DPBARCODE: D330401; **Reg. No. /FILE SYMBOL No.** 352-542, **PRODUCT**: Quizalofop-P-Ethyl Technical

September 25, 2006

FEE

SUBJECT: FEE. Secondary Product Chemistry Review of Quizalofop-P-ethyl Technical Herbicide

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TO: Vickie Walters / Mary Waller, RM 21
Herbicide Branch / RD (7505P)

DP BARCODE: D330401
EPA REG. NO.: 352-542
PRODUCT: Quizalofop-P-ethyl Technical
PCC: 128709
REGISTRANT: E. I. Du Pont Nemours & Company, Incorporation
USE: Herbicide

INTRODUCTION:

The registrant has submitted a CSF for alternate formulation (dated 05-12-06) which reflects two production sites in China for the technical quizalofop-p-ethyl. The technical was produced at the following two production facilities located in R.P. of China:

1. Anhui Fengle Agrochemical Company, Hefei, China.
2. Shandong Jingbo Agrochemicals Company, Ltd., Shandong Province, China.

In support of the alternate CSF, the registrant has submitted 830 series Subgroup A & Subgroup B product chemistry data under MRID nos. 468536-01 thru 468536-13.

The primary review of the product chemistry data submitted was performed by Dynamac Corporation. TRB has been asked to perform the secondary review of Dynamac Corporation's report and determine whether the data submitted support the CSF for alternate formulation.

SUMMARY OF FINDINGS

1. The registrant has submitted a Confidential Statement of Formula for alternate formulation (dated 05-12-06) for quizalofop-p-ethyl technical. The average purity of the technical was 97.80%, as determined by the five batch analysis of the batches produced at two manufacturing facilities. The nominal concentration concurs with the product label claim nominal concentration. The proposed certified limits for the active ingredient are based on the standard certified limit set-forth in 40CFR§158.175(b)(2). The proposed certified limits for the process related impurities were established based upon the five batch analysis and historical product development and/or production data. The product chemistry data submitted corresponding to guideline reference 830.1550 (product identity & composition) and 830.1750 (certified limits) satisfy the data requirements of 40CFR§158.155 and 158.175 respectively (MRID No.468536-01& 468536-04).

2. The product chemistry data submitted corresponding to guideline 830.1600 (description of materials use to produce the product) satisfy the data requirements of 40CFR§158.160. The registrant has provided the MSDS for all the starting materials used to produce the active ingredient, except one [redacted] The registrant has been contacted to provide the required information [MRID No. 468536-01].

3. The product chemistry data submitted corresponding to guideline reference 830.1620 (description of production process) satisfy the data requirements for 40CFR§158.162. The active ingredient was produced [redacted] The manufacturing process for the technical produced in commercial at both the sites has been described in details [MRID No. 468536-01].

4. The product chemistry data submitted corresponding to guideline reference 830.1670 (Discussion on the formation of impurities) satisfy the data requirements for 40CFR§158.167. The registrant has reported the formation of [redacted] are present at the concentration of < 0.1%. The discussion on the mechanism of formation of these impurities has been provided. No impurity of toxic concern has been reported in the CSF. The impurity profile of the alternate CSF is very similar to basic formulation CSF (dated 01-16-96). There appears to be one new impurity [redacted] < 0.1%) which is not present in the basic formulation [MRID No. 468536-01].

5. The data submitted corresponding the guideline reference 830.1700 (Preliminary analysis) satisfy the data requirements of 40CFR§158.170. Five representative batches of the technical at two different sites were analyzed for percent active ingredient using HPLC/UV (330 nm) (Normal phase chiral chromatography assay method) and [redacted] The methods were validated for accuracy, linearity, and precision [MRID No. 468536-02 & 468536-03].

6. The data submitted corresponding the guideline reference 830.1800 (Enforcement Analytical method) satisfy the data requirements of 40CFR§158.180. The HPLC-UV (330 nm) method described in item #5 can be used for the determination of the AI in the formulated products. The method was validated for accuracy, linearity, and precision [468536-02 & -03].

7. The registrant has submitted product chemistry data corresponding to guideline reference 830 Series Subgroup B (physical/chemical properties) for the technical produced in China. The data submitted satisfy the data requirements of 40CFR§158.190 [MRID No. See the Table].

CONCLUSIONS

TRB has reviewed the product chemistry data submitted for 830 series Subgroup A & B for quizalofop-P-ethyl technical produced at two sites in China and has concluded that:

1. The CSF for alternate formulation (dated 5-12-06) is acceptable. The alternate formulation CSF is substantially similar to the basic formulation (dated 01-16-96). It may be pointed out that there is significant difference in the density values for basic and alternate formulations (0.35 gm/cc in basic vs 1.36 gm/cc in alternate formulation).

2. The product chemistry data submitted corresponding to guidelines 830 series subgroup A for quizalofop-P-ethyl are acceptable.

3. The product chemistry data submitted corresponding to guidelines 830 series subgroup B (physical-chemical properties) for quizalofop-P-ethyl are acceptable, except for the guidelines 830.6317 (one year storage stability) and 830.6320 (corrosion characteristics).

4. The registrant must submit the results of one year storage stability (830.6317) and corrosion characteristics (830.6320) to the Agency on completion. It is recommended that the observations must be made at 0, 3, 6, 9, & 12 month intervals. The results must be submitted in a hard copy and an electronic format is also requested. If the results of these studies have been submitted previously, please provide the MRID numbers.

Note to PM

The registrant has been requested to provide additional information on one of the starting material [redacted] and also confirm the presence of an impurity (≤ 0.1%) which is not present in the basic formulation and confirming that it is not of toxicological concern. The information will be sent directly to PM team and can be reviewed at PM team.

Addressed in letter dated 9/29/06. Information is acceptable.

VKW 10/4/06

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DPBARCODE: D330401; **Reg. No. /FILE SYMBOL No.** : 352-542; **PRODUCT**: Quizalofop-P-Ethyl Technical

830.1550. Product identity & Composition: (MRID No. 46853601)

Common Name: Quizalofop-P-ethyl

Chemical name (CAS): Ethyl (*R*)-2-[4-[(6-chloro-2-quinoxalinyl)oxy]phenoxy]propionate
(IUPAC): Ethyl (*R*)-2-[4-(6-chloroquinoxalin-2-yloxy)phenoxy]propionate

CAS No.: 100646-51-3

PC Code No.: 128709

Empirical formula: $C_{19}H_{17}ClN_2O_4$

Molecular Weight: 372.81

Structural formula:

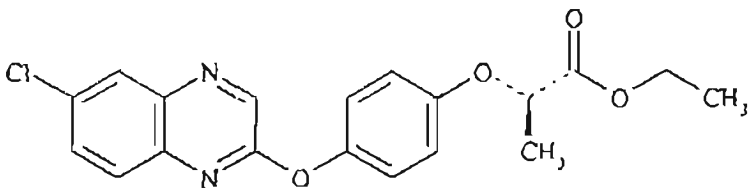

Table 1. Manufacturing and Impurity Data for TGAI/MUP				
GLN	Requirement	MRID	Status	Details and /or Deficiency
830.1550	Product Identity and composition	46853601	A	An alternate CSF (dated 5-12-06) has been submitted for the two production sites in China. The NC of the AI (97.8%) reflects the average preliminary analysis results for the two alternate manufacturing facilities. The nominal concentration of 97.8% concurs with the product label claim nominal concentration.
8301600	Description of materials used to produce the product	46853601	A	The description and composition for the starting materials used at both manufacturing facilities have been provided by the registrant for all materials except one, for which an MSDS is required. The MSDS for [redacted] is required.
830.1620	Description of production process	46853601	A	The AI is produced [redacted] process at both manufacturing facilities; [redacted] different chemical reactions are involved in the synthesis of quizalofop-P-ethyl. The details of the production process have been provided including the reaction conditions, relative amounts of chemicals in each step, yields from each step, and QA steps used.
830.1670	Discussion of formation of impurities	46853601	A	The registrant has provided the complete mechanisms of formation, quantification, and identification of all impurities (present at concentration of ≥ 0.1%). No impurities of toxicological concern have been reported by the registrant.
830.1700	Preliminary analysis	46853602 46853603	A	The registrant has submitted the results of preliminary analysis of five or six batches of the DuPont™ Quizalofop-P-ethyl Technical produced by two alternate manufacturers in China. The AI and impurities were determined using the methods summarized below under 830.1800. Closure was ~100% for both products.
830.1750	Certified limits	46853604	A	The proposed certified limits for the AI are based on the standard certified limit table; proposed upper certified limits for impurities reflect the manufacturing processes and preliminary analysis results for both manufacturing facilities. The proposed certified limits for the AI are in compliance with 40CFR158.175(b)(2) and for the impurities are based on the five batch analysis.
830.1800	Enforcement analytical method	46853602 46853603	A	The methods used in the preliminary analysis studies are proposed for enforcement. DuPont normal-phase HPLC/UV Method 79376.220.01.ES was used for the quantitation of the active ingredient. [redacted] were used for the quantitation of impurities. The analytical methods were adequately validated for specificity, linearity, and precision.
A = Acceptable; N = unacceptable (see Deficiency); N/A = Not Applicable; G = Data gap; I = In progress or need upgrade; U = Up-grade (additional information required)				

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830 Series Subgroup B (Physical-Chemical Properties)

Table 2: Physical and Chemical Properties of : TGAI/MUP				
GLN	Requirement	MRID	Status	Result or Deficiency
830.6302	Color	46853606	A	N9.3B Munsell value with a reflectance of 87.1% at 23 °C [97.5% TGAI]
830.6303	Physical state	46853606	A	Powdery solid at 23 °C (97.5% TGAI)
830.6304	Odor	46853606	A	Slight smell of pine or strong chemical insecticide [97.5% TGAI]
830.6313	Stability to normal and elevated temperatures, metals, and metal ions	46853608	A	Stable at ambient and elevated (54 °C) temperatures for 14 days, and on contact with metals iron and aluminum, and metal ions from iron (II) acetate and aluminum acetate at ambient temperatures for 14 days. (97.5% TGAI; HPLC quantitation)
830.6314	Oxidation/reduction: chemical incompatibility	46853614	A	Based on the molecular structure, quizalofop-P-ethyl is not likely to react with a combustible material and is non-oxidizing. Nitrogen atoms in the pyrazine moiety are in the highly reduced -3 oxidation state, chlorine is present as the -1 oxidation state and is non-oxidizing; and carbonyl and ether oxygens are in the -2 oxidation state and are non-oxidizing.
830.6315	Flammability	46853605	A	The technical product is not a flammable solid; no exothermic activity up to its melting point (~75 °C) was observed. [95.5% MUP; EEC Method A.10 (flammability of solids); EEC Method A.16 (relative self-ignition)]
830.6316	Explodability	46853605	A	The technical product is not sensitive to thermal, friction, or impact stimuli [95.5% MUP; EEC Method A.14 (thermal and friction sensitivity); ASTM E-680-79 (impact sensitivity)]
830.6317	Storage stability		G	
830.6319	Miscibility		N/A	The MUP is a solid at room temperature
830.6320	Corrosion characteristics		G	
830.7000	pH	46853606	A	7.29 ± 0.26 (1% suspension) [97.5% TGAI]
830.7050	UV/visible absorption	46853609	A	See Note 1
830.7100	Viscosity		N/A	The MUP is a solid at room temperature
830.7200	Melting point	46853606	A	75.2 ± 0.173 °C [97.5% TGAI; OECD Method No. 102]
830.7220	Boiling point		N/A	The TGAI is a solid at room temperature
830.7300	Density	46853606	A	1.3820 ± 0.00094 g/cm^3 at 21 °C [97.5% TGAI; OECD Method No. 109]
830.7370	Dissociation constants in water (DC)	46853610	A	Based on the molecular structure (no acidic, basic, or alcohol functional groups) and pH, quizalofop-P-ethyl is not likely to dissociate in an environmentally relevant pH range.
830.7550	Octanol/Water Partition coefficient	46853611	A	1.83 x 10^4 (log P_{ow} = 4.26) at 20 °C [97.5% TGAI, shake flask method]
830.7840	Water solubility	46853612	A	0.508 mg/L at 20 °C [97.5% TGAI; shake flask method; HPLC quantitation]
830.xxxx	Solvent solubility	46853613	A	7.85 g/L in n-hexane 24.2 g/L in n-octanol 38.7 g/L in methanol 213 g/L in acetonitrile ≥250 g/kg in acetone, ethyl acetate, dichloromethane, o-xylene, and toluene at 20 °C [97.5% TGAI; shake flask method; HPLC quantitation]
830.7950	Vapor pressure	46853607	A	<1.7 x 10^{-4} Pa at 20 °C <2.0 x 10^{-4} Pa at 25 °C [97.5% TGAI; OECD Method No. 104]

Table 2: Physical and Chemical Properties of : TGAI/MUP				
GLN	Requirement	MRID	Status	Result or Deficiency
A = Acceptable; N = unacceptable (see Deficiency); N/A = Not Applicable; G = Data gap; I = In progress or need upgrade; U = Up-grade (additional information required); W = waivers				

[1] Although the registrant did not identify the source (manufacturer) of the TGAI and MUP test substances used for the physical/chemical properties testing, because the product composition of the two products addressed in this review represent alternate formulations, the data are acceptable to support both products.

Note 1. 830.7050 UV/visible absorption

For the 97.5% TGAI:

Absorption Maxima	pH	Molar Absorption Coefficient (L/mol/cm)
204	<2	48,522
	7	47,723
	>10	47,874
236	<2	30,695
	7	30,128
	>10	30,140
244	<2	30,154
	7	29,719
	>10	29,983
338	<2	6,440
	7	6,048
	>10	6,272

830.1800. Enforcement of analytical method:

The methods used for preliminary analysis are proposed as the enforcement methods for the active ingredient (quizalofop-P-ethyl: Method 79376.220.01.ES) and impurities [redacted] Refer to the Confidential Appendix for complete descriptions of the methods for determination of impurities.

The active ingredient, quizalofop-P-ethyl was assayed using a normal-phase chiral HPLC/UV method.

Analytical Method No. 79376.220.01.ES for determination of the active ingredient, quizalofop-P-ethyl
Normal-phase HPLC operating conditions:
Detector: Fixed or variable wavelength UV (330 nm)
Column: Chiralcel OB-H 150 x 4.6 mm; 5 µm particle size
Column temperature: 40 °C
Isocratic mobile phase: 11% ethanol/89% hexane at 0.8 mL/minute
Sample size: 5 µL
Calibration: Internal standard of 2-methoxynapthalene; peak area ratios of DPX-79376/internal standard versus DPX-79376 concentration for quizalofop-P-ethyl external standards (calibration curve).
Retention time: 2-methoxynaphthalene (internal standard) 3.7 minutes
quizalofop-P-ethyl (DPX-79376; D(+) isomer) 6.5 minutes
L-isomer 10.2 minutes
Sample preparation: Technical samples are mixed with the internal standard solution, diluted with ethanol, and sonicated.

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Adequate validation data were submitted reflecting accuracy, linearity, and precision. The linearity correlation coefficient was 0.9998 in the range 0.482-1.501 mg/mL quizalofop-P-ethyl. Repeatability (precision) tests (5 replicate analyses of the technical product) yielded RSDs <0.3%. Recoveries in reproducibility testing (analysis of the same technical sample by 3 different laboratories) were 97.87 ± 0.46% (overall) for quizalofop-P-ethyl; recoveries for accuracy (using standard material as surrogate samples) were 99.5 ± 0.2% from four samples at 120x and 80x the method target concentration of 1 mg/mL. No additional data are required.

Attachment: Confidential Appendix

Pages 9-26 - *Manufacturing process information may be entitled to confidential treatment*