**DP BARCODE**: D332992; **Reg. No. /FILE SYMBOL No.**: 81598-L; **PRODUCT**: Rotam Imidacloprid Technical

March 20, 2007

SUBJECT: FEE. Secondary Product Chemistry Review on Rotam Imidacloprid Technical

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SBMathur 03-20-07

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DP BARCODE: D332992
EPA REG. NO.: 81598-L
PRODUCT: Rotam Imidacloprid Technical
PCC: 129099
REGISTRANT: Rotam Ltd.,
USE: Insecticide

INTRODUCTION:

The registrant Rotam has submitted an application for the registration of Rotam Imidacloprid Technical produced by Rotam Ltd., in [redacted] The applicant has provided a CSF for basic formulation (dated 09-15-06) and supporting product chemistry data under MRID Nos. 469425-01, -02, -03, & -04. 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 09-15-06) is filled out completely and correctly. The nominal concentration (NC) of the active ingredient (98.0%) 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 expected production variability. 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. 469425-01].

2. The data was submitted (by e-mail on 03-19-07 by Dr. Sobotka, hard copy has been sent to RM) corresponding to guideline 830.1600 (description of materials use to produce the product) satisfy the data requirements of 40CFR§158.160 [submitted as an addendum to MRID No. 469425-01].

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 active ingredient was produced [redacted] The production process has been described in full details [MRID No. 469425-01].

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. 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. 469425-01].

*Product ingredient source information may be entitled to confidential treatment*

*Manufacturing process information may be entitled to confidential treatment*

5. The data submitted corresponding the guideline reference 830.1700 (Preliminary analysis) satisfy the data requirements of 40CFR§158.170. Five representative batches of the 98.00% T, produced in [redacted] were analyzed for percent AI and the impurities. The active ingredient [redacted] [MRID No. 469425-02].

6. The data submitted corresponding the guideline reference 830.1800 (Enforcement Analytical method) satisfy the data requirements of 40CFR§158.180. The samples were extracted with acetonitrile and the AI was determined by reversed phase liquid chromatography using propiophenone as an internal standard. The method employs Nucleosil 100-5 C18 (125 mm x 3 mm, 5 µm) column with UV detector operating at 252 nm. The method was validated for precision, linearity and accuracy [MRID No. 4693425-02 and 469425-03].

7. The product chemistry data submitted corresponding to guideline reference 830 Series Subgroup B (physical/chemical properties) for the Rotam imidacloprid technical satisfy the data requirements of 40CFR§158.190, excluding the guidelines 830.6313 (stability to room and elevated temperatures, metal & metal ions), 830.6314 (oxidation/reduction), 830.6317 (storage stability), and 830.6320 (corrosion characteristics) [MRID No.469425-04].

**CONCLUSIONS**

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

1. The CSF for basic formulation (dated 09-15-06) is acceptable.

2. The product chemistry data submitted corresponding to guidelines 830 series subgroup A are acceptable.

3. The product chemistry data submitted corresponding to guidelines 830 series subgroup B are acceptable, except for the guidelines 830.6317 (storage stability), 830.6320 (corrosion characteristics), 830.6313 (stability to RT & elevated temperature, to metal & metal ions), and 830.6314 (oxidation/reduction). Data were provided reflecting stability on exposure to simulated sunlight; these data are not required. Data are required reflecting stability at normal and elevated temperatures and on exposure to metals and metal ions. Also data were provided reflecting oxidizing properties in terms of combustion; these data are not required. Data are required reflecting the chemical incompatibility with other substances.

4. The registrant is advised to generate & submit the results of the studies corresponding to the guidelines 830.6317 (one year storage stability) & 830.6320 (corrosion characteristics). The registrant is recommended to make observations at 0. 3, 6, 9, & 12 months time intervals. The results must be submitted in the hard copy as well as an electronic copy is requested.

5. Data must be provided for the guidelines 830.6313 & 830.6314 as indicated in item #3 above. The registrant agreed to conduct these studies and will submit the results and requests that a Conditional registration may be granted to the proposed technical.
**Note:** In a letter of March 20, 2007, the registrant has agreed to conduct these two studies and will submit the results on completion.

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*Manufacturing process information may be entitled to confidential treatment*

830.1550. Product Identity & Composition: (MRID No. 46942503)

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

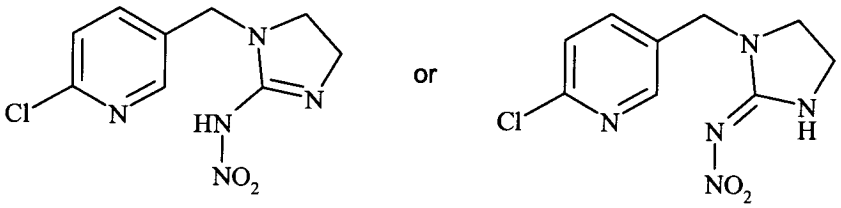
CAS No.: 138261-41-3

PC Code No.: 129099

Empirical formula: $C_9H_{10}ClN_5O_2$

Molecular Weight: 255.7

Structural formula:



*Manufacturing process information may be entitled to confidential treatment*

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| Table 1. Manufacturing and Impurity Data for the Rotam Ltd. 98% TGAI/MUP | | | | |
|---|---|---|---|---|
| GLN | Requirement | MRID | Status | Details and /or Deficiency |
| 830.1550 | Product identity and composition | 46942501; CSF 9/15/06 | A | The NC of the AI (98%) is supported by the 5-batch analysis and agrees with the label claim NC. [redacted] impurities (≥ 0.1%) are listed on the CSF. The proposed nominal concentration for one impurity is [redacted] the level found in preliminary analysis. The registrant must either revise the proposed nominal concentration for this impurity or provide an explanation for the proposed value. In addition, the registrant must confirm the producer of the 98% T. **Note: (3-20-07) deficiency was corrected. A revised CSF submitted.** |
| 830.1600 | Description of materials used to produce the product | 46942501 | A | The identity of the starting materials used to produce the 98% T has been provided by the registrant. Additional information is required concerning the specifications of the starting materials. As stated in OPPTS 830.1000(e)(1)(ii)(B), the registrant is required to submit a copy of available technical specifications by which the supplier of a beginning material describes its composition, properties, and/or toxicity as well as any other information available to the registrant concerning the composition and properties of the beginning material. Copies of Material Safety Data Sheets for all starting materials should be submitted. **Note: (3-14-07) the applicant submitted the MSDS's for all the starting materials. MSDS's received on 03-19-07** |
| 830.1620 | Description of production process | 46942501 | A | The 98%T is produced [redacted] chemical reaction is involved in the synthesis of the AI. The production process has been described in full detail. The reaction conditions, amounts of chemicals in each step, duration, and the yields in each step have been provided. Recovery/recycling measures and QA analysis have been addressed. |
| 830.1670 | Discussion of formation of impurities | 46942501 | A | The registrant has provided the complete mechanisms of formation and identification of all the impurities listed on the CSF at levels ≥0.1%. |
| 830.1700 | Preliminary analysis | 46942502 | A | Five representative batches of the 98% T were analyzed for percent AI and the impurities. The purity of the AI in the TGAI was determined by HPLC/UV with internal standard method. The [redacted] all batches. The registrant must identify the producer of the samples used for the preliminary analysis study. **Note: (3-14-07) the applicant provided the required information. The batches analyzed were obtained from the TGAI/MUP manufactured by Rotam in [redacted]** |
| 830.1750 | Certified limits | 46942501; CSF 9/15/06 | A | The proposed lower certified limit for the AI is based on the standard certified limit table. The registrant must provide an explanation concerning how upper certified limits for the impurities were established. In addition, the registrant must propose an upper certified limit for the AI and correct the proposed upper certified limit for one impurity. **Note: (3-14-07) a revised and corrected CSF was submitted.** |

*Product ingredient source information may be entitled to confidential treatment*

| Table 1. Manufacturing and Impurity Data for the Rotam Ltd. 98% TGAI/MUP | | | | |
|---|---|---|---|---|
| GLN | Requirement | MRID | Status | Details and /or Deficiency |
| 830.1800 | Enforcement analytical method | 46942502<br>46942503 | A | The methods submitted for preliminary analysis are suitable for enforcement purposes. The methods are adequate and are supported by acceptable method validation data. |
| 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: Rotam Ltd. 98% TGAI/MUP | | | | |
|---|---|---|---|---|
| GLN | Requirement | MRID | Status | Result or Deficiency [Test substance; method] |
| 830.6302 | Color | 46942504 | A | Off white |
| 830.6303 | Physical state | 46942504 | A | Very fine powder |
| 830.6304 | Odor | 46942504 | A | Slight characteristic odor |
| 830.6313 | Stability to normal and elevated temperatures, metals, and metal ions | 46942504 | I | Data were provided reflecting stability on exposure to simulated sunlight; these data are not required. Data are required reflecting stability at normal and elevated temperatures and on exposure to metals and metal ions. **Agreed to conduct the study.** |
| 830.6314 | Oxidation/reduction: chemical incompatibility | 46942504 | I | Data were provided reflecting oxidizing properties in terms of combustion; these data are not required. Data are required reflecting the chemical incompatibility with other substances. **Agreed to conduct the study.** |
| 830.6315 | Flammability | 46942504 | A | Nonflammable. No ignition observed on exposure to open flame 2 minutes.<br>[97.6% TGAI/MUP; NF-T 20-042; EEC Method A10]<br>Autoflammability temperature = 355 °C<br>[97.6% TGAI/MUP; ASTM E659/78] |
| 830.6316 | Explodability | | NA | |
| 830.6317 | Storage stability | | G | |
| 830.6319 | Miscibility | | N/A | The TGAI/MUP is a solid at room temperature |
| 830.6320 | Corrosion characteristics | | G | |
| 830.7000 | pH | 46942504 | A | 4.60; aqueous solution<br>[97.6% TGAI/MUP; CIPAC MT 75] |
| 830.7050 | UV/Visible absorption | 46942504 | A | See Note 1. |
| 830.7100 | Viscosity | | N/A | The TGAI/MUP is a solid at room temperature |
| 830.7200 | Melting point | 46942504 | A | 144.4 °C; melting range = 131.6-144.4 °C<br>[97.6% TGAI/MUP; Method EEC A1 and OECD 102] |
| 830.7220 | Boiling point | | N/A | The TGAI/MUP is a solid at room temperature |
| 830.7300 | Density | 46942504 | A | Relative density $d^{20}_4$ = 1.549 at 20 °C<br>[97.6% TGAI/MUP; NF-T 20-053; EEC Method A3] |
| 830.7370 | Dissociation constants in water (DC) | 46942504 | A | No dissociation observed in aqueous media<br>[97.6% TGAI/MUP; OECD 112] |
| 830.7550 | Octanol/water partition coefficient | 46942504 | A | $P_{ow}$ = 3.9 ± 0.2; log $P_{ow}$ = 0.60 at 23 °C<br>[97.6% TGAI/MUP; shake flask method (EEC A8 and OECD 107)] |
| 830.7840 | Water solubility | 46942504 | A | 0.71 g/L in pH 4 buffer<br>0.56 g/L in pH 7 buffer<br>0.61 g/L in pH 9 buffer<br>Average = 0.63 g/L at 25 °C<br>[97.6% TGAI/MUP; EEC Method A6; OEDC 105] |

| Table 2: Physical and Chemical Properties of: Rotam Ltd. 98% TGAI/MUP | | | | |
|---|---|---|---|---|
| GLN | Requirement | MRID | Status | Result or Deficiency [Test substance; method] |
| 830.xxxx | Solvent solubility | 46942504 | A | Solubility at 25 °C<br>n-Heptane 0.29 mg/L<br>Acetone 47 g/L<br>1,2-Dichloroethane 32 g/L<br>Ethyl acetate 8.0 g/L<br>Methanol 10 g/L<br>n-Octanol 0.93 g/L<br>Xylene 0.38 g/L<br>[97.6% TGAI/MUP; EEC Method A6] |
| 830.7950 | Vapor pressure | 46942504 | A | <4 x $10^{-7}$ Pa at 20 °C<br>[97.6% TGAI/MUP; EEC Method A.4; OECD 104] |
| 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 | | | | |

The TGAI test substance used for determination of physical/chemical characteristics was from Batch No. 20010806 of the 98% T. The AI content of the test substance was determined in MRID 46942503. Five replicate samples were analyzed using an HPLC/UV method based on CIPAC method MT 582/TC/M/3 which is the method used for determination of the AI in preliminary analysis. The mean AI content of the test substance was found to be 97.6%.

Note 1. 830.7050 UV/visible absorption

| Nature of solution | Absorption maxima, wavelength (nm) | Absorbance | Molar Extinction Coefficient, ε (L/mole/cm) | log (ε) |
|---|---|---|---|---|
| Neutral | 269.5 | 1.5852 | 19990 | 4.30 |
| Alkaline (pH 9.0 buffer) | 269.0 | 1.2586 | 15871 | 4.20 |
| Acidic (1 N HCl) | 271.0 | 1.7148 | 21624 | 4.33 |

[97.6% TGAI/MUP at ambient temperature; point 2.5 (Annex 1) of EEC Directive 94/37/CE modifying directive 91/414/EEC]

830.1800. Enforcement Analytical Method: (MRID No. 46942503)

HPLC/UV method CIPAC Method No. 582/TC/M/3 was used for determination of the AI in the preliminary analysis study, and appears to be an acceptable enforcement analytical method for the AI in the 98% T. This method with minor modifications was also submitted as a nonconfidential method for analysis of the AI content in the technical sample used for physical/chemical determinations. The method was adequately validated in conjunction with the preliminary analysis (refer to 830.1700; Confidential Appendix).

Analytical method CIPAC Method 582/TC/M/3 for determination of the active ingredient, imidacloprid
HPLC operating conditions:
Instrument: Waters Alliance
Detector: UV at 252 nm
Column: Nucleosil 100-5 C18, 125 x 3 mm (i.d.), particle size 5 µm
Column temperature: 40 °C
Mobile phase: Isocratic, acetonitrile:pH 3 water (35:65, v:v)
Flow rate: 0.5 mL/min
Sample size: 5 µL
Calibration: External standard of imidacloprid with the internal standard propiophenone; peak area
Retention time: ~2.3 minutes imidacloprid; ~4.3 minutes internal standard (propiophenone)
Sample preparation: Technical samples are prepared in acetonitrile.

Conclusion: The HPLC/UV method (CIPAC 582/TC/M/3) is adequate as an enforcement method for the AI in the technical product.

Attachment: Confidential Appendix

Page _____ is not included in this copy.

Pages 8 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.

830.1800. Enforcement Analytical Methods: (MRID No. 46942502 and 46942503)

The methods used in preliminary analysis appear to be suitable for enforcement purposes. The methods used for determination of the AI and impurities were adequately validated in conjunction with the preliminary analysis study. Details of the method equipment and parameters are presented above under 830.1700; the method (similar to the preliminary analysis method) used for analysis of the AI content in the test substance for physical/chemical characteristic determinations is reported in the public portion of this document under 830.1800.

Conclusions: The proposed enforcement methods for the AI and impurities are adequate and are supported by acceptable validation data.