Naptalam Reg. 524-
5

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

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

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Reregistration of Naptalam. Uniroyal Response to Product Chemistry Requirements: CBRS # 9443: DP Barcode D174935: MRID Nos. 421941-01 through -04 & 42130201.

FROM: William Smith, Chemist
Reregistration Section I
Chemistry Branch II: Reregistration Support (CBRS)
Health Effects Division (H7509C)

THROUGH: E. Zager, Chief
Chemistry Branch II: Reregistration Support
Health Effects Division (H7509C)

TO: Walter Waldrop/Susanne Cerrelli
Reregistration Branch
Special Review & Reregistration Division (H7508W)

Attached is the review of product chemistry data submitted in support of reregistration of a Naptalam product produced by an integrated system. This information was reviewed by Dynamac Corporation under supervision of CBRS, HED. The data assessment has undergone secondary review in the Branch and has been revised to reflect Branch policies.

A revised product chemistry data summary sheet is included.

Attachment 1: Naptalam CBRS No. 9443; DP Barcode D174935. Registrant's Response to Product Chemistry Data Requirements.

Attachment 2: Confidential Appendix to Naptalam CBRS No. 9443

cc (with attachments 1 & 2): W Smith (CBRS), Naptalam Reg. Std. File, SF, Dynamac.
cc (without attachments): RF

H7509C:CBRS:WOS:wos:CM#2:Rm805A:703-305-5353: 07/28/92
RDI: MMetzger:07/28/92 EZager:07/28/92

DYNAMAC
CORPORATION
Environmental Services

Final Report

NAPTALAM
Shaughnessy No. 030703
(CBRS No. 9443; DP Barcode D174935; Case 0183)

TASK 4
Registrant's Response to Product Chemistry Data Requirements

July 6, 1992

Contract No. 68-D2-0053

Submitted to:
U.S. Environmental Protection Agency
Arlington, VA 22202

Submitted by:
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NAPTALAM

Shaughnessy NO. 030703

(CBRS No. 9443; DP Barcode D174935; Case 0183)

Task 4

REGISTRANT'S RESPONSE TO PRODUCT CHEMISTRY DATA REQUIREMENTS

BACKGROUND

The Naptalam Registration Standard Update dated 7/25/90 stated that there are no registered manufacturing-use products (MPs) for naptalam/naptalam sodium. The Update required product chemistry data for the 23.7% end-use products (EPs; EPA Reg. Nos. 400-49, 400-166, and 400-345) containing naptalam sodium as the active ingredient since these EPs are manufactured by an integrated system in which the active ingredient is not isolated. According to the Agency Reference Files System search (conducted on 6/18/92), the registrations of EPA Reg. Nos. 400-166 and 400-345 have been canceled. No MPs are currently registered; only one EP (EPA Reg. No. 400-49) remains registered.

In response to an Agency Memorandum (R. Perfetti; CBRS No. 8322, dated 9/25/91) Uniroyal Chemical Company, Inc. has submitted five volumes of product chemistry data (CBRS No. 9443; 1991-92; MRIDs 421941-01 through -04, and 42130201) for the 23.7% EP (EPA Reg. No. 400-49). Data submitted in MRID 42194101 were previously submitted and deemed adequate under MRID 41385501 in the Naptalam Update dated 7/25/90. This MRID will not be presented in this document; all other submitted data and our conclusions are discussed below.

61-1. Product Composition

The Agency memorandum (R. Perfetti; CBRS No. 8322, dated 9/25/91) requires additional information concerning the product identity of the Uniroyal 23.7% EP (EPA Reg. No. 400-49). Uniroyal has submitted (1992; MRID 42194103) a Confidential Statement of Formula (CSF) dated 1/29/92 for the TGAI (40%) which is used to formulate the Uniroyal 23.7% EP (EPA Reg. No. 400-49). These data are presented in the Confidential Appendix and provide useful information regarding the identity and nominal concentrations of the active ingredient, solvents, and impurities in the TGAI (40%). They do not however, satisfy the requirements of 40 CFR §158.155 (Guideline Reference No. 61-1) regarding the product identity of the Uniroyal 23.7% EP (EPA Reg. No. 400-49) because the registrant must submit the chemical names (identity), purpose, and nominal concentrations required for the components of the registered 23.7% EP on EPA Form 8570-4 (Rev. 12/90). Additional data are required.

61-3. Discussion of Formation of Impurities

The Agency memorandum (R. Perfetti; CBRS No. 8322 dated 9/25/91) requires additional discussion of formation of impurities other than nitrosamines in the Uniroyal 23.7% EP (EPA Reg. No. 400-49). In response, Uniroyal has submitted a discussion (1992; MRID 42194102) of impurities formed during the production of the TGAI (40% aqueous) which is used to formulate the Uniroyal 23.7% EP. This discussion is presented in the Confidential Appendix. This information does not satisfy the requirements of 40 CFR §158.167 (Guideline Reference No. 61-3) regarding discussion of formation of impurities in the 23.7% EP (EPA Reg. No. 400-49) because possible degradation of ingredients after production, post-production impurities, and possible contamination from packaging materials or production equipment were not included in the discussion. Additional information is required.

62-1. Preliminary Analysis

The Agency memorandum (R. Perfetti; CBRS No. 8322, dated 9/25/91) requires additional preliminary analysis data other than nitrosamines for the Uniroyal 23.7% EP (EPA Reg. No. 400-49). In response, Uniroyal submitted (1992; MRID 42194103) data from the preliminary analysis of five batches of the TGAI (40%) used to formulate the 23.7% EP. The results of the preliminary analysis are presented in the Confidential Appendix. These data do not satisfy the requirements of 40 CFR §158.170 (Guideline Reference No. 62-1) regarding preliminary analysis because the analytical methods used in the preliminary analysis were not provided. The registrant must describe the methods used to determine the active ingredient and impurities; a statement of the method validations must be included. Additional data are required.

62-2. Certification of Limits

The Agency memorandum (R. Perfetti; CBRS No. 8322, dated 9/25/91) requires certification of ingredient limits for the 23.7% EP (EPA Reg. No. 400-49). Uniroyal submitted (1992; MRID 42194103) a Confidential Statement of Formula (CSF) dated 1/29/92 for the TGAI (40%) which is used to formulate the Uniroyal 23.7% EP (EPA Reg. No. 400-49). These data are presented in the Confidential Appendix and provide useful information regarding the limits of the active ingredients, solvents, and impurities in the TGAI. They do not however, satisfy the requirements of 40 CFR §158.175 (Guideline Reference No. 62-2) regarding certified limits of the Uniroyal 23.7% EP (EPA Reg. No. 400-49) because the registrant must submit the certified limits required for the components of

the registered 23.7% EP on EPA Form 8570-4 (Rev. 12/90). Additional data are required.

PHYSICAL AND CHEMICAL CHARACTERISTICS

The Agency memorandum (R. Perfetti; CBRS No. 8322, dated 9/25/91) requires additional data concerning the physical and chemical characteristics of the Uniroyal 23.7% EP (EPA Reg. No. 400-49).

Uniroyal has submitted (1991; MRID 42130201) data pertaining to the dissociation constant for the 23.7% EP. The dissociation constant of the TGAI was determined using the solubility method of A. Albert and E.P. Serjeant (The Determination of Ionization Constants: A Laboratory Manual. Third Edition, Chapman and Hall Ltd. London. 1984). The average reported pK_a value of three samples was 4.614 with a coefficient of variation of 0.44%.

Uniroyal has submitted (1992; MRID 42194104) a clarification of the test substance used to determine the octanol/water partition coefficient submitted previously for the 23.7% EP. The registrant stated that the previously reported K_{ow} value of 1.063 was generated using the pure active ingredient (PAI; 94.7% solid sodium naptalam) as the test substance. The registrant included information on the purification procedures of the technical naptalam sodium to the solid naptalam sodium.

These data satisfy the requirements of 40 CFR §158.190 (Guideline Reference Nos. 63-10 and 63-11) concerning dissociation constant and octanol/water partition coefficient, respectively, for the Uniroyal 23.7% EP (EPA Reg. No. 400-49). However, additional data remain outstanding concerning the odor and storage stability (Guideline Reference Nos. 63-4 and 63-17) of the 23.7% EP.

MASTER RECORD IDENTIFICATION NUMBERS

References used:

42194102 Pierce, J.B. (1992). Technical Sodium Naptalam: Theoretical Discussion of Impurities. Unpublished Study Prepared and Submitted by Uniroyal Chemical Company, Inc., Middlebury, CT. 9 pp.

42194103 Pierce, J.B. (1992). Sodium Naptalam 40% Aqueous Solution: Explanation of Certification of Ingredient Limits and Confidential Statement of Formula. Unpublished Study Prepared and Submitted by Uniroyal Chemical Company, Inc., Middlebury, CT. 8 pp.

42194104 Pierce, J.B. (1992). Commentary and Supplemental Data: EPA's Received Reviews of Octanol/Water Partition Coefficient for Alanap (Naptalam Sodium). Unpublished Study Prepared and Submitted by Uniroyal Chemical Company, Inc., Middlebury, CT. 6 pp.

42130201 Thomson, P.A. (1991). The Dissociation Constant of Alanap 40% Technical. Unpublished Study Prepared and Submitted by Uniroyal Chemical Company, Inc., Middlebury, CT. 12 pp.

References not used:
(This MRID contains data previously submitted and reviewed in the Naptalam Update dated 7/25/90)

42194101 Pierce, J.B. (1992). Alanap Technical: Description of Beginning Materials and Manufacturing Process. Unpublished Study Prepared and Submitted by Uniroyal Chemical Company, Inc., Middlebury, CT. 29 pp.

PRODUCT CHEMISTRY DATA SUMMARY
Uniroyal Naptalam Sodium 23.7% EP (EPA Reg. No. 400-49)

Guideline Number	Requirement	Requirement Fulfilled? [a]	MRID Number
61-1	Product Identity and Disclosure of Ingredients	N [b]	42194103
61-2	Beginning Materials and Manufacturing Process	Y	
61-3	Discussion of Formation of Impurities	N [c]	42194102
62-1	Preliminary Analysis	N [d]	42194103
62-2	Certification of Ingredient Limits	N [e]	42194103
62-3	Analytical Methods to Verify the Certified Limits	N	
63-2	Color	Y	
63-3	Physical State	Y	
63-4	Odor	N	
63-5	Melting Point	Y	
63-6	Boiling Point	N/A	
63-7	Density, Bulk Density or Specific Gravity	N	
63-8	Solubility	Y	
63-9	Vapor Pressure	Y	
63-10	Dissociation Constant	Y	42130201
63-11	Octanol/Water Partition Coefficient	Y	42194104
63-12	pH	Y	
63-13	Stability	Y	
63-14	Oxidizing or Reducing Action	Y	
63-15	Flammability	Y	
63-16	Explodability	Y	
63-17	Storage Stability	N	
63-18	Viscosity	Y	
63-19	Miscibility	Y	
63-20	Corrosion Characteristics	Y	

a. Y = Yes, N = No, N/A = Not Applicable. Data requirements footnoted in this table reflect conclusions determined in this document only.

b. The registrant must submit the chemical names (identity), purpose, and nominal concentrations required for the components of the registered 23.7% EP on EPA Form 8570-4 (Rev. 12/90).

c. The registrant must submit a discussion of the possible degradation of ingredients after production, post-production impurities, and possible contamination from packaging materials or production equipment.

d. The registrant must describe the methods used to determine the active ingredient and impurities; a statement of the method validations must be included.

e. The registrant must submit the certified limits required for the components of the registered 23.7% EP on EPA Form 8570-4 (Rev. 12/90).

NAPTALAM (UNIROYAL; CBRS No. 9443)

PRODUCT CHEMISTRY

TASK 4

(Final Report)

CONFIDENTIAL APPENDIX

5 Page(s)

Confidential Appendix to the Scientific Review of a Registration Standard Followup Report for the pesticide naptalam by the Chemistry Branch II Reregistration Support [Confidential FIFRA Trade Secret/CBI].

Page _____ is not included in this copy.

Pages __9__ through __13__ 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.

NAPTALAM (030703) RESIDUE CHEMISTRY DATA SUMMARY THROUGH 2/4/92[1]		
Guideline Number and Topic[2]	**Are data requirements satisfied?**	**MRID(s)[3]**
171-3 Directions for use	N	
171-4(a) Plant Metabolism	N[4]	41790501, -02 and <u>41790503</u>
171-4(b) Animal Metabolism	N	
171-4(c) Residue Analytical Methods - Plants	N	
171-4(d) Residue Analytical Methods - Animals	N	
171-4(e) Storage Stability	N	
171-4(k) Legume Vegetables (succulent/dried)		
Soybeans (Processed food/feed)	Y	
171-4(k) Foliage of Legume Vegetables		
Soybean forage and hay	Y	
171-4(k) Cucurbit Vegetables Group		
Cucumbers	Y	
Melons	Y	
171-4(k) Miscellaneous Commodities		
Peanuts (Processed food/feed)	Y	
171-4(l) Processed Food/Feed		
Peanuts	N	
Soybeans	N	
171-4(j) Meat/Milk/Poultry/Eggs	Reserved	
171-4(f) Potable Water	N/A	
171-4(g) Fish	N/A	
171-4(h) Irrigated Crops	N/A	
171-4(i) Food Handling Establishments	N/A	
171-5 Reduction of Residues	N/A	

[1]Registration Standard issued 6/85. Reregistration Standard Update issued 7/25/90.

[2]N/A = Guideline requirement not applicable.

[3]Underlining designates MRIDs that were reviewed in the current submission.

[4]CBRS No. 7773 dated 2/4/92 by R. Perfetti. Cucumber metabolism study potentially upgradeable. Numerous deficiencies. Refer to cited memo for details.

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	00153372 40274503	Yes[5]
171-4. Nature of the Residue (Metabolism) - Livestock	PAIRA & plant metabolites	No	N/A	Yes[6]
171-4. Residue Analytical Methods	TGAI & metabolites	Partially	N/A	Yes[7]
171-4. Storage Stability	TEP & metabolites	Partially	40274505 41664002	Yes[8]
171-4. Magnitude of Residue in Plants				
Legume Vegetables				
- Soybeans	TEP	Yes		No[9]
(processed commodities)	TEP	Partially	N/A	Yes[10]
Foliage of Legume Vegetables				
- Soybean forage and hay	TEP	Partially	N/A	No[11]

(Continued, footnotes follow)

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[12]
- Watermelons	TEP	Yes	40274504	No
Miscellaneous Commodities				
- Peanuts	TEP	No	N/A	No[13]
(processed commodities)	TEP	Partially	N/A	Yes[14]
171-4. Magnitude of residue in Meat/Milk/Poultry/Eggs	TGAI or plant metabolites	No	N/A	Reserved[15]

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 (Pesticide) Guidance Document dated (mm/dd/yy). 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.

TABLE A. (Continued).

5. 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 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.

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 "Qualitative Nature of the Residue in Plants" and "Qualitative Nature of the Residue in Animals" for additional details) reveals the presence of additional metabolites of concern or indicates a major portion of the total radioactive residue is not recovered and identified by the available methods, radiolabeled validation of new proposed 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 addendum. Storage stability data in support of previously submitted residue data are required only for those samples deemed to be useful for tolerance assessment. Data are also required which depict the decline

TABLE A. (Continued).

in levels of naptalam 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 Validity of Pesticide Residue Data available from NTIS under order no. PB 88112362/AS.

9. Data were not required by the Naptalam Guidance Document dated 3/85.

10. 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.

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

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

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

14. 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,

TABLE A. (Continued).

weathered residues. If residues concentrate in any product, an appropriate food/feed additive tolerance must be proposed.

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

13544

R115925

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

PC Code:
030702

HED File Code: 11100 Other Chemistry Documents
Memo Date: 7/30/1992
File ID: DPD174935
Accession #: 412-06-0011

HED Records Reference Center
9/14/2007