*Manufacturing process information may be entitled to confidential treatment*

**DP BARCODE**: D329849; **Reg. No. /FILE SYMBOL No.**: 70506-REE; **PRODUCT**: UPI Imidacloprid Technical Insecticide (98%)

FEE

October 30, 2006

SUBJECT: FEE. Secondary Product Chemistry Review on UPI Imidacloprid Technical Insecticide

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DP BARCODE: D329849
EPA REG. NO.: 70506-REE
PRODUCT: UPI Imidacloprid Technical Insecticide
PCC: 129099
REGISTRANT: United Phosphorous Incorporation (UPI)
USE: Insecticide-Rodenticide

INTRODUCTION:

The registrant UPI has submitted an application for the registration of UPI Imidacloprid Technical produced at Ankleshwar, Gujarat, India. The registrant has submitted CSF for basic formulation (dated 05-09-06) and supporting product chemistry data under MRID Nos. 468335-01 and 468335-02. The registrant has claimed that the proposed UPI imidacloprid TGAI/MUP is substantially similar to the registered product with Reg. No. 42750-104. The Dynamac Corporation conducted the primary review of the product chemistry data submitted (excluding CSF). TRB has been asked to perform the secondary review.

SUMMARY OF FINDINGS:

1. The CSF for basic formulation (dated 05-09-06) is filled out completely and correctly. The nominal concentration (NC) of the active ingredient (98%) concurs with the product label claim nominal concentration. The CSF is in compliance with PR Notice 91-2. The proposed certified limits for the AI are in compliance with standard certified limit table set-forth in 40CFR §158.175(b)(2). The proposed upper certified limits of the impurities are based on preliminary analysis and the potential for variations in the manufacturing process. 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. 468335-01].

2. The product chemistry data submitted corresponding to guideline 830.1600 (description of materials use to produce the product) satisfy the data requirements of 40CFR§158.160. The registrant has provided the MSDS for all the starting materials used to produce the active ingredient [MRID No. 468335-01].

3. The product chemistry data submitted corresponding to guideline reference 830.1620 (description of production process) do not satisfy the data requirements for 40CFR§158.162. The active ingredient was produced in [redacted] The production process has been described with detail, however some of the important information regarding the amounts of the chemical used in the each step and the yields of the product obtained in each step have not been provided [MRID No. 468335-01].

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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. The registrant has provided the mechanisms of formation and identification of all impurities identified in the 5-batch analysis at ≥0.1%. The registrant has listed [redacted] impurities on the CSF [MRID No. 468335-01].

5. The data submitted corresponding the guideline reference 830.1700 (Preliminary analysis) satisfy the data requirements of 40CFR§158.170. Five representative lots of the manufacturing concentrate were analyzed for weight percent of AI. Analyses were performed using HPLC-UV(252 nm) with internal standard method. Five representative batches of the 98% T were analyzed for percent AI and the impurities. Samples were analyzed [redacted] by HPLC/UV. Acceptable method validation data were submitted. The five-batch analysis supports the CSF [MRID No. 468335-01].

6. The data submitted corresponding the guideline reference 830.1800 (Enforcement Analytical method) satisfy the data requirements of 40CFR§158.180. The HPLC-UV (252 nm) with internal standard method was used for the determination of the AI [MRID No. 468335-01].

7. The product chemistry data submitted corresponding to guideline reference 830 Series Subgroup B (physical/chemical properties) for the UPI imidacloprid technical insecticide satisfy the data requirements of 40CFR§158.190, except for the guidelines 830.6317 (storage stability), and 830.6320 (corrosion characteristics).

**CONCLUSIONS**

TRB has reviewed the product chemistry data submitted for 830 series Subgroup A & Subgroup B for UPI Imidacloprid technical and has concluded that:

1. The CSF for basic formulation (both 05-09-06) is acceptable.

2. The product chemistry data submitted corresponding to guidelines 830 series subgroup A are acceptable, except for the guideline 830.1620 (description of production process). The registrant must provide information regarding the quantities of starting chemical used in each step of the synthesis along with the production yield in each step.

3. The product chemistry data submitted corresponding to guidelines 830 series subgroup B are acceptable, except for the guidelines 830.6317 (storage stability), and 830.6320 (corrosion characteristics).

4. The registrant must submit the results of one year storage stability (830.6317) and corrosion characteristics (830.6320) to the Agency on completion. It is recommended that the observations must be made at 0, 3, 6, 9, & 12 month intervals. The results must be submitted in a hard copy and an electronic format is also requested.

5. The proposed technical (File Symbol No. 70506-REE) was determined to be substantially similar to the registered product with Reg. No. 42750-104 from product chemistry point of view.

**Note to RM:** The reviewer tried two times to contact the registrant regarding the issue with the guideline 830.1620 but no response was received.

830.1550. Product identity & Composition: (MRID No. 46833501)

Common Name: Imidacloprid

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.: 138261-41-3

PC Code No.: 129099

Empirical formula: $C_9H_{10}N_5ClO_2$

Molecular Weight: 255.7

Structural formula

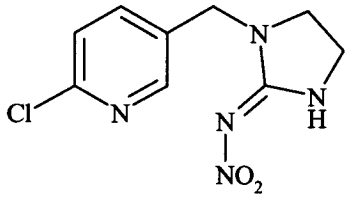

Table 1. Manufacturing and Impurity Data for the United Phosphorous, Inc. 98% TGAI/MUP

| GLN | Requirement | MRID | Status | Details and /or Deficiency |
|---|---|---|---|---|
| 830.1550 | Product Identity and composition | 46833501 | A | The NC of the AI (98%) is supported by the 5-batch analysis and agrees with the label claim [redacted] impurities >0.1% are listed on the CSF. |
| 830.1600 | Description of materials used to produce the product | 46833501 | A | The identity of the starting materials used to produce the technical product has been provided by the registrant. |
| 830.1620 | Description of production process | 46833501 | U | The 98% T is produced in [redacted] of the AI. Additional information is required concerning the quantity of product produced per theoretical batch size, and relative quantities in pounds or kilograms for each ingredient used in the process. |
| 830.1670 | Discussion of formation of impurities | 46833501 | A | The registrant has provided the mechanisms of formation and identification of all impurities identified in the 5-batch analysis at ≥0.1%, as well as [redacted] |
| 830.1700 | Preliminary analysis | 46833501 | A | Five representative batches of the 98% T were analyzed for percent AI and the impurities. Samples were analyzed for [redacted] by HPLC/UV. Acceptable method validation data were submitted. The five-batch analysis supports the CSF. |
| 830.1750 | Certified limits | 46833501 | A | The proposed certified limits for the AI are based on the standard certified limits of ±3% of the nominal concentration. The proposed upper certified limits for the impurities were based on preliminary analysis results and the potential for variations in the manufacturing process. |
| 830.1800 | Enforcement analytical method | 46833501 | A | The methods submitted for preliminary analysis are proposed for enforcement purposes. The AI is determined by a published HPLC/UV method, CIPAC Method 582. Impurities are determined by HPLC/UV and ion chromatography methods. |

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

830 Series Subgroup B (Physical-Chemical Properties)

| Table 2: Physical and Chemical Properties of: United Phosphorous, Inc. 98% TGAI/MUP | | | | |
|---|---|---|---|---|
| GLN | Requirement | MRID | Status | Result or Deficiency [Test substance; method] |
| 830.6302 | Color | 46833502 | A | White [TGAI/MUP] |
| 830.6303 | Physical state | 46833502 | A | Powder [TGAI/MUP] |
| 830.6304 | Odor | 46833502 | A | Odorless [TGAI/MUP] |
| 830.6313 | Stability to normal and elevated temperatures, metals, and metal ions | 46833502 | A | No change in appearance (color, odor, physical state, and pH) or the percent active ingredient after storage at 54 °C for 14 days. [TGAI; CIPAC MT 46.1.1.1]<br><br>Waiver requested for stability to metals and metal ions because the technical product will be packaged, stored, and shipped in fiber board drums lined with HDPE; therefore, there is no contact with metals or metal ions. The Agency recommends for this waiver.<br><br>Data are required demonstrating stability of the TGAI at ambient temperature. |
| 830.6314 | Oxidation/reduction: chemical incompatibility | 46833502 | N | "Not applicable for the TGAI" Data are required for the T/MUP. |
| 830.6315 | Flammability | 46833502 | N | "Not applicable for the TGAI" Data are required for the T/MUP. |
| 830.6316 | Explodability | 46833502 | N | "Not applicable for the TGAI" Data are required for the T/MUP. |
| 830.6317 | Storage stability | 46833502 | I | A one-year study is in progress; the final report will be submitted upon completion. |
| 830.6319 | Miscibility | | N/A | The T/MUP is a solid at room temperature |
| 830.6320 | Corrosion characteristics | 46833502 | I | A one-year study is in progress; the final report will be submitted upon completion. |
| 830.7000 | pH | 46833502 | A | 7.42 at 20 °C (1% w/w) [TGAI/MUP; CIPAC MT 75.3] |
| 830.7050 | UV/Visible absorption | 46833502 | A | See Note 1 |
| 830.7100 | Viscosity | | N/A | The T/MUP is a solid at room temperature. |
| 830.7200 | Melting point | 46833502 | A | 143.6 °C [99.04% PAI; OECD No. 102] |
| 830.7220 | Boiling point | | N/A | The TGAI is a solid at room temperature. |
| 830.7300 | Density | 46833502 | A | Specific gravity = 1.54 g/cm$^3$ at 20 °C [TGAI; CIPAC MT 3.2.1] |
| 830.7370 | Dissociation constants in water (DC) | 46833502 | A | Does not dissociate, and no dissociation constant could be determined. [99.04% PAI; pH changes on titration with 0.01 M HCl] |
| 830.7550 | Octanol/water partition coefficient | 46833502 | A | Log $K_{ow}$ = 0.57 [99.04% PAI; A.I. determination by HPLC/UV] |
| 830.7840 | Water solubility | 46833502 | A | At 20 °C:<br>0.61 at pH 5<br>0.59 at pH 7.0<br>0.58 at pH 9.0<br>[99.04% PAI; A.I. determination by HPLC/UV] |
| 830.xxxx | Solvent solubility | 46833502 | A | At 20 °C:<br>0.07 g/L n-heptane<br>0.10 g/L p-xylene<br>3.08 g/L ethyl acetate<br>5.20 g/L methanol<br>10-14 g/L 1,2-dichloroethane<br>25-29 g/L acetone<br>[99.04% PAI; CIPAC MT 181 and 157] |
| 830.7950 | Vapor pressure | 46833502 | N | "Cite-all"; 4 x 10$^{-7}$ mPa at 20 °C (literature value Data are required for the imidacloprid PAI produced by United Phosphorous, Inc. |

| Table 2: Physical and Chemical Properties of: United Phosphorous, Inc. 98% TGAI/MUP | | | | |
|---|---|---|---|---|
| GLN | Requirement | MRID | Status | Result or Deficiency [Test substance; method] |
| 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); W = waivers | | | | |

Note 1. 830.7050 UV/visible absorption
For the 98.08% TGAI at ambient temperature [spectrophotometer]:

| Nature of solution; pH | Absorption maxima, wavelength (nm) | Absorbance | Molar Extinction Coefficient, ε |
|---|---|---|---|
| Neutral; 6.75 | 212.0 | 0.677 | $1.34 \times 10^4$ |
| | 269.0 | 1.096 | $2.17 \times 10^4$ |
| Acidic; 1.64 | 212.0 | 0.635 | $1.31 \times 10^4$ |
| | 269.0 | 1.034 | $2.13 \times 10^4$ |
| Basic; 12.46 | 218.0 | 0.609 | $1.26 \times 10^4$ |
| | 269.0 | 0.708 | $1.46 \times 10^4$ |

830.1800. Enforcement Analytical Method: (MRID 46833501)

HPLC/UV CIPAC Method No. 582/TC/(M) is proposed as the enforcement analytical method for the active ingredient in the imidacloprid technical. Imidacloprid was quantitated in the preliminary analysis study using a similar method (without an internal standard).

Analytical CIPAC Method 582 for determination of the active ingredient, imidacloprid
HPLC operating conditions:
Instrument: HPLC able to generate more than 7 Mpa pressure
Detector: UV (252 nm)
Column: 250 x 4.6 mm (i.d.) packed with 5 µm octadecylsilane bonded silica gel
Column temperature: Ambient
Mobile phase: Isocratic, acetonitrile:water (60:40, v:v)
Flow rate: 1.2 mL/min
Sample size: 1 µL
Calibration: External standards of imidacloprid with the internal standard propiophenone; peak area
Retention time: ~2.1 minutes imidacloprid; ~4.1 minutes internal standard (propiophenone)
Sample preparation: Technical samples are prepared with internal standard and acetonitrile.

No validation data were provided for the CIPAC method; however, because this is an established (published) method for imidacloprid, no validation data are required for the United Phosphorous technical.

Attachment: Confidential Appendix

Page _____ is not included in this copy.

Pages 7 through 13 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.

_____ 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.