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

JAN 23 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES**MEMORANDUM**

SUBJECT: PP#9F3743-Clethodim (Select®) in/on Soybeans Cottonseed and Animal Commodities.
Review of the June 19, 1990 Amendments for Products Chemistry.

(MRID # 415433-01 thru -05) [DEB # 6966 and 7441]
(HED Project # 0-1812 and 1-0309)

FROM: Francis D. Griffith, Jr., Chemist
Chemistry Branch I - Tolerance Support
Health Effects Division (H-7509C)

A handwritten signature of Francis D. Griffith, Jr. in dark ink.

THRU: Richard D. Schmitt, Ph.D., Chief
Chemistry Branch I - Tolerance Support
Health Effects Division (H-7509C)

A handwritten signature of Richard D. Schmitt in dark ink.

TO: Joanne I. Miller, Acting, PM-23
Fungicide-Herbicide Branch
Registration Division (H-7509C)

Valent U.S.A. Corporation has submitted these amendments consisting of supplementary Product Chemistry data submitted in response to deficiencies outlined and summarized in our review of March 12, 1990 by M. J. Nelson. Attached is a revised Product Chemistry Review prepared by Dynamac Corporation under supervision of the Chemistry Branch (CBTS), Health Effects Division (HED).

This Dynamac review has undergone secondary and tertiary review in CBTS and reflects current Branch Policies.

Please note that Confidential Appendices A and B (pages 10 thru 14) of this Dynamac review will receive limited distribution since they contain Confidential FIFRA Trade Secret/CBI information.

Dynamac has also prepared Table A, Generic Data Requirements for the Clethodim Technical Grade, and Table B, Product Specific Data Requirements for Clethodim Manufacturing-Use Products. The

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2

footnotes to these tables detail the remaining unresolved deficiencies in Clethodim Product Chemistry.

If you need additional information please advise.

Attachment: "Clethodim (DEB No. 6966) Task 5: Product Chemistry Data Submitted in Support of Registration," 14 pages.

- cc [With Attachment consisting of the complete Dynamac review including the Confidential FIFRA Trade Secret/CBI portion in Confidential Appendices A and B (page 10-14)]:
Reading File,
TOX,
PP#9F3743,
Reviewer (FDG),
PIB/FOD (C. Furlow)
- cc [With Attachment consisting of the non-Confidential/non-CBI portion of the Dynamac review plus Table A and Table B (page 1-9 inclusively)]:
Circulation (7),
Dynamac (Paula A. Deschamp)

H7509C:CBTS:Reviewer:(FDG):CM#2:Rm814B:5570826:vg:1/3/91:
ed:fdg:1/4/91.

RDI:SecHd:RSQuick:1/8/91:BrSrSci:RALoranger:1/15/91.

2

DYNAMAC
CORPORATION

Final Report

CLETHODIM (DEB No. 6966)
**Task 5: Product Chemistry Data
Submitted in Support of Registration**

December 10, 1990

Contract No. 68-D8-0080

Submitted to:
Environmental Protection Agency
Arlington, VA 22202

Submitted by:
Dynamac Corporation
The Dynamac Building
11140 Rockville Pike
Rockville, MD 20852

CLETHODIMPRODUCT CHEMISTRY DATASUBMITTED IN SUPPORT OF REGISTRATIONTask 5 - DEB No. 6966BACKGROUND

In response to deficiencies cited in an Agency review (M.J. Nelson, DEB No. 5681, dated 3/12/90), Valent U.S.A. Corporation, as agent for Chevron Chemical Company, has submitted additional product chemistry data supplied by Chevron Chemical Co. (1990; MRIDs 41543301-41543305; DEB No. 6966) in support of PP#9F3743 and Valent's application for registration of their 90.5% technical (T; File Symbol 59639-E) and their 2 lb/gal EC (File Symbol 59639-G) formulations. The same product chemistry data are submitted in support of Chevron's application for registration of their 90.5% T (File Symbol 63499-GL) formulation.

These data and our conclusions are discussed below.

61-1. Product Identity and Disclosure of Ingredients

Chevron's submission (1990; MRID 41543301) of new Confidential Statements of Formula for the 90.5% Ts (File Symbol Nos. 59639-E and 63499-GL) listing the nominal concentration of each individual impurity present at $\geq 0.1\%$ by weight of the technical products, and modifying the lower certified limits does not satisfy the requirements of 40 CFR 158.155 (Guideline Reference No. 61-1) regarding product composition of the 95.5% T products. Refer to Confidential Appendix A for disclosure of the ingredients in the products. Chevron reports that the nominal concentration of clethodim on the statement of composition is derived from an analysis of five clethodim batches. This value differs significantly from the reported mean concentration and variability derived from the analyses of 31 pilot plant batches; Chevron reports that data from the pilot plant analyses were used to calculate the lower certified limit. Since an analysis of 31 batches more accurately reflects the nominal concentration, this mean should be used on the statement of composition. The raw data should be submitted for independent confirmation. In addition, Valent (not Chevron) should be listed on the CSF as the applicant/registrant for the product with the EPA File Symbol 59639-E. We note that the registrant has not adequately explained whether polar RE-45601 is herbicidally active. This polar conformer of clethodim is currently included in calculating the percent of active ingredient in the product. If it is not an herbicidally active ingredient, the concentration of this polar conformer needs to be subtracted from nominal concentration and a new CSF reflecting this change should be submitted. Additional data are required. See 62-3 below for details.

Although no additional data concerning product composition were required for the 2 lb/gal EC formulation (EPA File Symbol 59639-G), the requested change in the nominal concentration and upper certified limit for the technical must also be reflected in the CSF for this product.

61-2. Description of Beginning Materials and Manufacturing Process

No additional information was required for these products on this topic.

61-3. Discussion of Formation of Impurities

The registrants have complied with the request to provide a discussion of impurities that may occur in all three products both following production and through contamination during production or from packaging materials (MRIDs 41543301 [technicals] and 41543302 [2 lb/gal EC]). The discussion is presented in Confidential Appendix B. No additional information is required for this topic for these products.

62-1. Preliminary Analysis

No additional information was required for these products on this topic.

62-2. Certification of Limits

The procedure used by Chevron (1990; MRID 41543303; Confidential Appendix A) to establish certified limits for the active ingredient in the 90.5% Ts (EPA File Symbols 62499-GL and 59639-E) is not acceptable. The upper certified limit is based on a mean concentration derived from the analyses of five batches, while the lower certified limit is based on a different mean concentration derived from the analysis of 31 pilot plant batches over a period of one year. Since the latter analysis more accurately reflects the nominal concentration, we recommend that both the nominal concentration and upper certified limit be changed on the Confidential Statement of Formula to reflect this analysis. The petitioner need to submit all of the raw data used to make these calculations for independent confirmation. This information must be submitted on EPA Form 8570-4 (Rev. 2-85). Upon review of the raw data and correctly completed form, the data requirements for this topic will be considered fulfilled.

Additional data concerning certified limits were required for the 2 lb/gal EC (EPA File Symbol 59639-G) in the event that the certified limits for the technical used to formulate this product

were changed. Since a change in the reported nominal concentration (see 61-1 above) and upper certified limit for the technical is recommended, the CSF for the EC formulation must reflect these changes as well.

62-3. Analytical Methods to Verify Certified Limits

Previously submitted analytical methods and validation data for clethodim and its impurities were deemed acceptable; however, M.J. Nelson (DEB No. 5681) noted that the registrant did not indicate whether a peak containing a "polar form" of clethodim is herbicidally active or whether it is included in the reported weight percent active ingredient. Valent (1990; MRID 41543304) responds that the concentration of the polar peak is included in the weight percent active ingredient by quantitation using a calculation based upon an observed constant in peak height ratios. The registrant notes that when the polar and nonpolar HPLC peaks (established previously by NMR to be conformers of clethodim) were each collected, combined and rechromatographed, identical HPLC traces were obtained, and that the polar/non polar peak height ratio was constant. This same ratio is used in the analytical standard used for analysis. The registrant further claims that these experiments indicate that both conformers are herbicidal.

Herbicidal activity of a material cannot be assumed by observing its behavior using quantitative or qualitative analytical methods; it must be confirmed by initiating a biological assay. Further explanation as to the herbicidal activity of the polar form (RE-45601) of clethodim is needed. In lieu of biological testing of the "polar form" of clethodim, CBTS would accept data showing that the "polar form" isolated by HPLC converts to the mixture at a rate that would preclude meaningful testing of the polar form's herbicidal activity. The submitted method adequately separates the two conformers and satisfies guideline requirements pertaining to analytical methods. No additional data are required for the analytical method.

PHYSICAL AND CHEMICAL CHARACTERISTICS

The registrant has complied with the Agency's request to provide the physical/chemical properties 63-14 through 63-20 for the 90.5% Ts (EPA File Symbols 62499-GL and 59639-E). These data are included in Table 1. We note that the technical is usually formulated immediately into a more stable EC formulation; therefore, the requirement for stability tests lasting at least one year has been waived. No additional data are needed for these technical products for this topic.

Table 1. Physical and chemical properties of the clethodim 90.5%
Ts (EPA File Symbols 62499-GL and 59639-E). Data from
MRID 41543305.

Guidelines Reference

No., 40 CFR §158.190;

Name of Property

Description [Method; Test Substance*]

63-14. Oxidizing or reducing action	Oxidizable by KMNO_4 . The reaction is not abruptly exothermic. [40 CFR 16267; MP]
63-15. Flammability	Flash point (CC) >78 C [ASTM D-56; MP]. No apparent reaction when tested with solid or aqueous monoammonium phosphate. [40 CFR 16267; MP]
63-16. Explodability	Not explosive as shown by submitted studies on impact sensitivity [standard JANAF tests; MP] and differential scanning calorimetry of both the technical and PAI.
63-17. Storage stability	Twelve samples containing 85-92% ai were stored in amber glass bottles at 20 C. Samples were analyzed at 0 and 1 months, with some at ca 4, 6 or 10 months. Maximum % ai decomposition was 3.8% at 1 month, 14.2% at ca. 4 months, 37.4% at ca. 6 months, and 66.1% at ca. 10 months (one sample). Based upon a best fit curve, the product has a half-life of 8.4 months. [TGAI]
63-18. Viscosity	840 cps at 20 C [AM-26; MP]
63-19. Miscibility	Not required since the products are not emulsifiable liquids to be diluted with petroleum solvents.
63-20. Corrosiveness	No corrosion was observed during storage stability study discussed above. [TGAI]

* MP - Manufacturing-use product; TGAI - technical grade of the
active ingredient.

CLETHODIM
PRODUCT CHEMISTRY DATA
SUBMITTED IN SUPPORT OF REGISTRATION
TASK 5 - DEB No. 6966
(Final Report)

CONFIDENTIAL APPENDICES

Appendix A: 2 Page(s)
Appendix B: 3 Page(s)

Confidential Appendices to the Product Chemistry Data Review of
PP#9F3743 for the pesticide clethodim by the Dietary Exposure
Branch [Confidential FIFRA Trade Secret/CBI].

TABLE A. GENERIC DATA REQUIREMENTS FOR THE CLETHODIM TECHNICAL GRADE OF THE ACTIVE

Data Requirement	Test Substance	Guideline Status	Must additional data be submitted under FIFRA Sec. 3(c) (2) (B)?	
			[Yes]	[No]
<u>40 CFR §158.155-190 Product Chemistry</u>				
<u>Product Composition</u>				
61-1. Product Composition	TGAI	R	X ²	
61-2. Beginning Materials and Production Process	TGAI	R		X
61-3. Formation of Impurities	TGAI	R		X
<u>Analysis and Certification of Product Ingredients</u>				
62-1. Preliminary Analysis	TGAI	CR		
62-2. Certified Limits	TGAI	R	X ³	
62-3. Enforcement Analytical Methods	TGAI	R		X
<u>Physical and Chemical Characteristics</u>				
63-2. Color	TGAI	R		X
63-3. Physical State	TGAI	R		X
63-4. Odor	TGAI	R		X
63-5. Melting Point	TGAI	NA ⁴		X
63-6. Boiling Point	TGAI	R		X
63-7. Density, Bulk Density, or Specific Gravity	TGAI	R		X
63-8. Solubility	TGAI or PAI	R		X
63-9. Vapor pressure	TGAI or PAI	R		X
63-10. Dissociation Constant	TGAI or PAI	R		X

(Continued, footnotes follow)

TABLE A. (Continued).

Data Requirement	Test Substance	Guideline Status	Must additional data be submitted under FIFRA Sec. 3(c) (2) (B)?	
			[Yes]	[No]
63-11. Octanol/Water Partition Coefficient	PAI	CR		X
63-12. pH	TGAI	CR		X
63-13. Stability	TGAI	R		X

Other Requirements:

64-1. Submittal of Samples	TGAI or PAI	CR ⁵
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1. Data requirements pertain to the Chevron and Valent 90.5% Ts (EPA File Symbols 6 respectively). Additional data requirements are listed in the following Table E Requirements for Clethodim Manufacturing-Use Products", for registered technical
2. The nominal concentration of the active ingredient as reported on the Confidential Statement of Formula (CSF) should be modified to reflect the mean concentration obtained from the analysis of the product batches. In addition, Valent (not Chevron) should be listed on the CSF as the active ingredient with the EPA File Symbol 59639-E. We note that the registrant has not shown whether RE-45601 is herbicidally active. This conformer of clethodim is currently calculating the percent of active ingredient in the product. If it is not shown active ingredient, the concentration of this conformer should be subtracted from the total concentration and a new CSF should be submitted reflecting this change. In lieu of the "polar form" of clethodim, CBIS would accept data showing that the "polar form" converts to the mixture at a rate that would preclude meaningful testing of the activity.
3. The upper certified limit on the Confidential Statement of Formula should be modified to reflect variability around the mean obtained from the analysis of the 31 pilot plant batches. The registrant needs to submit all of the raw data used to make these calculations for independent verification.
4. Data are not required because the product is not a solid at room temperature.

(Continued, footnotes follow)

TABLE A. (Continued).

5. If samples are required, the Agency will request them.

TABLE B. PRODUCT SPECIFIC DATA REQUIREMENTS FOR CLETHODIM MANUFACTURING-USE PRODUCT

Data Requirement	Test Substance	Guideline Status	Must additional data be submitted under FIFRA Sec. 3(c) (2) (B)?	
			[Yes]	[No]
<u>40 CFR §158.155-190 Product Chemistry</u>				
<u>Product Composition</u>				
61-1. Product Composition	MP	R	X ²	
61-2. Beginning Materials & Production/Formulation Process	MP	R		X
61-3. Formation of Impurities	MP	R		X
<u>Analysis and Certification of Product Ingredients</u>				
62-1. Preliminary Analysis	MP	CR		X
62-2. Certified Limits	MP	R	X ³	
62-3. Enforcement Analytical Methods	MP	R		X
<u>Physical and Chemical Characteristics</u>				
63-2. Color	MP	R		X
63-3. Physical State	MP	R		X
63-4. Odor	MP	R		X
63-7. Density	MP	R		X
63-12. pH	MP	CR		X
62-14. Oxidizing/Reducing Action	MP	CR		X
62-15. Flammability	MP	CR		X
63-16. Explodability	MP	R		X
63-17. Storage Stability	MP	R		X
63-18. Viscosity	MP	CR		X
63-19. Miscibility	MP	CR		X
63-20. Corrosion Characteristics	MP	R		X

(Continued, footnotes follow)

TABLE B. (Continued).

Data Requirement	Test Substance	Guideline Status	Must additional data be submitted under FIFRA Sec. 3(c) (2) (B)?	
			[Yes]	[No]
<u>Other Requirements:</u>				
64-1. Submittal of Samples	MP	CR		X
1. Data requirements pertain to the 90.5% Ts (EPA File Symbols 62499-GL and 59639-I). Additional data requirements are listed in the preceding Table A, "Generic Data Clethodim Technical Grade of the Active Ingredient", for the TGAI of this manufa 2. The nominal concentration of the active ingredient as reported on the Confidential Statement of Formula (CSF) should be modified to reflect the mean concentration obtained from the analysis of the batches. In addition, Valent (not Chevron) should be listed on the CSF as the manufacturer of the product with the EPA File Symbol 59639-E. We note that the registrant has not shown whether RE-45601 is herbicidally active. This conformer of clethodim is currently calculating the percent of active ingredient in the product. If it is not shown that the active ingredient, the concentration of this conformer should be subtracted from the total concentration and a new CSF should be submitted reflecting this change. In lieu of the "polar form" of clethodim, CBTS would accept data showing that the "polar form" converts to the mixture at a rate that would preclude meaningful testing of the activity. 3. The upper certified limit on the Confidential Statement of Formula should be modified to reflect variability around the mean obtained from the analysis of the 31 pilot plant batches. The need to submit all of the raw data used to make these calculations for independence. 4. If samples are required, the Agency will request them.				

(Continued, footnotes follow)

RIN 1408-03

Clethodim Product Chemistry Review

Page is not included in this copy.

Pages 14 through 18 are not included.

The material not included contains the following type of information:

- Identity of product inert ingredients.
- Identity of product impurities.
- X Description of the product manufacturing process.
- X 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.
- 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.