110

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

725A

10

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

9/29/13

FEB 19 1986

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA File No. 10308-RN. (RS)-alpha-cyano-3-phenoxy-benzyl (1R)-cis,trans-chrysanthemate. Application for registration of technical. Accession Number 259842. [RCB# 150]

FROM: Richard Loranger, Chemist
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

R. Loranger

THRU: Charles L. Trichilo, Chief
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

TO: George LaRocca/Adam Heyward, PM Team 15
Registration Division (TS-767)

Sumitomo Chemical Company, Limited has submitted an application for registration of Gokilaht™ Technical, "An Insecticide for Formulating Use Only". The active ingredient is the new pyrethroid (RS)-alpha-cyano-3-phenoxybenzyl (1R)-cis,trans-chrysanthemate. Other designations for this pesticide include cyphenothrin (BSI accepted) and S-2703F. This represents the first submission for this compound to RCB. We have been requested to review the product chemistry data and the Confidential Statement of Formula (CSF).

Under "ACTIVE INGREDIENTS" the submitted label for Gokilaht™ states 87.4% (RS)-alpha-cyano-3-phenoxybenzyl (1R)-cis,trans-chrysanthemate and 4.6% other isomers. The remaining 8.0% is listed as "INERT INGREDIENTS". Although the label states "GOKILAHT™ TECHNICAL", we consider it to be only a manufacturing use product (MUP) since a stabilizer is added (see Appendix).

The various product chemistry requirements will be discussed below under the appropriate Guidelines Reference Numbers.

61-1 Product Identity and Dislosure of Ingredients

The full chemical name appears several times in the above paragraphs and the chemical structure is shown below.

Manufacturing process information is not included

Since this molecule possesses three chiral carbon atoms, a total of eight stereoisomers exist. We assume the cyano bearing carbon is present in equal quantities of the two configurations (R & S) based on the nature of the final synthetic step and the name given to the compound [i.e., "(RS)"]. The four different isomeric pairs which can result from the stereochemistry of the cyclopropane ring do not appear in equal quantities in Gokilaht. Analyses of the [redacted] Therefore, Sumitomo reports a $\geq$ 95% d or (1R) isomer content [sum of d-trans and d-cis] and a minimum of 75% trans isomer content [sum of d-trans and l-trans].

We conclude that the applicant has adequately identified the active ingredient in Gokilaht.

61-2 Description of Beginning Materials and Manufacturing Process

The synthesis of cyphenothrin is described in the Confidential Appendix to this review.

Although the applicant has provided the reaction pathway for the synthesis of Gokilaht, we want additional details on the following:
(1) Sources (manufacturers) of all reactants and some indication as to their purities and identification of contaminants.
(2) The relative quantities of each component in all steps as well as descriptions of physical conditions (eg., temperature) and duration of reaction.
(3) Descriptions of the purification procedures (extractions, distillations, recrystallizations, etc.), if any, used following each step.
(4) A description of the exact timing of addition of a certain component (see Confidential Appendix) to the product. Also, what is the intended percentage of this component? In regard to the latter question the applicant should explain why the observed levels of this stabilizer in the five batches fall in a much narrower range than indicated in the CSF?

Until the above information has been provided, the applicant has not satisfied this portion of the product chemistry requirements.

61-3 Discussion of Formation of Impurities

The applicant has submitted very little discussion on the likely impurities and side products to be found in this technical/MUP. We will require a more thorough discussion based on established chemical theory as to which side reactions may occur in various steps, what will be the fate of impurities introduced by the starting materials, and what effect the various purification procedures will have on unintentional inerts in cyphenothrin.

This requirement has not been filled.

62-1 Preliminary Analysis AND 62-2 Certification of Limits

The details of analyses of five pilot plant batches are discussed in the Confidential Appendix. The data are adequate to satisfy these portions of the Product Chemistry requirements. The 87.4% on the technical label for the 1R isomers is consistent with the minimum 92% total of all isomers and the minimum 95% 1R content within those isomers. We do note that the limits specified for one additive seem much wider than the levels observed in the 5 batches. The applicant is asked to address this under the information requested above under the manufacturing process.

62-3 Analytical Methods to Verify Certified Limits

The descriptions of analytical methods for the active ingredient and impurities are presented in the Confidential Appendix to this review. The methods appear adequate and satisfy the product chemistry requirements. However, Sumitomo should be notified that a non-confidential copy of the methods for the active ingredients (Document EEA-40-0010) must be provided prior to registration of Gokilaht.

63-2 to 63-21 Physical and Chemical Characteristics

Unless otherwise stated we consider the descriptions/data listed for each item below to be adequate. Although Sumitomo has not indicated whether technical or the MUP (i.e., stabilizer added) was used in these determinations, we believe that most of the properties would be the same for the two materials.

63-2, 63-3 Color and Physical State: yellowish viscous liquid
63-4 Odor: "faint characteristic"
63-5 Melting Point: not applicable.
63-6 Boiling Point: not provided. This is a data gap. The boiling point of the technical grade active ingredient (stabilizer not added) must be determined. From the vapor pressure data it can be seen that the boiling point is considerably over 300°C.
63-7 Specific Gravity: 1.080 at 25°C
63-8 Solubility: "soluble in ethanol, acetone, and most other organic solvents"; 0.1-1.0 ppm in water. More quantitative data are required for the organic solvents-the results are to be reported in grams/100 ml. Solubilities should be measured at 20 or 25°C.
63-9 Vapor Pressure: 8.7×10^{-7} mm Hg at 20°C, 3.0×10^{-6} at 30°C, 1.21 mm Hg at 200°C, 67.2 at 300°C.
63-10 Dissociation Constant: not applicable due to extremely low water solubility and no anticipated dissociation reaction.
63-11 Octanol/Water Partition Coefficient: log P=6.29 (room temp.)
63-12 pH: due to very low water solubility and absence of acidic and basic groups we will not require pH measurement.
63-13, 63-17 Stability and Storage Stability: 24 months stoppered at room temperature in coating-can and polyethylene bottle resulted in no change in % active ($\pm$ 0.2%). At 60°C four

samples (wet-dry, open-closed combinations) showed measurable degradation (93.6% down to 91.6-91.9%) over a 6 month period. At 40°C it is not clear whether changes are due to analytical variation or actual degradation (wet-closed sample showed 1.5% loss but wet-open sample gained 0.6% ai).

63-14 Oxidizing or Reducing Action: no information provided. The applicant should at least address this issue. Has the product (with stabilizer present) shown potential to act as an oxidizing or reducing agent under normal handling/use conditions? How do other similar compounds behave?

63-15 Flammability: flash point=130°C (although Sumitomo states elsewhere the technical is not flammable).

63-16 Explodability: no information provided. The applicant must address the question "Is the product explodable upon impact?"

63-18 Viscosity: 3400 cP at 20°C.

63-19 Misciblity: no information provided. We do consider this a requirement for Gokilaht since it will likely be mixed with petroleum hydrocarbon type solvents to prepare emulsifiable concentrates. Data on the miscibility with such solvents should be provided.

63-20 Corrosion Characteristics: "not corrosive"

63-21 Dielectric Breakdown Voltage: not applicable.

64-1 Submittal of Samples

The applicant should be told to submit samples of the pure active ingredient and technical grade Gokilaht (either with or without stabilizer) to the EPA Pesticides and Industrial Chemicals Repository.

CONCLUSIONS AND RECOMMENDATION

The following information/data are still needed for filling all the product chemistry requirements for Gokilaht:

61-2 Description of Beginning Materials and Manufacturing Process

(1) Sources (manufacturers) of all reactants and some indication as to their purities and identification of contaminants.
(2) The relative quantities of each component in all steps as well as descriptions of physical conditions (eg., temperature) and duration of reaction.
(3) Descriptions of the purification procedures (extractions, distillations, recrystallizations, etc.), if any, used following each step.
(4) A description of the exact timing of addition of a certain component (see Confidential Appendix) to the product. Also, what is the intended percentage of this component? In regard to the latter question the applicant should explain why the observed levels of this stabilizer in the five batches fall in a much narrower range than indicated in the CSF?

61-3 Discussion of Formation of Impurities

A more thorough discussion based on established chemical theory as to which side reactions may occur in various steps, what will be the fate of impurities introduced by the starting materials, and what effect the various purification procedures will have on unintentional inerts in cyphenothrin.

62-3 Analytical Methods to Verify Certified Limits

A non-confidential copy of the methods for the active ingredients (Document EEA-40-0010) must be provided.

63-6 Boiling Point
The boiling point of the technical grade active ingredient (stabilizer not added) must be determined.

63-8 Solubility
More quantitative data are required for the organic solvents- the results are to be reported in grams/100 ml. Solubilities should be measured at 20 or 25°C.

63-14 Oxidizing or Reducing Action
The applicant should address the following questions: Has the product (with stabilizer present) shown potential to act as an oxidizing or reducing agent under normal handling/use conditions? How do similar compounds behave?

63-16 Explodability
The applicant must address the question "Is the product explodable upon impact?"

63-19 Misciblity
Since Gokilaht is likely be mixed with petroleum hydrocarbon type solvents to prepare emulsifiable concentrates, data on the miscibility with such solvents should be provided.

64-1 Submittal of Samples
Samples of the pure active ingredient and technical grade Gokilaht (either with or without stabilizer) must be submitted to the EPA Pesticides and Industrial Chemicals Repository.

Until the product chemistry data described above have been provided, we recommend against registration of Gokilaht Technical.

Attachment:Confidential Appendix (Copies to PM-15, RF, SF, Loranger, PMSD/ISB)

cc: Circu, RF, Gokilaht SF, Loranger, PMSD/ISB
RDI:Section Head:ARRathman:2/18/86:RDSchmitt:2/18/86
TS-769:RCB:R.Loranger:557-7324:ral(6):CM#2:RM.810:Date:2/18/86

CONFIDENTIAL APPENDIX TO FILE NO. 10308-RN

[redacted]

Although the applicant has provided the reaction pathway for the synthesis of Gokilaht, we want some additional details such as the following: sources of all reactants and some indication as to their purities and identification of contaminants; the relative quantities of each component in all steps as well as descriptions of physical conditions (eg., temperature) and duration of reaction; description of the purification procedures (extractions, distillations, recrystallizations, etc.), if any, used following each step.

[redacted]

Analyses of five batches of cyphenothrin technical produced by a pilot plant have been submitted to satisfy the requirements under Sections 62-1 (Preliminary analysis) and 62-2 (Certification of Limits) of the Product Chemistry Guidelines. The following table summarizes the results of the five analyses and the certified limits presented by Sumitomo. The certified limits are the same values listed on the Confidential Statement of Formula (CSF).

Ingredient	% by weight	
	5 batches	CSF
[redacted]		

Manufacturing process information is not included

CONFIDENTIAL APPENDIX TO FILE NO. 10308-RN

[redacted]

We consider the above data adequate to satisfy Sections 62-1 and 62-2. However, in relation to [redacted] This question should be answered when the applicant replies to our query above under the manufacturing process description.

Analytical Methods

The determination of total isomers of the pyrethroid involves mixing a weighed sample with internal standard solution (di-2-ethylhexyl phthalate in acetone) and GC analysis (flame ionization detector). The proportions of the various isomers are determined by hydrolyzing the mixture with methanolic KOH to the corresponding chrysanthemic acids and esterifying with d-2-octanol to give diastereomers that are determined by GC. A sample chromatogram was included for each method.

[redacted]

Manufacturing process information is not included

150

(Contains [illegible] Confidential Information)

13544

R050671

Chemical:	**Cyclopropanecarboxylic acid, 2,2-dimethy**
PC Code:	**129013**
HED File Code	**11000 Chemistry Reviews**
Memo Date:	**02/19/86 12:00:00 AM**
File ID:	**00000000**
Accession Number:	**000-00-0048**

HED Records Reference Center
09/24/2003