAL TEST SHOWS THAT 3.2 AND 5.6 CAN BE
USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT
CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL
ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 4.41915

WHEN THERE ARE LESS THAN TWO CONCENTRATIONS AT WHICH THE
PERCENT DEAD IS BETWEEN 0 AND 100, NEITHER THE MOVING AVERAGE
NOR THE PROBIT METHOD CAN GIVE ANY STATISTICALLY SOUND RESULTS.

****

Shaughnessey # 111801 Chemical Name Poly(iminoimidocarbonylimi) Chemical Class _____ Page 1 of 1

Study/Species/Lab/ MRID #	Chemical % a.i.	Results	Reviewer/ Date	Validation Status
48-Hour EC_{50}	_____	EC_{50} - ppm (95% C.L. ( )) Control Mortality (%) - Solvent Control Mortality (%) - Slope - # Animals/Level - Temperature - 48-Hour Dose Level ppm /(% Effect) ( ), ( ), ( ), ( ), ( ) Comments:	_____	_____
96-Hour LC_{50}	20%	LC_{50} - 0.88 ppm a.i.* (95% C.L. 0.64-1.12) Control Mortality (%) - 0 Solvent Control Mortality (%) - NA Slope - NA # Animals/Level - 20 Temperature - 11.5-12.6°C 96-Hour Dose Level ppm a.i.*/(% Mortality) 0.36(0), 0.48(0), 0.64(0), 0.84(35), 1.12(100), 1.5(100), 2.0(100), 2.7(100) Comments: * Based on active ingredient of nominal concentrations. The concentration of test material in each test chamber was not measured. Therefore, the actual test concentrations to which the fish were exposed are unknown.	RGM 11/11/91	Invalid

Species: Salmo gairdneri

Lab: ICI Brixham Laboratory

MRID # 93191-003

(54) 91