DP BARCODE: D340005; **FILE SYMBOL No.:** 71368-61; **PRODUCT:** Imidacloprid Technical TGAI/MUP (Alternate source [redacted]

Date: August 6, 2007

SUBJECT: Product Chemistry Review of Imidacloprid Technical TGAI/MUP

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8/06/07

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DP BARCODE: D340005
DECISION No.: 378900
File Symbol No.: 71368-61
PRODUCT: Imidacloprid Technical TGAI/MUP
PCC: 129099
REGISTRANT: NuFarm Incorporation
USE: Insecticide
FOOD USE: Yes

INTRODUCTION:

The registrant has submitted a CSF for alternate formulation (dated 04-23-07) and the supporting product chemistry data for imidacloprid technical [redacted] The product chemistry data corresponding to 830 series subgroup A and Subgroup B have been submitted under MRID Nos. 471267-01 thru 471267-04. TRB has been asked to evaluate the alternate CSF and the supporting product chemistry data.

SUMMARY OF FINDINGS:

1. The registrant has submitted a Confidential Statement of Formula for alternate formulation (dated 04-23-07) for imidacloprid technical. The average purity of the technical/MUP is 98.0%, 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). There is present [redacted] new impurity (>0.1%) in the alternate formulation, which is not present in the basic formulation. The proposed limits for impurities ≥ 0.1% are based on the preliminary analysis and expected to occur in normal commercial production. The product chemistry data submitted corresponding to guideline reference 830.1550 (product identity & composition) and 830.1750 (certified limits) do not satisfy the data requirements of 40CFR§158.155 and 158.175 respectively [MRID No. 471267-01].

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. 471267-01].

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 imidacloprid technical was produced in a one step integrated batch procedure followed by the purification process. The applicant has provided the details of the chemical process with reaction conditions, equipment used, working up procedures, and quality assurance steps [MRID No. 471267-01].

PRODUCT INGREDIENT SOURCE/MANUFACTURING PROCESS INFORMATION HAS BEEN REMOVED

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 imidacloprid technical, the registrant discussed and reported the formation of [redacted] organic impurities in addition to [redacted]. These [redacted] organic impurities were present in preliminary analysis at average levels of ≥ 0.1% and it is expected that they will occur in proportional amounts of commercial production within the proposed certified limits. There is [redacted] new impurity identified in alternate formulation which was not detected & identified in the basic formulation [basic formulation CSF (dated 11-30-05)]. The registrant has provided discussion on the formation of these impurities. According to the registrant there is no possibility of the formation of the toxic impurities like, chlorinated phenols, benzene, PCDDs, hexachlorobenzene, and nitrosamine during the synthesis scheme followed to produce technical imidacloprid [MRID No. 471267-01].

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 [redacted] were analyzed (by Huntington Life Sciences Ltd., England) for percent active ingredient and the impurities. The identification & quantification of the AI and impurities were performed by HPLC-UV (252 nm) with internal and external standard methods. The analytical methods were validated for accuracy, linearity, and precision [MRID No. 471267-02].

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 (252 nm) by internal standard method. The method was validated for precision, accuracy and linearity [MRID No. 471267-02].

7. The data submitted corresponding to guidelines 830.7000 (pH) and 830.7300 (density) satisfy the data requirements of 40CFR§158.190 [MRID Nos. 471267-03 & 471267-04].

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CONCLUSIONS:

The TRB has reviewed the alternate CSF and the supporting product chemistry data submitted for imidacloprid TGAI / MUP [redacted] and has concluded that:

1. All the product chemistry data submitted corresponding to 830 Series Subgroup A are acceptable, except for the alternate CSF.

2. The CSF for alternate formulation (dated 04-23-07) is not acceptable. There is a new impurity present in the alternate formulation which is not present in the basic formulation CSF (dated 11-30-05). TRB has no knowledge on the toxicity of this impurity and, therefore, the alternate CSF is not in compliance with 40CFR§152.43.

3. The data submitted corresponding to the guidelines 830.7000 (pH) and 830.7300 (density) satisfy the data requirements of 40CFR§158.190 and are acceptable.

PRODUCT INGREDIENT SOURCE INFORMATION HAS BEEN REMOVED

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830.1550. Product identity & Composition: (MRID No. 471267-01)

Common Name: Imidacloprid

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

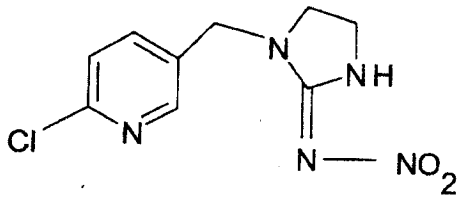
CAS No.: 138261-41-3

PC Code No.: 129099

Empirical formula: $C_9 H_{10} Cl N_5 O_2$

Molecular Weight: 255.7

Structural formula:



PRODUCT INGREDIENT SOURCE INFORMATION HAS BEEN REMOVED

DP BARCODE: D340005; **FILE SYMBOL No.:** 71368-61; **PRODUCT**: Imidacloprid Technical TGAI/MUP (Alternate source [redacted]

Table 1. Manufacturing and Impurity Data for Imidacloprid TGAI/MUP [redacted]

GLN	Requirement	MRID	Status	Details and /or Deficiency
830.1550	Product Identity and composition	Alternate CSF (04-23-07)	N	The NC of AI (98.0%) is supported by 5 batch analysis & agrees with the label claim NC. [redacted] impurities are listed on the CSF in addition to [redacted]
8301600	Description of materials used to produce the product	471267-01	A	The description & composition for all the starting materials used to produce the imidacloprid technical [redacted] have been provided by the registrant
830.1620	Description of production process	471267-01	A	The AI was produced in one step integrated process followed by purification 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.
830.1670	Discussion of formation of impurities	471267-01	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%. There is [redacted] additional impurity in alternate formulation which was not present in basic formulation. No toxic impurity was reported during the synthesis.
830.1700	Preliminary analysis	471267-02	A	Five representative batches of imidacloprid technical [redacted] were analyzed for percent active ingredient and the impurities. The identification & quantification of the AI and the impurities in the TGAI were determined by HPLC-UV (252 nm) with internal method. The five batch analysis supported the CSF for alternate formulation.
830.1750	Certified limits	471267-01	A	The proposed certified limits for the AI are based on standard certified limit table, whereas, those of impurities are based on five batch analysis.
830.1800	Enforcement analytical method	471267-02	A	The HPLC-UV (252 nm) with internal standard 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

PRODUCT INGREDIENT SOURCE/MANUFACTURING PROCESS INFORMATION HAS BEEN REMOVED

BARCODE: D325494; **Reg. No.** : 71368-AR **PRODUCT:** Imidacloprid Technical

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 (11-30-05)	A	The NC of AI (98.0%) is supported by 5 batch analysis & agrees with the label claim NC. Three impurities are listed on the CSF.
8301600	Description of materials used to produce the product	467076-01	A	The description & composition for all the starting materials used to produce the imidacloprid technical have been provided by the registrant
830.1620	Description of production process	467076-01	A	The AI was produced in [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.
830.1670	Discussion of formation of impurities	467076-01	A	The registrant has provided the complete mechanisms of formation, quantification and identification of all the impurities present at the levels of [redacted] Total of [redacted] impurities have been listed on the CSF at levels of [redacted] The related organic impurities have been grouped together with NC of [redacted] No toxic impurity was reported during the synthesis.
830.1700	Preliminary analysis	467219-01	A	Five representative batches of imidacloprid technical were analyzed for percent active ingredient and the impurities. The identification & quantification of the AI and the impurities in the TGAI were determined by HPLC-UV(270 nm) method. The five batch analysis supported the CSF for basic formulation.
830.1750	Certified limits	Basic CSF 11-30-05 467076-02	A	The proposed certified limits for the AI and the impurities are based on the standard certified limit table.
830.1800	Enforcement analytical method	467076-02	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

830 Series Subgroup B (Physical-Chemical Properties)

Table 2: Physical and Chemical Properties of : ImidaclopridTGAI/MUP

GLN	Requirement	MRID	Status	Result or Deficiency
830.6302	Color	467219-02	A	Off white
830.6303	Physical state	" " "	A	Solid Powder
830.6304	Odor	" " "	A	Odor free
830.6313	Stability to normal and elevated temperatures, metals, and metal ions	467219-03 467219-04	A	Stable at 54°C & RT for 14 days & also when treated with Zn dust, potassium dichromate, MAP, & turpentine
830.6314	Oxidation/reduction: chemical incompatibility	467219-04	A	None
830.6315	Flammability		NA	
830.6316	Explodability		NA	
830.6317	Storage stability	" " "	G	
830.6319	Miscibility		NA	
830.6320	Corrosion characteristics		G	
830.7000	**pH**	**471267-03**	A	7.34 ± 0.01 at 20°C [redacted]
830.7050	UV/Visible absorption	467076-08	A	**See Note 1**
830.7100	Viscosity		NA	
830.7200	Melting point	467219-06	A	144.1 ± 0.1°C
830.7220	Boiling point		NA	
830.7300	**Density**	**471267-04**	A	1.4803 ± 0.0069 g/ml at 20.05°C [redacted]
830.7370	Dissociation constants in water (DC)	e-mail 40-14-06	A	Average value 6.70
830.7550	Partition coefficient	467076-11	A	Log Po/w = 0.617 ± 0.008 @ 20°C
830.7840	Water solubility:	467219-08 467076-13	A	529.4 ppm @ 20°C **See Note 2**
830.7950	Vapor pressure (06-20-06)	e-mail 468123-01	A	0.077 mPa (15°C);0.158 mPa (20°C); 0.242 mPa (40°C); 0.098 mPa(20°C)*; 0.125 mPa (25°C)*

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)

* values of vapor pressure at 20°C and 25°C were calculated using slope and intercept of regression line.

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BARCODE: D325494; **Reg. No.** : 71368-AR **PRODUCT:** Imidacloprid Technical

Note1. 830.7050 (UV-VIS): (MRID Nos. 467076-08)

pH	Peak maximum Nm	Extinction Coefficient
Neutral	210	12649.66
	268	20611.07
Acidic	210	13203.39
	268	21558.57
Basic	210	11911.35
	268	20697.21

Note 2. Solubility in organic solvents at 20^0 C: (MRID No. 467076-13)

Acetone = 33-40 g/L; 1, 2-dichloro ethane = 20-25 g/L; MeOH = 7.10 ± 0.134 g/L;

EtOAc = 5.25 ± 0.14 g/L; p-xylene = 0.32 ± 0.0048 g/l.

830.1800. Enforcement of analytical method: (MRID No. 471267-02)

The analytical method was based on HPLC employing an internal standard technique using propiophenone with UV detection.

Equipment & Parameters

HPLC system: HP 1050 Liquid Chromatograph.
Column: Lichrospher 100-RP-18, 5 µm, 25 cm x 4.0 mm
Column temperature: Ambient
Mobile phase: Water : Acetonitrile (60 : 40 v/v)
Sample size: 5 µL
Flow rate: 1.2 ml/min
Detector wavelength: 252 nm
Internal standard: Propiophenone
Retention times: Imidacloprid – approximately 3 minutes; Propiophenone – approximately 12 minutes

9/6/07 Imidacloprid Product Chemistry Review
(MRID # 47126704)

Page _____ is not included in this copy.

Pages 8 through 16 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.

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_____ Claimed confidential by submitter upon submission to the Agency.

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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.