

BARCODE: D330793; **Reg. No. :** 83529-R **PRODUCT:** Imidacloprid Technical Insecticide

Date: December 7, 2006

SUBJECT: FEE. Product Chemistry Review of Imidacloprid Technical Insecticide TGAI/MUP

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12/07/06
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TO: Dani Daniel / Venus Eagle, RM 01
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DP BARCODE: D330793
DECISION No.: 367697
File Symbol No.: 83529-R
PRODUCT: Imidacloprid Technical Insecticide TGAI/MUP
PCC: 129099
REGISTRANT: Sharda USA LLC
USE: Insecticide, Food use

INTRODUCTION:

The registrant has submitted the product chemistry data to support the registration application of the proposed Imidacloprid Technical Insecticide TGAI/MUP produced by [REDACTED] in [REDACTED]. The product chemistry data corresponding to 830 series subgroup A and Subgroup B have been submitted under MRID Nos. 468445-01, 468445-03 and 468678-01. The registrant has also submitted a CSF for basic formulation (undated) and the product label. The registrant has claimed that the proposed Imidacloprid Technical Insecticide TGAI/MUP (File Symbol No. 83529-R) is substantially similar to the registered product with Reg. No. 264-755. TRB has been asked to evaluate the product chemistry data submitted for the proposed MUP and determine its similarity to the registered product.

SUMMARY OF FINDINGS:

1. The registrant has submitted a Confidential Statement of Formula for basic formulation (undated) for the Imidacloprid Technical Insecticide TGAI / MUP. The average purity of the technical/MUP is 98.53%, as determined by the five batch analysis. The proposed certified limits for the AI are based on the standard certified limits as set forth in 40CFR§158.175(b)(2), where as the certified limits for the impurities are based on the five batch analysis. 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. 468445-01].
2. The product chemistry data submitted corresponding to guideline reference 830.1600 (description of material used to produce the product) satisfy the data requirements of 40CFR§ 158.160 [MRID No. 468445-01].

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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 Imidacloprid Technical

[REDACTED] The details of the production process have been provided which included the amounts of each starting material used in the process, description of the equipment used, the reaction conditions (temperature, pH, etc.) and the yields of the final product and the steps taken to control the quality of the product [MRID No. 468445-01].

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. During the production of

[REDACTED] The registrant has provided discussion on the formation of these impurities [MRID No. 468445-01].

5. The data submitted corresponding the guideline reference 830.1700 (preliminary analysis) satisfy the data requirements of 40CFR§158.170. The study was conducted under GLP requirements in compliance with 40CFR§160. Five representative batches of the Imidacloprid Technical Insecticide MUP/technical were analyzed for percent active ingredient and the impurities by JAI Research Foundation in India. The active ingredient & the impurity contents were determined by HPLC-UV (252 nm) with internal standard method. The identification of the AI and the impurities was confirmed by LC-MS method. The analytical method was validated for accuracy, linearity, precision, LOD, and LOQ [MRID No. 468678-01].

6. The data submitted corresponding the guideline reference 830.1800 (enforcement analytical method) satisfy the data requirements of 40CFR§158.180. The purity of the AI in the TGAI was determined by HPLC-UV (252 nm) external standard method. The method was validated for precision, accuracy and linearity, LOQ and LOD [MRID No. 468678-03].

7. The data submitted corresponding to guidelines 830 Series Subgroup B (physical-chemical properties) satisfy the data requirements of 40CFR§158.190, except for 830.6313 (stability to room & elevated temperatures and metal & metal ions), explodability (830.6316), one year storage stability (830.6317), corrosion characteristics (830.6320), & UV/VIS (830.7050) studies. The registrant has reported that long term studies corresponding to guidelines 830.6317 & 830.6320 are in progress [MRID No. 468445-03].

8. On December 6, 2006, the registrant sent an e-mail requesting waivers for 830.6313 and 830.6316 providing the justifications. Also the registrant agreed to conduct the UV/VIS studies as a condition of registration. The registrant will conduct the one year storage and corrosion studies.

Manufacturing process information may be entitled to confidential treatment

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CONCLUSIONS:

The TRB has reviewed the product chemistry data submitted for Imidacloprid Technical Insecticide TGAI / MUP and has concluded that:

1. All the product chemistry data submitted corresponding to 830 Series Subgroup A are acceptable.
2. The CSF for basic formulation (undated) is acceptable.
3. The data submitted corresponding to the 830 Series Subgroup B (physical-chemical properties) are acceptable except for, except for 830.6313 (stability to room & elevated temperatures and metal & metal ions), explodability(830.6316) one year storage stability (830.6317), corrosion characteristics (830.6320), UV/VIS (830.7050) studies.
4. The registrant must generate studies corresponding to guidelines 830.6317(one year storage stability) and 830.6320 (corrosion characteristics). The observations must be made at 0, 3, 6, 9, & 12 months intervals. The results must be submitted to the Agency along with an electronic format also.
5. Based on the justifications provided, the Agency has no objection in granting waivers corresponding to guidelines 830.6313 (stability to room & elevated temperatures and metal & metal ions) and explodability (830.6316). The registrant has agreed to conduct studies for the guidelines 830.7050 (UV/VIS), 830.6317 (one year storage stability) and 830.6320 (corrosion characteristics) as a condition of registration for the proposed TGAI/MUP.
6. The proposed Imidacloprid Technical Insecticide TGAI/MUP (File symbol No. 83529-RI) was determined not to be substantially similar to the registered product with Reg. No. 264-755 (basic formulation, dated 9-13-91) from the product chemistry point of view. The impurity profile for the proposed MUP/TGAI and registered MUP/TGAI is significantly different [REDACTED] impurity). While the lack of the impurities is more environmentally favorable it may also affect the toxicity of the product. [REDACTED] The nominal concentration of registered Imidacloprid TGAI/MUP in the basic formulation (9-13-91) is 95.70%, whereas, the alternate formulation CSF (dated 6-15-94) has NC of 98.42% for imidacloprid. Label claim of the registered imidacloprid TGAI/MUP is 98% (accepted April 13, 2005).

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830.1550. Product identity & Composition: (MRID No. 468445-01)

Common name: Imidacloprid

IUPAC Chemical

Name: (EZ)-1-(6-chloro-3-pyridylmethyl)-N-nitroimidazolidin-2-ylideneamine

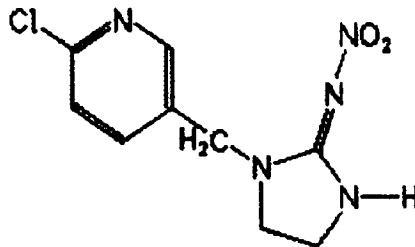
CAS Chemical Name: 1-[(6-chloro-3-pyridinyl)methyl]-N-nitro-2-imidazolidinimine

CAS Reg. No.: 138261-41-3

Empirical Formula: C₉H₁₀ClN₅O₂

Molecular Weight: 255.7

Structure:



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Table 1. Manufacturing and Impurity Data for Imidacloprid TGAI/MUP				
GLN	Requirement	MRID	Status	Details and /or Deficiency
830.1550	Product identity and composition	Basic CSF (undated)	A	The NC of AI (98.53%) is supported by 5 batch analysis & agrees with the label claim NC (98%). [REDACTED] impurities ($\geq 0.1\%$) are listed on the CSF.
830.1600	Description of materials used to produce the product	468445-01	A	The description & composition for all the starting materials used to produce the imidacloprid technical/mup have been provided by the registrant
830.1620	Description of production process	468445-01	A	The AI was produced in [REDACTED] [REDACTED] The production process has been described in full details. 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	468445-01	A	The registrant has provided the complete mechanisms of formation, quantification and identification of all the impurities present at the levels of $> 0.1\%$. Total of [REDACTED] impurities [REDACTED]
830.1700	Preliminary analysis	468678-01	A	Five representative batches of the imidacloprid technical/mup were analyzed for percent active ingredient and the impurities by JAI Research Foundation in India. The purity of the AI in the TGAI was determined by HPLC-UV (252 nm) with external standard method. The impurities were identified & quantified also by HPLC-UV (252nm) & HPLC-MS method. The AI and the impurities were quantified and their identity confirmed by LC-MS method. The five batch analysis supported the CSF for basic formulation.
830.1750	Certified limits	468445-01	A	The proposed certified limits for the AI are based on the standard certified limit table. Whereas proposed certified limits for the impurities are based on five batch analysis results.
830.1800	Enforcement analytical method	468678-01	A	The HPLC-UV (252 nm) method was used for the determination of the AI content in the TGAI/MUP. The method was validated for precision, linearity, accuracy, LOD, & LOQ.
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 : Imidacloprid TGAI/MUP				
GLN	Requirement	MRID	Status	Result or Deficiency
830.6302	Color	468445-03	A	White
830.6303	Physical state	" " "	A	Powder
830.6304	Odor	" " "	A	No characteristics odor
830.6313	Stability to normal and elevated temperatures, metals, and metal ions	e-mail 12-06-06	W	Waiver request accepted based on the justification provided (e-mail 12-06-6)
830.6314	Oxidation/reduction: chemical incompatibility	468445-03	A	Test substance is an oxidizer
830.6315	Autoflammability	468445-03	A	400°C by ASTM E659 method/not flammable
830.6316	Explosibility	e-mail 12-06-06	W	Waiver request accepted based on the justification provided (e-mail 12-06-6)
830.6317	Storage stability	468445-03	I	One year study in progress
830.6319	Miscibility		NA	
830.6320	Corrosion characteristics	468445-03	I	One year in progress
830.7000	pH	468445-03	A	4.68 at 20°C (1% aqueous, w/w)
830.7050	UV/Visible absorption	e-mail 12-06-06	I	Sharda agreed to conduct this study
830.7100	Viscosity		NA	
830.7200	Melting point	468445-03	A	143°C
830.7220	Boiling point		NA	
830.7300	Density	468445-03	A	1.517 g/ml at 20°C
830.7370	Dissociation constants in water (DC)	468445-03	A	No DC is observed for the test substance in aqueous solution
830.7550	Partition coefficient	468445-03	A	Log K o/w = 0.61
830.7840	Water solubility:	468445-03	A	See Note 1
830.7950	Vapor pressure	468445-03	A	< 10 ⁻⁴ Pa

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Note 1. 830.7840. Solubility in water & organic solvents: (MRID No. 468445-03)

Solubility in water (g/L at 25°C): 0.64 (pH=4.0); 0.64 (pH=7.0); 0.64 (pH=9.0); deionized water = 0.61 g/L

The solubility was determined in the following organic solvents (g/l at 25°C):

n-Heptane: 0.20 mg/l; Xylene: 0.36; 1, 2-dichloroethane: 28.9; Methanol: 8.20; Acetone: 42.2;

Ethyl acetate: 6.82; n-octanol: 0.81

830.1800. Enforcement of analytical method: (MRID No. 468678-01)

The imidacloprid active ingredient was determined by HPLC using external standard method. The method validation covered the aspects like: specificity, linear dynamic range (LDR), LOD, LOQ, precision (%RSD).

Equipment & Parameters

HPLC system: Agilent 1100 series with PDA detector.

Column: C-18, 5 µm, 250 mm x 4.6 mm

Mobile phase: Acetonitrile:0.5% acetic acid in water (40:60)

Sample size: 20 µL

Flow rate: 1.0 ml/min

Detector wavelength: 252 nm

Retention time: Imidacloprid = 5.589 minutes

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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.

 X The product confidential statement of formula.

 Information about a pending registration action.

 FIFRA registration data.

 The document is a duplicate of page(s) .

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 Proprietary information pertaining to the chemical composition of an inert ingredient provided by the source of the ingredient.

 Attorney-Client Privilege.

 Claimed Confidential by submitter upon submission to the Agency.

 Internal Deliberative 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.

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