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

APR 6 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Response to the Aldicarb Reregistration Standard: Residue Chemistry (MRID #'s 42436606, 42436603, 42017401, 42436604, 42436605, 42436602, 42436601, 42436501, 42467301, 42467302 and 00162562, CBRS #'s 10,186, 11,468 and 10,775, Barcode Nos.: D183798, D176694 and D180074).

FROM: R. B. Perfetti, Ph.D., Chemist
Reregistration Section 1
Chemistry Branch II: Reregistration Support
Health Effects Division (H7509C)

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

TO: Lois Rossi, Chief
Reregistration Branch
Special Review & Reregistration Division (H7508W)

and

E. Saito, Chief
Chemical Coordination Branch
Health Effects Division (H7509C)

Attached are reviews of residue chemistry data submitted in response to the aldicarb Reregistration Standard. These reviews were completed by Acurex Corporation (CBRS # 10,186) and Dynamac Corporation (CBRS # 10,775 and 11,468) under supervision of CBRS, HED. They have undergone secondary review in the branch and have been revised to reflect Agency policies.

A revised Tentative Residue Chemistry Summary sheet will follow.

If you need additional input please advise.

Attachment 1: Aldicarb Residue Chemistry Data Reviews.

cc (With Attachment 1): RBP, Aldicarb Reregistration Standard File, Aldicarb Subject File, RF, Circ., Dynamac and Acurex.

ALDICARB
(Chemical Code 098301)
(CBRS No. 10186; DP Barcode D180074)

TASK 3

Registrant's Response to Residue Chemistry Data Requirements

October 16, 1992

Contract No. 68-DO-0142

Submitted to:

U.S. Environmental Protection Agency
Arlington, VA 22202

Submitted by:

Acurex Environmental Corporation
Eastern Region Operations
4915 Prospectus Drive
P.O. Box 13109
Research Triangle Park, NC 27709

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ALDICARB

(Chemical Code 098301)

(CBRS No. 10186; DP Barcode D180074)

REGISTRANT'S RESPONSE TO RESIDUE CHEMISTRY REQUIREMENTS

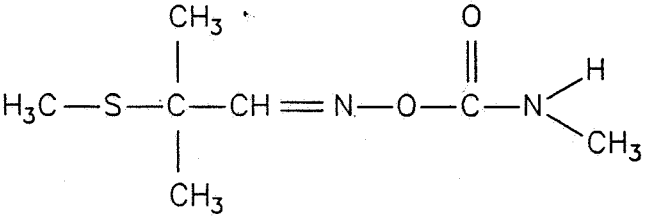
Task 3

BACKGROUND

The Aldicarb Guidance Document dated 4/84 required residue chemistry data on roasted coffee beans and instant coffee. In response, Union Carbide Agricultural Products Co. (1986; MRID 00162562) submitted data from a coffee bean processing study. These data are reviewed here for their adequacy in fulfilling residue chemistry data requirements. The Conclusions and Recommendations stated herein pertain to magnitude of the residue in coffee.

The qualitative nature of the residue in plants is not adequately understood. Metabolism studies are required on three dissimilar crops, including potatoes and an oil seed crop. Tolerances for residues in or on food/feed commodities are currently expressed in terms of the combined residues of aldicarb (2-methyl-2-(methylthio) propionaldehyde O-(methylcarbamoyl) oxime) and its cholinesterase-inhibiting metabolites aldicarb sulfoxide (2-methyl 2-(methylsulfinyl) propionaldehyde O-(methylcarbamoyl) oxime) and aldicarb sulfone (2-methyl 2-(methylsulfonyl) propionaldehyde O-(methylcarbamoyl) oxime) (40 CFR §180.269). Adequate tolerance enforcement methodology is available (Methods I and II in PAM, Vol. II, Sec. 180.269).

A Codex MRL (CXL) of 0.1 ppm has been established for the sum of aldicarb and its sulfoxide and sulfone in or on coffee beans. The corresponding U.S. tolerance is in harmony with this Codex MRL.



Aldicarb

CONCLUSIONS

1. The requirement for storage stability data to support all useful residue data remains outstanding. Storage stability data reflecting storage intervals of 6 months for green coffee beans and an additional 2 months for roasted beans and instant coffee are required to support the current study.

2. Provided that the storage stability data specified in conclusion 1 above are deemed adequate, the submitted coffee bean processing study is adequate. Aldicarb residues do not concentrate in roasted beans or instant coffee, but rather, are reduced to nondetectable levels. No food additive tolerance is required. No additional magnitude of the residue data are required for coffee.

DETAILED CONSIDERATIONS

Magnitude of the Residue - Crop Field Trials/Processing Studies

Coffee beans. A tolerance of 0.1 ppm has been established for the combined residues of aldicarb (2-methyl-2-(methylthio) propionaldehyde O-(methylcarbamoyl) oxime) and its cholinesterase-inhibiting metabolites aldicarb sulfoxide (2-methyl 2-(methylsulfinyl) propionaldehyde O-(methylcarbamoyl) oxime) and aldicarb sulfone (2-methyl 2-(methylsulfonyl) propionaldehyde O-(methylcarbamoyl) oxime) in or on coffee beans (40 CFR §180.269).

In 1977, under PP#7F1953, Union Carbide Corporation proposed use of the 10 and 15% G formulations on coffee in Latin America, Africa, Asia, and Oceania. Two soil incorporated applications may be made per season at 6.7-13.4 lb ai/A (1.5-3 g ai/tree or tree site; 5,000 individual trees/ha, or 1-4 tree/site with 1000 tree sites/ha). The first application is made between the first picking and the first rain, and the second is made 4 to 6 months later but not within 90 days of picking. Use of the 10% G formulation is also permitted on coffee in Puerto Rico under EPA SLN No. PR870001 (parent label EPA Reg No. 264-322; dated 4/20/89). NOTE: This EPA SLN label bears no use information and the parent label does not list the site coffee. The Agency has noted that this use has not been changed since the establishment of the coffee bean tolerance (R. Perfetti; CBRS No. 10193, dated 8/25/92). The 1984 Guidance Document required a processing study and residue data on roasted beans and instant coffee. In response, Union Carbide (1986; MRID 00162562) submitted data from a processing study. Coffee beans were harvested 90 days following two treatments using the 15% G formulation at 6 g ai/tree (4x). The beans were stored for approximately 6 months at 27 °C prior to processing and analysis, which were accomplished within the following 2 months. The beans were roasted, ground, and extracted with water in an autoclave extractor at 185 °C. The extract was then freeze dried to an "instant coffee" fraction. The report stated that the bench scale procedure paralleled commercial manufacturing.

Green coffee, roasted beans, spent grounds, and soluble "instant" coffee were analyzed using GLC/FPD method, which is essentially the same as Method II in PAM, Vol. II. Residues are extracted in water/acetone and aldicarb and aldicarb sulfoxide are oxidized to aldicarb sulfone with peracetic acid. The residues are partitioned into dichloromethane and cleaned up on Florisil prior to GLC analysis. The limit of detection was 0.02 ppm. Recoveries were 84% from green coffee beans, 92% from roasted beans, 141% from spent grounds, and 115% from instant coffee; samples were fortified at 0.2 or 0.4 ppm with a 1:1 mixture of aldicarb:aldicarb sulfone.

Residues were 0.11 ppm in or on green coffee beans and <0.02 ppm (nondetectable) in roasted beans, spent grounds, and soluble "instant" coffee. Duplicate analyses of one sample of each matrix were reported. Residues were <0.02 ppm (nondetectable) in or on control samples.

These data fulfill the outstanding requirements for a coffee processing study. Residues do not concentrate in roasted beans or instant coffee, but rather, are reduced to nondetectable levels. No food additive tolerance is required.

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References

Citations for the MRID documents referenced in this review are presented below. Submissions reviewed in this document are indicated by shaded type.

00162562 Romine, R. (1986) Temik Aldicarb Pesticide Residue in Instant Coffee: Laboratory Project Id.: 803R12. Unpublished study prepared by Union Carbide Agricultural Products Co. and General Foods Corp. 39 p.

Agency Memoranda

CBRS No.: 10193
Subject : Reregistration of Aldicarb. Comments on Draft DCI. Case No. 0140. Chemical No. 098301
To: L. Rossi
From: R. Perfetti
Dated: 8/25/92
MRID(s): None

DYNAMAC
CORPORATION
Environmental Services

Final Report

ALDICARB
Shaughnessy No. 098301 (CBRS No. 10775; DP Barcode D183798; Case 0140)

TASK 4
Registrant's Response To Residue Chemistry Data Requirements

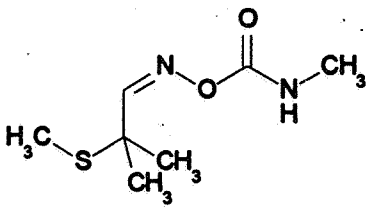
March 19, 1993

Contract No. 68-D2-0053

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

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

ALDICARB



Shaughnessy No. 098301; Case 0140

(CBRS No. 10775; DP Barcode D183798)

Task 4

REGISTRANT'S RESPONSE TO RESIDUE CHEMISTRY DATA REQUIREMENTS

BACKGROUND

The Aldicarb Guidance Document, dated 3/30/84, previously determined that the qualitative nature of the residue in plants was adequately understood based on studies in cotton, peanuts, potatoes, and sugar beets. However, the Aldicarb Reregistration Standard Update, dated 8/20/90, concluded that because the acceptance criteria for plant metabolism data have since become more stringent, the available data from these studies are suspect for the following general reasons: (i) data pertaining to the total recovered radioactive residues present at the time of harvest are either lacking or unclear; (ii) solvent extraction efficiencies were not reported; and (iii) although identification of radiolabeled moieties was typically by two-dimensional TLC in multiple solvent systems, confirmation by MS was either unsupported by MS scans or not attempted. Consequently, the Update and the ensuing Aldicarb Data Call-In Notice of 3/14/91 require new plant metabolism studies on three dissimilar crops. Alternatively, the Update concluded that if the registrant wishes to rely on plant metabolism studies which have been previously submitted and evaluated for reregistration, then the registrant(s) must submit and summarize the data in a reformatted form according to current acceptance criteria of Guideline 171-4(a) of Subdivision O.

In response to the Update and the DCI Notice, Rhone-Poulenc submitted data depicting the metabolism of [^{14}C]aldicarb in cotton (1992; MRID 42436606), peanuts (1992; MRID 42436603), potatoes (1991; MRID 42017401 and 1992; MRIDs 42436604 and 42436605), sugar beets (1992; MRID 42436602), and various plant commodities (1992; MRID 42436601). It should be noted that the data in MRIDs 42436602, 42436603, 42436604, 42436605, and 42436606 are reformatted versions of previously evaluated plant metabolism studies which were submitted between 1967 and 1980 and reviewed in the Aldicarb Residue Chemistry Science Chapter dated 11/83. The data in MRID 42017401 are unacceptable according to plant metabolism study guidelines because the study mainly pertains to the metabolism of aldicarb in callus tissue cultures of potato tubers and citron fruit, and were submitted in the form of a Ph.D. dissertation with incomplete raw data. The data in MRID 42436601 are duplicate summaries of the studies for cotton, peanuts, potatoes, and sugar beets as well as published information (without raw data) on the metabolism of aldicarb in lettuce, spearmint, and tobacco. Only the acceptable plant metabolism studies are evaluated in this document.

Additionally, Rhone-Poulenc submitted data pertaining to the analysis of aldicarb residues of concern using multiresidue methods (1992; MRID 42436501) and storage stability data for the processed commodities of potatoes (1992; MRID 42467301) and soybeans (1992; MRID 42467302). CBRS will forward the multiresidue method submission to FDA for review.

Tolerances are currently expressed in terms of the combined residues of aldicarb [2-methyl-2-(methylthio)propionaldehyde-O-(methyl carbamoyl) oxime], and its cholinesterase-inhibiting metabolites aldicarb sulfoxide [2-methyl-2-(methylsulfinyl)propionaldehyde-O-(methyl carbamoyl) oxime] and aldicarb sulfone [2-methyl-2-(methylsulfonyl)propionaldehyde-O-(methyl carbamoyl) oxime] in/on plant and in animal commodities [40 CFR §180.269, 40 CFR §185.150 (a), and 40 CFR §186.150].

The Pesticide Analytical Manual (PAM) Vol. II lists three GC methods (Methods I, II, and III), each with flame photometric detection (FPD), as available for enforcement of aldicarb tolerances. A colorimetric method (Method A) and an alternate GC/FPD method (Method B) are listed in PAM Vol. II as confirmatory methods.

The submitted data are reviewed and evaluated in this document for adequacy in fulfilling outstanding residue chemistry data requirements. The Conclusions and Recommendations stated below apply only to the following residue chemistry topics: (i) the nature of the residue of aldicarb in/on cotton, peanuts, potatoes, and sugar beets; and (ii) frozen storage stability of aldicarb residues of concern in processed commodities of potatoes and soybeans. No other data requirements of the Update are addressed herein.

CONCLUSIONS

Qualitative Nature of the Residue in Plants:

1. Cotton: The qualitative nature of aldicarb residues in cotton is not adequately understood. The reformatted study does not present any new data and is inadequate to fulfill 171-4 (a) guideline requirements for similar reasons as those explained in the Update and additional deficiencies which are listed below: (i) data pertaining to the total radioactive residues present at the time of harvest are lacking since the registrant did not combust the cottonseed and forage samples prior to residue extraction; (ii) the study failed to characterize/identify the aqueous-soluble fractions from the at-planting plus sidedress portion of the study which accounted for 32-72% (12-81 ppm) of the extractable radioactivity in forage and 70% (2.0 ppm) in seed; (iii) information pertaining to the magnitude or nature of non-extractable residues was not provided; (iv) the organosoluble metabolites tentatively identified by two-dimensional TLC were not confirmed by a second method; (v) raw data (e.g. dpm data for extractions in a flow chart, sample weights, counting efficiencies, quantitative data associated with chromatograms, sample calculations, etc.) were not reported making it difficult to validate the reported results; and (vi) information pertaining to the storage intervals of samples between harvest, extraction, and analysis was not provided. CBRS does not believe that this study is upgradeable since it is unlikely that the registrant would be able to conduct further analyses on samples collected before 1973 and provide supporting storage stability data.

2. Peanuts: The qualitative nature of aldicarb residues in peanuts is not adequately understood. The reformatted study does not present any new data and is inadequate to fulfill 171-4 (a) guideline requirements for similar reasons as those explained in the Update and additional deficiencies which are listed below: (i) data pertaining to the total radioactive residues present at the time of harvest are lacking since the registrant did not combust the peanut commodity samples prior to residue extraction; (ii) the study failed to characterize/identify the aqueous-soluble and non-extractable fractions, the radioactivity of which exceeds the Agency's metabolism study trigger values; (iii) the organosoluble metabolites tentatively identified by two-dimensional TLC were not confirmed by a second method; (iv) raw data (e.g. dpm data for extractions in a flow chart, sample weights, counting efficiencies, quantitative data associated with chromatograms, sample calculations, etc.) were not reported making it difficult to validate the reported results; and (v)

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storage stability data and information pertaining to the storage intervals of samples between harvest, extraction, and analysis were not provided. CBRS does not believe that this study is upgradeable since it is unlikely that the registrant would be able to conduct further analyses on samples collected before 1972 and provide supporting storage stability data.

3. Potatoes: The qualitative nature of aldicarb residues in potatoes is not adequately understood. The reformatted study does not present any new data and is inadequate to fulfill 171-4 (a) guideline requirements for similar reasons as those explained in the Update and additional deficiencies which are listed below: (i) data pertaining to the total radioactive residues present at the time of harvest are lacking since the registrant did not combust the potato tuber and foliage samples prior to residue extraction; (ii) the study failed to characterize/identify the aqueous-soluble fractions which accounted for ca. 31-66% (0.42 and 0.52 ppm) of the extractable residues in tubers and 21-30% (0.96-1.81 ppm) in foliage; (iii) information pertaining to the magnitude or nature of non-extractable residues was not provided; (iv) the organosoluble metabolites tentatively identified by two-dimensional TLC were not confirmed by a second method; (v) raw data (e.g. dpm data for extractions in a flow chart, sample weights, counting efficiencies, quantitative data associated with chromatograms, sample calculations, etc.) were not reported making it difficult to validate the reported results; and (vi) information pertaining to the storage intervals of samples between harvest, extraction, and analysis was not provided. CBRS does not believe that this study is upgradeable since it is unlikely that the registrant would be able to conduct further analyses on samples collected between 1972 and 1978 and provide supporting storage stability data.

4. Sugar beets: The qualitative nature of aldicarb residues in sugar beets is not adequately understood. The reformatted study does not present any new data and is inadequate to fulfill 171-4 (a) guideline requirements for similar reasons as those explained in the Update and additional deficiencies which are listed below: (i) data pertaining to the total radioactive residues present at the time of harvest are lacking since the registrant did not combust the sugar beet top and root samples prior to residue extraction; (ii) the soil application study failed to characterize/identify the aqueous-soluble fractions which accounted for ca. 62-74% (1.6-2.0 ppm) of the extractable residues in sugar beet roots and ca. 15-48% (6-15 ppm) of the extractable residues in sugar beet tops; (iii) information pertaining to the magnitude or nature of non-extractable residues was not provided; (iv) the organosoluble metabolites tentatively identified by two-dimensional TLC were not confirmed by a second method; (v) raw data (e.g. dpm data for extractions in a flow chart, sample weights, counting efficiencies, quantitative data associated with chromatograms, sample calculations, etc.) were not reported making it difficult to validate the reported results; and (vi) information pertaining to the storage intervals of samples between harvest, extraction, and analysis was not provided. CBRS does not believe that this study is upgradeable since it is unlikely that the registrant would be able to conduct further analyses on samples collected before 1970 and provide supporting storage stability data.

Storage Stability Data:

5. The submitted storage stability data for potato processed commodities and soybean processed commodities do not fulfill 171-4(e) guideline requirements because the submissions were not supported by complete raw data. Summary data unsupported by raw data are unacceptable; individual analyses representing each residue value must be reported to enable the agency to verify the reported residue results. Furthermore, a complete description of the HPLC method used to determine aldicarb residues of concern in potato processed commodities (RPAC SOP 90015) must be submitted. These studies are potentially upgradeable if the registrant is able to submit the required raw data for potato and soybean processed commodities, and a complete method description for the determination of aldicarb residues of concern in potato processed

commodities. If the required plant metabolism studies indicate that other metabolites of concern are identified, then additional storage stability data of these metabolites in the processed commodities of potatoes and soybeans may be required.

6. Although incomplete, the storage stability studies indicate that residues of aldicarb, aldicarb sulfoxide, and aldicarb sulfone were stable for up to six weeks of frozen storage in potato wet peel, dry peel, and flake; residues of aldicarb sulfoxide and aldicarb sulfone were stable for up to six weeks of frozen storage in potato chips and granules. Residues of aldicarb were stable for up to four weeks of frozen storage in potato chips and granules. In addition, the available storage stability data indicate that residues of aldicarb, aldicarb sulfoxide, and aldicarb sulfone were stable for up to six weeks of frozen storage in/on soybeans and in soybean meal, hulls, crude and refined oil, and grain dust. The data also indicate that residues of aldicarb were stable for up to six weeks of frozen storage in soybean soapstock but that residues of aldicarb sulfoxide and aldicarb sulfone declined to <5% after two weeks of frozen storage.

RECOMMENDATIONS

1. The registrant should be informed that the metabolism of aldicarb in plants is inadequately understood based on reasons stated in Conclusions 1 through 4. The following additional data are required: Data depicting the uptake, distribution, and metabolism of [S-methyl-^{14}C]aldicarb in three dissimilar crops which are presently registered. We recommend that potatoes and an oil seed crop be included in the list. Radiolabeled purified active ingredient must be applied under conditions representing normal cropping practices and at rates high enough to permit characterization of ^{14}C-residues. The identities and quantities of residues in mature plant parts must be determined in order to elucidate terminal residues. Data depicting the distribution of all total terminal residue components at the time of harvest should be expressed as the percentage of the total radioactivity and concentration (ppm). Confirmation of the identities of residues using a suitable method such as MS or HPLC is also required. Representative samples from these studies must also be analyzed by the residue analytical methods developed for collection and tolerance enforcement to ascertain that the methods are capable of adequately recovering and quantifying all metabolites of concern.

2. We recommend that the registrant be provided copies of recently published guidance documents regarding the conduct of metabolism and storage stability studies, and the submission of raw data.

3. To upgrade the submitted storage stability data for the processed commodities of potatoes and soybeans, the registrant should comply with the requirements stated in Conclusion 5.

Based on available plant metabolism data, the registrant proposed a metabolic pathway for aldicarb in plants. It involves the oxidation of aldicarb to form aldicarb sulfoxide and aldicarb sulfone. Aldicarb sulfoxide may react further to form the oxime sulfoxide, nitrile sulfoxide, alcohol sulfoxide, acid sulfoxide, and acid sulfone. Aldicarb sulfone may react further to form the oxime sulfone, alcohol sulfone, and the acid sulfone. Conjugates may be formed from the oxime and alcohol sulfoxides and sulfones.

The molecular structures of aldicarb along with the metabolites tentatively identified in the commodities of cotton, peanuts, potatoes, and sugar beets are presented in Table 1.

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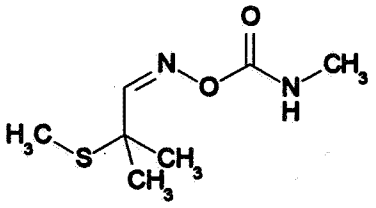
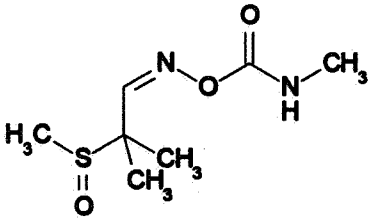
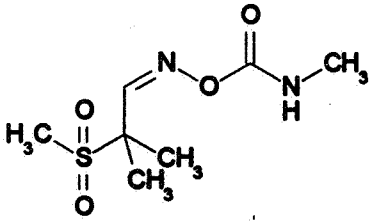
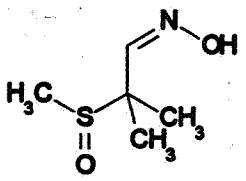
Table 1. Aldicarb and its putative metabolites in cotton, peanuts, potatoes, and sugar beets.

Code	Chemical Name / Structure	Substrate	MRID
			Common Name
I.	2-Methyl-2-(methylthio)propionaldehyde-O-(methylcarbamoyl)oxime		
		cotton forage	42436606
		peanuts and peanut foliage, shells, roots, and pegs	42436603
		sugar beets and sugar beet tops	42436602
			Aldicarb
II.	2-Methyl-2-(methylsulfinyl)propionaldehyde-O-(methylcarbamoyl)oxime		
		cotton forage and cottonseed	42436606
		peanuts and peanut foliage, shells, roots, and pegs	42436603
		potatoes and potato foliage	42436605
		sugar beets and sugar beet tops	42436602
			Aldicarb sulfoxide
III.	2-Methyl-2-(methylsulfonyl)propionaldehyde-O-(methylcarbamoyl)oxime		
		cotton forage and cottonseed	42436606
		peanuts and peanut foliage, shells, roots, and pegs	42436603
		potatoes and potato foliage	42436605
		sugar beets and sugar beet tops	42436602
			Aldicarb sulfone
IV.	2-Methyl-2-(methylsulfinyl)propionaldehyde oxime		
		cotton forage and cottonseed	42436606
		peanuts and peanut foliage, shells, roots, and pegs	42436603
		potatoes and potato foliage	42436605
		sugar beets and sugar beet tops	42436602
			Oxime sulfoxide

(continued; footnotes follow)

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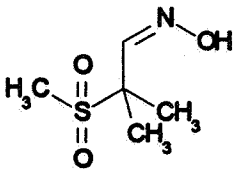
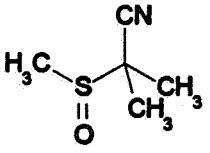
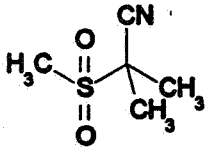
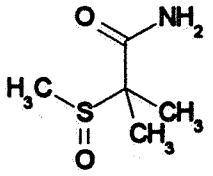
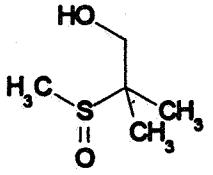
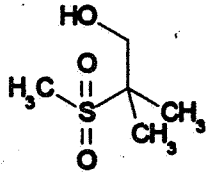
Table 1 continued.

Code	Chemical Name Structure	Substrate	MRID Common Name
V.	2-Methyl-2-(methylsulfonyl)propionaldehyde oxime		
		cotton forage and cottonseed	42436606
		peanuts and peanut foliage, shells, roots, and pegs	42436603
		potatoes and potato foliage	42436605
		sugar beets and sugar beet tops	42436602
			Oxime sulfone
VI.	2-Methyl-2-(methylsulfinyl)propionitrile		
		cotton forage and cottonseed	42436606
		peanuts and peanut foliage, shells, roots, and pegs	42436603
		sugar beets and sugar beet tops	42436602
			Nitrile sulfoxide
VII.	2-Methyl-2-(methylsulfonyl)propionitrile		
		cotton forage	42436606
		peanuts and peanut foliage, shells, roots, and pegs	42436603
		sugar beets and sugar beet tops	42436602
			Nitrile sulfone

(continued; footnotes follow)

Table 1 continued.

Code	Chemical Name Structure	Substrate	MRID Common Name
VIII.	2-Methyl-2-(methylsulfinyl)propionamide		
		cotton forage[a]	42436606
			Amide sulfoxide
IX.	2-Methyl-2-(methylsulfinyl)propanol		
		cotton forage[a]	42436606
		peanuts and peanut foliage, shells, roots, and pegs	42436603
		sugar beets and sugar beet tops	42436602
			Alcohol sulfoxide
X.	2-Methyl-2-(methylsulfonyl)propanol		
		cotton forage[a] and cottonseed	42436606
			Alcohol sulfone

(continued; footnotes follow)

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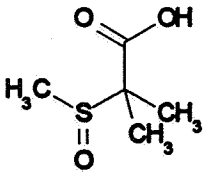
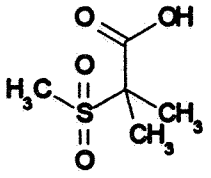
Table 1 continued.

Code	Chemical Name Structure	Substrate	MRID Common Name
XI.	2-Methyl-2-(methylsulfinyl)propionic acid 	cotton forage	42436606 **Acid sulfoxide**
XII.	2-Methyl-2-(methylsulfonyl)propionic acid 	cotton forage	42436606 **Acid sulfone**

[a] Identification confirmed by a second method.

DETAILED CONSIDERATIONS

Qualitative Nature of the Residue in Plants

Cotton

In-life phase

Rhone-Poulenc submitted data (1992; MRID 42436606) depicting the metabolism of [^{14}C]aldicarb in cotton forage and seed. The submission is a reformatted version of a previously evaluated cotton metabolism study which was submitted in 1973 under MRID 00101977 and reviewed in the Aldicarb Residue Chemistry Science Chapter dated 11/83. The present report includes and describes metabolism studies conducted on: (i) cotton grown to maturity following soil application of the formulated [^{14}C]aldicarb under field conditions; and (ii) cottonseed following application of [^{14}C]aldicarb directly to developing bolls (not reflecting registered use) in the greenhouse. The purpose of the second study was to demonstrate that aldicarb metabolites are formed by the plant-boll system rather than solely by soil metabolism and plant uptake. The results of the second study were discussed in the Science Chapter and are not re-reviewed in this document since they will not contribute to the overall understanding of metabolism in cotton. References pertaining to a published study on the metabolism of radiolabeled aldicarb in greenhouse grown cotton plants were also made to support the residue extraction efficiency of the first study. The first study is described below.

Cotton plants (Carolina Queen variety) received a single, at-planting, in-furrow application of [S-methyl-^{14}C]aldicarb (5.85 mCi/mmol; >98.5% radiochemical purity) at a field-equivalent rate of 1 lb ai/A (1x the maximum registered rate for at-planting application). This portion of the study will be referred to in this document as the "at-planting study". The test substance was prepared by mixing radiolabeled aldicarb with unlabeled aldicarb to give a final specific activity of 0.11 mCi/mmol. Fifty eight days after planting, half of the treated plants received an additional single sidedress application of the test substance at a field-equivalent rate of 2 lb ai/A (0.7x the maximum registered rate for sidedress application). This portion of the study will be referred to as the "at-planting plus sidedress study". Cotton forage samples were harvested 9, 14, 22, 37, and 58 days after the first application; additional forage samples were collected 7, 14, 28, 42, and 88 days after the second application. Cottonseed samples were harvested at maturity (88 days after the second application). Samples were stored frozen at -20 C prior to analysis. The registrant did not report the storage intervals prior to laboratory analysis.

Total radioactive residues (TRR)

The registrant calculated total radioactive residues by summation of the ^{14}C-activity present as tentatively identified components, material retained at the TLC origin, and aqueous-soluble residues. These values reflect only the total extractable ^{14}C-activity. The extractable radioactivity was determined by scraping radioactive zones from TLC plates and analyzing by liquid scintillation spectrometry (LSS). The LSS limit of detection was 10 dpm above background.

The registrant did not combust the samples prior to residue extraction. For metabolism studies, CBRS prefers that the treated raw agricultural commodities be initially analyzed for TRR by combustion/LSS prior to any solvent extraction and further laboratory workup. This procedure will allow CBRS to determine the material balance on the commodities of interest and check whether any losses occurred during extraction and other analytical phases of the study.

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Extraction/characterization of residues

Forage and seed samples were homogenized with ethanol:water (1:1; v:v) and filtered. The resulting solid residues were further extracted with ethanol:water (1:1; v:v) and filtered. The filtrates were combined and concentrated under vacuum at 40 C; aliquots were removed for analysis by LSS. The aqueous extracts were partitioned four times with chloroform:acetonitrile (1:1; v:v). The organosoluble extracts were combined, dried over anhydrous sodium sulfate, and filtered. The aqueous-soluble and organosoluble fractions were analyzed for radioactivity by LSS. The registrant did not provide raw data (e.g. dpm data for extractions in a flow chart, sample weights, counting efficiencies, etc.) pertaining to LSS analysis of extracts. The extraction efficiencies could not be calculated since combustion analysis of samples prior to extraction was not conducted. The registrant provided data pertaining to extraction efficiencies from another study pertaining to the metabolism of radiolabeled aldicarb in greenhouse grown cotton forage; these data indicate that up to 56% of radioactive residues in cotton forage were non-extractable. No information pertaining to the amount of non-extractable residues was provided in the present study.

The distribution of radioactivity in the aqueous-soluble and organosoluble fractions of cotton forage was presented as "organic/aqueous" ratios instead of values depicting ppm and %TRR in each fraction. This information is presented below in Table 2. The registrant did not provide information on the distribution of radioactivity in/on cottonseed.

Table 2. Distribution of radioactivity (presented as the ratio of radioactivity in organosoluble and aqueous-soluble fractions) in cotton forage treated with [^{14}C]aldicarb.

PTI [a] (days)	Organic/Aqueous Ratios	
	At-planting	At-planting plus sidedress
9	4.00	--
14	4.55	--
22	2.95	--
37	1.44	--
58	1.41	--
65/7 [b]	1.33	1.76
72/14	0.90	2.02
86/28	1.72	2.12
100/42	0.89	1.22
146/88	0.27	0.38

[a] Posttreatment interval.
[b] Days after first application/days after second application.

Metabolite identification

The organosoluble extracts were analyzed by two-dimensional TLC on silica-gel plates presumably developed with ether:hexane (2:1; v:v) containing 20% acetone in the first dimension and chloroform:acetonitrile (3:2; v:v) in the second dimension. There were discrepancies as to what TLC solvent systems were actually used. [On page 19 of the study report, the registrant reported 18 other solvent systems.] Radioactive areas were detected by autoradiography and tentatively identified by co-chromatography with reference standards having known R_f values. Non-radioactive standards were

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visualized by short-wave UV light, exposure to iodine vapors, and/or spraying with potassium permanganate solution.

Tables 3 and 4 show the distribution of tentatively identified metabolites in forage and seed, respectively. Table 5 shows the distribution of tentatively identified metabolites in the aqueous-soluble extract of 22-day PTI forage. We emphasize that the registrant reported the results in summary tables and did not provide any raw data (e.g. quantitative data associated with chromatograms, sample calculations, etc.). Therefore, independent verification of these residue values cannot be made.

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Table 3. Distribution of tentatively identified metabolites in cotton forage treated with [^{14}C]aldicarb.

Method	Radioactivity as ppm [^{14}C]aldicarb equivalents (% total extractable residues)				
Metabolite	PTI (days)				
At-planting	9	14	22	37	58
Aldicarb	2.2 (1.0)	1.1 (0.5)	1.0 (0.8)	0.4 (0.8)	T[a]
Aldicarb SO[b]	147.6 (70.6)	146.8 (60.7)	45.3 (35.7)	13.0 (24.3)	2.5 (12.5)
Aldicarb SO_2[b]	14.8 (7.1)	37.7 (15.6)	39.2 (30.9)	12.9 (24.1)	7.3 (36.5)
Combined residues[c]	164.6 (78.6)	185.6 (76.7)	85.5 (67.4)	26.3 (49.2)	9.8 (49.0)
Oxime SO	0.4 (0.2)	1.1 (0.5)	1.1 (0.9)	1.1 (2.1)	1.2 (6.0)
Oxide SO_2	ND[d]	1.0 (0.4)	1.4 (1.1)	0.7 (1.3)	0.3 (1.5)
Nitrile SO	ND	4.8 (2.0)	4.7 (3.7)	2.0 (3.7)	0.1 (0.5)
Nitrile SO_2	ND	ND	ND	T	T
Alcohol SO_2	ND	1.1 (0.5)	1.1 (0.9)	0.4 (0.7)	ND
Total identified	**165.0 (78.9)**	**193.6 (80.0)**	**92.7 (73.1)**	**30.5 (57.0)**	**11.4 (57.0)**
TLC Origin	2.2 (1.0)	3.1 (1.3)	0.9 (0.7)	1.0 (1.9)	0.3 (1.5)
Aqueous-soluble	41.8 (20.0)	43.6 (18.0)	32.1 (25.3)	22.0 (41.1)	8.3 (41.5)
Total	209.0	241.9	126.8	53.5	20.0

At-planting (continued)	65	72	86	100	146
Aldicarb	T	T	T	T	T
Aldicarb SO	2.1 (10.4)	0.7 (7.6)	0.2 (8.3)	0.7 (9.9)	0.4 (4.5)
Aldicarb SO_2	7.5 (37.1)	2.5 (27.2)	1.1 (45.8)	2.0 (28.2)	0.6 (6.7)
Combined Residues[c]	9.6 (47.5)	3.2.(34.8)	1.3 (54.2)	2.7 (38.0)	1.0 (11.2)
Oxime SO	1.3 (6.4)	0.7 (7.6)	0.2 (8.3)	0.6 (8.5)	0.5 (5.6)
Oxime SO_2	0.4 (2.0)	0.2 (2.2)	T	T	T
Nitrile SO	0.2 (1.0)	0.1 (1.1)	T	T	T
Nitrile SO_2	T	T	T	T	T
Alcohol SO_2	ND	ND	ND	ND	ND
Total identified	**11.5 (56.9)**	**4.2 (45.7)**	**1.5 (62.5)**	**3.3 (46.5)**	**1.5 (16.9)**
TLC origin	T	T	T	T	0.2 (2.2)
Aqueous-soluble	8.7 (43.1)	5.0 (54.3)	0.9 (37.5)	3.8 (53.5)	7.2 (80.9)
Total	20.2	9.2	2.4	7.1	8.9

At-planting + sidedress	7	14	28	42	88
Aldicarb	0.1 (0.3)	0.2 (0.5)	T	T	T
Aldicarb SO	12.5 (37.5)	17.9 (45.8)	25.5 (36.3)	8.9 (20.8)	10.8 (9.7)
Aldicarb SO_2	7.2 (21.6)	5.7 (14.6)	16.2 (23.0)	11.7 (27.3)	13.1 (11.7)
Combined residues[c]	19.8 (59.5)	23.8 (60.9)	41.7 (59.3)	20.6 (48.1)	23.9 (21.4)
Oxime SO	0.5 (1.5)	0.6 (1.5)	1.1 (1.6)	1.2 (2.8)	2.5 (2.2)
Oxime SO_2	0.1 (0.3)	0.2 (0.5)	0.7 (1.0)	0.5 (1.2)	0.5 (0.4)
Nitrile SO	T	0.6 (1.5)	2.9 (4.1)	ND	1.1 (1.0)
Nitrile SO_2	T	T	0.7 (1.0)	0.5 (1.2)	1.4 (1.3)
Alcohol SO_2	0.6 (1.8)	0.7 (1.8)	0.5 (0.7)	0.3 (0.7)	0.1 (0.1)
Total identified	**21.0 (63.1)**	**25.9 (66.2)**	**47.6 (67.7)**	**23.1 (54.0)**	**29.5 (26.4)**
TLC origin	0.2 (0.6)	0.3 (0.8)	0.2 (0.3)	0.4 (0.9)	1.5 (1.3)
Aqueous-soluble	12.1 (36.3)	12.9 (33.0)	22.5 (32.0)	19.3 (45.1)	80.8 (72.3)
Total	33.3	39.1	70.3	42.8	111.8

[a] Traces of residues; <0.1 ppm.
[b] SO = sulfoxide; SO_2 = sulfone.
[c] Combined residues of aldicarb, aldicarb sulfoxide, and aldicarb sulfone; calculated by study reviewer.
[d] Not detected; registrant reported LSS detection limit as 10 dpm above background.

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Table 4. Distribution of tentatively identified metabolites in cottonseed treated with [^{14}C]aldicarb.

Metabolite	Extractable radioactive residues	
	ppm [a]	% [b]
Aldicarb	ND [c]	ND
Aldicarb SO [d]	0.196	6.97
Aldicarb SO_2 [d]	0.213	7.57
Combined residues [e]	0.409	14.54
Oxime SO	0.003	0.10
Oxide SO_2	0.031	1.12
Nitrile SO	0.028	1.01
Alcohol SO_2	0.029	1.02
Total identified	**0.500**	**17.79**
Solvent front	0.062	2.19
TLC origin	0.288	10.25
Aqueous-soluble	1.96	69.77
Total	**2.81**	**100**

[a] Calculated by study reviewer from registrant-provided data on percent radioactivity.
[b] Percent of extractable radioactive residues.
[c] Not detected; the reported LSS detection limit was 10 dpm above background.
[d] SO = sulfoxide; SO_2 = sulfone.
[e] Combined residues of aldicarb, aldicarb sulfoxide, and aldicarb sulfone; calculated by study reviewer.

Table 5. Distribution of tentatively identified metabolites in the aqueous-soluble extract of 22-day PTI cotton forage treated with [^{14}C]aldicarb.

Metabolite	Extractable radioactive residues	
	ppm [a]	% [b]
Oxime sulfoxide glycoside conjugate	4.4	3.5
Alcohol sulfoxide	9.9	7.8
Amide sulfoxide	2.0	1.6
Acid sulfoxide	0.8	0.6
Acid sulfone	1.4	1.1
Unknown	2.8	2.2
Unhydrolyzed conjugate	10.8	8.5

[a] Calculated by study reviewer from registrant-provided data on percent radioactivity.
[b] Percent of extractable radioactive residues.

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Of the extractable radioactivity from the at-planting plus sidedress study, approximately 26-68% (21-48 ppm) was tentatively identified in cotton forage and 18% (0.5 ppm) in cottonseed. The major metabolites found were aldicarb sulfoxide and aldicarb sulfone. In the same study, the registrant did not characterize/identify the aqueous-soluble fractions which accounted for 32-72% (12-81 ppm) of the extractable radioactivity in forage and 70% (2.0 ppm) in seed.

The registrant provided a single TLC chromatogram, but it could not be determined as to which extract the chromatogram represented. The tentatively identified metabolites were not confirmed by a second method. However, the identities of some of the metabolites in the aqueous-soluble extracts of cotton forage were confirmed using MS in a separate study (see below). The identification of organosoluble ^{14}C-residues found in cotton forage and seed remains tentative.

Confirmation of metabolites in aqueous-soluble residues: A separate study was conducted to confirm metabolite identification in aqueous-soluble residues. The roots of cotton plants were immersed in an aqueous acetone solution of [S-methyl-^{14}C]aldicarb (5.5 mCi/mmol; unspecified radiochemical purity) at a field-equivalent rate of 0.81 lb ai/A. We note that this application method does not reflect normal cropping practices. Cotton forage samples were harvested (the interval between application and harvest was not specified) and stored frozen until analysis; storage intervals and temperatures were not specified. Samples were homogenized with ethanol:water (1:1; v:v) and filtered. The filtrate was concentrated and partitioned with chloroform:acetonitrile (1:1; v:v) to separate organosoluble and aqueous-soluble fractions. Very little quantitative information on radioactive residues was provided. The aqueous-soluble fraction was then subjected to anion exchange chromatography (Amberlite IRA-400) using a continuous gradient of aqueous ammonium carbonate of increasing ionic strength. Ion exchange chromatography resulted in the separation into three fractions. The registrant noted that TLC analysis of the aqueous-soluble extracts prior to and following ion exchange chromatography indicated that no degradation of metabolites was occurring on the column.

The first fraction from the ion exchange column, comprising 70-80% of the radioactivity applied to the column according to the registrant, was found to contain minor amounts of three metabolites which were identified to be the amide sulfoxide, alcohol sulfoxide, and alcohol sulfone using MS. The majority of the first fraction (60-85%, according to the registrant) consisted of highly polar products. Enzyme hydrolysis with β-glucosidase converted 80-90% of these products to the alcohol sulfoxide; the registrant concluded that the polar unknowns were glycoside conjugates.

The second fraction was analyzed by TLC using four unspecified solvent systems and was identified to be the acid sulfoxide by cochromatography with a standard. The third fraction was resolved into two peaks, present at a ca. 2:1 ratio. Treatment of the mixture with acetic acid:30% hydrogen peroxide (1:1; v:v) resulted in the conversion of the major compound to the minor compound. The registrant concluded that the two peaks corresponded to sulfoxide-sulfone analogues. Hydrolyses with peptidase, carboxypeptidase, and 2 N HCl (reflux for two hours) did not release any identifiable metabolites.

Residue method validation

The registrant performed radiolabeled validation of samples using two methods. Samples of cottonseed were analyzed using a GLC/FPD method which is similar to Method I of PAM Vol. II. Samples of foliage were analyzed by an undescribed method which does not appear to be an enforcement method since residues of aldicarb, aldicarb sulfoxide, and aldicarb sulfone were separately determined; therefore, data pertaining to validation of this method will not be reviewed herein.

Cottonseed samples from the at-planting plus sidedress study were extracted with chloroform:acetone (1:1; v:v) instead of acetone:water (3:1; v:v). The samples were then subjected to the remainder of Method I (PAM Vol. II) procedures. The registrant reported total combined residues of 0.23 ppm using this method. The reported total combined residues as determined by radiometric techniques were 0.29 ppm. This value differs from the value reported in Table 4 with no explanation by the registrant. No raw data were submitted to support these results.

Storage stability

Samples were stored frozen at -20 C prior to analysis. The registrant did not report the storage intervals prior to laboratory analysis.

In summary, the qualitative nature of aldicarb residues in cotton is not adequately understood. The reformatted study does not present any new data and is inadequate to fulfill 171-4 (a) guideline requirements for similar reasons as those explained in the Update and additional deficiencies which are listed below: (i) data pertaining to the total radioactive residues present at the time of harvest are lacking since the registrant did not combust the cottonseed and forage samples prior to residue extraction; (ii) the study failed to characterize/identify the aqueous-soluble fractions from the at-planting plus sidedress portion of the study which accounted for 32-72% (12-81 ppm) of the extractable radioactivity in forage and 70% (2.0 ppm) in seed; (iii) information pertaining to the amount or nature of non-extractable residues was not provided; (iv) the organosoluble metabolites tentatively identified by two-dimensional TLC were not confirmed by a second method; (v) raw data (e.g. dpm data for extractions in a flow chart, sample weights, counting efficiencies, quantitative data associated with chromatograms, sample calculations, etc.) were not reported making it difficult to validate the reported results; and (vi) information pertaining to the storage intervals of samples between harvest, extraction, and analysis was not provided. CBRS does not believe that this study is upgradeable since it is unlikely that the registrant would be able to conduct further analyses on samples collected before 1973 and provide supporting storage stability data.

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Peanuts

In-life phase

Rhone-Poulenc submitted data (1992; MRID 42436603) from two studies depicting the metabolism of [^{14}C]aldicarb in field-grown peanuts. The submission is a reformatted version of previously evaluated studies which were submitted in 1972 under MRID 00102009 and reviewed in the Aldicarb Residue Chemistry Science Chapter dated 11/83. In the first study, [S-methyl-^{14}C]aldicarb (specific activity 6.92 mCi/mmol; 96% radiochemical purity) was applied at planting as a 10% G formulation at a rate equivalent to 6 lb ai/A (2x the maximum registered rate). Plants were harvested 21, 35, 56, 98, and 126 days after planting (DAP; three samples/interval). The 21, 35, and 56 DAP harvests consisted of foliage and root samples while the 98 and 126 DAP harvests consisted of foliage, roots, pegs, kernels, and shells. In the second study, the test substance was applied as a soil band application at pegging (56 DAP) as a 10% G formulation at 6 lb ai/A (2x). Plants were harvested 70 days posttreatment and the foliage and nuts were sorted. In both tests, all peanut commodity samples were stored frozen at -5 C prior to analysis. The storage intervals were not reported.

Total radioactive residues (TRR)

The registrant calculated total radioactive residues by summation of the ^{14}C-activity present as extractable and non-extractable residues. The extractable residues were calculated by summation of ^{14}C-activity present as tentatively identified components, material retained at the TLC origin, and aqueous-soluble residues, and were determined by scraping radioactive zones from TLC plates and analyzing by liquid scintillation spectrometry (LSS). The LSS limit of detection was 10 dpm above background. Non-extractable residues were determined by combustion/LSS. The registrant did not combust the samples prior to residue extraction. For metabolism studies, CBRS prefers that the treated raw agricultural commodities be initially analyzed for TRR by combustion/LSS prior to any solvent extraction and further laboratory workup. This procedure will allow CBRS to determine the material balance on the commodities of interest and check whether any losses occurred during extraction and other analytical phases of the study. Table 6, which presents the registrant-calculated TRR in/on peanut commodities, indicates that sufficient amounts of extractable ^{14}C-residues were obtained for characterization/identification. The registrant did not conduct any further analytical work on the non-extractable residues. Since the levels of non-extractable residues in/on peanut foliage and mature peanuts exceed the Agency's trigger values, additional work on these residues should have been conducted.

Extraction/characterization of residues

Samples of peanut commodities were homogenized in ethanol:water (1:1; v:v) then filtered. The remaining solid residues were washed twice with ethanol:water (1:1; v:v) and filtered. The filtrates were combined, concentrated under vacuum at 40 C, and diluted with water. Aliquots were removed for analysis by LSS. The aqueous extract was partitioned four times with chloroform:acetonitrile (1:1; v:v). The organosoluble extracts were combined, dried over anhydrous sodium sulfate, and filtered. The aqueous-soluble and organosoluble fractions were analyzed for radioactivity by LSS. The extraction efficiencies could not be calculated since combustion analysis of samples prior to extraction was not conducted. The registrant provided data pertaining to samples of cotton leaves to demonstrate extraction efficiency. However, these data cannot be translated to peanut commodities.

The distribution of radioactivity in the aqueous-soluble and organosoluble fractions of peanut commodities was presented as "organic/aqueous" ratios instead of values depicting ppm and %TRR in each fraction. This information is presented in Table 7. The partitioning data indicate that the major portion of extractable radioactivity on mature samples is found in the aqueous fraction.

Table 6. Registrant-calculated total radioactive residues in/on peanut matrices following a single at-planting or soil-band application of [^{14}C]aldicarb at 6 lb ai/A to field-grown peanuts.

Method Peanut Matrix	PTI [a] (days)	Registrant-calculated TRR, [^{14}C]aldicarb equivalents Extractable ppm	 % [b]	 Nonextractable ppm	 % [b]	 Total ppm
At-planting						
Foliage	21	173.33	98.2	3.18	1.8	176.51
Foliage	35	127.72	97.2	3.65	2.8	131.37
Foliage	56	60.91	96.3	2.02	3.2	62.93
Foliage	98	3.56	88.8	0.45	11.2	4.01
Foliage	126	3.47	87.6	0.51	12.4	3.96
Peanuts	98	0.62	59.6	0.42	40.4	1.04
Peanuts	126	0.52	61.2	0.33	38.8	0.85
Pegs	98	0.80	58.8	0.56	41.2	1.36
Pegs	126	1.53	68.0	0.72	32.0	2.25
Roots	21	18.57	72.1	7.17	27.9	25.74
Roots	35	12.53	71.5	5.00	28.5	17.53
Roots	56	4.45	62.9	2.62	37.1	7.07
Roots	98	0.98	54.1	0.85	45.9	1.81
Roots	126	1.28	47.6	1.41	52.4	2.69
Shells	98	0.51	48.6	0.54	51.4	1.05
Shells	126	0.19	32.3	0.39	67.7	0.58
Soil-band						
Green foliage	70	4.08	–	–	–	4.08
Dry foliage	70	27.44	–	–	–	27.44
Green peanuts	70	2.72	60.4	1.78	39.6	4.50
Dry peanuts	70	2.84	48.3	3.04	51.7	5.88
Green shells	70	0.75	62.5	1.20	37.5	1.95
Dry shells	70	1.42	38.2	2.30	61.8	3.72

[a] Posttreatment interval.
[b] Based on registrant-calculated TRR values.

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Table 7. Distribution of extractable radioactivity (presented as the ratio of radioactivity in organosoluble and aqueous-soluble fractions) in peanut commodities treated with [^{14}C]aldicarb.

PTI[a]	Organic/Aqueous Ratios				
(days)	Foliage	Roots	Peanuts	Shells	Pegs
21	2.15	1.64	-	-	-
35	2.14	0.98	-	-	-
56	1.79	0.43	-	-	-
98	0.54	0.22	0.11	0.24	0.21
126	0.30	0.15	0.06	0.26	0.21

[a] Posttreatment interval.

Metabolite identification

The organosoluble extracts were analyzed by two-dimensional TLC on silica-gel plates presumably developed with ether:hexane (2:1; v:v) in 20% acetone in the first direction and methylene chloride:acetonitrile (3:2; v:v) in the second direction. Additional solvent systems may have been used since the registrant referenced two published journal articles which contain additional information pertaining to solvent systems. Radioactive areas were detected by autoradiography and tentatively identified by co-chromatography with reference standards having known R_f values. Non-radioactive standards were visualized by short-wave UV light, exposure to iodine vapors, and/or spraying with potassium permanganate solution.

The distribution of tentatively identified metabolites in peanut commodities following at-planting application is presented in Table 8 for foliage and roots and in Table 9 for peanuts, shells, and pegs. Table 10 shows the distribution of tentatively identified metabolites in commodities following soil-band application. We emphasize that the registrant reported the results in summary tables and provided meager or no raw data (e.g. quantitative data associated with chromatograms, sample calculations, etc.). Therefore, independent verification of these residue values cannot be made. No confirmatory analyses were conducted. The registrant reported data pertaining to the confirmation of aqueous-soluble metabolites identified in a cotton metabolism study; these data cannot be translated to the study in review. The identification of ^{14}C-residues found in peanut commodities remains tentative.

In the study reflecting at-planting application, approximately 18-67% (0.7-118 ppm) and 5.7% (0.06 ppm) of the registrant-calculated TRR in foliage and mature peanuts, respectively, were initially identified. In the study reflecting soil-band application, approximately 27.5% (1.1 ppm) and 8.5% (0.2 ppm) of the registrant-calculated TRR in foliage and shell, respectively, were initially identified. The registrant did not characterize/identify the aqueous-soluble fractions which accounted for 31-73% of registrant-calculated TRR in all foliage samples, 44-56% in all peanut samples, and 26-39% in all shell samples. The major metabolites tentatively identified were aldicarb sulfoxide and aldicarb sulfone.

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Table 8. Distribution of tentatively identified metabolites in peanut foliage and roots following a single at-planting soil-incorporated application of [^{14}C]aldicarb at 2x.

Matrix	Percent of registrant-calculated TRR [a]				
	PTI (days)				
Metabolite	21	35	56	98	126
Foliage					
Aldicarb	ND [b]	ND	ND	ND	ND
Aldicarb SO [c]	42.3	33.5	16.7	4.7	0.9
Aldicarb SO_2 [c]	18.5	23.2	32.6	13.4	2.3
Combined residues [d]	60.8	56.7	49.3	18.1	3.2
Oxime SO	1.4	1.3	0.6	0.3	0.9
Oxide SO_2	1.2	1.1	2.8	2.5	5.4
Nitrile SO	1.8	2.9	2.0	0.8	6.9
Nitrile SO_2	0.5	0.8	1.6	0.8	0.4
Alcohol SO_2	1.0	2.1	4.7	5.9	2.6
Total identified	66.7	64.9	61.0	28.4	17.6
TLC origin	0.5	1.4	2.1	2.8	1.0
Aqueous-soluble	31.1	30.8	34.4	57.6	67.3
Roots					
Aldicarb	ND	ND	ND	ND	ND
Aldicarb SO	32.8	20.8	7.0	2.2	1.8
Aldicarb SO_2	8.6	9.1	18.0	1.4	0.8
Combined Residues [d]	41.4	29.9	25.0	3.6	2.6
Oxime SO	0.6	1.0	0.2	0.2	0.2
Oxime SO_2	0.2	0.6	0.3	0.5	0.3
Nitrile SO	0.4	0.6	0.1	0.4	0.3
Nitrile SO_2	0.3	0.4	0.8	0.4	0.8
Alcohol SO_2	0.5	0.6	0.9	0.6	0.4
Total identified	43.4	33.1	27.3	5.7	4.6
TLC origin	1.6	2.1	2.5	4.1	1.9
Aqueous-soluble	27.3	22.7	43.9	44.3	41.1

[a] Based on registrant-calculated TRR instead of percent of extractable radioactivity.
[b] Not detected; registrant reported LSS detection limit as 10 dpm above background.
[c] SO = sulfoxide; SO_2 = sulfone.
[d] Combined residues of aldicarb, aldicarb sulfoxide, and aldicarb sulfone; calculated by study reviewer.

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Table 9. Distribution of tentatively identified metabolites in peanut nuts, shells, and pegs following a single at-planting soil-broadcast application of [^{14}C]aldicarb at 2x.

	Percent of registrant-calculated TRR [a]					
	98 days posttreatment			126 days posttreatment		
Metabolite	Peanuts	Shells	Pegs	Peanuts	Shells	Pegs
Aldicarb	ND [b]	ND	ND	(3.7) [c]	(6.8) [c]	ND
Aldicarb SO [d]	1.0	1.6	1.5	–	–	1.1
Aldicarb SO_2 [d]	2.0	3.4	3.3	–	–	2.9
Combined Residues [e]	3.0	5.0	4.8	–	–	4.0
Oxime SO	0.1	0.1	0.2	–	–	0.2
Oxime SO_2	0.2	0.7	0.8	–	–	0.9
Nitrile SO	0.5	0.6	1.1	–	–	2.0
Nitrile SO_2	1.2	1.3	1.1	–	–	0.7
Alcohol SO	0.7	1.2	1.8	–	–	2.7
Total identified	**5.7**	**8.9**	**9.8**	**–**	**–**	**10.5**
TLC origin	0.3	0.6	0.4	–	–	1.2
Aqueous-soluble	53.8	39.1	48.5	56.3	25.9	83.5

[a] Based on registrant-calculated TRR instead of percent of extractable radioactivity.
[b] Not detected; registrant reported LSS detection limit as 10 dpm above background.
[c] Combined residues of aldicarb, aldicarb sulfoxide, aldicarb sulfone, oxime sulfoxide, oxime sulfone, nitrile sulfoxide, nitrile sulfone, alcohol sulfoxide, and material retained at TLC origin. The registrant did not state whether all metabolites were identified in these samples.
[d] SO = sulfoxide; SO2 = sulfone.
[e] Combined residues of aldicarb, aldicarb sulfoxide, and aldicarb sulfone; calculated by study reviewer.

Table 10. Distribution of tentatively identified metabolites in peanut commodities following a single postemergence, soil-band (sidedress) application of [^{14}C]aldicarb at 2x.[a]

	Percent of registrant-calculated TRR					
	Green			Desiccated		
Metabolite	Foliage	Peanuts	Shells	Foliage	Peanuts	Shells
Aldicarb	ND[b]	(8.4)[c]	ND	ND	ND	ND
Aldicarb SO[d]	4.3	--	1.0	4.0	0.6	0.6
Aldicarb SO_2[d]	9.0	--	2.0	7.4	1.0	1.6
Combined Residues[e]	13.3	--	3.0	13.7	1.6	2.2
Oxime SO	1.3	--	2.9	1.1	0.7	0.1
Oxime SO_2	3.1	--	0.3	3.9	0.2	0.6
Nitrile SO	3.2	--	0.5	4.5	0.2	1.0
Nitrile SO_2	1.6	--	0.9	3.0	0.3	0.7
Alcohol SO	2.8	--	0.9	2.7	0.1	0.6
Total identified	**27.5**	**--**	**8.5**	**28.9**	**3.1**	**5.2**
TLC origin	2.2	--	0.5	1.9	0.7	0.2
Aqueous-soluble	72.5	52.0	31.9	71.3	44.3	32.7

[a] Based on registrant-calculated TRR instead of percent of extractable recovery.
[b] Not detected; registrant reported LSS detection limit as 10 dpm above background.
[c] Combined residues of aldicarb, aldicarb sulfoxide, aldicarb sulfone, oxime sulfoxide, oxime sulfone, nitrile sulfoxide, nitrile sulfone, alcohol sulfoxide, and material retained at TLC origin. The registrant did not state whether all metabolites were identified in these samples.
[d] SO = sulfoxide; SO_2 = sulfone.
[e] Combined residues of aldicarb, aldicarb sulfoxide, and aldicarb sulfone; calculated by study reviewer.

Residue method validation

Representative samples from this study were not analyzed by an enforcement method.

Storage stability

All plant samples were stored frozen at -5 C prior to analysis; storage intervals were not reported.

In summary, the qualitative nature of aldicarb residues in peanuts is not adequately understood. The reformatted study does not present any new data and is inadequate to fulfill 171-4 (a) guideline requirements for similar reasons as those explained in the Update and additional deficiencies which are listed below: (i) data pertaining to the total radioactive residues present at the time of harvest are lacking since the registrant did not combust the peanut commodity samples prior to residue extraction; (ii) the study failed to characterize/identify the aqueous-soluble and non-extractable fractions, the radioactivity of which exceeds the Agency's metabolism study trigger values; (iii) the organosoluble metabolites tentatively identified by two-dimensional TLC were not confirmed by a second method; (iv) raw data (e.g. dpm data for extractions in a flow chart, sample weights, counting efficiencies, quantitative data associated with chromatograms, sample calculations, etc.) were not reported making it difficult to validate the reported results; and (v) storage stability data and information pertaining to the storage intervals of samples between harvest, extraction, and analysis were not provided. CBRS does not

believe that this study is upgradeable since it is unlikely that the registrant would be able to conduct further analyses on samples collected before 1972 and provide supporting storage stability data.

Potatoes

In-life phase

Rhone-Poulenc submitted data (1991; MRID 42017401 and 1992; MRIDs 42436604 and 42436605) from several studies depicting the metabolism of [^{14}C]aldicarb in potatoes. The data in MRIDs 42436604 and 42436605 represent reformatted versions of previously evaluated peanut metabolism studies which were submitted in 1972-78 under MRIDs 00101930 and 00101996, respectively, and reviewed in the Aldicarb Residue Chemistry Science Chapter dated 11/83. We note that data in MRID 42436604 are duplicated in MRID 42436605. We further note that MRID 42436605 contains additional studies pertaining to metabolism following application by stem injection and metabolism in immature potato plants. These additional studies are unacceptable according to the current 171-4(a) guidelines and are not re-reviewed in this document since they will not contribute to the overall understanding of the metabolism in potatoes. The data in MRID 42017401 are also unacceptable since the study mainly pertains to the metabolism of aldicarb in callus tissue cultures of potato tuber and citron fruit and were submitted in the form of a Ph.D. dissertation with incomplete raw data. Only the acceptable potato metabolism studies are described below.

Field-grown Irish potatoes (Cobbler variety; MRID 42436605) received a single in-furrow application of [S-methyl-^{14}C]aldicarb (specific activity 29.3 μCi/mmol; >98.5% radiochemical purity) at a rate equivalent to 3 lb ai/A. The rate is 1x the maximum registered rate for the 10% and 15% G formulations. Two plants from each formulation class were harvested 30, 60, and 90 days posttreatment and stored frozen at -20 C prior to analysis. The sample storage intervals were not reported.

Total radioactive residues (TRR)

The registrant calculated total radioactive residues by summation of the ^{14}C-activity present as tentatively identified components, material retained at the TLC origin, and aqueous-soluble residues. These values reflect only the total extractable ^{14}C-activity. Table 11 presents the extractable radioactive residues in potato tuber and foliage. The extractable radioactivity was determined by scraping radioactive zones from TLC plates and analyzing by liquid scintillation spectrometry (LSS). The LSS detection limits were 0.01 ppm in crude ethanol:water extracts and 0.003 ppm in organic extracts after partitioning. The registrant did not combust the samples prior to residue extraction. For metabolism studies, CBRS prefers that the treated raw agricultural commodities be initially analyzed for TRR by combustion/LSS prior to any solvent extraction and further laboratory workup. This procedure will allow CBRS to determine the material balance on the commodities of interest and check whether any losses occurred during extraction and other analytical phases of the study.

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Table 11. Distribution of tentatively identified metabolites in potato tuber and foliage treated with [^{14}C]aldicarb at 1x the maximum registered rate.

Matrix	Extractable radioactive residues					
	30-day PTI		60-day PTI		90-day PTI	
Metabolite	ppm	%	ppm	%	ppm	%
Foliage						
Aldicarb	ND[a]	ND	ND	ND	ND	ND
Aldicarb SO[b]	2.11	45.3	1.53	22.9	0.29	6.6
Aldicarb SO_2[b]	1.20	25.8	2.92	43.9	2.45	55.9
Combined Residues[c]	3.31	71.1	4.45	66.8	2.74	62.5
Oxime SO	0.05	1.1	0.06	0.9	0.05	1.1
Oxime SO_2	0.07	1.4	0.10	1.6	0.18	4.0
Total identified	3.43	73.6	4.61	69.3	2.97	67.6
TLC origin	0.27	5.7	0.24	3.6	0.11	2.6
Aqueous-soluble	0.96	20.5	1.81	27.2	1.30	29.8
Total[d]	4.66	100	6.66	100	4.38	100
Tuber						
Aldicarb	--[e]	--	ND	ND	ND	ND
Aldicarb SO	--	--	0.46	33.4	0.03	4.6
Aldicarb SO_2	--	--	0.42	30.0	0.08	10.1
Combined residues[c]	--	--	0.88	63.4	0.11	14.7
Oxime SO	--	--	0.02	1.6	0.09	11.3
Oxime SO_2	--	--	0.06	4.0	0.06	8.0
Total identified	--	--	0.96	69.0	0.26	34.0
TLC origin	--	--	0.01	0.3	0.01	0.3
Aqueous-soluble	--	--	0.42	30.7	0.52	65.7
Total[d]	--	--	1.39	100	0.79	100

[a] Nondetectable; detection limits were not reported.
[b] SO = sulfoxide; SO_2 = sulfone.
[c] Combined residues of aldicarb, aldicarb sulfoxide, and aldicarb sulfone; calculated by the reviewer.
[d] Calculated by study reviewer.
[e] Potato tuber was not collected at this interval.

Extraction/characterization

Samples of potato tuber and foliage were homogenized in ethanol:water (1:1; v:v) and then filtered. The remaining solid residues were washed twice with ethanol:water (1:1; v:v) and filtered. The filtrates were combined, concentrated under vacuum at 40 C, and diluted with water; aliquots were analyzed by LSS. The aqueous extract was partitioned four times with chloroform:acetonitrile (1:1; v:v) while the organosoluble extracts were combined, dried over anhydrous sodium sulfate, and then filtered. Both fractions were analyzed for radioactivity by LSS. The registrant did not provide raw data (e.g. dpm data for extractions in a flow chart, sample weights, counting efficiencies, etc.) pertaining to LSS analysis of extracts. The extraction efficiencies could not be calculated since combustion analysis of samples prior

to extraction was not conducted. The registrant provided data pertaining to extraction efficiencies from another unacceptable cotton metabolism studies. However, these data cannot be translated to this study. No information pertaining to the amount of non-extractable residues was provided.

Metabolite identification

The organosoluble extracts were analyzed by one- and two-dimensional TLC on silica gel plates developed with the solvent systems listed below:

Ether:hexane (2:1; v:v) containing 20% acetone;
Methylene chloride:acetonitrile (2:1; v:v);
Ethyl acetate:methanol (5:1; v:v);
Dioxane:hexane (1:1; v:v);
Dioxane:methanol (1:1; v:v);
Dioxane:benzene (1:1; v:v);
Chloroform:methanol (6:1; v:v);
Dioxane:benzene (3:1; v:v);
Methylene chloride:acetonitrile (3:1; v:v);
Ether:benzene:formic acid (3:1:1; v:v:v);
Benzene:methanol:acetic acid (4:1:1; v:v:v);
Dioxane:methanol (9:1; v:v); and
Chloroform:ethyl acetate:hexane:dioxane (5:1:1:1; v:v:v:v).

Metabolites were tentatively identified by co-chromatography with reference standards having known R_f values. Radioactive areas were detected by autoradiography and tentatively identified by co-chromatography with reference standards having known R_f values. Non-radioactive standards were visualized by short-wave UV light, exposure to iodine vapors, and/or spraying with potassium permanganate solution. The registrant provided a single TLC chromatogram but it could not be determined as to which extract the chromatogram represented. The registrant reported the results in summary tables and provided meager or no raw data (e.g. quantitative data associated with chromatograms, sample calculations, etc.). Therefore, independent verification of these residue values cannot be made. No confirmatory analyses were conducted. The tentatively identified metabolites were not confirmed by a second method. The registrant reported data pertaining to the confirmation of aqueous-soluble metabolites identified in a cotton metabolism study; these data cannot be translated to the study in review. The identification of ^{14}C-residues found in potato tuber and foliage remains tentative.

Table 11 indicates that the registrant tentatively identified ca. 34-69% (0.26-0.96 ppm) of the extractable residues in tuber and 68-74% (2.97-4.61 ppm) in foliage. The major metabolites found were aldicarb sulfoxide and aldicarb sulfone. The registrant did not characterize/identify the aqueous-soluble fractions which accounted for ca. 31-66% (0.42 and 0.52 ppm) of the extractable residues in tuber and 21-30% (0.96-1.81 ppm) in foliage.

Residue method validation

Samples from this study were not analyzed by an enforcement method.

Storage stability

Samples were stored frozen at -20 C prior to analysis; sample storage intervals were not reported.

In summary, the qualitative nature of aldicarb residues in potatoes is not adequately understood. The reformatted study does not present any new data and is inadequate to fulfill 171-4 (a) guideline requirements for similar reasons as those explained in the Update and additional deficiencies which are listed below: (i) data pertaining to the total radioactive residues present at the time of harvest are lacking since the registrant did not combust the potato tuber and foliage samples prior to residue extraction; (ii) the study failed to characterize/identify the aqueous-soluble fractions which accounted for ca. 31-66% (0.42 and 0.52 ppm) of the extractable residues in tuber and 21-30% (0.96-1.81 ppm) in foliage; (iii) information pertaining to the magnitude or nature of non-extractable residues was not provided; (iv) the organosoluble metabolites tentatively identified by two-dimensional TLC were not confirmed by a second method; (v) raw data (e.g. dpm data for extractions in a flow chart, sample weights, counting efficiencies, quantitative data associated with chromatograms, sample calculations, etc.) were not reported making it difficult to validate the reported results; and (vi) information pertaining to the storage intervals of samples between harvest, extraction, and analysis was not provided. CBRS does not believe that this study is upgradeable since it is unlikely that the registrant would be able to conduct further analyses on samples collected between 1972 and 1978 and provide supporting storage stability data.

Sugar beets

In-life phase

Rhone-Poulenc submitted data (1992; MRID 42436602) from two studies depicting the metabolism of [^{14}C]aldicarb in sugar beets. These data represent reformatted versions of previously submitted sugar beet metabolism studies submitted in 1970 under MRID 00102178 (1970) and reviewed in the Aldicarb Residue Chemistry Science Chapter dated 11/83. In the first study, sugar beets (Spreckels monogram variety) were grown in clay pots containing either a mixture of peat moss and red mortar sand (C-mix; 1:1; w:w) or Norfolk sandy loam soil. [S-methyl-^{14}C]Aldicarb (5.85 mCi/mmol; radiochemical purity >98.5%) was applied 28 days after planting into the soil at an equivalent rate of 20 lb ai/A. This rate is 4.9x the maximum registered postemergence application rate. Radiolabeled aldicarb was mixed with unlabeled granular formulation of aldicarb to give a final specific activity of 0.11 mCi/mmol. Samples of tops were collected 7, 14, 28, 67, 90, and 140 days posttreatment while samples of sugar beets were collected 90 and 140 days posttreatment. Two plants were collected at each sampling date. Sample storage conditions and intervals between sampling, extraction, and analysis were not reported.

A second study was conducted for the purpose of obtaining samples bearing detectable radioactive residues of aldicarb and its metabolites for residue method validation. Greenhouse-grown sugar beets were grown for 80 days in C-mix and then treated with [S-methyl-^{14}C]aldicarb by injecting a stock solution (containing radiolabeled aldicarb in acetone; 3024 dpm/μg specific activity) into the beet portion of each plant using a glass capillary; ca. 200 μg was applied to each beet. Samples of tops and beets were collected 20 days following treatment. Sample storage conditions and intervals between sampling, extraction, and analysis were not reported.

Total radioactive residues (TRR)

Soil application study: The registrant calculated total radioactive residues by summation of the ^{14}C-activity present as tentatively identified components, material retained at the TLC origin, and aqueous-soluble residues. These values reflect only the total extractable ^{14}C-activity. Tables 12 and 13 present the extractable radioactive residues in tops and roots, respectively. The extractable radioactivity was determined by scraping radioactive zones from TLC plates and analyzing by liquid scintillation spectrometry (LSS). The LSS limit of detection was not reported.

The registrant did not combust the samples prior to residue extraction. For metabolism studies, CBRS prefers that the treated raw agricultural commodities be initially analyzed for TRR by combustion/LSS prior to any solvent extraction and further laboratory workup. This procedure will allow CBRS to determine the material balance on the commodities of interest and check whether any losses occurred during extraction and other analytical phases of the study.

Injection study: The registrant calculated total radioactive residues by summation of the ^{14}C-activity present as extractable and non-extractable residues. The extractable residues were calculated by summation of ^{14}C-activity present as tentatively identified components, material retained at the TLC origin, and aqueous-soluble residues, and were determined by scraping radioactive zones from TLC plates and analyzing by liquid scintillation spectrometry (LSS). Non-extractable residues were determined by combustion/LSS. The registrant did not combust the samples prior to residue extraction.

Extraction/characterization of residues

Soil application study: The top and root samples were homogenized in ethanol:water (1:1; v:v) and then filtered. The remaining solid residues were washed twice with ethanol:water (1:1; v:v) and filtered. The filtrates were combined, concentrated under vacuum at 40 C, then diluted with water; aliquots were removed for analysis by LSS. The aqueous extract was partitioned three times with chloroform:acetonitrile (1:1; v:v). The organosoluble extracts were combined, dried with anhydrous sodium sulfate, and filtered. Both fractions were analyzed for radioactivity by LSS. The registrant did not provide raw data (e.g. dpm data for extractions in a flow chart, sample weights, counting efficiencies, etc.) pertaining to LSS analysis of extracts. The extraction efficiencies could not be calculated since combustion analysis of samples prior to extraction was not conducted. The registrant provided data pertaining to extraction efficiencies from another unacceptable cotton metabolism studies. However, these data cannot be translated to this study. No information pertaining to the amount of non-extractable residues was provided.

Injection study: Top and root samples were extracted in the same manner as described for the soil application study. The registrant did not provide raw data (e.g. dpm data for extractions in a flow chart, sample weights, counting efficiencies, etc.) pertaining to LSS analysis of extracts. The extraction efficiencies could not be calculated since combustion analysis of samples prior to extraction was not conducted. The distribution of radioactivity in the organosoluble, aqueous-soluble, and non-extractable fractions of tops and beets is presented in Table 12. No further work was conducted on the extracts of sugar beets.

Table 12. Registrant-calculated total radioactive residues in/on sugar beet tops and sugar beets following a single application of [^{14}C]aldicarb by injection into the beet.

	Registrant-calculated TRR, [^{14}C]aldicarb equivalents [a]						
	Organosoluble		Aqueous-soluble		Nonextractable		Total
Commodity	ppm	% [b]	ppm	% [b]	ppm	% [b]	ppm
Sugar beet tops	2.44	64.7	1.26	33.4	0.07	1.9	3.77
Sugar beets	0.01	6.3	0.14	87.5	0.01	6.3	0.16

[a] Average of three determinations.
[b] Based on registrant-calculated TRR values.

Metabolite identification

Soil application study: The organosoluble extracts were analyzed by two-dimensional TLC on silica gel plates developed with various solvent systems. Solvent systems of ether:hexane (2:1; v:v) in 20% acetone and methylene chloride:acetonitrile (3:2; v:v) were listed. The registrant referenced two published journal articles which contain additional solvent systems. Metabolites were tentatively identified by co-chromatography with reference standards having known R_f values. Radioactive areas were detected by autoradiography and tentatively identified by co-chromatography with reference standards having known R_f values. Non-radioactive standards were visualized by short-wave UV light, exposure to iodine vapors, and/or spraying with potassium permanganate solution. The registrant reported the results in summary tables and provided meager or no raw data (e.g. quantitative data associated with chromatograms, sample calculations, etc.). Therefore, independent verification of these residue values cannot be made.

The tentatively identified metabolites were not confirmed by a second method. The registrant reported data pertaining to the confirmation of aqueous-soluble metabolites identified in a cotton metabolism study; these data cannot be translated since only organosoluble metabolites were identified in the study in review. The identification of ^{14}C-residues found in sugar beet tops and roots remains tentative. Tables 13 and 14 indicate that the registrant tentatively identified ca. 50-82% (9-82 ppm) of the extractable residues in sugar beet tops. Table 14 indicates that the registrant tentatively identified ca. 25-35% (0.67-0.88 ppm) of the extractable residues in sugar beet roots. The major metabolites found were aldicarb sulfoxide and aldicarb sulfone. The registrant did not characterize/identify the aqueous-soluble fractions which accounted for ca. 62-74% (1.6-2.0 ppm) of the extractable residues in sugar beets and ca. 15-48% (6-15 ppm) of the extractable residues in sugar beet tops.

Table 13. Distribution of tentatively identified metabolites in sugar beet tops following a single soil broadcast application of [^{14}C]aldicarb at 4.9x.

Growth Medium	Total extractable residues							
	7-day PTI		14-day PTI		28-day PTI		67-day PTI	
Metabolite	%	ppm	%	ppm	%	ppm	%	ppm
C-mix-grown								
Aldicarb	1.07	0.64	1.50	1.49	ND [b]	ND	ND	ND
Aldicarb SO [a]	68.45	41.65	61.73	61.66	35.11	16.92	18.01	5.64
Aldicarb SO_2 [a]	7.92	4.82	15.02	15.00	24.53	11.82	27.04	8.47
Combined Residues [c]	77.44	47.11	78.25	78.15	59.64	28.74	45.05	14.11
Oxime SO	0.10	0.06	0.19	0.19	1.36	0.66	0.35	0.11
Oxime SO_2	0.08	0.04	0.45	0.45	0.53	0.26	0.68	0.21
Nitrile SO	0.75	0.46	3.23	3.23	4.41	2.13	1.35	0.42
Nitrile SO_2	ND	ND	ND	ND	3.12	0.50	2.17	0.68
Alcohol SO_2	ND	ND	ND	ND	ND	ND	1.01	0.32
Total identified	78.37	47.67	82.12	82.02	69.06	32.29	50.61	15.85
TLC origin	1.19	0.73	2.55	2.55	1.18	0.57	4.55	1.42
Aqueous-soluble	20.44	12.12	15.33	15.31	29.76	14.34	44.84	14.04
Total	100	60.53	100	99.98	100	47.20	100	31.31
Soil-grown								
Aldicarb	–	–	1.39	0.32	ND	ND	ND	ND
Aldicarb SO	–	–	43.35	9.83	30.51	5.78	39.98	7.62
Aldicarb SO_2	–	–	12.53	2.84	29.30	5.56	22.23	4.24
Combined Residues [c]	–	–	57.27	12.99	59.81	11.34	62.21	11.86
Oxime SO	–	–	0.17	0.04	0.68	0.13	0.44	0.08
Oxime SO_2	–	–	0.43	0.10	0.74	0.14	0.50	0.10
Nitrile SO	–	–	3.64	0.83	1.74	0.33	1.22	0.23
Nitrile SO_2	–	–	ND	ND	0.82	0.16	1.29	0.25
Alcohol SO_2	–	–	ND	ND	0.47	0.09	0.07	0.01
Total identified	–	–	61.51	13.96	64.26	12.19	65.73	12.53
TLC origin	–	–	1.12	0.25	1.85	0.35	1.53	0.29
Aqueous-soluble	–	–	37.37	8.48	33.89	6.43	32.74	6.24
Total	–	–	100	22.69	100	18.97	100	19.06

[a] SO = sulfoxide; SO_2 = sulfone.
[b] Not detected; detection limits were not reported.
[c] Combined residues of aldicarb, aldicarb sulfoxide, and aldicarb sulfone; calculated by study reviewer.

Table 14. Distribution of tentatively identified metabolites in sugar beet tops and roots following a single soil broadcast application of [^{14}C]aldicarb at 4.9x.

	Total extractable residues							
	90-day PTI				140-day PTI			
	Tops		Roots		Tops		Roots	
Metabolite	%	ppm	%	ppm	%	ppm	%	ppm
Aldicarb	ND[a]	ND	ND	ND	ND	ND	ND	ND
Aldicarb SO[b]	13.48	2.47	12.17	0.33	9.84	2.67	12.73	0.32
Aldicarb SO_2[b]	25.35	4.64	8.75	0.24	30.81	8.36	11.25	0.28
Combined Residues[c]	38.83	7.11	20.92	0.57	40.65	11.03	23.98	0.60
Oxime SO	0.21	0.04	1.21	0.03	0.10	0.03	1.64	0.04
Oxime SO_2	1.11	0.20	0.34	0.01	1.18	0.32	3.46	0.09
Nitrile SO	0.62	0.11	ND	ND	2.43	0.66	1.18	0.03
Nitrile SO_2	0.71	0.13	0.40	0.01	2.43	0.66	0.47	0.01
Alcohol SO_2	8.92	1.63	1.93	0.05	12.37	3.36	4.45	0.11
Total identified	**50.40**	**9.22**	**24.80**	**0.67**	**59.09**	**16.06**	**35.18**	**0.88**
TLC origin	1.29	0.24	1.20	0.03	3.09	0.84	2.71	0.07
Aqueous-soluble	48.31	8.85	74.00	2.00	37.75	10.25	62.11	1.57
Total	**100**	**18.31**	**100**	**2.70**	**100**	**27.15**	**100**	**2.52**

[a] Not detected; detection limits were not reported.
[b] SO = sulfoxide; SO_2 = sulfone.
[c] Combined residues of aldicarb, aldicarb sulfoxide, and aldicarb sulfone; calculated by study reviewer.

Injection study: Organosoluble extracts of sugar beet tops were analyzed in the same manner as described for the soil application study. The metabolites identified in sugar beet tops are presented in Table 15. The registrant reported the results in summary tables and provided meager raw data. No confirmatory analyses were conducted; therefore, the identification of ^{14}C-residues remains tentative. The registrant tentatively identified ca. 63% (2.4 ppm) of registrant-calculated TRR in sugar beet tops. The registrant did not characterize/identify the aqueous-soluble fraction which accounted for ca. 34% (1.3 ppm) of registrant-calculated TRR.

Table 15. Distribution of tentatively identified metabolites in sugar beet tops following a single application of [^{14}C]aldicarb by injection into the beet.

Metabolite	Registrant-calculated TRR	
	% [a]	ppm
Aldicarb	ND [b]	ND
Aldicarb SO [c]	31.09	1.18
Aldicarb SO_2 [c]	25.04	0.94
Combined Residues [d]	56.13	2.12
Oxime SO	0.43	0.02
Oxime SO_2	1.46	0.06
Nitrile SO	2.44	0.10
Nitrile SO_2	2.33	0.09
Alcohol SO_2	0.49	0.02
Total identified	**63.28**	**2.41**
TLC origin	0.92	0.04
Aqueous-soluble	33.94	1.26
Total	**98.14**	**3.71**

[a] Data were recalculated by study reviewer to reflect percent of registrant-calculated TRR instead of percent extractable radioactivity.
[b] Not detected; detection limits were not reported.
[c] SO = sulfoxide; SO_2 = sulfone.
[d] Combined residues of aldicarb, aldicarb sulfoxide, and aldicarb sulfone; calculated by study reviewer.

Residue method validation

Samples from the injection study were analyzed by an undescribed GC method. The total combined residues of aldicarb, aldicarb sulfoxide, and aldicarb sulfone were 2.40 ppm in sugar beet tops as determined by GC; this compares well with the value of 2.12 ppm as determined by TLC analysis (see Table 15). The registrant did not provide raw data nor information (descriptions, conducting laboratory, etc.) pertaining to the GC method of analysis. This study may be useful in satisfying requirements for radiovalidation of the analytical method provided that a complete description of the GC method used to analyze the samples is submitted.

Storage stability

Sample storage conditions and intervals between sampling, extraction, and analysis were not reported.

In summary, the qualitative nature of aldicarb residues in sugar beets is not adequately understood. The reformatted study does not present any new data and is inadequate to fulfill 171-4 (a) guideline requirements for similar reasons as those explained in the Update and additional deficiencies which are listed below: (i) data pertaining to the total radioactive residues present at the time of harvest are lacking since the registrant did not combust the sugar beet top and root samples prior to residue extraction; (ii) the soil application study failed to characterize/identify the aqueous-soluble fractions which accounted for ca. 62-74% (1.6-2.0 ppm) of the extractable residues in sugar beet roots and ca. 15-48% (6-15 ppm) of the extractable residues in sugar beet tops; (iii) information pertaining to the

magnitude or nature of non-extractable residues was not provided; (iv) the organosoluble metabolites tentatively identified by two-dimensional TLC were not confirmed by a second method; (v) raw data (e.g. dpm data for extractions in a flow chart, sample weights, counting efficiencies, quantitative data associated with chromatograms, sample calculations, etc.) were not reported making it difficult to validate the reported results; and (vi) information pertaining to the storage intervals of samples between harvest, extraction, and analysis was not provided. CBRS does not believe that this study is upgradeable since it is unlikely that the registrant would be able to conduct further analyses on samples collected before 1970 and provide supporting storage stability data.

Storage Stability Data

Potato Processed Commodities

Rhone-Poulenc (1992; MRID 42467301) submitted data depicting the frozen storage stability of aldicarb residues of concern in potato processed commodities. Samples of processed fractions (potato chips, flakes, granules, and wet and dry peel) that were obtained from Texas A&M University each were fortified with a mixture of aldicarb, aldicarb sulfoxide, and aldicarb sulfone at 0.3 ppm. The fortified samples were frozen at ca. -20 C, then removed from storage after 2-, 4-, and 6-week intervals and analyzed using an HPLC method (RPAC SOP 90015). One untreated control and one fortified sample, as well as the stored samples, were analyzed at each interval. The registrant reported results in summary tables and did not submit raw data, other than representative chromatograms.

The frozen storage stability data for potato processed commodities are presented in Table 14. The available storage stability data indicate that residues of aldicarb, aldicarb sulfoxide, and aldicarb sulfone were stable for up to six weeks of frozen storage in potato wet peel, dry peel, and flake; residues of aldicarb sulfoxide and aldicarb sulfone were stable for up to six weeks of frozen storage in potato chips and granules. Residues of aldicarb were stable for up to four weeks of frozen storage in potato chips and granules.

Samples of potato processed commodities were analyzed using an HPLC method (RPAC SOP 90015). The registrant included a brief description of the method; however, a complete description of this method was not submitted. We note that the data collection methods discussed in the Residue Chemistry Chapter of the Reregistration Standard and the enforcement methods listed in PAM Vol. II are GC/FPD methods. Samples of granules and peels (wet and dry) were extracted with methanol:water (75:25; v:v); chip and flake samples were extracted with acetone:water (3:1; v:v). The extracts were partitioned with methylene chloride and purified on a Florisil column. Residues of aldicarb, aldicarb sulfoxide, and aldicarb sulfone were separated by reverse-phase HPLC using an unspecified mobile phase and an unspecified column. Following separation, metabolites were subjected to post-column hydrolysis which releases methylamine from each compound. Methylamine was derivatized with o-phthalaldehyde and mercaptoethanol to yield a fluorescent product, 1-(2-hydroxyethyl)thio-2-methyl isoindole, which was detected using a fluorescence detector. Parent and metabolite concentrations were quantified from a calibration curve prepared from peak area responses of standards. The detection limit was 0.02 ppm for each compound. Analyses were conducted by Rhone-Poulenc (Research Triangle Park, NC). Sample chromatograms were included. The registrant provided data from concurrent method recoveries; these data are presented in Table 15. The data indicate that this method is adequate for data collection from potato processed commodities. However, a complete description of the method must be submitted.

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Table 14. Frozen storage stability of aldicarb residues of concern in processed potato commodities fortified with aldicarb, aldicarb sulfoxide, and aldicarb sulfone at 0.3 ppm.

Matrix	No. of	Percent Recovery [a]		
Storage Interval (days)	Samples	Aldicarb	Aldicarb Sulfoxide	Aldicarb Sulfone
Wet peel				
19	3	94.0-94.7	89.7-104.0	87.0-96.3
33	3	88.3-91.6	91.0-96.7	91.7-96.0
47	3	87.0-103.0	90.3-113.6	103.6-122.3
Flake				
14	3	86.0-91.7	90.7-97.7	87.3-94.0
28	3	82.0-101.3	89.3-93.0	86.7-101.7
43	3	85.7-97.3	92.3-105.0	80.3-89.3
Chips				
15	3	85.3-107.0	71.3-79.0	81.3-89.7
28	3	65.7-105.3	66.0-76.0	67.0-83.7
43	3	52.0-74.3 [b]	100.3-125.7	78.3-96.7
Granules				
19	3	82.7-90.3	89.3-91.3	97.7-100.7
33	3	58.0-97.0	92.3-94.7	89.7-94.3
53	3	23.7-30.0 [b]	109.0-117.3	72.0-75.3
Dry Peel				
22	3	85.3-98.7	84.0-96.7	83.3-98.7
36	3	101.0-104.7	101.3-118.3	96.0-104.7
50	3	84.3-94.3	85.7-95.0	80.3-87.7

[a] All values are corrected for concurrent method recoveries (see Table 15).
[b] Average recovery less than 70%.

Table 15. Analytical method validation and concurrent method recovery data for potato processed commodities fortified with aldicarb, aldicarb sulfoxide, and aldicarb sulfone fortified at 0.3 ppm (concurrent method recovery data) and 1.0 ppm (method validation data).

Matrix	Storage Interval (days) [a]	No. of Samples	Percent Recovery		
			Aldicarb	Aldicarb Sulfoxide	Aldicarb Sulfone
Dry peel	-- [b]	5	80.7-85.4	67.5-75.1	79.2-88.6
	22	1	83.1	79.9	86.9
	36	1	78.3	70.4	84.4
	50	1	80.7	85.3	85.6
Wet peel	--	5	76.0-84.4	76.0-79.5	85.3-89.3
	19	1	86.5	74.1	88.1
	33	1	85.3	77.6	82.9
	47	1	76.9	87.2	83.0
Granules	--	5	80.7-90.6	74.6-104.3	82.8-90.6
	19	1	81.2	90.2	83.7
	33	1	89.4	77.6	90.4
	53	1	82.6	85.2	85.3
Flakes	--	4	71.6-88.6	66.6-75.7	78.3-88.0
	14	1	91.5	76.2	95.7
	28	1	71.6	100.7	91.7
	43	1	85.2	78.2	92.2
Chips	--	4	71.7-84.6	84.6-96.0	84.6-91.6
	15	1	61.0	115.7	92.6
	28	1	60.5	118.9	94.4
	43	1	76.7	78.3	83.4

[a] Concurrent method recovery at the indicated storage stability study interval.
[b] Method validation data.

Soybean Processed Commodities

Rhone-Poulenc (1992; MRID 42467302) submitted data depicting the frozen storage stability of aldicarb residues of concern in/on soybeans and in soybean processed commodities. Samples of soybeans and soybean processed fractions (hulls, meal, crude oil, refined oil, soapstock, and grain dust) obtained from Texas A&M University were fortified with aldicarb, aldicarb sulfoxide, and aldicarb sulfone at 0.02 ppm. The fortified samples were frozen at ca. -20 C, then removed from storage at ca. 2-, 4-, and 6-week intervals and analyzed using an HPLC method (RPAC SOP 90025). One untreated control and one fortified sample, as well as the stored samples, were analyzed at each interval. The registrant reported results in summary tables and did not submit raw data, other than representative chromatograms. We note that the registrant stated that the method limit of detection was 0.02 ppm for each compound; however, results as low as 0.001 ppm were reported by the registrant.

The frozen storage stability data for soybean processed commodities are presented in Table 16. The available storage stability data indicate that residues of aldicarb, aldicarb sulfoxide, and aldicarb sulfone were stable for up to six weeks of frozen storage in/on soybeans and in soybean meal, hulls, crude and refined oil, and grain dust. The data also indicate that residues of aldicarb were stable for up to six weeks of frozen storage in soybean soapstock but that residues of aldicarb sulfoxide and aldicarb sulfone declined to less than 5% after two weeks frozen storage.

Samples of soybean processed commodities were analyzed using an HPLC method employing fluorescence detection (RPAC SOP 90025). Samples of soybeans and soybean hulls, meal, and grain dust were extracted with methanol:water (65:35; v:v) and filtered. The filtrate was partitioned with methylene chloride and the organic layer was passed through anhydrous sodium sulfate. Samples of soybean crude and refined oil were extracted with hexane and filtered. The filtrate was partitioned with acetonitrile. Samples of soybean soapstock were extracted with acetonitrile and filtered. Water was added and the pH of the extract was adjusted to 5-7 by dropwise addition of concentrated hydrochloric acid. The neutralized extract was partitioned four times with hexane and passed through anhydrous sodium sulfate. Organosoluble residues were evaporated to dryness at 45 C under a stream of air. Dried residues were redissolved in acetone, purified on a column containing activated charcoal, evaporated to dryness (as previously), and redissolved in water. Samples were injected onto a Zorbax phenyl column equipped with and a post-column reactor to hydrolyze aldicarb, aldicarb sulfoxide, and aldicarb sulfone, resulting in the release of methylamine. Methylamine was derivatized with o-phthalaldehyde and mercaptoethanol yielding a fluorescent product, 1-(2-hydroxyethyl)thio-2-methyl isoindole, which was detected using a fluorescence detector. A gradient mobile phase of acetonitrile:water was used (10:90, v:v to 75:25, v:v). Parent and metabolite concentrations were quantified from a calibration curve prepared from peak area responses of standards. The limit of detection was 0.02 ppm for each compound. Analyses were conducted by Rhone-Poulenc (Research Triangle Park, NC). Sample chromatograms were included. The registrant included data from concurrent method recoveries; these data are presented in Table 17. The data indicate that this method is adequate for data collection from soybean processed commodities.

In summary, the submitted storage stability data for potato processed commodities and soybean processed commodities are incomplete to satisfy data requirements because data were not supported by complete raw data. Summary data unsupported by raw data are unacceptable; individual analyses representing each residue value must be reported to enable the agency to verify the reported residue results. Furthermore, a complete description of the HPLC method used to determine aldicarb residues of concern in potato processed commodities (RPAC SOP 90015) must be submitted. These studies are potentially upgradeable if the registrant submits the required raw data for potato and soybean processed commodities and a complete method description for the determination of aldicarb residues of concern in potato processed commodities. If the required plant metabolism studies indicate that other metabolites of concern are identified, then additional storage stability data of these metabolites in the processed commodities of potatoes and soybeans may be required.

Table 16. Frozen storage stability of aldicarb residues of concern in/on soybeans and in soybean processed commodities fortified with aldicarb, aldicarb sulfoxide, and aldicarb sulfone at 0.02 ppm.

Matrix	No. of	Percent Recovery [a]		
Storage Interval (days)	Samples	Aldicarb	Aldicarb Sulfoxide	Aldicarb Sulfone
Soybeans				
20	3	80-90	85-110	80-95
28	3	70-75	65-85	65-90
44	3	80-90	100	85-100
Meal				
14	3	90	85-100	90
28	3	90-100	90-115	60-90
44	3	90-95	85-120	95-105
Hulls				
20	3	85	95	80-85
27	3	90-100	105-120	125-135
47	3	90-120	90-120	100-130
Refined oil				
14	3	95-100	80-90	95-100
28	3	95-110	100	90-115
48	3	100-105	95-100	130-135
Crude oil				
14	3	95-105	85-100	115-120
28	3	105-110	90-110	100-105
48	3	105	100-110	110
Soapstock				
14	3	80-85	ND [b]-5	ND
28	3	50-70 [c]	ND	ND
48	3	60-90	ND	ND
Grain dust				
44	2	80, 85	90, 110	80, 85

[a] All values are corrected for concurrent method recoveries (see Table 17).
[b] Not detected.
[c] Average recovery less than 70%.

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Table 17. Analytical method validation and concurrent method recovery data for soybean processed commodities fortified with aldicarb, aldicarb sulfoxide, and aldicarb sulfone at 0.02 ppm.

Matrix	Storage Interval (days) [a]	No. of Samples	Percent Recovery		
			Aldicarb	Aldicarb Sulfoxide	Aldicarb Sulfone
Soybeans	– [b]	4	74.6-81.9	72.3-85.9	84.9-89.7
	20	1	85.5	77.1	88.9
	28	1	80.7	70.6	79.6
	44	1	93.2	74.1	86.1
Hulls	–	4	75.4-82.9	67.6-77.9	85.9-89.0
	20	1	83.1	75.0	100.1
	27	1	75.9	61.3	78.8
	47	1	93.0	87.4	84.0
Meal	–	4	77.4-79.0	68.2-102.2	83.5-88.1
	14	1	83.0	70.9	81.6
	28	1	75.8	61.3	77.1
	44	1	93.6	83.6	89.1
Refined oil	–	4	92.1-103.2	86.7-96.7	79.6-118.8
	14	1	98.0	95.1	100.2
	28	1	92.9	85.7	92.2
	48	1	90.1	94.7	73.1
Crude oil	–	4	90.0-102.9	71.0-83.7	80.3-89.1
	14	1	96.3	91.5	97.2
	28	1	87.8	82.6	95.0
	48	1	89.0	83.0	92.2
Soapstock	–	4	85.7-92.8	74.3-99.2	85.5-90.8
	14	1	76.2	84.8	64.4
	28	1	77.0	55.4	91.4
	48	1	76.9	108.4	77.2
Grain dust	–	1	75.8	71.6	87.2
	44	1	92.6	77.7	95.0

[a] Concurrent method recovery at the indicated storage stability study interval.
[b] Method validation data.

MASTER RECORD IDENTIFICATION NUMBERS

The citations for the MRID documents referred to in this review are presented below.

References Used:

42436602 Bagley, W.P. and N.R. Andrawes (1992) Metabolism and associated residues of TEMIK (2-methyl-2-(methylthio)propionaldehyde-O-(methylcarbamoyl)oxime (TEMIK) in sugar beet plants: Project No. 111B19, File No. 12694. Unpublished study prepared by Rhone-Poulenc Ag Company (Research Triangle Park, NC) in cooperation with Hazard Evaluation & Regulatory Affairs Company (H.E.R.A.C., Greensboro, NC). 52 p.

42436603 Andrawes, N.R. (1992) The metabolism and terminal residues of "TEMIK" aldicarb pesticide in peanut plants under field conditions: Project No. 111A12, File No. 17613. Unpublished study prepared by Rhone-Poulenc Ag Company (Research Triangle Park, NC) in cooperation with Hazard Evaluation & Regulatory Affairs Company (H.E.R.A.C., Greensboro, NC). 47 p.

42436604 Bagley, W.P. and N.R. Andrawes (1992) Metabolism and associated residues of TEMIK (2-methyl-2-(methylthio) propionaldehyde-O-(methylcarbamoyl)oxime (TEMIK) in potato foliage: Project No. 111B19, File No. 10495. Unpublished study prepared by Rhone-Poulenc Ag Company (Research Triangle Park, NC) in cooperation with Hazard Evaluation & Regulatory Affairs Company (H.E.R.A.C., Greensboro, NC). 44 p.

42436605 Bagley, W.P. and N.R. Andrawes (1992) Metabolism of (2-methyl-2-(methylthio) propionaldehyde-O-(methylcarbamoyl)oxime (TEMIK aldicarb pesticide) in potato plants. Unpublished study prepared by Rhone-Poulenc Ag Company (Research Triangle Park, NC) in cooperation with Hazard Evaluation & Regulatory Affairs Company (H.E.R.A.C., Greensboro, NC). 60 p.

42436606 Bagley, W.P., R.R. Romaine, and N.R. Andrawes (1992) Metabolism and residues of TEMIK aldicarb pesticide in cotton foliage and seed under field conditions. Unpublished study prepared by Rhone-Poulenc Ag Company (Research Triangle Park, NC) in cooperation with Hazard Evaluation & Regulatory Affairs Company (H.E.R.A.C., Greensboro, NC). 82 p.

42467301 Tew, E.L. (1992) Aldicarb - Stability of residues on frozen potato processed fractions. RPAC Project No. EC-92-201, File No. 41265. Unpublished study prepared by Rhone-Poulenc Ag Company (Research Triangle Park, NC). 62 p.

42467302 Tew, E.L. (1992) Aldicarb - Stability of residues on frozen soybean processed fractions. RPAC Project No. EC-92-200, File No. 41256. Unpublished study prepared by Rhone-Poulenc Ag Company (Research Triangle Park, NC). 54 p.

References Not Used:

[The following MRID was not reviewed in this document since the study is unacceptable according to plant metabolism study guideline because the study mainly pertains to the metabolism of aldicarb in callus tissue cultures of potato tuber and citron fruit, and were submitted in the form of a Ph.D. dissertation with incomplete raw data.]

42017401 Stratton, G.D. (1986) Metabolism of aldicarb, aldicarb sulfoxide, and aldicarb sulfone in potato plants and in plant callus tissue cultures of potato tuber and citron fruit. A dissertation presented to the graduate school of the University of Florida in partial fulfillment of the requirements for the degree of Doctor of Philosophy. 261 p.

[The following MRID was not reviewed in this document since the data are duplicate summaries of the studies for cotton, peanuts, potatoes, and sugar beets as well as published information (without raw data) on the metabolism of aldicarb in lettuce, spearmint, and tobacco.]

42436601 Honeycutt, R.C. and N.R. Andrawes (1992) Summary report on the nature of the residues of [^{14}C]aldicarb in plants. Summary report prepared by Rhone-Poulenc Ag Company (Research Triangle Park, NC) in cooperation with Hazard Evaluation & Regulatory Affairs Company (H.E.R.A.C., Greensboro, NC). H.E.R.A.C. Report No. 92-102. 70 p.