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

MAY 9 1994

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Registration of REJEX-IT™ AG-36 (Methyl Anthranilate, File Symbol 58035-O). Product Chemistry and Mammalian Toxicology Data (Case # 040651; Chemical # 128725; Submission # S456763; DP Barcode # D198502)

TO: Robert Forrest, Product Manager (PM-14)
Daniel Peacock, Reviewer (PM-14)
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Registration Division (7505C)

FROM: Sheryl K. Reilly, Ph.D., Biological Section SKR 5/5/94
Science Analysis Branch
Health Effects Division (7509C)

THROUGH: William L. Burnam, Branch Chief
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and

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INERT INGREDIENT INFORMATION IS NOT INCLUDED

ACTION REQUESTED: PMC Specialties Group, Inc. has submitted a registration application for an end-use product, REJEX-IT™ AG-36 (14.5% a.i.), which consists of REJEX-IT™ TP-40 (40% a.i.). [redacted] for use in repelling birds from golf course or other turf areas. The active ingredient (methyl anthranilate) is considered GRAS under 21 CFR 182.60, and is used as a flavoring agent in foods (alcoholic and nonalcoholic beverages, ice cream, candy, baked goods, gelatins and puddings, chewing gum), and is also a component of perfumes.

CONCLUSIONS: The registrant did not submit a list of impurities, their percentages, or reasons for occurrence (Guideline Reference Number 151-12). No data were submitted to indicate the efficacy of the methodologies used to detect MA for identifying or quantitating impurities. All of the studies submitted for acute mammalian toxicology were graded Supplementary but are upgradeable, provided the lot number of the test material used in these studies and its purity are specified.

DETAILED CONSIDERATIONS:

A. Product Characterization

The following product data are required under 40 CFR § 158 Subpart C, in accordance with Subdivision M § 151-10 to -18 of the Pesticide Assessment Guidelines:

1. Guideline 151-10: Identity of the Active Ingredient

Product Identity

REJEX-IT™ AG-36 (end-use product, 14.5% a.i.)

Confidential Statement of Formula (CSF)

The registrant has provided the CSF, and a photocopy is located in the attached Confidential Appendix.

Information on Active Ingredient

The following table summarizes information submitted regarding the active ingredient:

Chemical Name	methyl 2-aminobenzoate
CAS Registry No.	134-20-3
Common Name	Methyl Anthranilate (MA)
Empirical Formula	$C_8H_9NO_2$
Molecular Formula	$COOCH_3-C_6H_4-NH_2$
Molecular Weight	151.17
Source of biochemical	grape varieties, flower oils, synthetic process (see below)
Mode of Action	Bird repellant; presumably by taste or irritation owing to the aromatic nature of MA

2. Guideline 151-11: Manufacturing Process

The manufacturing process for REJEX-IT™ AG-36 was not provided. The Technical Bulletin (#BA-4811) indicated that all ingredients are food grade, and therefore, the manufacturing process is not required. The manufacturing process for the technical other REJEX-IT™ end-use products is described in HED Doc. # 010940 (S. Reilly to R. Forrest and D. Peacock memorandum dated 4/29/94).

3. Guideline 151-12: Discussion of the Formation of Unintentional Ingredients

The petitioner did not submit a list of impurities, their percentages, or reasons for occurrence. The test substance was analyzed and quantitated by HPLC; this showed only one peak of significance (i.e., MA), but no data were submitted to indicate the efficacy of the method for determining impurities.

4. Guideline 151-13: Analysis of Samples

Method Validation:

REJEX-IT™ AG-36 Lot/batch/ID # ES 930106A

Analytical Standard (>99% pure): REJEX-IT™ MA

HPLC Column: HP C-18 (200 x 4.6 mm x 5.0 µm)
Column Temperature: 40°C
Mobile phase: 50% acetonitrile/50% deionized H_2O
Flow rate: 0.75 mg/min
UV Detector: 230 nm
Limits of detection: 57.4 ± 0.4 µg/ml
Retention Time: 5.954 minutes

Linearity: Coefficient of correlation = 0.999 for concentrations 58.5, 93.6, 117.0 140.0 and 176.0 µg/ml

Precision: Relative standard deviation (%) was 0.70

Recovery: Mean % recovery = 101.5%

5. Guideline 151-15: Certification of Ingredient Limits

The Certifications of Ingredient Limits for technical MA and REJEX-IT™ AP-50 are provided in the attached Confidential Appendix. The certified limits (upper and lower) are found in column 14 of the CSFs. The petitioner did not submit 5-batch analysis data.

6. Guideline 151-16: Analytical Methods for Certified Limits

As mentioned previously (see Manufacturing Process, above), the petitioner submitted HPLC methodology and data for assaying MA.

7. Guideline 151-17: Physical and Chemical Characteristics

The following table summarizes the data that satisfy the requirements of 40 CFR § 158.190:

Guideline No.	Characteristics	TGAI (REJEX-IT™ MA)*	REJEX-IT™ AG-36
63-2	Color	Pale yellow	light blue to tan
63-3	Physical State	liquid or crystals	slurry
63-4	Odor	oranges blossoms; grapes	concord grapes
63-5	Melting Point	23.5-25°C	NR
63-6	Boiling Point (760 mm Hg)	256°C	100°C
63-7	Density**	1.2	1.02 g/l
63-8	Water Solubility: (g/100 ml)	0.29	0.196
63-9	Vapor Pressure	0.012 mm @ 20°C	NR
63-10	Dissociation Constant	K(25°C)= 1.7×10^{-12}	NR
63-11	Octanol/Water Partition Coefficient	42 ± 11.6	NR
63-12	pH	Waived	5.6
63-13	Stability	Waived	NR
63-15	Flammability	Waived	NR
63-16	Explodability	Waived	NR
63-17	Storage Stability***	100%	NR
63-18	Viscosity	NR	NR
63-19	Miscibility	NR	Miscible in H20; any ratio
63-20	Corrosion Characteristics	None	None

* Information on the TGAI taken from HED Doc. 010940, dated 4/29/94.

** Relative density is reported for TGAI; bulk density for AG-36.

*** Thirty days @ 50°C; accountability in % Total.

NR = Not required

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8. Data Waivers

a. pH - These data were waived because there were no acute toxicity concerns (all acute mammalian toxicity categories were III or IV).

b. Flammability - The waiver request for flammability is granted because the product does not contain combustible liquids.

c. Stability - This data requirement was waived for the TGAI because manufacturing process indicates MA is stable at high distillation temperatures; also, the registrant submitted storage stability data which indicated the product is stable for at least 30 days at elevated temperatures (50°C).

d. Explodability - this requirement was waived because the flash point is over 248°F.

9. Data Gaps: The following product chemistry data gap exists for this petition:

Guideline	
151-12:	Discussion of the Formation of Unintentional Ingredients for the technical and both end-use products

B. Human Health Assessment

1. Mammalian Toxicology Data Base

The acute toxicity study battery for the similar end-use product, REJEX-IT™ TP-40, has been reviewed by SAB (HED Doc. # 010940: S. Reilly to R. Forrest and D. Peacock memorandum dated 4/29/94). The only differences between TP-40 and AG-36 is that the latter contains 14.5% a.i. (instead of 40%), and includes an additional inert [redacted]. Based on the lack of significant toxicity of the technical a.i (REJEX-IT™ MA; also reviewed in HED Doc. # 010940) and of REJEX-IT™ TP-40, SAB would have recommended that the toxicology studies on the a.i. under TP-40 would also have been sufficient to satisfy the data requirements for AG-36. [redacted] presents no additional toxicological concerns. Therefore, SAB is not providing formal Data Evaluation Reports for the toxicology studies submitted for REJEX-IT™ AG-36, but rather will only summarize the study results for REJEX-IT™ AG-36 in the table below. This summary review is sufficient to assign toxicity categories to the studies, especially in view of the lack of toxicity for REJEX-IT™ MA, REJEX-IT™ TP-40, and REJEX-IT™ AP-50. SAB recommends that these studies need not be upgraded, provided the Registrant upgrades the studies submitted to support the registration of TP-40 (i.e., identifes the test material lot numbers).

TOXICOLOGY DATA BASE FOR REJEX-IT™ AG-36

STUDY (Species)	MRID No.	RESULTS	TOX. CATEGORY	Coregrade
Acute Oral Toxicity (rat)	42999502	LD_{50} > 5g/kg	IV	S
Acute Dermal Toxicity (rabbit)	42999503	LD_{50} > 2g/kg[1]	III	S
Acute Inhalation Toxicity (rat)	Waived			
Eye Irritation (rabbit)	42999504	Minimal irritant[2]	IV	S
Dermal Irritation (rabbit)	42999505	Not an irritant	IV	S
Dermal Sensitization - modified Buehler (guinea pig)	42999506	Not a sensitizer	N/A	S
Immune Response	Waived			

1 Slight to Moderate irritation (Draize scores for erythema and edema 1-2 through day 7), slight desquamation in 1 female, days 7 and 10.

2 Slight conjunctival irritation clearing within 24 hours (avg. Draize score 1.7 @ 1 hour).

S Supplementary, due to lack of information on lot/batch #, purity and stability

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2. **Data Waivers:**

a. Guideline Ref. No. 81-3 - The registrant requested a waiver for acute inhalation studies since the label will require the wearing of a respirator as protective clothing.

SAB does not support this waiver request for the studies solely on the basis of the "product will not result in repeated inhalation exposure at concentrations likely to be toxic. No exposure data were submitted to support this claim. SAB believes that pulmonary exposure will not result at a toxic concentration only because of the label specification that a respirator should be worn by applicators. The type of respirator that is required for this use is a dust/mist filtering respirator (MSHA/NIOSH approval number prefix TC-21C; personal communication with A. Nielson, Occupational and Residential Exposure Branch).

b. Guideline Ref. No. 152-18 - The immune response waiver requested because the product is an FDA GRAS list material, widely consumed for many years, etc. is not supported by SAB for the reasons presented by the petitioner; however, SAB will support a waiver of 152-18 because the use patterns and protective clothing as proposed is not likely to increase exposure to that which already occurs via the diet.

Attachment:

1. Confidential Appendix

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CONFIDENTIAL APPENDIX

METHYL ANTHRANILATE TOXR 010959

Page 9 is not included in this copy.

Pages _____ through _____ are not included.

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.

X 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.

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.
