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

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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Naptalam Product Chemistry and Residue Chemistry Registration Standard Updates.

FROM: Richard D. Schmitt, Ph.D., Chief
Dietary Exposure Branch (DEB)
Health Effects Division (H7509C)

TO: Lois Rossi, Chief
Reregistration Branch
Special Review & Reregistration Division (H7508C)

and

Reto Engler, Ph.D., Chief
Science Analysis and Coordination Branch
Health Effects Division (H7509C)

Attached are updates to the Product and Residue Chemistry Chapters of the Naptalam Registration Standard prepared by Dynamac Corporation under supervision of the Dietary Exposure Branch, HED. They have undergone secondary review in the branch and have been revised to reflect Agency policies.

These documents provide an in-depth analysis of the status of the Naptalam Product and Residue Chemistry data bases as of 02/20/90. Revised data requirement tables are included.

Please note that Confidential Business Information accompanies the Product Chemistry Update as Appendices A, B, C and D.

If you need additional input please advise.

Attachment 1: Naptalam Product Chemistry Registration Standard Update

Attachment 2: Confidential Appendices A, B, C and D.

Attachment 3: Naptalam Residue Chemistry Registration Standard Update

cc (with attachments 1, 2 & 3): W. Smith, Naptalam Registration Standard file, Naptalam Subject File, C. Furlow (PIB/FOD), J. Burrell (FOD), Dynamac.

cc (without attachments): RF, Circ.(8)

DYNAMAC CORPORATION

Final Report

NAPTALAM
Task 4: Product Chemistry Registration Standard Update

May 11, 1989

Revised Final Report dated June 28, 1990

Contract No. 68-D8-0080

Submitted to:
Environmental Protection Agency
Arlington, VA 22202

Submitted by:
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NAPTALAM

REGISTRATION STANDARD UPDATE

PRODUCT CHEMISTRY

TASK 4

INTRODUCTION

A Product Search Listing conducted 3/29/90 identifies three naptalam 23.7% end-use products (EPs) produced by Uniroyal Chemical Company: EPA Reg. Nos. 400-49, 400-166, and 400-345. Uniroyal is the only registrant of products with naptalam sodium as the sole active ingredient. There are no registered technical or manufacturing-use products for naptalam/naptalam sodium, and the Naptalam Science Chapter dated 1/9/85 stated that the acid form of naptalam (N-1-naphthylphthalamic acid) is no longer in commercial production.

The Naptalam Guidance Document dated March 1985 identifies generic data requirements for several product chemistry topics concerning naptalam/naptalam sodium; naptalam sodium is the technical grade of the active ingredient (TGAI). Naptalam sodium end-use products are manufactured by an integrated system in which the active ingredient is not isolated; therefore, product chemistry information is required for all EPs. In response to the Guidance Document requirements, Uniroyal Chemical Company has submitted data (1985; MRID 00154116, 1986; MRIDs 00157183 and 40003301, and 1990; MRID 41385501) pertaining to two 23.7% EPs (EPA Reg. Nos. 400-49 and 400-345). These data are reviewed below for their adequacy in fulfilling outstanding data requirements. No data were submitted for the 23.7% EP (EPA Reg. No. 400-166).

Corresponding to each of the Topical Discussions listed below are the Guideline Reference Numbers from "Pesticide Assessment Guidelines - Subdivision D - Product Chemistry", referred to in Title 40 of the Code of Federal Regulations (40 CFR), Part 158, "Data Requirements for Registration", Subpart C, "Product Chemistry Data Requirements". These regulations and guidelines explain the minimum data that the Agency needs to adequately assess the product chemistry of naptalam.

	Guidelines Reference No. from 40 CFR §158.155-190
Product Composition and Manufacture	61-(1-3)
Analysis and Certification of Product Ingredients . .	62-(1-3)
Physical and Chemical Characteristics	63-(2-20)

SUMMARY

The following Product Chemistry data are required:

- For the Uniroyal 23.7% EP (EPA Reg. No. 400-49), additional data must be submitted pertaining to product composition, discussion of formation of impurities, preliminary analysis, certified limits, enforcement analytical methods, odor, density, dissociation constant, octanol/water partition coefficient, pH, and storage stability.

- For the Uniroyal 23.7% EP (EPA Reg. No. 400-166), data on all product chemistry topics must be submitted.

- For the Uniroyal 23.7% EP (EPA Reg. No. 400-345), additional data must be submitted pertaining to product composition, beginning materials and manufacturing process, discussion of formation of impurities, preliminary analysis, certified limits, enforcement analytical methods, odor, density, dissociation constant, octanol/water partition coefficient, pH, and storage stability.

PRODUCT IDENTITY AND COMPOSITION

61-1. Product Composition

The Naptalam Guidance Document dated March 1985 does not require additional generic data concerning product composition for the naptalam sodium TGAI. Uniroyal Chemical Company has submitted product-specific data (1986; MRID 00157183) for two 23.7% EPs (EPA Reg. Nos. 400-49 and 400-345). These data are presented in Confidential Appendix A. The submitted data do not satisfy the requirements of 40 CFR §158.155 (Guideline Reference No. 61-1) regarding product composition for the two 23.7% EPs because the registrant did not provide nominal concentrations for the impurities and the nominal concentration listed for the active ingredient was not based on the nominal concentration of the active ingredient in the source product. Additional information is required.

Uniroyal did not submit data pertaining to product composition for the 23.7% EP ((EPA Reg. No. 400-166). All data requirements related to this topic remain outstanding.

61-2. Beginning Materials and Manufacturing Process

The Naptalam Guidance Document dated March 1985 specifies generic data requirements for naptalam regarding beginning materials and

the manufacturing/formulation process. The Guidance Document also noted the potential for nitrosamine formation if nitrite nitrogen were used in the formulation process, and requested the registrant to acknowledge any use of this compound as a corrosion inhibitor. In response to the Guidance Document, Uniroyal Chemical Company submitted information (1990; MRID 41385501) for the 23.7% EP (EPA Reg. No. 400-49). This information is presented in Confidential Appendix B. These data satisfy the requirements of 40 CFR §158.160-162 ((Guideline Reference No. 61-2) for the 23.7% EP (EPA Reg. No. 400-49) and its naptalam sodium TGAI. No additional information is required on this topic for these products.

Uniroyal did not submit data pertaining to the beginning materials and the formulation process for the 23.7% EP (EPA Reg. No. 400-345). However data submitted for the 23.7% EP (EPA Reg. No. 400-49) may be applied to the 23.7% EP (EPA Reg. No. 400-345) since the CSFs list the same technical source. Additional information is required, however, for beginning materials and manufacturing process of the end-use product.

Uniroyal did not submit data pertaining to the beginning materials and the formulation process for the 23.7% EP (EPA Reg. No. 400-166). All data requirements related to this topic remain outstanding.

61-3. Discussion of the Formation of Impurities

The Naptalam Guidance Document dated March 1985 specifies generic data requirements for naptalam regarding discussion of the formation of impurities, including the possibility of formation of nitrosamines and other impurities of toxicological significance at <0.1% in the TGAI. Uniroyal has not responded to this requirement. All data requirements for 40 CFR §158.167 (Guideline Reference No. 61-3) remain outstanding for the three 23.7% EPs (EPA Reg. Nos. 400-49, 400-345, and 400-166).

ANALYSIS AND CERTIFICATION OF PRODUCT INGREDIENTS

62-1. Preliminary Analysis

The Naptalam Guidance Document dated March 1985 specifies generic data requirements for naptalam regarding preliminary analysis for the TGAI, including analysis for nitrosamines. In response to the Guidance Document, Uniroyal submitted preliminary analysis data (1986; MRID 40003301) for dilute solutions of naptalam sodium in water (ca. 25% active ingredient). These data are presented in Confidential Appendix C. The submitted data do not fully satisfy the requirements of 40 CFR §158.150 (Guideline Reference No. 62-1) because the registrant did not analyze

samples for all impurities associated with the TGAI, as identified on the CSF for the 23.7% EP (EPA Reg. No. 400-49). If a discussion of the formation of impurities reveals the potential for formation of nitrosamines or other compounds of toxicological significance at levels <0.1% of the TGAI, these compounds too must be included in preliminary analysis.

Preliminary analysis is required for all impurities present in the naptalam sodium solid at levels <0.1% of the TGAI. If additional preliminary analysis data are collected from the 25% dilute naptalam sodium solution, the registrant must identify impurities present in the solution at ≥0.025% and must include analysis for nitrosamines or other compounds of toxicological significance at <0.025% if warranted by further discussion of formation of impurities. Additional data are required.

No data have been submitted for the other two Uniroyal 23.7% EPs (EPA Reg. Nos. 400-166 and 400-345). However data submitted for the 23.7% EP (EPA Reg. No. 400-49) may be applied to the 23.7% EP (EPA Reg. No. 400-345) since the CSFs list the same technical source. For the 23.7% EP (EPA Reg. No. 400-166), the registrant must submit information on the technical source; if the product is manufactured in an integrated system from the same technical source and has no additional impurities than the other two 23.7% EPs, then the above data may also be applied towards satisfying the preliminary analysis requirements of this product. Additional data are required.

62-2. Certified Limits

The Naptalam Guidance Document dated March 1985 specifies generic data requirements for naptalam regarding certification of ingredient limits. In response to the Guidance Document, Uniroyal submitted CSFs (1986; MRID 00157183) dated 3/10/86 for two 23.7% EPs (EPA Reg. Nos. 400-49 and 400-345). These data, presented in Confidential Appendix A, do not satisfy the requirements of 40 CFR §158.175 (Guideline Reference No. 62-2) because the registrant did not submit upper certified limits for impurities, as determined in preliminary analysis, and certified limits for the active ingredient were not based on the nominal concentration of the active ingredient in the source product. When submitting a new Confidential Statement of Formula (CSF), the registrant should provide CAS Registry Numbers for ingredients, and record upper and lower certified limits in the correct columns of EPA Form 8570-4 (Rev. 2-85). Additional information is required.

Uniroyal did not submit certified limits data for the 23.7% EP (EPA Reg. No. 400-166). Data requirements pertaining to this topic remain outstanding for the product.

62-3. Enforcement Analytical Methods

The Naptalam Guidance Document dated March 1985 specifies generic data requirements for naptalam regarding analytical methods to verify certified limits. In response to the Guidance Document, Uniroyal Chemical Company submitted analytical methods (1986; MRID 40003301) pertaining to the naptalam sodium active ingredient and its impurities. The method for determining the active ingredient is discussed below; methods for determining impurities are discussed in Confidential Appendix D.

High performance liquid chromatography (HPLC) method AC-1134A was submitted for the determination of the active ingredient. Samples and standards are injected onto an HPLC system with a C18 column and a UV detector set at 250 nm. An internal standard solution of phenol in 80% methanol in water is used for quantitation; a gradient mixture of aqueous and methanolic tetrabutylammonium phosphate is used for the mobile phase. Linearity for the active ingredient was determined on a five-point standard curve of r^2=0.9935 over a range of 0.582 to 1.182 mg/mL. Ten analyses of a sodium naptalam standard yielded a mean concentration of 90.8% and a coefficient of variation of 0.7%.

The analytical method submitted for determination of naptalam sodium satisfies the requirements of 40 CFR §158.180 (Guideline Reference No. 62-3) regarding enforcement analytical methods. The methods submitted for the determination of the impurities of the TGAI in the 23.7% EPs (EPA Reg. No. 400-49 and 400-345), do not fully satisfy the requirements of 40 CFR §158.180 (Guideline Reference No. 62-3) regarding enforcement analytical methods because methods were not submitted for all impurities of toxicological significance. If these impurities are present in the TGAI at levels ≥0.1%, analytical methods are required for these impurities as well. If discussion of the formation of impurities reveals the potential for formation of nitrosamines or other compounds of toxicological significance, methods will be required for determining these impurities at <0.1% in the TGAI. Additional data are required.

No enforcement analytical methods have been submitted for the Uniroyal 23.7% EP (EPA Reg. No. 400-166). The registrant must submit information on the source of the TGAI. If the 23.7% EP (EPA Reg. No. 400-166) is manufactured in an integrated system from the same technical source and has no additional impurities, then the above methods may also be applied towards satisfying data requirements for enforcement analytical methods for this product.

PHYSICAL AND CHEMICAL CHARACTERISTICS

The Naptalam Guidance Document dated March 1985 requires additional data pertaining to the odor, specific gravity, dissociation constant, octanol/water partition coefficient and pH for the naptalam sodium TGAI. The registrant responded to data requirements for odor and specific gravity information in a letter to the Agency dated 10/8/85 (Jackets, EPA Reg. Nos. 400-49 and 400-345), indicating that the odor of the TGAI resembles aromatic amines and the specific gravity determinations were made at 25 C. This information satisfies the requirements of 40 CFR §158.190 (Guideline Reference Nos. 63-4 and 63-7) pertaining to odor and specific gravity for the TGAI.

In addition to the requirements listed above for the TGAI, the following physical chemical characteristics are required for end-use products produced from this TGAI: color, physical state, odor, density/specific gravity, pH, oxidizing/reducing action, flammability, explodability, storage stability, viscosity, and corrosion characteristics. In response to the Guidance Document, Uniroyal has submitted data (1985, 1986; MRIDs 00154116 and 00157183) pertaining to physical and chemical characteristics for the two Uniroyal 23.7 EPs (EPA Reg. No. 400-49 and 400-345). These data are presented in Table 1.

Data pertaining to the dissociation constant, octanol/water partition coefficient and pH may satisfy the requirements of 40 CFR §158.190 (Guideline Reference Nos. 63-10 through 63-12) for the 23.7% EPs (EPA Reg. Nos. 400-49 and 400-345) once the registrant has clearly identified the test substances used. Determination of the dissociation constant and pH must be based on the TGAI and the octanol/water partition coefficient must be determined from the PAI.

Information submitted for the end-use products pertaining to odor and storage stability (Guideline Reference Nos. 63-4 and 63-17) is inadequate to satisfy data requirements for the 23.7% EPs (EPA Reg. Nos. 400-49 and 400-345) because a more descriptive term is required for odor, and quantitative storage stability data are required for the active ingredient.

For the 23.7% EPs (EPA Reg. Nos. 400-49 and 400-345) data pertaining to the octanol/water partition coefficient (Guideline Reference No. 63-11) must be submitted for the PAI, and odor, density/specific gravity and storage stability data must be submitted for the end-use products (Guideline Reference Nos. 63-4, 63-7, and 63-17). Data submitted for these products may satisfy requirements for the 23.7% EP (EPA Reg. No. 400-166), if the registrant indicates that the technical source is the same; otherwise, all data requirements pertaining to physical and chemical characteristics (Guideline Reference Nos. 63-2 through 63-20) must be submitted as required for the TGAI, PAI, and EP.

Table 1. Physical and chemical properties of the naptalam purified active ingredient (PAI), technical grade of the active ingredient (TGAI), and end-use products (EPs).

Guidelines Reference No., 40 CFR §158.190; Name of Property	Description [Method] (Substrate; EPA Reg. No.; MRID)[a]
63-2. Color	**light purple** (23.7% EP; 400-49, 400-345; 00157183)
63-3. Physical state	**liquid** (23.7% EP; 400-49, 400-345; 00157183)
63-4. Odor	**unpleasant** (23.7% EP; 400-49, 400-345; 00157183)
63-10. Dissociation constant	**$K = 2 \times 10^{-6}$** [OECD Guidelines, May 1981, Section 1, No. 112] (00157183)
63-11. Octanol/water partition coefficient	**K_{ow} = 1.063 (mean value; pH range 5-9)** [OECD Guidelines, May 1981, Section 107] (00154116)
63-12. pH	**7.12 (1% solution, 25 C)** (00157183) **10.5** (23.7% EPs; 400-49, 400-345; 00157183)
63-14. Oxidizing or reducing action	**mild exothermic reaction with dilute potassium permanganate; no reaction with zinc granules** (23.7% EPs; 400-49, 400-345; 00157183)
63-15. Flammability	**none to 566 C (1050 F)** (23.7% EPs; 400-49, 400-345; 00157183)
63-16. Explodability	**negative to 302.5 at 50 cm** (23.7% EPs; 400-49, 400-345; 00157183)

(Continued.)

Table 1. (Continued.)

Guidelines Reference No., 40 CFR §158.190; Name of Property	Description [Method] (Substrate; EPA Reg. No.; MRID)[a]
63-17. Storage Stability	**no change observed following 4 to 5 yrs ambient storage; ppts at -1 C; imide forms at 60 to 65 C and ppts.** (23.7% EPs; 400-49, 400-345; 00157183)
63-18. Viscosity	**5.5 cps at 60 rpm** [Brookfield viscometer] (23.7% EPs; 400-49, 400-345; 00157183)
63-19. Miscibility	**completely soluble in water at 20 C** (23.7% EPs; 400-49, 400-345; 00157183)
63-20. Corrosiveness	**incompatible with acids; corrodes unlined steel containers** (23.7% EPs; 400-49, 400-345; 00157183)

[a] PAI = purified active ingredient. TGAI = technical grade of the active ingredient. MP = manufacturing-use product. FI = formulation intermediate. EP = end-use product. Hyphenated numbers represent EPA Registration Numbers. Eight-digit numbers are MRID documents from the Pesticide Document Management System (PDMS).

Product Chemistry Citations (used):

00154116 Larrivee, C.; Parkins, M. (1985) Octanol/Water Partition Coefficient of Alanap: Project No. 8579. Unpublished study prepared by Uniroyal Chemical. 9 p.

00157183 Uniroyal, Inc. (1986) Product Chemistry Requirements [of Alanap]. Unpublished compilation. 27 p.

40003301 Blaszczynski, E. (1986) Determination of Percent Active and Impurities in Sodium Alanap Technical: Proj. No. 8651. Unpublished study prepared by Uniroyal Chemical Co., Inc. 18 p.

41385501 Pierce, J. (1990) Description of Beginning Materials and Manufacturing Process: Lab Project Number: 9005. Unpublished study prepared by Uniroyal Chemical Co., Inc. 44 p.

TABLE A. GENERIC DATA REQUIREMENTS FOR THE NAPTALAM/NAPTALAM SODIUM TECHNICAL GRADE OF THE ACTIVE INGREDIENT.[1]

Data Requirement	Test Substance[2]	Does EPA have data to satisfy this requirement?	Bibliographic Citation[3]	Must additional data be submitted under FIFRA Sec. 3(c)(2)(B)?
40 CFR §158.155-190 Product Chemistry				
Product Composition				
61-2. Beginning Materials and Production Process	TGAI	Partially	41385501	Yes[4]
61-3. Formation of Impurities	TGAI	No	N/A	Yes[5]
Analysis and Certification of Product Ingredients				
62-1. Preliminary Analysis	TGAI	Partially	40003301	Yes[6]
Physical and Chemical Characteristics[7]				
63-2. Color	TGAI	Yes	N/A	No
63-3. Physical State	TGAI	Yes	N/A	No
63-4. Odor	TGAI	Yes	Reg. Jackets 400-49, 400-345	No
63-5. Melting Point	TGAI	Yes	N/A	No
63-6. Boiling Point	TGAI	N/A	N/A	No
63-7. Density, Bulk Density, or Specific Gravity	TGAI	Yes	Reg. Jackets 400-49, 400-345	No
63-8. Solubility	TGAI or PAI	Yes	N/A	No
63-9. Vapor Pressure	TGAI or PAI	N/A	N/A	No
63-10. Dissociation Constant	TGAI or PAI	Partially	00157183	Yes[8]
63-11. Octanol/Water Partitioning Coefficient	PAI	Partially	00154116	Yes[8]
63-12. pH	TGAI	Partially	00157183	Yes[8]
63-13. Stability	TGAI	Yes	N/A	No
Other Requirements:				
64-1. Submittal of Samples	N/A	N/A	N/A	No

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TABLE A. (Continued).

1. Data requirements pertain to the TGAI (solid naptalam sodium) of the Uniroyal Chemical Company 23.7% EPs (EPA Reg. Nos. 400-49, 400-166, and 400-345). Additional data requirements are listed in the following Table C, "Product Specific Data Requirements for Naptalam End-Use Products".

2. Test substance: PAI = purified active ingredient; TGAI = technical grade of the active ingredient; MP = manufacturing-use product; EP = end-use product.

3. Underlining indicates documents that have been reviewed in this Update document.

4. Uniroyal has not responded to data requirements for the 23.7% EP (EPA Reg. Nos. 400-166). The following information must be provided: (i) the name and address of the producer of the technical grade of the active ingredient; (ii) the brand name, trade name or other commercial designation, the name and address of the producer, and information concerning the composition of each starting material; (iii) a general characterization of the process (e.g., batch or continuous); (iv) a flow chart of the chemical equations of each intended reaction occurring at each step of the process, the necessary reaction conditions, and the duration of each step of the process and of the entire process; (v) the identity of the materials used to produce the product, their relative amounts, and the order in which they are added; (vi) a description of the equipment used; (vii) a description of the conditions (e.g., temperature, pressure, pH, humidity) that are controlled during each step of the process; (viii) a description of any purification procedures (including procedures to recover or recycle starting materials, intermediates or the substance produced); and (ix) a description of the procedures used to assure consistent composition of the substance produced (quality control methods). Uniroyal has responded for the 23.7% EP (EPA Reg. No. 400-49); the data submitted are adequate for this topic. The technical source listed on the CSF of the 23.7% EP (EPA Reg. No. 400-345) is the same as for the 23.7% EP (EPA Reg. No. 400-49); thus the TGAI data submitted will satisfy requirements for both 23.7% EPs (EPA Reg. Nos. 400-49 and 400-345) for this topic.

5. Uniroyal has not responded to data requirements for any of the three 23.7% EPs listed in Footnote 1. For these products, a discussion regarding the origin of the following potential impurities must be provided: (i) each impurity associated with the active ingredient which was found to be present in any analysis of the product conducted by or for the registrant, and (ii) each impurity which the registrant has reason to believe may be present at a level equal to or greater than 0.1% (w/w) based on the composition of each starting material, (iii) possible formation of nitrosamines and other impurities of toxicological significance at <0.1%, (iv) intended and side reactions which may occur during production, (v) the possible degradation of ingredients after production, post-production reactions between ingredients, possible

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TABLE A. (Continued).

contamination from packaging materials or production equipment, and (vi) process control, purification and quality control measures.

6. Uniroyal has responded to data requirements for the 23.7% EPs (EPA Reg. No. 400-49 and 400-345). However, the registrant must submit additional data regarding all impurities of the TGAI at 0.1% or greater, as listed on the CSFs. If the discussion of the formation of impurities reveals the potential for nitrosamines or other compounds of toxicological significance at levels <0.1% of the TGAI, these compounds too must be included in the preliminary analysis study. Additional preliminary analysis data may be collected using the 25% dilute naptalam sodium solution; however, the registrant will then be required to identify impurities present in the solution at ≥0.025% and nitrosamines or other compounds of toxicological significance at <0.025% as warranted by discussion of formation of impurities. Uniroyal has not responded to data requirements for the 23.7% EP (EPA Reg. No. 400-166). For this product, five or more representative samples must be analyzed for the amount of active ingredient and each impurity present at 0.1% or greater. If the product is produced by a batch process, five separate batches should be represented in preliminary analyses. Complete and detailed descriptions of the methods used for sample analysis must be submitted, including statements of their precision and accuracy. The preliminary analysis report should include the identity and quantity of each ingredient for which analysis is conducted along with the mean and relative standard deviation of the analytical results. Based on the preliminary analysis, a statement of the composition of the technical grade of active ingredient must be provided. If the source of the technical product is the same as for the other two 23.7% EPs, then the submitted data may apply to the 23.7% EP (EPA Reg. No. 400-166) as well.

7. As required by 40 CFR §158.190 and more fully described in the Pesticide Assessment Guidelines, Subdivision D, Guidelines Reference Nos. 63-2 through 63-13, data must be submitted on physicochemical characteristics (color, physical state, odor, melting point, boiling point, specific gravity, solubility, vapor pressure, dissociation constant, octanol/water partition coefficient, pH, and stability). There are additional data requirements listed in Table C pertaining to physicochemical characteristics of end-use products.

8. Uniroyal has responded for the 23.7% EPs (EPA Reg. Nos. 400-49 and 400-345); however, the registrant must specify which test substance was used. Uniroyal has not responded for the 23.7% EP (EPA Reg. No. 400-166) on this topic; if the source of the technical product is the same as for the other two 23.7% EPs, then the submitted data may apply to the 23.7% EP (EPA Reg. No. 400-166) as well.

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TABLE C. PRODUCT SPECIFIC DATA REQUIREMENTS FOR NAPTALAM/NAPTALAM SODIUM END-USE PRODUCTS.[1]

Data Requirement	Test Substance[2]	Does EPA have data to satisfy this requirement?	Bibliographic Citation[3]	Must additional data be submitted under FIFRA Sec. 3(c)(2)(B)?
40 CFR §158.155-190 Product Chemistry				
Product Composition				
61-1. Product Composition	EP	Partially	00157183	Yes[4]
61-2. Beginning Materials & Production/Formulation Process	EP	Partially	41385501	Yes[5]
61-3. Formation of Impurities	EP	No	N/A	Yes[6]
Analysis and Certification of Product Ingredients				
62-1. Preliminary Analysis	EP	Partially	40003301	Yes[7]
62-2. Certified Limits	EP	Partially	00157183	Yes[8]
62-3. Enforcement Analytical Methods	EP	Partially	40003301	Yes[9]
Physical and Chemical Characteristics[10]				
63-2. Color	EP	Partially	00157183	Yes[11]
63-3. Physical State	EP	Partially	00157183	Yes[11]
63-4. Odor	EP	Partially	00157183	Yes[12]
63-7. Density, Bulk Density, or Specific Gravity	EP	No	N/A	Yes
63-12. pH	EP	Partially	00157183	Yes[11]
62-14. Oxidizing or Reducing Action	EP	Partially	00157183	Yes[11]
62-15. Flammability	EP	Partially	00157183	Yes[11]
63-16. Explodability	EP	Partially	00157183	Yes[11]
63-17. Storage Stability	EP	Partially	00157183	Yes[13]
63-18. Viscosity	EP	Partially	00157183	Yes[11]
63-19. Miscibility	EP	Partially	00157183	Yes[11]
63-20. Corrosion Characteristics	EP	Partially	00157183	Yes[11]
Other Requirements:				
64-1. Submittal of Samples	N/A	N/A	N/A	No

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TABLE C. (Continued).

1. Data requirements pertain to the Uniroyal Chemical Company 23.7% EPs (EPA Reg. Nos. 400-49, 400-166, and 400-345). Additional data requirements are listed in the preceding Table A, "Generic Data Requirements for the Naptalam/Naptalam Sodium Technical Grade of the Active Ingredient".

2. Test substance: PAI = purified active ingredient; TGAI = technical grade of the active ingredient; MP = manufacturing-use product; EP = end-use product.

3. Underlining indicates documents that have been reviewed in this Update document.

4. Uniroyal has not responded to data requirements for the 23.7% EP (EPA Reg. No. 400-166). Since this product is produced by an integrated system, the following information must be provided: (i) the CA-approved chemical name, CAS Registry Number, any common names, the nominal concentration, upper and lower certified limits in accordance with 40 CFR §158.175, and the purpose of each active and inert ingredient in the product; (ii) the molecular, structural and empirical formulas, and the molecular weight or weight range of each active ingredient in the product; (iii) the chemical name and nominal concentration of each impurity of toxicological significance associated with the active ingredient or present in any sample at a level equal to or greater than 0.1% by weight of the TGAI; and (iv) sufficient information to enable the Agency to identify the source and qualitative composition of all ingredients that are not characterized. Impurities must be identified as such. Uniroyal has responded for the 23.7% EPs (EPA Reg. Nos. 400-49 and 400-345); however, the registrant must submit nominal concentrations for the impurities listed on the CSFs and the nominal concentration of the active ingredient should be based on the nominal concentration in the source product.

5. *Uniroyal has not responded to data requirements for the 23.7% EPs (EPA Reg. No. 400-166 and 400-345).* Since these products are produced by an integrated system, the following information must be provided: (i) the brand name, trade name or other commercial designation of each starting material, the name and address of its producer, and information concerning its composition; (ii) the brand name, trade name, or other commercial designation and information concerning the composition of each inert ingredient; (iii) a general characterization of the formulation or production process (e.g., batch or continuous); the identity of the materials used to produce the product, their relative amounts, and the order in which they are added; (iv) a description of the equipment used; (v) a description of the conditions (e.g., temperature, pressure, pH, humidity) that are controlled during each step of the process; (vi) a flow chart of the chemical equations of each intended reaction occurring at each step of the process and of the entire process; and (vii) a description of any purification procedures (including procedures to recover or recycle starting materials, intermediates or the substance produced); and (viii) a description of the procedures used to assure

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TABLE C. (Continued).

consistent composition of the substance produced (quality control methods). Uniroyal has responded for the 23.7% EP (EPA Reg. No. 400-49); data are adequate for this topic.

6. Uniroyal has not responded to data requirements for the 23.7% EPs listed in footnote 1. Since these products are produced by an integrated system, a discussion regarding the origin of the following potential impurities must be provided: (i) each impurity associated with the active ingredient which was found to be present in any analysis of the product conducted by or for the registrant, and (ii) each impurity which the registrant has reason to believe may be present in the product at a level equal to or greater than 0.1% (w/w) based on the composition of each starting material, (iii) intended and side reactions which may occur in the production of the product, (iv) the possible degradation of ingredients in the product after production, (v) post-production reactions between the ingredients in the product, (vi) possible contamination from packaging materials or production equipment, and (vii) process control, purification and quality control measures.

7. Uniroyal has not responded to data requirements for the 23.7% EP (EPA Reg. No. 400-166). Since this product is produced by an integrated system, the registrant must provide preliminary analyses of five or more representative samples of each technical grade of active ingredient contained in the product to identify all impurities present at 0.1% or greater of the TGAI. If the product is produced by a batch process, at least five separate batches should be represented. The preliminary analysis should be conducted at the point in the production process after which no further chemical reactions designed to produce or purify the substance are intended. Complete descriptions of suitably validated methods used for sample analysis must be submitted. The preliminary analysis report should include the identity and quantity of each ingredient for which analysis is conducted, along with the mean and relative standard deviation of the analytical results. Based on the preliminary analysis, a statement of the composition of the technical grade of active ingredient must be provided. If the technical grade of active ingredient cannot be isolated, a statement of the composition of the practical equivalent of the technical grade of active ingredient must be submitted. In addition, if nitrosamine formation is possible, then these must be identified and quantified by methods sensitive to 1 ppm of N-nitroso contaminants in six samples of the product; two samples of each must be analyzed shortly after production, two at 3 months after production, and two at 6 months after production. Upper limits must be proposed for all nitrosamines found. Uniroyal has responded for the 23.7% EPs (EPA Reg. No. 400-49 and 400-345); however, the registrant must submit preliminary analysis on all impurities listed on the CSFs. If a discussion of impurities reveals the potential for the formation of nitrosamines or other toxicologically significant compounds at levels <0.1% of the TGAI, then these too must be included in the preliminary analysis study. Nitrosamines must be identified and quantified by methods sensitive to 1 ppm of N-nitroso contaminants in six samples of the

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TABLE C. (Continued).

product; two samples of each must be analyzed shortly after production, two at 3 months after production, and two at 6 months after production. Upper limits must be proposed for all nitrosamines found.

8. Uniroyal has not responded to data requirements for the 23.7% EP (EPA Reg. No. 400-166). The registrant must propose upper and lower certified limits for each active and inert ingredient, if such limits would differ from the standard certified limits determined by the Agency according to 40 CFR §158.175(b)(2). Also, since the product is produced by an integrated system, upper limits must be proposed for each toxicologically significant impurity associated with the active ingredients and found to be present in any sample of the product (standard certified limits cannot be used for impurities). Certified limits should be based on the sources and magnitude of variability in the manufacturing process and the stability of the ingredients following production. The registrant must certify the accuracy of the information presented, and that the certified limits will be maintained. An explanation of how each certified limit was established (e.g., sample analysis using a validated analytical procedure, quantitative estimate based on the amounts of ingredients used, etc.) must be provided, along with suitable validation data on any analytical procedures used. Certifications must be submitted on EPA Form 8570-4 (Rev. 2/85). Uniroyal has responded for the 23.7% EPs (EPA Reg. Nos. 400-49 and 400-345); however the registrant must submit the following: (i) upper certified limits for toxicologically significant impurities present, as determined in preliminary analysis, and (ii) certified limits for the active ingredient based on the nominal concentration of the active ingredient in the source product.

9. Uniroyal responded to data requirements for the 23.7% EPs (EPA Reg. Nos. 400-49 and 400-345), however further information is required for this topic. The registrant must submit suitably validated analytical methods for all impurities of toxicological significance listed on the CSFs. If a discussion of impurities reveals the potential for the formation of nitrosamines, analytical methods must be submitted for determining these impurities at <0.1% in the TGAI. Uniroyal has not responded for the 23.7% EP (EPA Reg. No. 400-166). Analytical methods which are suitable for enforcement purposes must be provided for each active ingredient and each additional ingredient or impurity that is determined to be toxicologically significant. Suitability for enforcement purposes shall be determined from validation studies of methods submitted by the registrant. If the impurities and the source of the technical product are the same as for the other two 23.7% EPs, then the submitted methods may apply to the 23.7% EP (EPA Reg. No. 400-166) as well.

10. As required in 40 CFR §158.190 and more fully described in the Pesticide Assessment Guidelines, Subdivision D, Guidelines Reference Nos. 63-2 through 63-20, data must be submitted on physicochemical characteristics of each end-use product (color, physical state, odor, specific gravity, pH, oxidizing or

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TABLE C. (Continued).

reducing action, flammability, explodability, storage stability, viscosity, miscibility, and corrosion characteristics). Additional data requirements regarding physicochemical properties of the technical grade of the active ingredient are listed in Table A, "Generic Data Requirements for the Naptalam Technical Grade of the Active Ingredient."

11. Uniroyal has not responded for the 23.7% EP (EPA Reg. No. 400-166); data requirements for this topic are still outstanding. Uniroyal has responded for the 23.7% EPs (EPA Reg. Nos. 400-49 and 400-345); these data are adequate for this topic.

12. Uniroyal has not responded for the 23.7% EP (EPA Reg. No. 400-166); data requirements are still outstanding for this topic. Uniroyal has responded for the 23.7% EPs (EPA Reg. No. 400-49 and 400-345), however, the registrant must submit a more detailed description of the odor.

13. Uniroyal has not responded for the 23.7% EP (EPA Reg. No. 400-166); data requirements for this topic are still outstanding. Uniroyal has responded for the 23.7% EPs (EPA Reg. No. 400-49 and 400-345); however, the registrant must submit the quantitative storage stability data.

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NAPTALAM

REGISTRATION STANDARD UPDATE

PRODUCT CHEMISTRY

TASK 4

(Final Report)

CONFIDENTIAL APPENDICES

Appendix A: 3 Page(s)
Appendix B: 1 Page(s)
Appendix C: 2 Page(s)
Appendix D: 1 Page(s)

Confidential Appendices to the Scientific Review of the Registration Standard Update Report for the pesticide naptalam by the Dietary Exposure Branch [Confidential FIFRA Trade Secret/CBI].

Page _____ is not included in this copy.

Pages __22___ through ___28___ are not included in this copy.

The material not included contains the following type of information:

__X__ 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.

_____ Internal deliberative information.

_____ Attorney-Client work product.

__ __ Claimed Confidential by submitter upon submission to the Agency.

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.

DYNAMAC
CORPORATION

Final Report

NAPTALAM
Task 4: Residue Chemistry Registration Standard Update

Contract No. 68-D8-0080

May 11, 1990

Submitted to:
Environmental Protection Agency
Arlington, VA 22202

Submitted by:
Dynamac Corporation
The Dynamac Building
11140 Rockville Pike
Rockville, MD 20852

NAPTALAM

REGISTRATION STANDARD UPDATE

RESIDUE CHEMISTRY

Task - 4

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NAPTALAM

REGISTRATION STANDARD UPDATE

RESIDUE CHEMISTRY

Task - 4

INTRODUCTION

The 4/26/89 update of the Index of Pesticide Chemicals identifies registered food/feed uses for the sodium salt of the herbicide naptalam on the following crops: cucurbits (including cantaloupe, cucumber, muskmelon, and watermelon), peanuts, and soybeans. Sodium Naptalam formulations registered for preemergence, preplant, and postemergence applications to food/feed crops include the 2 lb/gal emulsifiable concentrate (EC) and the 2 lb/gal soluble concentrate/liquid (SC/L).

The Naptalam Guidance Document, dated 3/85, identifies residue chemistry data gaps for plant and animal metabolism, storage stability, and magnitude of the residue in soybean forage and hay, cucurbits (including cantaloupes, cucumbers, muskmelons, and watermelons), and peanut forage and hay. In response to these requirements, Uniroyal Chemical Co., Inc. has submitted data pertaining to plant metabolism (1987; MRID 40274503), storage stability (1987; MRID 40274505), and residues in cucurbits (1987; MRID 40274504). The available data up to February 20,1990, have been reviewed by the Agency or are otherwise reviewed here for their adequacy in fulfilling the outstanding data requirements.

Tolerances for residues of naptalam (N-1-naphthyl phthalamic acid) in or on raw agricultural commodities are currently expressed in terms of naptalam *per se* [40 CFR §180.297].

SUMMARY

The following residue chemistry data are outstanding:

- Data on plant and animal metabolism, residue analytical methods, and storage stability.
- Data pertaining to the processing of peanuts and soybeans.

QUALITATIVE NATURE OF THE RESIDUE IN PLANTS

Conclusions:

The Naptalam Guidance Document, dated 3/85 concludes that the qualitative nature of the residue in plants is not adequately

understood, and requires additional data regarding [^{14}C]naptalam ring-labeled in the phthalic acid moiety and a separate study with the label in the 1-naphthylamine moiety (or one study using [^{14}C]naptalam labeled in both moieties). Studies were required in soybeans and a cucurbit vegetable. In response to these requirements, Uniroyal Chemical Co., Inc. (1987; MRID 40274503) submitted data pertaining to cucumber and soybean metabolism.

The qualitative nature of the residue in plants is not adequately understood because mature, edible tissues were not analyzed (only cucumber leaves and cucumber and soybean callus tissue were tested). It should be noted that the metabolite identifications reported are considered tentative, since no successful confirmatory analyses were conducted.

The following additional data are required:

- Data depicting the distribution and metabolism of [^{14}C]naptalam ring-labeled in the phthalic acid moiety and a separate study with the label in the 1-naphthylamine moiety (or one study using [^{14}C]naptalam labeled in both moieties) in soybeans and a cucurbit vegetable. A completely characterized test substance representative of technical naptalam used in commercial formulations (including impurities) must be applied under conditions representing normal cropping practices and at levels sufficient to make residue identification and quantification possible. Residues must be characterized in edible mature plant parts. Confirmation of the identities of residues using a suitable method such as mass spectrometry (MS) or high performance liquid chromatography (HPLC) is also required. In addition, representative samples from these tests must be analyzed by the residue analytical methods developed for data collection and tolerance enforcement to ascertain that these methods will recover and quantify all metabolites of concern.

Although incomplete, the available metabolism data indicate that naptalam is metabolized in cucumbers and soybeans to 1-naphthyl-phthalimide and/or 1-naphthylamine and phthalic acid; 1-naphthylamine may become conjugated to glucose. The molecular structures and chemical names of naptalam and its possible metabolites in plants are presented in Table 2.

References (used):

MRID(s): 40274503.

Discussion of the data:

Uniroyal Chemical Co., Inc. (1987; MRID 40274503, Report No. 8727) submitted data from a test pertaining to metabolism of [^{14}C]naptalam in cucumber plants and soybean callus. Cucumbers planted in a greenhouse received preemergence soil application at a rate equivalent to 8 lb ai/A (2x the maximum registered rate) using [^{14}C]naptalam (label positions not clearly specified; specific activity 11.86 mCi/mmol, radiochemical purity 90%; diluted to 0.4 mCi/mL using the 2 lb/gal SC/L formulation). Leaf samples were collected 14 weeks after treatment. In addition, a previously untreated 2-month-old cucumber plant was transplanted into nutrient solution containing 55 ppm of [^{14}C]naptalam; the entire plant was harvested after wilting at 5 days posttreatment. In a third test, callus tissue derived from aseptically germinated cucumber or soybean seeds was injected with 15 µg [^{14}C]naptalam and incubated for 11 days before analysis.

Total Radioactive Residues (TRR)

TRR were 0.054 ppm in or on leaves from the preemergence treatment, determined using combustion/liquid scintillation spectrometry (LSS). The limit of detection of the radioassay was not reported. Combustion/LSS analyses were not conducted on samples from the other two experiments.

Extraction

Cucumber leaf or callus samples from the three experiments were extracted with methanol:chloroform:water (2:1:0.8); the soluble residues from the preemergence-treated plants were analyzed directly by high-performance liquid chromatography (HPLC) without further cleanup. Soluble residues extracted from callus tissue and the plant in nutrient solution were cleaned up on a Supelco C18 column eluted with methanol prior to HPLC analysis. Residues in methanol from the hydroponically treated plant were partitioned into chloroform and aqueous phases; the nonextractable residues from this plant were subjected to protease and cellulase hydrolysis, although no procedural details were provided.

A "trace" (unspecified) of ^{14}C-residues was reported as having been extractable from the preemergence-treated leaf tissue; unextractable residues amounted to 0.065 ppm, ca. 120% of the residues detected in combustion analysis. In the hydroponically treated plant, chloroform-soluble, aqueous, and non-extractable residues accounted for 7.2, 23.6, and 69.2%, respectively, of the total residues recovered after extraction; protease solubilized <1% of the total residue from the non-extracted fraction and it was reported that none of the solid residues were hydrolyzed by cellulase. Extractable residues accounted for 80.3 and 55.6%,

respectively, of the total ^{14}C-activity in cucumber and soybean callus; 7.5 and 22.3% of the residues in these samples were non-extractable.

Characterization

Residues in methanol extracts and C18 column eluates were characterized using HPLC. The chloroform soluble phase partitioned from methanol soluble, hydroponic plant extracts was analyzed by two-dimensional thin-layer chromatography (TLC). Identification of naptalam and its metabolites phthalic acid, 1-naphthylamine, and 1-naphthyl-phthalimide was based on HPLC retention times or TLC Rf values for standard compounds. A major peak isolated from the cucumber callus and hydroponic plant tissue (purported to be the 1-naphthylamine-glucose conjugate) was analyzed by hydrolyzing the eluted residue fraction with hydrochloric acid or ß-glucosidase, resulting in a compound with the same HPLC retention time as 1-naphthylamine; GC/MS analysis of the unhydrolyzed compound revealed the presence of a glucose moiety, but was otherwise inconclusive. The results are summarized in Table 1.

Table 1. Partial characterization of ^{14}C-activity in soluble fractions from tissues following extraction of naptalam-treated cucumber and soybean.

Component	% Extractable (% TRR[a]) Cucumber preemergence	Cucumber hydroponic	Soybean callus
Phthalic acid	--	--	12.3 (6.8)
1-Naphthylamine-glucose	12.8	50.4 (15.5)	7.4 (4.1)
1-Naphthylamine	14.7	21.9 (6.7)	6.0 (3.3)
naptalam	25.6	--	10.2 (5.7)
1-Naphthyl-phthalimide	2.0	--	1.2 (0.7)
Unknown a	--	--	10.5 (5.8)
Unknown b	9.6	8.3 (2.6)	6.5 (3.6)
Unknown c	11.0	--	18.3 (10.2)
Unknown d	--	4.4 (1.4)	18.1 (10.1)
Unexplained		(4.7)	(5.3)
Total extracted	NS[b]	(30.8)	(55.6)
Non-extracted	NS	(69.2)	(22.3)

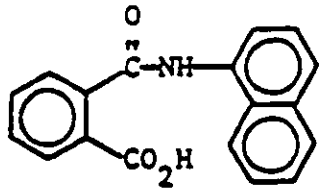
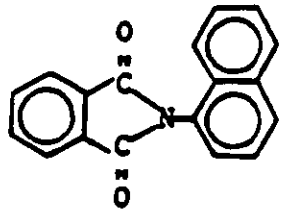
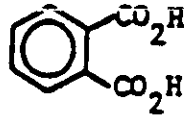
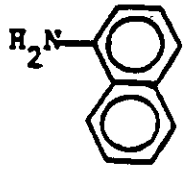
[a] The percentage of the TRR accounted for by each component could not be calculated because the percent of the TRR extracted was not reported.

[b] NS = not specified.

The chloroform extractable portion from the methanol extract of hydroponically treated cucumbers was analyzed by two-dimensional thin-layer chromatography (TLC) using two solvent systems chloroform:acetone:formic acid (7:3:0.5) and hexane:chloroform (4:6), and found to contain 5.8% naptalam and 45% 1-naphthyl-phthalimide, with four other components comprising 6-20% each; these additional components were neither further identified nor explained. Radioactive components characterized from cucumber callus tissue did not contain metabolites differing from those in extracts from preemergence or hydroponically treated plants; residue levels in these samples were not quantified.

In summary, the qualitative nature of the residue in plants is not adequately understood because mature, edible tissues were not analyzed. It should be noted that the metabolite identifications reported are considered tentative, since no successful confirmatory analyses were conducted.

Table 2. Naptalam and its metabolites in plants.

Code	Chemical name Structure	Substrate	MRID Common name
I	N-1-Naphthyl phthalamic acid		
		cucumber seedlings soybean callus	40274503 40274503 **Naptalam** **Alanap**
II	N-1-Naphthyl phthalimide		
		cucumber seedlings soybean callus	40274503 40274503
III	Phthalic acid		
		soybean callus	40274503
IV	N-1-Naphthylamine		
		cucumber seedlings hydroponic cucumber soybean callus	40274503 40274503 40274503
V	1-Naphthylamine glucose-conjugate		
		cucumber seedlings hydroponic cucumber soybean callus	40274503 40274503 40274503

QUALITATIVE NATURE OF THE RESIDUE IN ANIMALS

Conclusions:

The Naptalam Guidance Document, dated 3/85, concludes that the qualitative nature of the residue in animals is not adequately delineated, and requires data on ruminant and poultry metabolism, unless the registrant can show that there are no detectable residues in animal feeds by a sensitive method, or that practical restrictions can be imposed on the use of naptalam which will preclude from animal feeds detectable residues of concern. However, current guidelines require additional data on the metabolism of [^{14}C]naptalam in ruminants and poultry, since there are registered uses on crops with commodities used as livestock feed. No data have been submitted in response to the Guidance Document; therefore, data requirements for this topic are still outstanding. The following additional data are required:

- Metabolism studies utilizing ruminants and poultry must be conducted. Animals must be dosed orally for a minimum of 3 days with both ring-labeled [phthalic acid- and 1-naphthylamine-^{14}C]naptalam in the diet at a level sufficient to make residue identification and quantification possible. Eggs and milk must be collected twice daily during the dosing period. Animals must be sacrificed within 24 hours of the final dose. The distribution and identity of residues must be determined in eggs, milk, muscle, fat, kidney (except poultry), and liver. Representative samples from these studies must be analyzed using a suitable confirmatory method such as MS or HPLC. In addition, representative samples from these studies must be analyzed using a currently accepted or proposed enforcement analytical method in order to ascertain that the method is capable of adequately recovering and identifying all residues of concern.

References (used):

N/A.

Discussion of the data:

N/A.

RESIDUE ANALYTICAL METHODS

Conclusions:

The qualitative nature of the residue in plants and animals has not been adequately described. Therefore, the adequacy of the available analytical methods cannot be ascertained. The Naptalam Guidance Document, dated 3/85, requires no additional data

pertaining to analytical methodology unless additional metabolites of concern are identified in plant or animal tissues.

For all food uses, data on whether the FDA multiresidue methodology would detect and identify a pesticide are required (40 CFR 158.240). The FDA Pestrak database (PAM Vol. I, Appendix dated 12/13/89) indicates that recovery of naptalam using protocols A, D, or E is not likely. Additionally, the FDA Pestrak database lists naptalam as undergoing method development research on anilines.

The currently preferred method for data collection and tolerance enforcement is a colorimetric procedure that determines residues of naptalam per se. PAM Vol. II lists the colorimetric methods of Smith and Stone (Method A in PAM Vol. II) and Lane et. al. (Method B in PAM Vol. II).

The following data are required:

- If radiolabeled validation of existing analytical methodology for plants and animals (refer to metabolism studies requested in the sections "Qualitative Nature of the Residue in Plants" and "Qualitative Nature of the Residue in Animals" for additional details) reveal the presence of additional metabolites of concern or indicates a major portion of the total radioactive residue is not recovered and identified by these methods, radiolabeled validation of new proposed analytical methodology will be required.

References (used):

N/A.

Discussion of the data:

N/A.

STORAGE STABILITY DATA

Conclusions:

The Naptalam Guidance Document, dated 3/85, concludes that additional data are required to show the stability of residues of naptalam in or on residue samples subjected to the same conditions under which the residue samples collected by the registrant were stored.

In response to these requirements, Uniroyal Chemical Co., Inc. (1987; MRID 40274505) submitted data depicting the stability of naptalam in cucumbers and cantaloupes stored for 3 and 8 months,

respectively, at sub-freezing temperatures. These data indicate that residue decline of naptalam in cucumber and cantaloupe stored frozen for 3-6 months is limited; however, in cantaloupes, residue decline may occur between 6 and 8 months of storage; recovery of naptalam from fortified samples was 86-92% at 6 months and 38-69% at 8 months.

The data do not fulfill the requirements for the topic because: (i) details regarding the test compound used for fortification (purity, concentration) were not supplied; (ii) specific details of storage conditions (containers, temperatures, lighting, humidity) were not indicated; and (iii) no data were supplied for soybeans and peanuts. The following additional data are required:

- The sample storage intervals and conditions must be supplied for all residue data submitted in support of tolerances, whether previously submitted or required in this update. Storage stability data in support of previously submitted residue data must reflect the actual storage conditions and intervals for samples used to generate the residue data. If residue depletion occurs, data will be required which depict the decline in levels of pesticide residues of concern in commodities stored under the range of conditions and for the range of intervals specified. Crop samples bearing measurable weathered residues or fortified with naptalam residues of concern must be analyzed immediately after harvest or fortification and again after storage intervals that allow for reasonable unforeseen delays in sample analysis. In laboratory tests using fortified samples, the pure active ingredient and pure metabolites must be used. However, if field-weathered samples are used, the test substance must be a typical end-use product. For additional guidance on conducting storage stability studies, the registrant is referred to an August, 1987 Position Document on the Effects of Storage on the Validity of Pesticide Residue Data available from NTIS under order no. PB 88112362/AS.

The nature of the residue in plants and animals is not adequately understood. If the requested data on plant and animal metabolism indicate the presence of additional metabolites of concern, data depicting the stability of those residues during storage will be required.

References (used):

MRID(s): 40274505.

Discussion of the data:

Uniroyal Chemical Co., Inc. (1987; MRID 40274505, Report No. UR301) submitted data from a test pertaining to the storage stability of residues of naptalam in or on cantaloupes and cucumbers. Commodities were macerated and fortified at 0.1-0.4 ppm and maintained frozen at unspecified temperatures for up to 244 days. Data were collected using a colorimetric method (Lane et. al., 1958). The limit of detection was 0.05 ppm. Three control samples each of cantaloupe and cucumber bore residues of <0.05 ppm (nondetectable). Recoveries of initial fortification levels at various storage intervals are detailed in Table 3; values obtained for the zero-day storage interval were fortified and analyzed at the time of the last analysis.

Table 3. Stability of naptalam in cantaloupes and cucumbers frozen storage.

Commodity[b]	Storage Interval (days)	Recovery (%)[a] naptalam
Cantaloupe (0.1)	0	94, 100
	125	76, 88
	182	86, 92
	244	38, 69
Cucumber (0.4)	0	110, 116
	28	115, 116
	87	97, 120

[a] Method recoveries at time of analysis 86-123%.

[b] Initial fortifications given in parentheses.

In summary, these data indicate that residue decline of naptalam in cucumbers and cantaloupes stored frozen for 3-6 months appears limited, however, in cantaloupes residue decline may occur between 6 and 8 months of storage. The registrant states that these are partial results, and that additional data will be submitted.

These data do not fulfill the requirements for the topic because: (i) details regarding the test compound used for fortification (purity, concentration) were not supplied; (ii) specific details of storage conditions (containers, temperatures, lighting, humidity) were not indicated; and (iii) no data were supplied for soybeans, peanuts, and cranberries. Additional data are required.

MAGNITUDE OF THE RESIDUE IN PLANTS

The Naptalam Guidance Document, dated 3/85, identifies field residue data requirements for soybean forage and hay, cucurbits (including cantaloupes, cucumbers, muskmelons, and watermelons), and peanut forage and hay. Uniroyal Chemical Co., Inc. responded to these requirements by submitting residue data for cantaloupes, cucumbers, and watermelons; data concerning these crops can be translated to muskmelons. Outstanding data gaps (refer to Table A. Generic Data Requirements for Naptalam) reflect recent changes in Agency policy regarding requirements for residue chemistry data.

The Guidance Document did not require additional data pertaining to the processing of peanuts or soybeans. However, the data reviewed for the Guidance Document concerned the processing of samples bearing no detectable residues from treatment at ca. 1x the maximum registered rate. Current Agency policy requires that processing studies be conducted using commodities bearing measurable weathered residues. Therefore, additional data pertaining to the processed commodities of peanuts and soybeans are required.

Although a tolerance has been established for residues of naptalam in or on cranberries, the Index Update does not include this site. The naptalam Residue Chemistry Chapter indicates that an 8.1% granular (G) formulation was registered for use on cranberries; however, the Product Search Listing (4/21/89) does not list this formulation. If naled is no longer registered for use on cranberries, this tolerance should be revoked.

Since issuance of the Naptalam Guidance Document, dated 3/85, Uniroyal Chemical Co., Inc. has amended their product label (EPA Reg. No. 400-49, 2 lb/gal SC/L, acceptance date 4/8/88) to (i) delete directions for application to cucurbits using aerial equipment; (ii) impose a livestock feeding restriction on forage and hay from treated soybeans and peanuts; and (iii) impose a 60-day PHI for soybeans.

The conclusions stated in this section regarding the adequacy of established tolerances may change on receipt of the required data on plant metabolism, residue analytical methods, and storage stability. The registrant should be urged to complete and submit all required plant metabolism studies prior to initiation of required storage stability or residue studies.

Cucurbit Vegetables Group

Cantaloupes

Tolerance(s):

A tolerance of 0.1 ppm has been established for residues of N-1-naphthyl phthalamic acid in or on cantaloupes [40 CFR §180.297].

Use directions and limitations:

The 2 lb/gal SC/L formulation is registered for preemergence application to cantaloupes after seeding and postemergence application before vine formation at 3-4 lb ai/A in 20-40 gal/A. These use directions were obtained from the product label for the 2 lb/gal SC/L (EPA Reg. No. 400-49, approved 4/8/88).

Conclusions:

The Naptalam Guidance Document, dated 3/85, requires additional data depicting residues of naptalam in or on cantaloupes resulting from a preemergence application of the 2 lb/gal SC/L formulation at 6 lb ai/A using ground equipment followed by a postemergence application at 4 lb ai/A using aerial and ground equipment. However, directions for aerial application do not appear on the current labels and the maximum rate for each application is 4 lb ai/A. In response to the Guidance Document, Uniroyal submitted additional data (MRID 40274504) which indicate that residues of naptalam will not exceed the established tolerance of 0.1 ppm in or on cantaloupes harvested 47-54 days following treatments at the maximum registered rate. No additional data are required.

References (used):

MRID(s): 40274504.

Discussion of the data:

Uniroyal Chemical Co., Inc. (1987; MRID 40274504) submitted data from four tests conducted in CA(1), FL(2), and IN(1) depicting residues of naptalam in or on cantaloupes. Residues were <0.1 ppm (nondetectable) in or on four samples of cantaloupes harvested 47-54 days following the last application of a regimen that included single preemergence and postemergence applications using the 2 lb/gal SC/L formulation each at 4 lb ai/A (1x the maximum registered rate). Control samples also bore nondetectable residues. Samples were stored frozen (temperature unspecified) for 123-325 days prior to residue analysis using a colorimetric method (Lane et. al., 1958). The limit of detection

was 0.1 ppm. Recovery was 73-82% from four samples fortified with naptalam at 0.1 ppm.

Geographic representation of the data is adequate since the test states of CA(52%), FL(1%), and IN(2%) accounted for ca. 60% of the 1982 U.S. cantaloupe production (1982 Census of Agriculture, Vol. 1, Part 51, p. 339). The available data indicate that residues of naptalam will not exceed the established tolerance of 0.1 ppm in or on cantaloupes harvested 47-54 days following two ground applications of the 2 lb/gal SC/L formulation at 1x the maximum registered rate. No additional data are required.

Cucumbers

Tolerance(s):

A tolerance of 0.1 ppm has been established for residues of N-1-naphthyl phthalamic acid in or on cucumbers [40 CFR §180.297].

Use directions and limitations:

The 2 lb/gal SC/L formulation is registered for preemergence application to cucumbers after seeding and postemergence application before vine formation. Applications are made at 4 lb ai/A in 20-40 gal/A. These use directions were obtained from the product label for the 2 lb/gal SC/L (EPA Reg. No. 400-49, approved 4/8/88).

Conclusions:

The Naptalam Guidance Document, dated 3/85, requires additional data depicting residues of naptalam/naptalam sodium in or on cucumbers resulting from a preemergence application of the 2 lb/gal SC/L formulation at 6 lb ai/A using ground equipment followed by a postemergence application at 4 lb ai/A using aerial and ground equipment. However, directions for aerial application do not appear on the current labels and the maximum rate for each application is 4 lb ai/A. In response to the Guidance Document, Uniroyal submitted additional data (MRID 40274504) which indicate that residues of naptalam will not exceed the established tolerance of 0.1 ppm in or on cucumbers harvested 14-64 days following treatments at the current registered rate. No additional data are required.

References (used):

MRID(s): 40274504.

Discussion of the data:

Uniroyal Chemical Co., Inc. (1987; MRID 40274504) submitted data from seven tests conducted in CA(1), FL(1), IN(1), NC(1), TX(1), and OR(2) pertaining to the residues of naptalam in or on cucumbers. Residues were <0.1 ppm (nondetectable) in or on six samples of cucumbers harvested 14-57 days following the last application of a regimen that included single preemergence and postemergence applications using the 2 lb/gal SC/L formulation each at 4 lb ai/A (1x the maximum registered rate). Residues were also <0.1 ppm (nondetectable) in or on one sample of cucumbers harvested 64 days after a single postemergence application using the 2 lb/gal SC/L formulation at 4 lb ai/A. Control samples also bore nondetectable residues. Samples were stored frozen (temperature unspecified) for 194-317 days prior to residue analysis using a colorimetric method (Lane et. al., 1958). The limit of detection was 0.1 ppm. Recovery was 72-100% from six samples fortified with naptalam at 0.1 ppm. Reported residue values were corrected for method recovery.

Geographic representation is adequate since the test states CA(11%), FL(6%), IN(2%), NC(15%), OR(4%), and TX(8%) accounted for ca. 65% of the 1988 U.S. processing cucumber production, if IN is representative of MI(19%) (Agricultural Statistics Board, NASS, USDA, Vegetables, 1988 Summary, June 1989, p.40). The available data indicate that residues of naptalam will not exceed the established tolerance of 0.1 ppm in or on cucumbers harvested 14-64 days following preemergence and postemergence applications of the 2 lb/gal SC/L formulation at the maximum registered rate. No additional data are required.

Watermelons

Tolerance(s):

A tolerance of 0.1 ppm has been established for residues of N-1-naphthyl phthalamic acid in or on watermelons [40 CFR §180.297].

Use directions and limitations:

The 2 lb/gal SC/L formulation is registered for preemergence application to watermelons after seeding and postemergence application before vine formation. Applications are made at 4 lb ai/A in 20-40 gal/A. These use directions were obtained from product label for the 2 lb/gal SC/L (EPA Reg. No. 400-49, approved 4/8/88).

Conclusions:

The Naptalam Guidance Document, dated 3/85, requires additional data depicting residues of naptalam in or on watermelons

resulting from a preemergence application of the 2 lb/gal SC/L formulation at 6 lb ai/A using ground equipment followed by a postemergence application at 4 lb ai/A using aerial and ground equipment. However, directions for aerial application do not appear on the current labels and the maximum rate for each application is 4 lb ai/A. In response to the Guidance Document, Uniroyal submitted (MRID 40274504) additional data which indicate that residues of naptalam will not exceed the established tolerance of 0.1 ppm in or on watermelons harvested 33-68 days following treatments at the current registered rate. No additional data are required.

References (used):

MRID(s): 40274504.

Discussion of the data:

Uniroyal Chemical Co., Inc. (1987; MRID 40274504) submitted data from five tests conducted in CA(1), FL(1), MO(1), NC(1), and TX(1) depicting residues of naptalam in or on watermelons. Residues were <0.1 ppm (nondetectable) in or on five samples of watermelons harvested 33-68 days following the last application of a regimen that included single preemergence and postemergence applications of the 2 lb/gal SC/L formulation each at 4 lb ai/A (1x the maximum registered rate). Control samples also bore nondetectable residues. Samples were stored frozen (temperature unknown) for 124-318 days prior to residue analysis using a colorimetric method (Lane et. al., 1958). The limit of detection was 0.1 ppm. Recoveries were 75-99% from four samples fortified with naptalam at 0.1 ppm. Reported residue values were corrected for method recovery.

Geographical representation of the data is adequate since the tests states of CA(10%), FL(20%), MO(2%), NC(4%), and TX(24%) accounted for ca. 60% of the 1982 U.S. watermelon production (1982 Census of Agriculture, Vol. 1, Part 51, p. 356). The available data indicate that residues of naptalam will not exceed the established tolerance of 0.1 ppm in or on watermelons harvested 33-68 days following two ground application of the 2 lb/gal SC/L formulation at the maximum registered rate. No additional data are required.

MAGNITUDE OF THE RESIDUE IN MEAT, MILK POULTRY AND EGGS

Milk and the Fat, Meat, and Meat Byproducts of Cattle, Goats, Hogs, Horses, and Sheep

Conclusions:

The Naptalam Guidance Document, dated 3/85, does not require additional data concerning this topic. Presently, data gaps exist concerning the nature of naptalam residues in ruminants and the magnitude of naptalam residues in or on forage and hay of soybeans and peanuts. Therefore, the requirement for additional data regarding the magnitude of residues in milk, and the fat, meat, and meat byproducts of ruminants is reserved, pending submission and evaluation of the requested data. Following receipt of the requested data from ruminant metabolism and field crop trials, the expected dietary intake for ruminants will be calculated and the need for additional feeding studies will be reevaluated.

References (used):

N/A.

Discussion of the data:
N/A.

Eggs and the Fat, Meat, and Meat Byproducts of Poultry

Conclusions:

The Naptalam Guidance Document, dated 3/85, does not require additional data on this topic. Presently, a data gap exists concerning the nature of naptalam residues in poultry. Therefore, the requirement for additional data regarding the magnitude of residues in eggs, and the fat, meat, and meat byproducts of poultry is reserved, pending submission and evaluation of the requested data regarding the nature of the residue in poultry. Following receipt of the requested poultry metabolism data, the expected dietary intake for poultry will be calculated and the need for additional feeding studies will be reevaluated.

References (used):

N/A.

Discussion of the data:

N/A.

MASTER RECORD IDENTIFICATION NUMBERS

40274503 Lengen, M. (1987) Metabolism of :Carbon 14: Naptalam (Alanap) in Cucumbers: Uniroyal Proj. No. 8727. Unpublished study prepared by Uniroyal Chemical Co., Inc. 22 p.

40274504 Ball, J. (1987) Magnitude of the Residue of Naptalam Sodium in Cucumbers, Cantaloupe and Watermelon. Unpublished compilation prepared by Morse Laboratories, Inc. 25 p.

40274505 Ball, J. (1987) Storage Stability of Naptalam Sodium in Cucumbers and Cantaloupe: Status Report: Lab. Nos. 42693, 40787. Unpublished compilation prepared by Morse Laboratories, Inc. 12 p.

TABLE A. GENERIC DATA REQUIREMENTS FOR NAPTALAM.

Data Requirement	Test Substance[1]	Does EPA have data to satisfy this requirement?	Bibliographic Citation[2]	Must additional data be submitted under FIFRA Sec. 3(c)(2)(B)?
40 CFR §158.240 Residue Chemistry				
171-2. Chemical Identity[3]				
171-3. Directions for Use		(See Index)[4]		
171-4. Nature of the Residue (Metabolism) - Plants	PAIRA	Partially	40274503	Yes[5]
171-4. Nature of the Residue (Metabolism) - Livestock	PAIRA & plant metabolites	Partially	N/A	Yes[6]
171-4. Residue Analytical Methods	TGAI & metabolites	Partially	N/A	Yes[7]
171-4. Storage Stability	TEP & metabolites	Partially	40274505	Yes[8]
171-4. Magnitude of Residue in Plants				
Legume Vegetables				
- Soybeans	TEP	Yes		No
(processed commodities)	TEP	Partially	N/A	Yes[9]
Foliage of Legume Vegetables				
- Soybean forage and hay	TEP	Partially	N/A	No[10]

(Continued, footnotes follow)

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TABLE A. (Continued).

Data Requirement	Test Substance[1]	Does EPA have data to satisfy this requirement?	Bibliographic Citation[2]	Must additional data be submitted under FIFRA Sec. 3(c)(2)(B)?
Cucurbit Vegetables				
- Cantaloupes	TEP	Yes	40274504	No
- Cucumbers	TEP	Yes	40274504	No
- Muskmelons	TEP	Partially	N/A	No[11]
- Watermelons	TEP	Yes	40274504	No
Miscellaneous Commodities				
- Peanuts	TEP	No	N/A	No[12]
(processed commodities)	TEP	Partially	N/A	Yes[13]
171-4. Magnitude of residue in Meat/Milk/Poultry/Eggs	TGAI or plant metabolites	No	N/A	Reserved[14]

1. Test substance: PAI = purified active ingredient; PAIRA = purified active ingredient, radiolabeled; TEP = Typical end-use product; TGAI = technical grade of the active ingredient; MP = manufacturing-use product.

2. These references were submitted in response to the Naptalam Guidance Document dated 3/85. Underlining indicates documents that have been reviewed for this update.

3. The same chemical identity data are required as under 40 CFR §158.150-190, with emphasis on impurities that could constitute residue problems. Refer to Product Chemistry Data Requirements tables.

4. The 4/26/89 Update to the Naptalam Index was used to create this document.

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TABLE A. (Continued).

5. The submitted data do not reflect analysis of any mature, edible tissues of cucumbers or soybeans. Therefore, data are required depicting the distribution and metabolism of [^{14}C]naptalam ring-labeled in the phthalic acid moiety and a separate study with the label in the 1-naphthylamine moiety (or one study using [^{14}C]naptalam labeled in both moieties) in soybeans and a cucurbit vegetable. A completely characterized test substance representative of technical naled used in commercial formulations (including impurities) must be applied under conditions representing normal cropping practices and at levels sufficient to make residue identification and quantification possible. Residues must be characterized in edible mature plant parts. Confirmation of the identities of residues using a suitable method such as mass spectrometry (MS) or high performance liquid chromatography (HPLC) is also required. In addition, representative samples from these tests must be analyzed by the residue analytical methods developed for data collection and tolerance enforcement to ascertain that these methods will recover and quantify all metabolites of concern.

6. No data have been submitted in response to the Guidance Document. Metabolism studies utilizing ruminants and poultry must be conducted. Animals must be dosed orally for a minimum of 3 days with both ring-labeled [phthalic acid- and 1-naphthylamine-^{14}C]naptalam in the diet at a level sufficient to make residue identification and quantification possible. Eggs and milk must be collected twice daily during the dosing period. Animals must be sacrificed within 24 hours of the final dose. The distribution and identity of residues must be determined in eggs, milk, muscle, fat, kidney (except poultry), and liver. Representative samples from these studies must be analyzed using a suitable confirmatory method such as MS or HPLC. In addition, representative samples from these studies must be analyzed using a currently accepted or proposed enforcement analytical method in order to ascertain that the method is capable of adequately recovering and identifying all residues of concern.

7. If radiolabeled validation of existing analytical methodology for plants and animals (refer to metabolism studies requested in the sections "Qualitative Nature of the Residue in Plants" and "Qualitative Nature of the Residue in Animals" for additional details) reveal the presence of additional metabolites of concern or indicates a major portion of the total radioactive residue is not recovered and identified by these methods, radiolabeled validation of new proposed analytical methodology will be required.

8. The data do not fulfill the requirements for the topic because: (i) details regarding the test compound used for fortification (purity, concentration) were not supplied; (ii) specific details of storage conditions (containers, temperatures, lighting, humidity) were not indicated; and (iii) no data were supplied for soybeans and peanuts. Therefore, the sample storage intervals and conditions must be supplied for all residue data submitted in support of tolerances, whether previously submitted or required in this update. Storage stability data in support of previously submitted residue data are required only for those

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TABLE A. (Continued).

samples deemed to be useful for tolerance assessment. Data are also required which depict the decline in levels of naled residues of concern in commodities stored under the range of conditions and for the range of intervals specified. Crop samples bearing measurable weathered residues or fortified with naled residues of concern must be analyzed immediately after harvest or fortification and again after storage intervals that allow for reasonable unforeseen delays in sample analysis. In laboratory tests using fortified samples, the pure active ingredient and pure metabolites must be used. However, if field-weathered samples are used, the test substance must be a typical end-use product. For additional guidance on conducting storage stability studies, the registrant is referred to an August, 1987 Position Document on the Effects of Storage on the Validity of Pesticide Residue Data available from NTIS under order no. PB 88112362/AS.

9. The Guidance Document did not require additional data pertaining to the processing of soybeans. However, the data reviewed for the Guidance Document concerned the processing of samples bearing no detectable residues from treatment at ca. 1x the maximum registered rate. Current Agency policy requires that processing studies be conducted using commodities bearing measurable weathered residues. Therefore, a processing study is required depicting the potential for concentration of naptalam residues of concern in products (meal, hulls, soapstock, crude oil, and refined oil) from the processing of soybeans bearing measurable, weathered residues. If residues concentrate in any product, an appropriate food/feed additive tolerance must be proposed.

10. No data are required, since a feeding restriction has been imposed.

11. The data submitted for cantaloupes will translate to muskmelons.

12. Additional data on peanut forage and hay are not required since a feeding restriction has been imposed.

13. The Guidance Document did not require additional data pertaining to the processing of peanuts. However, the data reviewed for the Guidance Document concerned the processing of samples bearing no detectable residues from treatment at ca. 1x the maximum registered rate. Current Agency policy requires that processing studies be conducted using commodities bearing measurable weathered residues. Therefore, a processing study is required depicting the potential for concentration of naptalam residues of concern in products (meal, soapstock, crude oil, and refined oil) from the processing of peanuts bearing measurable, weathered residues. If residues concentrate in any product, an appropriate food/feed additive tolerance must be proposed.

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TABLE A. (Continued).

14. The nature of the residue in animals is not understood. Following receipt of the requested animal metabolism data, the need for and nature of tolerances for residues of naled in meat, milk, poultry, and eggs will be determined, and feeding trials may be required.

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R115930

Chemical: Benzoic acid, 2-((1-naphthalenylamino)carbonyl)-

PC Code:
030702

HED File Code: 11100 Other Chemistry Documents
Memo Date: 7/25/1990
File ID: 00000000
Accession #: 412-06-0011

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9/14/2007