Date: 24 Jan 2007

SUBJECT: Product Chemistry Review of XDE-LAT Technical

FROM: Bruce F. Kitchens, Chemist
Technical Review Branch/RD (7505P)
Registration Division (7505P)

TO: RM #23, Joanne Miller/James Stone
Herbicide Branch
Registration Division (7505P)

DP BARCODE: D332130
DECISION No.: 369824
File Symbol No.: 62719-LAT
PRODUCT: TGAI
PCC: 108702
REGISTRANT: Dow AgroSciences LLC
USE: Manufacturing Use Product

INTRODUCTION:

The registrant, Dow AgroSciences LLC, is submitting an application for the registration of the new manufacturing use product, XDE-742 Technical. In addition, the registrant is seeking a NAFTA review for the proposed active ingredient in the United States, Canada, and Australia. The active ingredient in this product is Pyroxsulam (N-5,7-dimethoxy[1,2,4]triazolo[1.5-a]pyrimidin-2-yl)-2-methoxy-4-(trifluromethyl)-3-pyridinesulfonamide) at a label nominal concentration of 99.0% a.i. This product is intended for use in the manufacture of food use herbicide end-use products. In support of this request, the registrant has submitted a basic Confidential Statement of Formula (CSF) dated 03 July 2006, a draft label, and product chemistry data contained in MRID#s 469083-01, 469083-03, and 469085-14. The Technical Review Branch (TRB) has been asked to review this submission.

SUMMARY OF FINDINGS:

TRB has reviewed this submission and reports the following findings:

1. This product is produced from an integrate formulation process. This means that the active ingredient is produced as a result of intended chemical reactions.

2. All impurities have been identified and quantified by the registrant. In addition, all impurities listed on the basic CSF have a nominal concentration and an upper certified limit. The registrant has not declared this product to contain impurities of toxicological concern.

3. The nominal concentration of the active ingredient listed on the proposed CSFand the draft label are the same.

4. The draft label contains the appropriate storage and disposal statements.

5. The active ingredient's certified limits as proposed on the basic CSF are acceptable.

CONCLUSIONS:

TRB has reviewed this submission and concludes the following:

1. The basic formula CSF for the proposed end-use product, XDE-742 Technical dated 03 July 2006 is acceptable.

2. This submission satisfies the data requirements as specified in 40 CFR 158.155, 158.160, 158.165, 158.167, 158.175, and 158.180 with respect to product identity and composition, description of materials used to produce the product, description of formulation process, discussion of formation of impurities, certified limits, and enforcement analytical method.

3. This submission satisfies the data requirements as specified in 40 CFR 158.190 with respect to physical and chemical properties.

BARCODE:D332130; **Reg. No.** : 62719-LAT **PRODUCT**: XDE-742 Technical TGAI/MUP

830.1550. Product identity & Composition:

Common Name: XDE-742 Technical

Chemical Name (CAS): N-(5,7-dimethoxy[1,2,4] triazolo[1,5-a]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide

(IUPAC): N-(5,7-dimethoxy[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide

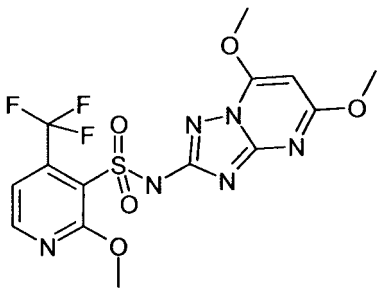
CAS No.: 422556-08-9

PC Code No.: 108702

Empirical formula: $C_{14}H_{13}F_3N_6O_5S$

Molecular Weight: 434.4

Structural Formula:



BARCODE:D332130; **Reg. No.** : 62719-LAT **PRODUCT**:XDE-742 Technical TGAI/MUP

Table 1. Manufacturing and Impurity Data for XDE-742 Technical

GLN	Requirement	MRID	Status	Details and /or Deficiency
830.1550	Product Identity and composition	469083-01	A	The NC of AI (99.0%) is supported by 5 batch analysis & agrees with the label claim NC. [redacted] impurities (> 0.1%)are listed on the CSF
8301600	Description of materials used to produce the product	469083-01	A	The product specification sheets (MSDS) for all the starting materials have been provided by the registrant
830.1620	Description of production process	469083-01	A	The AI was produced in [redacted] The production process has been described in full detail. The reaction conditions, amounts of chemicals in each step, duration of time, and the yields in each step have been provided. The QA steps involved in each step have been described.
830.1670	Discussion of formation of impurities	469083-01	A	The registrant has provided the complete mechanisms of formation, quantification and identification of all the impurities present at the levels of ≥ 0.1%. [redacted] impurities have been listed on the CSF including [redacted] No toxic impurities were reported during the analyses.
830.1700	Preliminary analysis	469083-01	A	The registrant has provided batch analysis for the TGAI. Seven batches were analyzed. The AI & impurities were identified and quantified by using HPLC/UV internal standard method. The methods were validated for accuracy, linearity, and precision. The LOQ and LOD for the AI & each impurity have been determined. The five batch analysis supported the CSF for basic formulation.
830.1750	Certified limits	469083-01	A	The proposed certified limits for the AI & for the impurities are based on the five batch analytical results.
830.1800	Enforcement analytical method	469083-01	A	An internal standard LC/UV method was used for the determination of the AI content in the TGAI/MUP. ESI/ LC/MS in the PI and NI mode was used to further identify the AI and its components. Method validation is acceptable.

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

BARCODE:D332130; **Reg. No.** : 62719-LAT **PRODUCT**: XDE-742 Technical TGAI/MUP

830 Series Subgroup B (Physical-Chemical Properties)

Table 2: Physical and Chemical Properties of XDE-742 Technical

GLN	Requirement	MRID	Status	Result or Deficiency
830.6302	C o l o r	469083-03	Y	Off- white
830.6303	Physical state	469083-03	Y	Solid @ 22.6^{O}C
830.6304	Odor	469083-03	Y	Spicy odor
830.6313	Stability to normal and elevated temperatures, metals, and metal ions	469083-03	Y	Product is stable at normal & elevated temperatures. Product is stable in the presence of 304 stainless steel, 316 stainless steel, brass, & copper. Product is also stable when mixed with CuCl, $NiCl_2$, & $FeCl_3$. Degradation products were not observed during the course of the study.
830.6314	Oxidation/reduction: chemical incompatibility	469083-03	Y	No temperature change when mixed with water, zinc dust, monoammonium phosphate, & potassium permanganate. A color change to pink was noted after the addition of potassium permanganate.
830.6315	Flammability	469083-03	NA	Product is a solid which does not contain flammable liquids
830.6316	Explodability	469083-03	NA	Product not explosive after thermal, shock, and friction tests.
830.6317	Storage stability		N	
830.6319	Miscibility	469083-03	NA	Product is not an emulsifiable liquid nor mixed with petroleum solvents
830.6320	Corrosion characteristics		N	
830.7000	pH	469083-03	Y	4.06 at 24.4°C (1% wt/wt aqueous solution)
830.7050	UV/Visible absorption	469083-03	Y	Neutral: λ_{max} 297; ϵ = 8000 Acidic: λ_{max} 297; ϵ = 7600 Basic: :λ_{max} 292; ϵ = 11100
830.7100	Viscosity	469083-03	NA	Product is a solid.
830.7200	Melting point	469083-03	Y	208.3°C
830.7220	Boiling point	469083-03	NA	Product is not a liquid at room temperature. Product decomposed at ≈ 213^{O}C.
830.7300	Density	469083-03	Y	Relative: 1.618 g/cc @ 20^{O}C Bulk: 0.383 g/cc @ 22.6 ^{0}C
830.7370	Dissociation constants in water	469083-03	Y	pKa = 4.67 $\pm$ 0.01; pH = 3.87 to 5.47

Table 2: Physical and Chemical Properties of XDE-742 Technical

GLN	Requirement	MRID	Status	Result or Deficiency
830.7550	Partition coefficient	469083-03	Y	Shake flask method: Log Po/w = 1.77 pH 4 12.1 $\pm$ 0.3 ($\log_{10} P_{ow}$ = 1.08 $\pm$ 0.01) pH 7 0.097 $\pm$ 0.1 ($\log_{10} P_{ow}$ = -1.01 $\pm$ 0.05) pH 9 0.024 $\pm$ 0.007 ($\log_{10} P_{ow}$ = -1.60 $\pm$ 0.12)
830.7840	Water solubility:	469083-03	Y	0.0626 g/L **See Note 1** for solubility I organic solvents
830.7950	Vapor pressure	469083-03	Y	$<1 \times 10^{-7}$ Pa @ 20^{O}C (PAI)

Y = Acceptable; N = unacceptable (see Deficiency); N/A = Not Applicable; G = Data gap; I = In progress or need upgrade; U = Up-grade (additional information required

Note 1. Solubility in organic solvents (g/100 ml): methanol (1.01), Xylene (0.0352), heptane (< 0.001), 1,2- Dichloromethane (3.94); Octanol (0.073);Acetone (2.79); Ethyl acetate (2.17)

BARCODE:D332130; **Reg. No.** : 62719-LAT **PRODUCT**: XDE-742 Technical TGAI/MUP

830.1800. Enforcement of analytical method: (MRID No. 469083-01)

Study Title: Analytical Method and Validation for the Determination of Active Ingredient in XDE-742 Technical by Liquid Chromatography

This method is applicable for the determination of XDE-742 Technical in TGAI or PAI. The technique consists of internal standard high performance liquid chromatography (HPLC) method and detection by ultraviolet (UV) absorption. The sample was also analyzed by electrospray ionization-liquid chromatography-mass spectrometry (ESI/LC/MS) in the positive (PI) and negative (NI) ion modes for the identification of XDE-742 Technical. Quantification was made by peak area measurements with internal standardization. The method was validated for precision, accuracy linearity, stability, ruggedness, and interferences.

Equipment & operating conditions:

High Performance Liquid Chromatography

Instruments: Perkin-Elmer High Performance Liquid Chromatograph (HPLC), Series 200 autosampler, Series 200 pump, Perkin-Elmer 785A detector or equivalent

Waters ZMD Quadrupole Mass Spectroscopy system

Detector:	Ultraviolet (UV) detector
Wavelength:	270 nm
Column:	Zorbax RX-C8 4.6 x 250 mm, 5 µm or equivalent
Oven temperature:	30°C
Mobile Phase A:	Water/Acetonitrile/Methanol (85:7.2:7.8 v/v) with 0.05% Trifluoroacetic acid
Mobile Phase B:	Acetonitrile with 0.05% Trifluoroacetic acid
Mobile C:	Methanol with 0.05% Trifluoroacetic acid
Flow rate:	1.0 ml/min
Injection volume:	20 µL
Internal Standard:	o-toluic acid
Gradient Program:	Equilibrate 7.0 min. at 100%A prior to injection. After injection, hold 0.5 min at 100%A. Linear gradient 57.6%A/18.4%B/24%C over 8.0 min. Hold 57.6%A/18.4%B/24%C for 13.5 minutes. Linear gradient to 23.5%A/29.7%B/46.8%C over 4.0 minutes. Hold 23.5%A/29.7%B/46.8%C for 5.0 minutes.
Run Time:	31 minutes
Retention Time:	o-toluic acid - 14.9 min XDE-742 - 16.9 min.

Step	Time (min)	%A	%B	%C	Curve
0	7.0	100	0	0	Equilibrium
1	0.5	100	0	0	
2	8.0	57.6	18.4	24	1 (linear)
3	13.5	57.6	18.4	24	
4	4.0	23.5	29.7	46.8	1 (linear)
5	5.0	23.5	29.7	46.8	

.

830.1800. Enforcement of analytical method (con't): (MRID No. 469083-01)

Electroscopy Ionization-Liquid Chromatography-Mass Spectrometry (ESI/LC/MS)

Chromatographic Conditions:

Instrument: Waters Alliance 2690 ternary gradient liquid chromatograph coupled to a Waters ZMD quadrupole MS system via a Micromass Z-spray electrospray (ESI) interface in the PI and NI modes
Column: Zorbax RX-C8, 5µm, 250 x 4.6 mm
Column Temp.: 30^{O}C
Mobile phase A: 0.05% Trifluoroacetic acid in DI Water
Mobile phase B: 0.05% Trifluoroacetic acid in Acetonitrile
Mobile phase C: 0.05% Trifluoroacetic acid in Methanol
Flow Rate: 1.0 ml/min
Gradient Run Conditions:
0 to 0.5 min, hold at 85%/7.2%/7.8% A/B/C
0.5 to 6.5 min, ramp to 49%/22.5%/28.5% A/B/C
8.5 TO 22 min, hold at to 49%/22.5%/28.5% A/B/C
22 to 26 min, ramp to 20%/31.4%/48.6% A/B/C
26 to 31 min, hold at 20%/31.4%/48.6% A/B/C
31 to 31.5 min, ramp to 85%/7.2%/7.8% A/B/C
31.5 to 38 min, hold at 85%/7.2%/7.8% A/B/C
Total run time: 38 minutes
Detector: Ultraviolet (UV) diode array 20 to 400
Wavelength: 270 nm
ESI conditions: Source block = 110^{O}C Desolvation = 300^{O}C
Capillary = 2.5kV Extractor = 4V

RF Lens = ~0.3V Cone = 24V (+) and 54V (+)
Gas flow = ~2.6 liters/hour
MS Conditions: Photomultiplier = 650V Ion Energy = 0.7V
Resolution = 15/15 mode = +Q1MS; centroid
Scan = 120 to 1200 amu (+) @ 24V and 54V cone
Rate = 1.2 sec/scan

Methods of Calculation
Relative Response Factor for XDE-742

$$RRF_i = \frac{W_i \times A_{is}}{W_{is} X A_i}$$

Where
RRF_i = Relative response factor of component, I
W_i = Weight of component, I, added to calibration solution in mg, corrected for purituy
A_{is} = Peak area of internal standard peak
W_{is} = Weight of internal standard solution added to calibration solution in mg
A_i = Peak area of component, i

830.1800. Enforcement of analytical method (con't): (MRID No. 469083-01)

Concentration for XDE-742

$$Wt\% = \frac{RRF_i \times A_i \, W_{IS} \times 100}{A_{IS} \times W_s}$$

Where
Wt% = weight percent of component, i
RRF_i = Relative response factor of component, i
A_1 = Peak areas of component, I
W_{IS} = Weight of internal standard solution added to sample in mg
A_{IS} = Peak area of internal standard peak
W_s = weight of sample in mg

Horwitz Equation

$$RSDr = 2^{\frac{(1-\log C)}{2}} \times 0.67$$

where

RSDr = Expected relative standard deviation
C = Concentration of component as weight percent fraction ($\frac{wt\%}{100}$)

108702-1-24-2007 – Product Chemistry Rev of ZDE-LAT Technical , MRID #'a 469083-01, -03 & 46908514_

Page _____ is not included in this copy.

Pages 10 through 20 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.

_X___ 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.

_____ FIFRA registration data.

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

_____ The document is not responsive to the request.

_____ Internal deliberative information.

_____ Attorney-client communication.

_____ Claimed confidential by submitter upon submission to the Agency.

_____ Personal privacy Information

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.