FEE

Date: August 14, 2006

SUBJECT: Product Chemistry Review of Imidacloprid (ENS-010) TGAI/MUP

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8/14/06

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DP BARCODE: D325434
DECISION No.: 363042
File Symbol No.: 82957-R
PRODUCT: Imidacloprid (ENS-010) TGAI/MUP
PCC: 129099
REGISTRANT: Ensystex III, Incorporation
USE: Food Handling establishments: places other than private residences in which food is held, processed, prepared and served.

INTRODUCTION:

The registrant has submitted the product chemistry data to support the registration application of the proposed imidacloprid (ENS-010) technical [redacted] The product chemistry data corresponding to 830 series subgroup A and Subgroup B have been submitted under MRID Nos. 467096-01, 467096-02, 467096-07 to -09, 467096-11, 467096-13, and 467225-01 thru 467225-05. The registrant has also submitted a CSF for basic formulation (dated 12-01-05) and the product label. The registrant has claimed that the proposed TGAI/MUP imidacloprid ENS-010 (File Symbol No. 82957-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 (dated 12-01-05) for the ENS-010 TGAI / MUP. The average purity of the technical/MUP is 99.0%, 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 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. 467096-01].

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. 467096-01].

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 ENS-10 TGAI/MUP was manufactured in two step integrated batch process. 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. 467096-01].

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 ENS-010 (involving two synthetic steps), the registrant discussed and reported the formation of [redacted] major impurities present at the levels of > 0.1% in addition to [redacted] In addition the registrant also discussed about an impurity of toxicological concern (nitroso compound) associated with the TGAI/MUP, which is quantified at the level allowed (maximum 1ppm) by the agency. During the 5 batch analysis, the toxic impurity was not detected (instrument LOD = 0.13 ppm & LOQ = 0.26 ppm). The registrant has provided discussion on the formation of these impurities [MRID No. 467096-01].

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 ENS-010 MUP/technical were analyzed for percent active ingredient and the impurities. The active ingredient & the impurities were determined by HPLC-UV (270 nm). The identification of the AI and the impurities were confirmed by LC-MS. The analysis for the toxic impurity was conducted following LC-MS with the level of detection (LOD) of 0.13 ppm and LOQ of 0.26 ppm. The nitroso impurity was not detected at this LOD. The analytical method was validated for accuracy, linearity, and precision [MRID No. 467096-02].

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 (270 nm) external standard method. The method was validated for precision, accuracy and linearity [MRID No. 467096-02].

7. The data submitted corresponding to guidelines 830 Series Subgroup B (physical-chemical properties) satisfy the data requirements of 40CFR§158.190, except for stability to normal & elevated temperature, metal & metal ions (830.6314), one year storage stability (830.6317) & corrosion characteristics (830.6320) studies [MRID No. See Table II].

8. The registrant has requested waivers for the following guidelines: [MRID No. 467096-13]

830.6313. Stability to normal & elevated temperature, metal & metal ions
830.6314. Oxidation/Reduction: Justification: seeking waiver on the basis that the test substance does not contain any oxidizing and reducing agents.
830.6315. Flammability
830.6316. Explodability
830.6317. Storage stability
830.6319. Miscibility
830.6320. Corrosion characteristics
830.6321. Dielectric breakdown voltage
830.7100. Viscosity
830.7220. BP
830.7950. Vapor pressure. Justification: seeking waiver on the basis that data are not required for materials that are solid at room temperature and have a low vapor pressure.

BARCODE: D325434; **Reg. No.** : 82957-R **PRODUCT**: Imidacloprid (ENS-010)TGAI/MUP

CONCLUSIONS:

The TRB has reviewed the product chemistry data submitted for imidacloprid (ENS-010) 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 (dated 12-01-05) is acceptable.

3. The data submitted corresponding to the 830 Series Subgroup B (physical-chemical properties) are acceptable except for stability to room & elevated temperature, metal & metal ions (830.6313), one year storage stability (830.6317) & corrosion characteristics (830.6320) studies.

4. The Agency has no objections in granting waivers for the physical-chemical properties identified in Item #8 of Summary of Findings above, except for stability to room & elevated temperature, metal & metal ions storage stability & corrosion studies.

5. The registrant must generate studies corresponding to guidelines 830.6313 (stability to room & elevated temperature, metal & metal ions), 830.6317(one year storage stability) and 830.6320 (corrosion characteristics). The observations must be made at 0, 3, 6, 9, & 12 months intervals for storage stability & corrosion studies. The accelerated study (14 days for 54°C) submitted on storage stability will not substitute for one year study. The results must be submitted to the Agency along with an electronic format also.

6. The proposed product (File symbol No. 81959-RG) was determined not to be substantially similar to the registered product with Reg. No. 264-755 from the product chemistry point of view for the following reasons:

- The impurity profile of the two products is significantly different.
- The proposed uses for imidacloprid (ENS-010) are not the same as for the registered product.
- The ENS-010 may contain very low amounts (not detectable at LOD of 0.13 ppm) of nitroso compound which was not even reported in the registered product.

BARCODE: D325434; **Reg. No.** : 82957-R **PRODUCT**: Imidacloprid (ENS-010)TGAI/MUP

30.1550. Product identity & Composition: (MRID No. 467096-01)

Common Name: Imidacloprid [ENS-010]

Chemical Name (CAS): 1-[(6-chloro-3-pyridinyl) methyl]-N-nitro-2-imidazolidinimine
(IUPAC): (EZ)-1-(6-chloro-3-pyridylmethyl)-N-nitroimidazolidin-2-ylideneamine

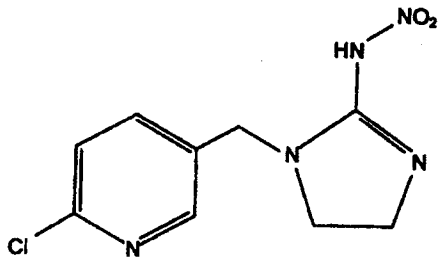
CAS No.: 105827-78-9

PC Code No.: 129099

Empirical formula: $C_9H_{10}ClN_5O_2$

Molecular Weight: 255.67

Structural formula:



Imidacloprid

BARCODE: D325434; **Reg. No.** : 82957-R **PRODUCT**: Imidacloprid (ENS-010)TGAI/MUP

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 (12-01-05)	A	The NC of AI (99%) is supported by 5 batch analysis & agrees with the label claim NC. [redacted]mpurities (≥ 0.1%) are listed on the CSF.
8301600	Description of materials used to produce the product	467096-01	A	The description & composition for all the starting materials used to produce the EN-010 technical have been provided by the registrant
830.1620	Description of production process	467096-01	A	The AI was produced in two stage integrated batch process. 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	467096-01	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 have been listed on the CSF at levels of ≥ 0.1%. The TGAI was analyzed for impurity of tox concern (nitroso) but was not detected at LOD of 0.13ppm.
830.1700	Preliminary analysis	467096-02	A	Five representative batches of the ENS-010 technical were analyzed for percent active ingredient and the impurities. The purity of the AI and impurities in the TGAI were determined by HPLC-UV (270 nm) with external standard method. The analysis for nitroso compound was carried out using LC-MS at LOD of 0.13 ppm and LOQ of 0.26 ppm, but was not detected. The five batch analysis supported the CSF for basic formulation.
830.1750	Certified limits	467096-02	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	467096-02	A	The HPLC-UV (270 nm) method was used for the determination of the AI content in the TGAI/MUP. The method was validated for precision, linearity and accuracy..

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

MANUFACTURING PROCESS INFORMATION HAS BEEN REMOVED

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30 Series Subgroup B (Physical-Chemical Properties)

Table 2: Physical and Chemical Properties of : ENS-010 TGAI/MUP

GLN	Requirement	MRID	Status	Result or Deficiency
830.6302	Color	467225-01	A	White
830.6303	Physical state	" " "	A	Solid powder
830.6304	Odor	" " "	A	Odorless
830.6313	Stability to normal and elevated temperatures, metals, and metal ions	467096-13	W	Waiver denied. Must determine stability at room and elevated temperatures and also towards metal & metal ions at RT & 54°C. The study submitted at the elevated temperature (MRID 467225-02) can be cited.
830.6314	Oxidation/reduction: chemical incompatibility	467096-13	W	TS does not contain any oxidizing or reducing agents
830.6315	Flammability	467096-13	W	
830.6316	Explodability	" " "	W	
830.6317	Storage stability	" " "	W	Waiver denied
830.6319	Miscibility		NA	
830.6320	Corrosion characteristics	467096-13	W	Waiver denied
830.7000	pH	467225-03	A	6.72 at 20.2°C (1% aqueous solution)
830.7050	UV/Visible absorption	467225-04	A	**See Note 1**
830.7100	Viscosity	467096-13	W	
830.7200	Melting point	467096-07	A	142.2°C
830.7220	Boiling point	467096-13	W	
830.7300	Specific gravity	467096-08	A	1.54 at 20°C
830.7370	Dissociation constants in water (DC)	467096-09	A	Could not be established
830.7550	Partition coefficient	467225-05	A	Log P o/w = 0.57
830.7840	Water solubility:	467096-11	A	See **Note 2**
830.7950	Vapor pressure	467096-13	W	

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8/14/96 Imidacloprid Product Chemistry Review
(MRID #s 41679608 & 41722503)

Page _____ is not included in this copy.

Pages 8 through 15 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 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.