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HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Uniroyal Chemical Company: Response to the Naptalam Reregistration Standard: Plant Metabolism Data (MRID #'s 41790501, -02 and -03, CBRS # 7733, Barcode No. D162084.)

FROM: R. B. Perfetti, Ph.D., Chemist
Reregistration Section
Chemistry Branch II: Reregistration Support
Health Effects Division (H7509C)

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

TO: W. Burnam, Acting Chief
Science Analysis and Coordination Branch
Health Effects Division (H7509C)

and

L. Rossi, Chief
Reregistration Branch
Special Review and Reregistration Division (H7508C)

Attached please find a review of Uniroyal Chemical Company's response to the Naptalam Reregistration Standard. This data was reviewed by Dynamac Corporation under supervision of CBRS, HED.

This information has undergone secondary review in CBRS and has been revised to reflect the Branch policies.

Please see our conclusions in the attachment regarding the adequacy of the information provided by the Registrant.

A Residue Chemistry Summary Data Table has also been provided.

If you need additional input please advise.

Attachment : Review of Naptalam Metabolism Information.

cc (With Attachment): R. B. Perfetti, J. Burrell/C. Furlow (PIB/FOD), Naptalam Reregistration Standard File, Naptalam Subject File, Circ. (7) and Dynamac.

cc (Without Attachments): RF

DYNAMAC CORPORATION

Final Report

NAPTALAM (CBRS No. 7733) Task 4: Registrant's Response to Residue Chemistry Data Requirements

September 12, 1991

Contract No. 68-D8-0080

Submitted to:
Environmental Protection Agency
Arlington, VA 22202

Submitted by:
Dynamac Corporation
The Dynamac Building
2275 Research Boulevard
Rockville, MD 20850-3268

NAPTALAM (CBRS No. 7733)

REGISTRANT'S RESPONSE TO THE RESIDUE CHEMISTRY DATA REQUIREMENTS

Task - 4

BACKGROUND

The Naptalam Guidance Document, dated 3/85, identifies residue chemistry data gaps for the nature of the residue in plants and animals, storage stability, and the magnitude of the residue in various crops. Plant metabolism data (1987; MRID 40274503) reviewed in the Naptalam Reregistration Update, dated 7/25/90 were not adequate because mature edible tissues were not analyzed (only cucumber leaves and cucumber and soybean callus tissue were tested) and metabolite identifications were considered tentative, since no successful confirmatory analyses were conducted.

In response to data requirements, Uniroyal submitted (1976; MRID 00153372) data concerning the metabolism of naptalam in mature soybeans treated with [1-naphthylamine-^{14}C]naptalam. The data were reviewed in the Naptalam Reregistration Standard Update Addendum #1, dated 1/22/91 and determined to be inadequate to satisfy data requirements for reregistration because of the following reasons: (i) only 40-46% of detectable ^{14}C-residues in soybean seed were characterized; (ii) suitable confirmatory methods were not used for those ^{14}C-residues that were identified; and (iii) raw data and supporting calculations for the reported concentration of ^{14}C-activity recovered in hexane-soluble, methanol-soluble, and insoluble fractions were not provided. The Naptalam Reregistration Standard Update Addendum #1, dated 1/22/91 specifically requires 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 the edible mature plant parts of soybeans and a cucurbit vegetable. Data requirements in the Update Addendum #1 were made following reconsideration of the Registrants's earlier argument against conducting plant metabolism studies using material labeled in the napthylamine moiety and in the phthalic acid ring or a single study using a double labeled compound (EPA Memoranda CBRS Nos. 7333 and 7343, E. Zager, 4/17/91).

In response to the Update Addendum #1, Uniroyal Chemical Co. (CBRS No. 7733) submitted data concerning the metabolism of [1-naphthylamine-^{14}C]naptalam in soybeans (1976; MRIDs 41790501 and 41790502) and in cucumber fruit (1991; MRID 41790505). The soybean studies duplicate data submitted under MRID 00153372, previously reviewed and considered to be inadequate in the Update

Addendum #1. Uniroyal also submitted a letter to S. Cerrelli, dated 2/15/91 requesting a waiver from the requirement to use double-labeled naptalam in the metabolism studies. The registrant states that in biological systems naptalam hydrolyses to phthalic acid and 1-naphythylamine. The registrant also states that [napthyl-1-^{14}C]naptalam is metabolized to ^{14}C-phthalic acid. Therefore, Uniroyal requests the Agency to consider a waiver from the requirement to use double-labeled material.

Tolerances for residues of naptalam in or on raw agricultural commodities and animal products are currently expressed in terms of naptalam applied as its sodium salt [40 CFR §180.297].

Deficiencies Remaining to be Resolved

The remaining residue chemistry data requirements concerning the qualitative nature of the residue animals, storage stability, and the magnitude of the residues in the processed commodities of soybeans and peanuts that were identified in the Guidance Document, and/or the Reregistration Standard Update, and/or Addendum #1 have not been addressed in this document and remain unresolved.

The Conclusions and Recommendations stated below apply only to the qualitative nature of the residue in cucumbers and soybeans. The other data requirements stated above remain outstanding.

CONCLUSIONS

1. The nature of the naptalam residue in soybeans is not adequately understood. No new soybean metabolism data were presented. The submitted data regarding the metabolism of [1-naphthylamine-^{14}C]naptalam in soybeans (1976; MRIDs 41790501 and 41790502) duplicates data submitted under MRID 00153372, previously reviewed and considered to be inadequate in the Update Addendum #1. As previously stated by CBRS (EPA Memoranda CBRS Nos. 7333 and 7343, E. Zager, 4/17/91) the registrant's argument against conducting plant metabolism studies using material labeled in the napthylamine moiety and in the phthalic acid ring or a single study using a double labeled compound has been reconsidered and rejected. The submitted soybean metabolism studies have been reviewed and determined inadequate to satisfy data requirements for reregisteration.

2. The nature of the naptalam residue in cucumbers is not adequately understood. No data were submitted using material labeled in the phthalic acid ring or a single study using a double labeled compound. The submitted data concerning the metabolism of [1-naphthylamine-^{14}C]naptalam in cucumber fruit

(1991; MRID 41790503) is inadequate for the reasons detailed below:

2a. The registrant has not adequately described the experimental treatment protocols used in the cucumber study. The nature of the test substance, amount of active ingredient (ai), and the precise rate of application were not presented.

2b. None of the residues in the cucumber peels (0.026 ppm)were characterized or identified. This identification is required.

RECOMMENDATIONS

The registrant should be given a copy of this review and informed that the nature of the naptalam residue is not adequately understood in soybeans and cucumbers. Data required in the Naptalam Reregistration Standard Update Addendum #1, dated 1/22/91, restated below, remain outstanding:

Data depicting the distribution and metabolism of [1-naphthylamine-^{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 [1-naphthylamine -^{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.

There are currently no Codex MRL's or Mexican or Canadian tolerances for naptalam, therefore no compatibility questions exist for this chemical.

DETAILED CONSIDERATIONS

Uniroyal (1991; MRID 41790503) submitted data concerning the metabolism of [1-naphthylamine-^{14}C]naptalam in cucumbers. Potted cucumbers received a single pre-emergence application of [1-naphthylamine-^{14}C]naptalam (specific activity 11.86 mCi/mmole, 3643.7 dpm/ g; >98% radiochemical purity) at 4 gal/A (equivalent to 2-4x the maximum registered rate). The formulation used and

the rate in lb ai/A were not specified. Additional information pertaining to field experimental protocols is required to accurately assess the residue data. Cucumber fruit were harvested 82-days posttreatment and stored refrigerated (temperature unspecified) overnight. The fruit was then peeled, and peels and peeled fruit were stored frozen (-20 C) for an unspecified period of time prior to analysis.

Total Radioactive Residues (TRR)

Samples of peel and peeled fruit were separately homogenized, dried, and analyzed for TRR by combustion/liquid scintillation spectrometry (LSS). The limits of detection were 0.01 ppm for peels and 0.006 ppm for peeled fruit. Residue data were reported as the average of one sample each of cucumber peel and peeled fruit, that were separately and repeatedly (six times for peel and seven times for peeled fruit) subsampled and reanalyzed. Total radioactive residues were 0.026 ppm naptalam equivalents in peel, <0.006 ppm (ND; nondetectable) in peeled fruit, and 0.0096 ppm in whole fruit. Residues for whole fruit were calculated from the sum of the peeled fruit and peels using the total μg radioactivity recovered and the sample fresh weight. Direct measurement of whole fruit samples were not conducted. Residues in cucumber samples were not subjected to further characterization or identification.

In summary, the qualitative nature of the residue in cucumber fruit is not adequately understood. The experimental treatment protocols are not adequately described. Cucumbers were harvested 82 days following a single preemergence application of test substance. Residue data reviewed in the Reregistration Standard Update indicate naptalam may be applied pre- and postemergence. We recommend that future studies include the postemergence applications and that fruit are harvested at the established PHI. Residues in peels were >0.01 ppm, but were not characterized; these data are needed. Additional data are required.

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 41790503
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.

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R115926

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

PC Code:
030702
HED File Code: 11100 Other Chemistry Documents
Memo Date: 2/4/1992
File ID: DPD162084
Accession #: 412-06-0011

HED Records Reference Center
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