

US EPA ARCHIVE DOCUMENT

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

FROM: Shyam B. Mathur, Ph.D
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03-20-07

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[Signature]

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

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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

[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.

Product ingredient source information may be entitled to confidential treatment

Manufacturing process information may be entitled to confidential treatment

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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

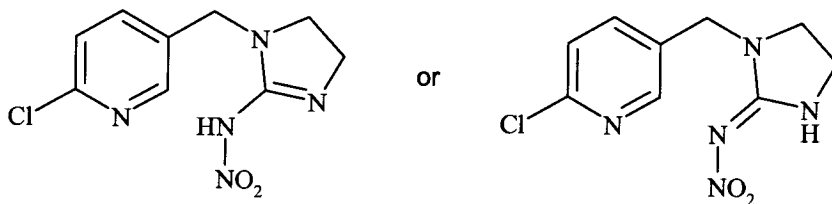
CAS No.: 138261-41-3

PC Code No.: 129099

Empirical formula: C₉H₁₀ClN₅O₂

Molecular Weight: 255.7

Structural formula:



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Table 1. Manufacturing and Impurity Data for the Rotam Ltd. 98% TGA/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 ($\geq 0.1\%$) 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 $\geq 0.1\%$.
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 TGA 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 TGA/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.

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 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. [97.6% TGAI/MUP; NF-T 20-042; EEC Method A10] Autoflammability temperature = 355 °C [97.6% TGAI/MUP; ASTM E659/78]
830.6316	Explosibility		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 [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 [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 $d_4^{20} = 1.549$ at 20 °C [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 [97.6% TGAI/MUP; OECD 112]
830.7550	Octanol/water partition coefficient	46942504	A	$P_{ow} = 3.9 \pm 0.2$; $\log P_{ow} = 0.60$ at 23 °C [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 0.56 g/L in pH 7 buffer 0.61 g/L in pH 9 buffer Average = 0.63 g/L at 25 °C [97.6% TGAI/MUP; EEC Method A6; OECD 105]

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GLN	Requirement	MRID	Status	Result or Deficiency [Test substance; method]
830.xxxx	Solvent solubility	46942504	A	<u>Solubility at 25 °C</u> n-Heptane 0.29 mg/L Acetone 47 g/L 1,2-Dichloroethane 32 g/L Ethyl acetate 8.0 g/L Methanol 10 g/L n-Octanol 0.93 g/L Xylene 0.38 g/L [97.6% TGAI/MUP; EEC Method A6]
830.7950	Vapor pressure	46942504	A	$<4 \times 10^{-7}$ Pa at 20 °C [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 μ m

Column temperature: 40 °C

Mobile phase: Isocratic, acetonitrile:pH 3 water (35:65, v:v)

Flow rate: 0.5 mL/min

Sample size: 5 μ L

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.

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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.
 - 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.
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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.

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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.