3-23-93

DP Barcode : D186220
PC Code No : 108501
EEB Out : 3/23/93

To: Walter Waldrop
Product Manager 71
Special Review and Reregistration Division (H7508W)

From: Anthony F. Maciorowski, Chief
Ecological Effects Branch/EFED (H7507C)

Attached, please find the EEB review of...

Reg./File # : 108501
Chemical Name : Pendimethalin
Type Product : Herbicide
Product Name :
Company Name : American Cyanamid
Purpose : Response to registrant's rebuttal to EEB's review of Tier 2 phytotoxicity studies.

Action Code : 629 Date Due : 03/20/93
Reviewer : Tracy L. Perry

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)	42372201 42372202	N N
71-4(B)			72-3(E)			123-1(B)	42372203	N
71-5(A)			72-3(F)			123-2	42372205 42372206 42372207	Y Y Y
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

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

MAR 22 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Pendimethalin: American Cyanamid's rebuttal to EEB's review of Tier 2 phytotoxicity studies.

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

TO: Walter Waldrop, PM 71
Reregistration Branch
Special Review and Reregistration Division (H7508W)

Background

On October 14, 1992, EEB completed its review of seven Tier 2 phytotoxicity studies for pendimethalin (MRID Nos. 423722-01-07). Six of the seven studies (all except 42372204) were found to be invalid. American Cyanamid is rebutting EEB's classification of these studies with the current submission.

Tier 2 Aquatic Plant Studies

Three of the four aquatic plant studies were classified as invalid due to apparent contamination of the solvent controls with the test material. Although other discrepancies with guideline requirements were commented on by the registrant, only the contamination point will be discussed in this response as this was the reason for invalidation.

After review of the registrant's comments, the reviewer has determined that these studies may be upgraded from invalid to core. Although the solvent control was apparently contaminated in all three studies, the 5-day algae/diatom cell counts were not statistically different between the no-treatment controls and the solvent controls. Therefore, the possible contamination of the solvent controls had no significant impact on algae/diatom growth.

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control when a solvent (acetone) was used to dissolve the test material. The registrant feels that this omission is minor as the concentration of acetone used was not high enough to cause phytotoxic symptoms in the test organisms. However, the registrant has no data to prove this. In addition, the registrant claims that Subdivision J Guidelines do not specify the need for a no-treatment control when a solvent is used. On page 21 of Subdivision J, it states: "Where a carrier, vehicle, or adjuvant other than water is used, appropriate experiments and controls should be included to distinguish the possible action of the carrier, vehicle or adjuvant." The action of acetone cannot be determined unless there is a water only control to compare it with.

Therefore, based on the above, the terrestrial plant studies remain invalid. These studies may possibly be upgraded to supplemental/ core (depending on the study) if the registrant can provide information demonstrating that the concentrations of acetone used in these studies are not phytotoxic to the plant species tested.

If you have any questions, please contact Tracy Perry at 305-6461 or Henry Craven at 305-5320.

TRACY PERRY PENDIMETHALIN SKELETONEMA COSTATUM EC50

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
23.2	100	96	96	0
11.3	100	94	94	0
5	100	45	45	0
2.7	100	18	18	0
1.5	100	29	29	0
.7	100	4	4	0

THE BINOMIAL TEST SHOWS THAT 5 AND 11.3 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 5.361849

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
5	1.190022E-02	4.137341	3.659327	4.692284

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
3	.3350071	9.570804	0

A PROBABILITY OF 0 MEANS THAT IT IS LESS THAN 0.001.

SINCE THE PROBABILITY IS LESS THAN 0.05, RESULTS CALCULATED
USING THE PROBIT METHOD PROBABLY SHOULD NOT BE USED.

SLOPE = 2.299801
95 PERCENT CONFIDENCE LIMITS = .9686808 AND 3.630921

LC50 = 4.173468
95 PERCENT CONFIDENCE LIMITS = 2.191364 AND 8.369531

LC10 = 1.170241
95 PERCENT CONFIDENCE LIMITS = .1804027 AND 2.219921

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TRACY PERRY PENDIMETHALIN NAVICULA PELLICULOSA EC50

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB. (PERCENT)
56.2	100	99	99	0
28.4	100	98	98	0
12.6	100	83	83	0
6	100	61	61	0
3.2	100	4	4	0

BECAUSE THE NUMBER OF ORGANISMS USED WAS SO LARGE, THE 95 PERCENT CONFIDENCE INTERVALS CALCULATED FROM THE BINOMIAL PROBABILITY ARE UNRELIABLE. USE THE INTERVALS CALCULATED BY THE OTHER TESTS.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 5.423178

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
3	1.268907E-02	6.685684	6.048959	7.339373

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
5	.836489	11.71798	0

A PROBABILITY OF 0 MEANS THAT IT IS LESS THAN 0.001.

SINCE THE PROBABILITY IS LESS THAN 0.05, RESULTS CALCULATED USING THE PROBIT METHOD PROBABLY SHOULD NOT BE USED.

SLOPE = 3.484039

95 PERCENT CONFIDENCE LIMITS = .297545 AND 6.670534

LC50 = 6.522581

95 PERCENT CONFIDENCE LIMITS = 1.154899 AND 21.02334

LC10 = 2.817734

95 PERCENT CONFIDENCE LIMITS = 1.605369E-04 AND 5.260404

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CYANAMID

This Submission Contains No 40 CFR 158 Data

American Cyanamid Company
Agricultural Research Division
P.O. Box 400
Princeton, NJ 08543-0400
(609) 799-0400

December 18, 1992

Ms. Terri Stowe
Reregistration Branch I
Special Review and Reregistration Branch
Office of Pesticide Programs
U. S. Environmental Protection Agency
Crystal Mall No. 2
1921 Jefferson Davis Highway
Arlington, VA 22202

Re: Pendimethalin Reregistration
Response to LS to MG Letter of November 16, 1992
Concerning EEB Phytotoxicity Studies 40 CFR 158 GN 123

Dear Ms. Stowe:

Thank you for sending us the referenced letter and review (attached for your ease of reference). We have examined the comments made by the EEB reviewer and we believe that a response on our part to have all the studies classified as "invalid" changed to "core" is warranted.

The Guideline Studies Number 123-1A & 1B were classified as invalid primarily due to the lack of an non-treatment control. The Guideline Studies Number 123-2 were classified as invalid, with the exception of the core-approved Selanastrum capricornutum, primarily due to solvent controls contaminated with the test materials. Both these objections are based on correct statements of fact, however, we differ with the review as to the significance of these facts. In summary, we believe that the data provided to the Agency are adequate to reclassify these studies as valid and to assess environmental risk.

We have prepared a response for each of the studies as follows:

The Standard Evaluation Procedures (SEP) for this study specifies that if a solvent was used to dissolve the test compound, the concentration used should not result in phytotoxicity and that a solvent control should be used. Since the concentration of acetone was not sufficient to cause phytotoxic symptoms and an acetone control was used, both of these requirements were fulfilled in the submitted studies. In addition, neither the Nontarget Hazard Evaluation Guidelines nor the SEP specify the need for a water control when a solvent is used to dissolve the test compound.

Page 6 of Review, Item 14B..

The reviewer calculated the EC values for the ryegrass dry weight parameter to be 0.016 pound active ingredient per acre (lb ai/A) and suggested rounding the value to 0.02 lb ai/A. The report stated the value was 0.0138 lb ai/A which was rounded to 0.01 lb ai/A. To determine the EC values, the reviewer analyzed the treatment mean percent effect levels while the values presented in the report are based on analysis of the replicate percent effect levels. Analyses based on individual replicate effect levels would generally be more sensitive than those conducted on treatment effect levels. Therefore, we believe that the values presented in the study report should be retained since they were calculated on all available data.

Page 6 of Review, Item 14C.

Since the dose response in many of the parameters was either not adequate for analysis or the highest treatment concentration of 4.0 lb ai/A did not result in a significant phytotoxic effect, all EC_{25} and EC_{50} values could not be calculated. An asterisk or a "ND" was used to designate crops where EC values could not be determined. The reviewer suggested changing all of these designations to ">4.0 lb ai/A". If the study is reclassified by the EPA as valid, we will issue an amended report, changing the report tables where appropriate.

To restate our position, a second (water-only) control was not a requirement and, furthermore, such a control would not provide any additional information useful to hazard analysis. For these reasons, we request that this study be reclassified as valid.

3. A Tier 2 Plant Phytotoxicity Study For Vegetative Vigor Using AC 92,553. Pan-Ag Laboratory Study Number BL91-454, American Cyanamid Study Number 941-91-127, EPA MRID No. 423722-03.

This study was classified as invalid because a second (water-only) control was not included. We wish to address this issue as well as other comments made by the reviewer.

Page 6 of Review, Item 14A.

The reviewer declared the above study invalid due to the lack of a second (water-only) control. The study was conducted by dissolving the test compound technical grade active ingredient in 67% acetone and treating the test system at the equivalent of 50 gallons per acre (gal/A). Using the calculations presented in the report, each 4.90 ft^2 plot was treated with 21.3 mL of spray solution. Therefore, each pot (7.5 cm X 7.5 cm) was treated with 0.26 mL of spray solution (0.18 mL acetone). Calculations are presented below.

$$\frac{21.3 \text{ mL spray}}{4.90 \text{ sq ft}} \times \frac{\text{sq ft}}{144 \text{ sq in}} \times \frac{\text{sq in}}{6.45 \text{ sq cm}} \times \frac{56.25 \text{ sq cm}}{\text{pot}} = \frac{0.26 \text{ mL spray}}{\text{pot}}$$

$$\frac{0.26 \text{ mL spray}}{\text{pot}} \times \frac{0.67 \text{ mL acetone}}{1.0 \text{ mL spray}} = \frac{0.18 \text{ mL acetone}}{\text{pot}}$$

Acetone is a commonly used solvent in the conduct of plant phytotoxicity studies. Acetone has no residual phytotoxic properties, therefore all phytotoxicity in a vegetative vigor study would result from acetone's ability to dissolve plant cuticle. The removal of plant cuticle would result in tissue desiccation and visible signs of phytotoxicity. Since no phytotoxicity was observed in any of the vegetative vigor study controls, the application of 0.18 mL of acetone to the control pots during the warm conditions occurring at application on June 19 in Madera, California, was of insufficient quantity and exposure duration to result in phytotoxicity prior to evaporation. The use of acetone in this study did not result in any detrimental effects and should be considered a sufficient control.

The Standard Evaluation Procedures (SEP) for this study specifies that if a solvent was used to dissolve the test compound, the concentration used should not result in phytotoxicity and that a solvent control should be used. Since the concentration of acetone was not sufficient to cause phytotoxic symptoms and an acetone control was used, both of these requirements were fulfilled in the submitted studies. In addition, neither the Nontarget Hazard Evaluation Guidelines nor the SEP specify the need for a water control when a solvent is used to dissolve the test compound.

Guideline Number 123-2, Aquatic Plant Growth. Comments are provided on reviews for four aquatic plant studies (Selenastrum, Anabaena, Navicula, and Skeletonema); note that the Lemna study was approved by EEB on October 23, 1992 (W.W. letter to M.G. of December 11, 1992).

1. Effect of AC 92,553 on Growth of the Green Alga, Selenastrum capricornutum; Malcolm Pirnie Study Number B400-32-1; Cyanamid Study Number 941-91-131; MRID No. 423722-04.

This study was classified as core. However, there were some comments made by the reviewer that we would like to address.

Page 2 of Review, Item B, Paragraph 3.

The reviewer did correctly identify a typographical error on Page 14 of the report. The correct concentrations of the stock solutions were: 10, 31.25, 62.5, 125, 250 and 500 μg/mL. A report amendment will be written to correct this error.

Page 4 of Review, Item 14A, Paragraph 2.

The study was criticized because cell count measurements were not taken on test days 1 and 2. However, with the low inoculum density (3,000 cells/mL), it is extremely difficult to obtain accurate cell counts during the lag phase of growth during the first two days of the test. Cell counts performed on test days 3, 4, and 5 are sufficient to define the shapes of the growth curves and assess the response of algae to test substances. In the past, EPA reviewers have found this practice to be acceptable.

Page 4 of Review, Item 14A, Paragraph 3.

The report was criticized for not containing the results of the continuous temperature measurements. This information is available in log book pages which have been filed with the raw data package. If necessary, this information can be added to the report by a report amendment.

2. Effect of AC 92,553 on Growth of the Marine Diatom, Skeletonema costatum; Malcolm Pirnie Study Number B400-32-4; Cyanamid Study Number 941-91-134; MRID No. 423722-05.

This study was classified as invalid because "the solvent control was apparently contaminated". The reviewer had a few additional comments that we would like to address in addition to the effect of possible contamination on the outcome of the study.

Page 4 of Review, Item 14A, Paragraph 2.

The study was criticized because cell count measurements were not taken on test days 1 and 2. However with the low inoculum density (10,000 cells/mL), it is extremely difficult to obtain accurate cell counts during the lag phase of growth during the first two days of the test. Cell counts performed on test days 3, 4, and 5 are sufficient to define the shapes of the growth curves and assess the response of algae to test substances. In the past, EPA reviewers have found this practice acceptable.

Page 4 of Review, Item 14A, Paragraph 3.

The report was criticized for not containing the results of the continuous temperature measurements. This information is available in log book pages which have been filed with the raw data package. If necessary, this information can be added to the report by a report amendment.

Page 4 of Review, Item 14A, Paragraph 4.

The study was criticized for using a 14-hour light photoperiod as opposed to the 16-hour light to 8-hour dark photoperiod that is recommended in the guidelines. However, a 14-hour photoperiod is recommended by Dr. Gerald Walsh of the Gulf Breeze Laboratory, who is EPA's foremost authority on marine algal toxicity testing (Reference: Walsh and Alexander, 1980, "A marine algal bioassay method, results with pesticides and industrial wastes:, Water, Air and Soil Pollution, Vol. 13, pp. 45-55). In addition, growth of the control organisms was acceptable in this study.

We have recalculated the results of this study based solely on the comparison of the test substance treatment levels with the no-treatment control, which would provide the most conservative estimate of toxicity. Percent inhibition based on mean day-5 cell counts, relative to the no-treatment control range from 3.9 to 95.5% (see Table 1 of attachments to this letter). As determined by weighted least squares non-linear regression, the 5-day EC25 is 3.0 µg/L (95% confidence limits of 1.6 to 5.9 µg/L) and the 5-day EC50 is 5.0 µg/L (95% confidence limits of 3.4 to 7.5 µg/L). These values are essentially the same as when calculated using the combined controls. As determined by ANOVA and Dunnett's test, the NOEC is 5.0 µg/L, which is higher than previously reported based on the combined controls. The reviewer's statistical analysis also concluded that the NOEC was 5.0 µg/L. However, the reviewer made the judgement that since 27% inhibition occurred at 1.5 µg/L, that this should be considered an effect level and that the NOEC was 0.7 µg/L. This judgement was apparently based on the belief that the NOEC must always be less than the EC50.

We agree that statistical significance does not necessarily correlate with biological significance, and that it does seem illogical to report an NOEC value that is equal to or greater than an EC50 value. However, as long as the NOEC is defined according to statistical considerations, it is quite possible for this to occur. If "within-treatment" variability is large, which is not uncommon in tests with Skeletonema, it is difficult to demonstrate significant differences, and the NOEC may very well be greater than the EC50. We must point out that is it not always appropriate to make a direct comparison of the EC50 value and the NOEC in these types of studies. The NOEC is derived by hypothesis testing procedures and is therefore sensitive to the selection of the level of significance, the statistical technique chosen, the sample size and the selection of test concentrations. No confidence limits can be placed on an NOEC. The EC50 on the other hand is a point estimate derived from a regression technique and is therefore less sensitive to the above listed parameters. Detailed information on this subject can be found in the follo ing references: (1) "Advantages of Using Regression Analysis to Calculate Results of Chronic Toxicity Tests" by Stephan and Rodgers, Aquatic Toxicology and Hazard Assessment: Eighth Symposium, ASTM STP 891, R.C. Bahner and D.J. Hansen, eds., 1985, pp. 328-338; (2) An Evaluation of Appropriate Expressions of Toxicity in Aquatic Plant Bioassays as Demonstrated by the Effects of Atrizine on Algae and Duckweed" by Hughes et al., Aquatic Toxicology and Hazard Assessment, 10th Volume, ASTM STP 971, W.J. Adams, G.A. Chapman and W.G. Landis, eds., 1988, pp. 531-547; and (3) Supplement to Short-Term Methods for Estimating the Chronic Toxicity of Effluents and Surface Waters to Fresh Water Organisms"; EPA 600/4-89-001a.

3. Effect of AC 92,553 on Growth of the Freshwater Diatom, Navicula pelliculosa; Malcolm Pirnie Study Number B400-32-1; Cyanamid Study Number 941-91-133; MRID No. 423722-06.

This study was classified as invalid because "the solvent control was apparently contaminated". The reviewer had a few additional comments that we would like to address in addition to the effect of possible solvent control contamination on the outcome of the study.

Page 4 of Review, Item 14A, Paragraph 2.

The study was criticized because cell measurements were not taken on test days 1 and 2. However, with the low inoculum density (3,000 cells/mL), it is extremely difficult to obtain accurate cell counts during the lag phase of growth during the first two days of the test. Cell counts performed on test days 3, 4, and 5 are sufficient to define the shapes of growth curves and assess the response of algae to test substances. In the past, EPA reviewers have found this practice acceptable.

Page 3 of Review, Item 14A, Paragraph 3.

The report was criticized for not containing the results of continuous temperature measurements. This information is available in log book pages which have been filed with the raw data package. If necessary, this information can be added to the report by a report amendment.

Page 4 of Review, Item 14B

The reviewer used EPA's TOXANAL program to recalculate the EC50 value. However, the procedures contained in the program are not appropriate for aquatic plant toxicity test data, which is continuous and not dichotomous. The use of probit analysis, moving average, Spearman-Karber, and the binomial procedure require, in the calculations, inputting the number of organisms affected relative to the number of organisms tested. In aquatic plant toxicity tests, the number of organisms in the test increase over time. It is not appropriate to convert percent inhibition values into the number of organisms relative to 100. For example, 28% inhibition of population growth is not equivalent to 28 out of 100 organisms affected.

In this study, we used a weighted least squares non-linear regression technique that has been described by Bruce and Versteeg ("A Statistical Procedure for Modelling Continuous Toxicity Data", Environ. Toxicol. and Chem., Vol. 11, No. 10, pp. 1485-1494, 1992). Other methods that may be applicable include the Bootstrap Procedure (obtainable from Teresa Norberg-King, EPA, ERL-Duluth) and the curve-fitting techniques discussed by Nyholm et al. in the paper entitled "Statistical Treatment of Data from Microbial Toxicity Tests"; Environ. Toxicol. and Chem., Vol. 11, No. 2, pp. 157-167, 1992.

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4. Effect of AC 92,553 on Growth of the Blue-Green Alga, Anabaena flos-aquae, Malcolm Pirnie Study Number B400-32-2; Cyanamid Study Number 941-91-132; MRID No. 423722-07.

This study was classified as invalid because "the solvent control was apparently contaminated". The reviewer had a few additional comments that we would like to address in addition to the effect of possible contamination on the outcome of the study.

Page 4 of Review, Item 14A, Paragraph 2.

The study was criticized because cell measurements were not taken on test days 1 and 2. However, with the low inoculum density (3,000 cells/mL), it is extremely difficult to obtain accurate cell counts during the lag phase of growth during the first two days of the test. Cell counts performed on test days 3, 4, and 5 are sufficient to define the shapes of the growth curves and assess the response of algae to test substances. In the past, EPA reviewers have found this practice to be acceptable.

Page 4 of Review, Item 14A, Paragraph 3.

The report was criticized for not containing results of the continuous temperature measurements. This information is available in log book pages which have been filed with the raw data package. If necessary, this information can be added to the report by a report amendment.

Page 4 of Review, Item 14C.

On test day-0, the test substance was apparently detected in the solvent control at a level that was slightly higher than the validated limit of detection. As we stated in the report, we were not able to ascertain whether this low level of detection represented an analytical artifact or was actual contamination. It must be pointed out that the growth in the no-treatment controls and the solvent controls was similar throughout the test. Therefore, the solvent itself, the "contamination" in the solvent or the combination did not have any effect on cell growth in the solvent controls. In addition, as the reviewer correctly states in their review "the test material had little effect on A. flos-aquae growth" (page 3 of Review, Item 12, paragraph 2). Therefore, since the test substance was tested at concentrations up to its limit of solubility, the results clearly indicate that the test substance is non-toxic to A. flos-aquae and that minor contamination, if it is contamination, of the solvent control would not affect these results and conclusions. In this study, since growth in the no-treatment controls and the solvent controls was statistically equivalent, the control groups were combined and mean growth of each treatment group was compared with the mean growth of the combined controls. This was done to increase the power of the statistical procedures that were used to determine whether the effects at different concentrations were significantly different.

Currently, an analysis of the rejection rate and the reasons for rejection of studies is being carried out in EEB. We believe that one of the reasons for high rejection rates in EEB is the lack of a core minimum category in this branch that exists in other branches. This category allows for acceptance of studies that may not be exactly to the letter core guideline but despite this fact provide all the necessary information to satisfy the requirements for the data guideline. We also believe that in these present cases it is clear that there are sufficient data available to satify all necessary requirements for these guidelines even if the EEB reviewer disagrees with some of the details of the study. It is our hope that after reconsideration by the EEB, they will concur with our proposals, however, if they do not sign off, then we request that you, as the risk manager for these studies, accept them as satisfying the requirements. Repeating the studies will not change the bottom line decision on the toxicity of pendimethalin to these plants but will cost more money and certainly delay the time for pendimethalin to undergo a Registration Evaluation Decision.

Thank you for your continued good management of the reregistration of pendimethalin.

Respectfully submitted,

Agricultural Research Division
American Cyanamid Company

Mark W. Galley
Manager
U.S. Plant Regulatory Affairs

Attachment

MWG/dt

Pendimethalin

Page _____ is not included in this copy.

Pages 15 through 16 are not included in this copy.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product inert impurities.

_____ Description of the product manufacturing process.

_____ Description of product 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 confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.