FEE

Date: JUNE 6, 2005

SUBJECT: **FEE**: Product Chemistry Review of IR5878 Technical

FROM: Debra Rate
Product Chemistry Team
Technical Review Branch/RD (7505C)

Debra M. Rate 6/8/05
6/8/05

TO: James Tompkins / Erik Kraft RM 25
Herbicide Branch / RD (7505C)

DECISION NO: 342749
DP BARCODE: D304195
EPA REG. NO.: 80289-EUP-1
PRODUCT: IR5878 Technical
PCC: 108209
REGISTRANT: ISAGRO S.P.A.
USE: Herbicide

INTRODUCTION:

The registrant has submitted a Confidential Statement of Formula (CSF) for basic formulation (dated 02/FEB/2004) for the experimental-use product, IR5878 Technical. [redacted] The 830 Series Subgroup A and B data have been submitted under the MRID Nos. 462190-01 through 462190-14 and 465590-01. The Technical Review Branch (TRB) has been asked to evaluate the submitted studies and determine if the studies support the registration of the subject product.

SUMMARY OF FINDINGS:

1. The manufacturing site where this product is produced by [redacted] The 5 batch analysis was performed on test substances [redacted]

2. The registrant has submitted a basic formulation CSF (dated 02/FEB/2004) for IR5878 Technical. The nominal concentration (98.0%) of the AI (orthosulfamuron) concurs with the product label claim nominal concentration of 98.0%. 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.

3. The subject product is produced in an integrated system, [redacted] The data submitted in MRID No. 462190-01detailing the production and manufacturing processes corresponding to guidelines 830.1600 and 830.1620, satisfy the requirements of 40CFR§158.160 and158.162, respectively.

4. The registrant has provided an adequate explanation of the impurities that are known to be associated with the subject product and potential impurities of the subject product. This submitted data corresponding to guideline 830.1670 (discussion on the formation of impurities) satisfy the data requirements of 40CFR§158.167. The preliminary 5-batch analysis provided by the registrant concurs with the data the registrant presented on the impurities. [MRID Nos. 462190-01]

5. The product chemistry data submitted corresponding to the guideline reference 830.1700 (preliminary analysis) satisfy the data requirements for 40CFR§158.170. The % AI and the impurities were determined for the test substance. See the Confidential Appendix for details. [MRID No. 462190-02]

6. The data submitted corresponding to reference guideline 830.1800 (Enforcement Analytical Method) satisfies the data requirements of 40CFR§158.180. The method of analysis of the active ingredient (AI) is high-performance liquid chromatography (HPLC) with UV detection (265 nm). The method was validated for precision, linearity, and accuracy. See Confidential Appendix for details. [MRID No. 462190-03]

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7. The data corresponding to 830 Series Subgroup B (physical-chemical properties) are acceptable and fulfill the data requirements for 40CFR§158.190. [MRID No. 462190-04 through 462190-14 and 465590-01]

CONCLUSIONS:

TRB has reviewed the product chemistry data submitted for IR5878 Technical and has concluded that:

1. All of the product chemistry data submitted corresponding to 830 Series Subgroup A are acceptable and satisfy the data requirements of 40CFR§158.155.

2. The data submitted corresponding to reference guidelines 830 Series Subgroup B data are acceptable, and satisfy the data requirements of 40CFR§158.190.

3. The CSF for basic formulation (dated 02/FEB/2004) is acceptable.

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Common Name: Orthosulfamuron

Chemical name: IUPAC: 1-(4,6-dimethoxypyrimidin-2-yl)-3-[2-(dimethylcarbamoyl)-phenylsulfamoyl]urea

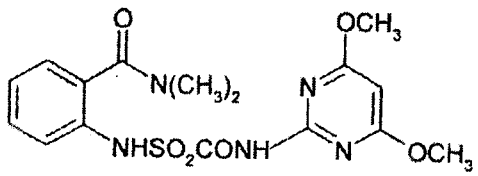
CAS No.: 213464-77-8

PC Code No.: 108209

Empirical formula: $C_{16}H_{20}N_6O_6S$

Molecular Weight: 424.44

Structural formula:



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ATTACHMENT II

REVIEW OF PRODUCT CHEMISTRY, OPPTS 830 SERIES

Chemical Name (IUPAC, CAS)	Orthosulfamuron, 1-(4,6-dimethoxypyrimidin-2-yl)-3-[2-(dimethylcarbamoyl)-phenylsulfamoyl]urea
Chemical Number (CAS; PC Code)	CAS No. 213464-77-8 PC Code:108209
Registration/Symbol No.	80289-EUP-1
Type of Product (T, MP, EP)	98.0 % TGAI
DP Barcode	D304195
Reviewer	Debra Rate
Branch Chief	Deborah McCall

Table 1: Manufacturing and Impurity Data for the IR5878 Technical.

GLN	Requirement	MRID	Status[1]	Details and/or Deficiency[2]
830.1550	Product Identity & Disclosure of Ingredients	CSF (dated 02/FEB/2004)	A	The nominal concentration of the AI (98.0%) is supported by the 5 batch analyses.
830.1600 830.1620	Starting Materials & Manufacturing Process	462190-01	A	The MSDS for the starting materials have been submitted. The subject product is produced in an integrated system [redacted]
830.1670	Discussion of Impurities	462190-01	A	An adequate explanation of the known and potential impurities found in the technical product has been provided by the registrant.
830.1700	Preliminary Analysis	462190-02	A	The registrant has provided 5 batch analysis for the TGAI.
830.1750	Certification of Limits	CSF (dated 02/FEB/2004) 462190-01, 462190-02	A	The registrant based the upper certified limits on the results obtained from the 5 batch analyses. Although the Certified Limits do not follow the Agency Standards set forth in 40CFR§158.175(b)(2), they are reasonable due to manufacturing and batch variation.
830.1800	Analytical Methods	462190-03	A	Method was submitted for determination of the %AI in the product. HPLC / UV (265 nm) detector was used for the %AI determination. The method was validated for precision, linearity and accuracy.

[1] A = Acceptable; N = Unacceptable (see Deficiency); U = Upgradable data; N/A = Not Applicable.

Table 2: Physical and Chemical Properties of IR5878 Technical

GLN	Requirement	MRID	Status	Result or Deficiency
830.6302	Color	462190-04	A	White (N9.5/90.0%R, Munsell System @ 22.0°C)
830.6303	Physical state	462190-05	A	Fine Powder @ 20.0 °C
830.6304	Odor	462190-06	A	Odorless @ 20.0 °C

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MANUFACTURING PROCESS INFORMATION IS NOT INCLUDED

Table 2: Physical and Chemical Properties of IR5878 Technical

GLN	Requirement	MRID	Status	Result or Deficiency
830.6313	Stability to normal and elevated temperatures, metals, and metal ions	462190-14	A W	The TGAI was exposed to elevated temperatures over a period of 14 days and showed no decomposition or loss of %AI. Waiver was requested and granted for stability to metals and metal ions. See File Jacket.
830.7000	pH	462190-13	A	pH = 4.35 @ 25 ^{0}C (1% aqueous dispersion)
830.7050	UV/Visible Absorption	465590-01	A	Acidic (pH 0.89): A = 0.4567 $\epsilon = 1.95 \times 10^4$ (236 nm) Neutral (pH 6.9): A = 0.4938 $\epsilon = 2.11 \times 10^4$ (238 nm) Alkaline (pH 12.8): A = 0.6535 $\epsilon = 2.79 \times 10^4$ (241 nm)
830.7100	Viscosity		NA	Not applicable to a solid.
830.7200	Melting point	462190-07	A	151°C (Melted with decomposition.)
830.7220	Boiling point		NA	Technical is a solid.
830.7300	Relative Density	462190-08	A	1.45 g/ml @ 20.0 ^{0}C using the pycnometer method.
830.7370	Dissociation constants in water	462190-11	A	The test material is predicted to have 5 overlapping dissociation constants. The test material becomes increasingly less soluble in water as the pH is lowered and undergoes degradation (hydrolysis) at neutral through to acidic pH's. (See MRID for predicted dissociation constants.)
830.7550	Partition coefficient	462190-12	A	pH: 4: $Log_{10}P_{ow} = 2.02$ pH: (~7): $Log_{10}P_{ow} = 1.31$ pH: 10: $Log_{10}P_{ow} = <0.3$
830.7840	Water solubility:	462190-09	A	pH 4.0 Buffer: 2.62×10^{-2} g/L @ 20.0 ^{0}C pH 7.0 Buffer: 0.629 g/L @ 20.0 ^{0}C pH 8.5 Buffer: 38.9 g/L @ 20.0 ^{0}C
830.7950	Vapor pressure	462190-10	A	1.116×10^{-4} Pa @ 20 ^{0}C $< 1.4 \times 10^{-4}$ Pa @ 25 ^{0}C

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830.1800. Enforcement analytical method: (MRID No. 462190-03)

Analytical Method for Determination of the% orthosulfamuron in the subject product. [MRID No. 462190-03]

Reagents and Standards:
IR 5878; certified analytical standard
Acetonitrile; HPLC grade
Water; HPLC grade
Acetonitrile; reagent grade
Potassium dihydrogen phosphate; reagent grade
Sodium bicarbonate; reagent grade
Solvent Mix: Acetonitrile/aqueous sodium bicarbonate 0.33M (7:3 v/v)

Apparatus and Operating Conditions:

Liquid Chromatograph:	Perkin Elmer Series 200 Pump
Diode Array Detector:	Perkin Elmer Series 200 DAD
Autosampler:	Perkin Elmer Series Autosampler
Software for Chromatographic Data:	Perkin Elmer Turbochrom WS
Column:	Hypersil 5 μm C-18, 4 X 250 mm Phenomenex

Balance accurate to 0.1 mg
Volumetric glassware
Filtering apparatus

Eluent:	Solvent A: Water KH_2PO_4 0.004M / Solvent Acetonitrile
Column Temperature:	40 °C
Flow Rate:	1.0 ml / min
Detection:	UV at 265 nm
Injection Volume:	10 μl

Retention Time:
Orthosulfamuron: ~8.9 min

Gradient Program:

STEP	Time (min)	Solvent A	Solvent B
1	0	75	25
2	1	75	25
3	10	20	80
4	1	20	80
5	10	75	25

DER for MRID #46219001-14 + 45559001

Page _____ is not included in this copy.

Pages 7 through 12 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.

_____ FIFRA registration data.

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

_____ The document is not responsive to the request.

_____ Internal deliberative information.

_____ Attorney-Client work product.

_____ Claimed Confidential by submitter upon submission to the Agency.

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.