Key Hard File 12-10-90

Case No.: 2675
Chemical No(s).: 114501



## CBRS TRANSMITTAL SHEET FOR PHASE 4 REVIEWS

Transmitted to HED on 9/29/90
Case name: Thiodicarb
Chemical name(s): Thiodicarb
Data submitter(s): Rhone-Poulenc Ag Company

CRM: Linda Deluise Phone #: 308-8066

Issues/flags:

This action contains a request for a DATA WAIVER ( )
TIME EXTENSION ( )
ALTERED/DELETED USE ( )

Other: LUIS output dated 10/25/90 and labels acquired from the Registration Division were used when reviewing this package.

Branch: CBRS, Phase 4 Review Team
Reviewed by: Christine L. Olinger CLO Date: 12-7-90

12/7/90

Approvals:

Section Head: Andrew Rathman ARR Date: 12/10/90

Branch Approval: Edward Zager EZ Date: 12/10/90

cc: CLOlinger, List B File, Ciru. (7), B. Grim (EFED), C. Furlow (FOD/PIB)

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Response, by Guideline

Guideline #: 171-4(a) Description: Nature of residue - plants
Is requirement applicable? (Y/N): Y
Does the summary/available information indicate that the MRID is a candidate for Phase 5 review?: N
MRID Nos.: 40170401, 40116705, 44068, 44069, 44070, 44071, 44072, 44073, 44068, 44069, 71182, 72237, 159815, 92185-033 through -037, 92185-040, 92185-042, 92185-062 through -067
Discussion: Most of these studies do not completely satisfy the acceptance criteria. Particularly there has not been complete characterization of the Total Radioactive Residue (TRR) and/or the residues in the RAC used as food were not characterized. However there may be sufficient information from these studies and the metabolism of methomyl (the monomer of thiodicarb) to propose a metabolic pathway and the metabolites/degradates which require regulation. Additional information is required before these studies may be reviewed and is outlined under "Data Gap".
Data gap: Residues of thiodicarb and its metabolites/degradates are quantified only as percent of the applied dose or TRR, and not in parts per million in/on the plant matrix. The amount of plant matrix used for analysis was not provided, which would allow CBRS to calculate the concentrations. Before CBRS can concur with the registrant's assessment that the residues in/on the food items are too low to characterize, the concentration values must be added to the reformatted reports.

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Guideline #: 171-4(b) Description: Nature of residue - animals
Is requirement applicable? (Y/N): Y
Does the summary/available information indicate that the MRID is a candidate for Phase 5 review?: P-additional data are required to fulfill this requirement
MRID Nos.: 40824802, 40824805, 00044075, 92185044, 92185068
Discussion: The registrant has committed to provide a new ruminant metabolism study and has submitted a summary of a laying hen metabolism study.

Three groups of laying hens were dosed with radiolabelled thiodicarb for 21 days at a level of 15.4, 28.6, or 102 ppm. Hens were sacrificed six hours, three days, or seven days after the final dose. Thiodicarb, methomyl, and methomyl derivatives were not detected in any sample at an unreported limit of determination. Acetonitrile was detected

in all tissues (with the exception of fat) at all dose levels; acetamide was found in some tissues only at the highest dose level. Only 0-35% of the total radioactive residue (TRR) was characterized in any tissue. The TRR ranged from a minimum of 0.46 ppm (thiodicarb equivalents) in breast muscle at the 15.4 ppm feeding level to 10.89 ppm (thiodicarb equivalents) in liver at the 102 ppm feeding level. Given the high levels found CBRS would have expected a greater degree of residue characterization.

The degree of characterization is below the level typically accepted. The registrant believes further characterization of the TRR would be extremely difficult since they have concluded thiodicarb is extensively metabolized and incorporated into natural constituents. This study may be considered acceptable if the ruminant metabolism study corroborates these findings.

Data gap: The registrant must provide a ruminant metabolism study. Thiodicarb labelled in a non-labile part of the molecule should be fed to the livestock for a minimum of three days. Orally treated test animals must be sacrificed within 24 hours of the final dose. The dose administered and the specific activity should be high enough to allow for adequate identification of the metabolites/degradates. The tissues from the metabolism study should be tested using the data collection method(s) and enforcement analytical method(s).

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Guideline #: 171-4(c) Description: Res. analyt. method - plant
Is requirement applicable? (Y/N): Y
Does the summary/available information indicate that the MRID is a candidate for Phase 5 review?: P - additional data are required to fulfill this requirement

MRID No.: 41250009, 92185045

Discussion: The registrant has committed to providing additional data, but hasn't specified the type of study to be conducted. Most of the methods (including the enforcement method) previously submitted were determined to be inadequate. However the PAM II method has been successfully validated in Agency laboratories. Adequate fortifications have been conducted with the crop field trials. The registrant may be able to fulfill this requirement with a description of existing methodology along with a summary of fortifications conducted in conjunction with acceptable field trials.

Data gap: The registrant must present descriptions (including

validation data) of **all** enforcement and data collection methods for the determination of thiodicarb and its metabolite methomyl in/on plant matrices. If sufficient fortification data exist (e.g. from a crop field trial or processing study) for a method and the raw data are available to support the study, then the registrant may be able to combine the method report with existing fortification and radiovalidation data. If not then new data must be presented. Any **new** regulatory methods submitted will require an independent method validation as described in PR Notice 88-5 (July 15, 1988).

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Guideline #: 171-4(d) Description: Res. anal. method - animals
Is requirement applicable? (Y/N): Y
Does the summary/available information indicate that the MRID is a candidate for Phase 5 review?: P - additional data are required to fulfill this requirement
MRID Nos. 41250010, 41250011, 00144618, 92185046, 92185047
Discussion: Tolerances have not been established for residues of thiodicarb or any metabolites in/on any animal commodities. The registrant has submitted methods for the determination of the metabolites acetamide in milk and acetonitrile and acetamide in meat, milk, and eggs. These methods may be adequate if it is determined during or before Phase 5 that these chemicals will require regulation. At this time CBRS considers this a data gap because additional metabolites which require regulation may be found in the metabolism study.
Data gap: The registrant must submit data collection and regulatory analytical method(s) for the determination of thiodicarb and its metabolites in/on animal commodities. If metabolites (which require regulation) are found in the new animal metabolism studies, then analytical method(s) must be developed for them as well. Any regulatory methods submitted will require an independent method validation as described in PR Notice 88-5 (July 15, 1988). Any new metabolites found in the new metabolism study must be tested through multi-residue Protocol(s) C, D, and E (and possibly B as well).

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Guideline #: 171-4(e) Description: Storage stability
Is requirement applicable? (Y/N): Y
Does the summary/available information indicate that the MRID is a candidate for Phase 5 review?: N/A
Discussion: Registrant has committed to do the study.
Data gap: Storage stability studies must be conducted on all

crops and processed products for which a field trial and/or processing study has been (or will be) conducted, as well as representative livestock commodities. Use of field-weathered samples is strongly recommended. Storage conditions must reflect the storage conditions of the treated samples (from the field trial and processing studies) with respect to temperature, length of storage, containers, lighting, etc. If there are any metabolites and/or degradates included in the tolerance expressions, then they must be tested as well. The chosen intervals must allow for unforeseen delays in sample storage.

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Guideline #: 171-4(f) Description: Mag. res. - potable water
Guideline #: 171-4(g) Description: Magnitude residue - fish
Guideline #: 171-4(h) Description: Mag. res. - irrigated crop
Guideline #: 171-4(i) Description: Mag. res. - food handling
Are requirements applicable? (Y/N): N

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Guideline #: 171-4(j) Description: Mag. meat/milk/poultry/eggs
Is requirement applicable? (Y/N): Y
Does the summary/available information indicate that the MRID is a candidate for Phase 5 review?: N
MRID No. 41250012, 92185048
Discussion: Registrant has committed to provide a poultry feeding study but has requested EPA reserve the cattle study. CBRS cannot recommend for reserving this requirement in the absence of adequate justification.

The registrant has submitted a study describing endogenous residues of acetamide in milk and eggs. Milk and eggs purchased in supermarkets were analyzed for acetamide, a known metabolite of thiodicarb. Levels ranging from 274 to 707 ppm in milk and 72 to 258 ppm in eggs were detected.

This information does not fulfill the requirement for livestock feeding studies, but will be considered when reviewing the livestock metabolism and feeding studies.

Data gap: Thiodicarb must be fed to dairy cattle and laying hens for 28 days or until residues plateau in the milk or eggs. Following oral treatment, test animals should be sacrificed within 24 hours of the final dose. Feeding levels should be determined based on the most recent crop residue data generated or to be generated. When determining the feeding levels the registrant should consider the maximum crop residue

levels possible and the dietary burden based on Table II Subdivision O - Residue Chemistry Guidelines.

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Guideline #: 171-4(k/l) Description: Soybean field trials/process
Is requirement applicable? (Y/N): Y
Does the summary/available information indicate that the MRID is a candidate for Phase 5 review?: P - additional data are required to fulfill requirement

MRID Nos.: 40926801, 92185054

Discussion: Summaries of crop field trial studies were submitted describing residues in/on soybeans from aerial application or application as a seed treatment. Seed treatments will not be addressed as there are no currently registered seed treatment uses.

Aerial applications were made in ten trials in seven states. Two applications of 0.45 lb a.i./A (equivalent to 0.6X) in 1 gal were made six or seven days apart. No maximum seasonal application rate has been specified on the current labels. Pre-harvest intervals of 28-31 days were observed. The highest residue found on any sample was 0.05 ppm, which is well below the tolerance level of 0.2 ppm. These data are adequate if the registrant amends the label to a maximum rate of 0.45 lb a.i./A and a seasonal rate of 0.9 lb a.i./A for aerial applications. Alternatively the registrant could develop data at the current maximum rate of 0.75 lb a.i./A. Acceptance of this study is contingent upon submission of adequate storage stability data.

Additional residue data are needed to complete geographical representation and all application techniques. Once additional residue data are generated the registrant should modify the label to include a seasonal maximum application rate, maximum number of applications, and minimum retreatment interval.

Data gap: Data depicting residues of thiodicarb and the regulated metabolites in/on soybeans must be submitted. The aqueous flowable and dry flowable formulations must be applied (each in separate tests) at the maximum label rate (currently 0.75 lb a.i./A), the maximum seasonal rate, the maximum number of applications, minimum retreatment interval, and a PHI of 28 days. Labels must be amended to incorporate all these use pattern variables. The use of conventional ground and chemigation application equipment must be represented in separate tests. The tests must be conducted in MS/LA, TN, AR, IN/IL, IA/NE, MN, MO which represent the major soybean

production regions. (If a slash appears between states then either site may be chosen.) The registrant must amend the label to a maximum rate of 0.45 lb a.i./A and a seasonal rate of 0.9 lb a.i./A for aerial applications. Alternatively the registrant could develop aerial application data at the current maximum rate of 0.75 lb a.i./A and the proposed seasonal maximum.

A processing study must be conducted for soybeans bearing detectable residues of the parent and the regulated metabolites. The soybeans should be processed into hulls, meal, soapstock, crude oil, refined oil, and grain dust to determine the residue concentration or reduction factor(s). If the soybeans are treated at exaggerated rates equivalent to at least the maximum theoretical concentration factor due to processing and no detectable residues are found on the RAC, then processing studies are not required.

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Guideline #: 171-4(k/l) Description: Cotton field trials/process
Is requirement applicable? (Y/N): Y
Does the summary/available information indicate that the MRID is a candidate for Phase 5 review?: P - additional data are required to fulfill requirement

MRID Nos. 41019101, 92185052

Discussion: Summaries of crop field trial studies were submitted describing residues in/on cottonseed from foliar application in CA and AZ or application as a seed treatment. Seed treatments will not be addressed as there are no currently registered seed treatment uses.

Aerial and ground applications were made in separate tests for a total of seven trials in CA and AZ. Two applications of 0.9 lb a.i./A (1X rate) were made in all trials, with the exception of one trial where the rate was 0.6 lb a.i./A. The last application was made prior to boll opening for an average PHI of 43 days. Residues in/on all cottonseed samples were below the established tolerance. These data do not reflect the general directions for use, but they are representative of AZ directions for use; the label does not permit application in CA. Acceptance of this study is contingent upon submission of adequate storage stability data.

Additional residue data are needed to complete geographical representation and all application techniques. Once additional residue data are generated the registrant should modify the label to

include a seasonal maximum application rate, maximum number of applications, and retreatment intervals.

Data gap: Data depicting residues of thiodicarb and the regulated metabolites in/on cottonseed must be submitted. The aqueous and dry flowable formulations must be applied (each in separate tests) at the maximum label rate (currently 0.9 lb a.i./A), the maximum seasonal rate, the maximum number of applications, minimum retreatment interval, and a PHI of 28 days. Labels must be amended to incorporate these use pattern variables. The use of aerial, chemigation, and ground equipment must be represented in separate tests. The tests must be conducted in MS, TX, and LA which represent the major cottonseed production regions.

A processing study must be conducted for cottonseed bearing detectable residues of the parent and the regulated metabolites should be processed into hulls, crude oil, refined oil, soapstock, and meal to determine the residue concentration or reduction factor(s). If the cottonseed is treated at exaggerated rates equivalent to at least the maximum theoretical concentration factor due to processing and no detectable residues are found on the RAC, then processing studies are not required.

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Guideline #: 171-4(k/l) Description: Sweet Corn field trial/process
Is requirement applicable? (Y/N): Y
Does the summary/available information indicate that the MRID is a candidate for Phase 5 review?: P - additional data are required to fulfill requirement

MRID Nos.: 122772, 92185049, 92185051

Discussion: Summaries of crop field trial studies were submitted describing residues in/on sweet corn from foliar applications or application as a seed treatment. Seed treatments will not be addressed as there are no currently registered seed treatment uses. A processing study summary was also presented.

Field trials were conducted in fourteen states using ten ground or simulated aerial applications at the maximum application rate of 0.75 lb a.i./A for a maximum seasonal application rate of 7.5 lb a.i./A. The retreatment intervals were not specified, and the PHIs ranged from 0-7 days. Wettable powder and aqueous flowable formulations were used. Residues of thiodicarb and its regulated metabolite were all below the tolerance for sweet corn kernels and cobs with the husks removed.

Thirteen field trials in nine states were conducted at an application rate of 0.75 lb a.i./A. A minimum of 10 applications were made using ground or simulated aerial equipment. At PHIs ranging from 0 to 7 days residues of thiodicarb and metabolites in/on sweet corn forage did not exceed 260 ppm. These data appear to be sufficient to support ground applications only. There is a grazing/feeding restriction on the Sec. 3 label and no tolerances have been established for forage/fodder. Sec 24(c) registrations have been established for use on sweet corn in DE, GA, LA, MA, MD, MI, MS, NC, NJ, NY, OH, PA, AND VA. CBRS does not accept feeding restrictions for sweet corn in states other than FL. The registrant must propose sweet corn forage tolerances to support these 24(c) registrations.

Dates of storage were not recorded. If the registrant cannot determine the length and condition of sample storage, then the study may not be acceptable. Acceptance of this study is also contingent upon submission of adequate storage stability data.

These data may be adequate to support ground application uses only. Additional aerial data must be submitted since simulated aerial applications do not adequately reflect aerial use.

Sweet corn was treated at the maximum application rate at sites in 10 states. Kernels were separated from the cobs and husks, ground, and composited with the husks and cobs. The registrant should provide justification that this study reflects commercial practice. Substantially greater residues were found in/on the cannery waste. Residues in/on cannery waste would be covered by a forage tolerance once it has been established.

Data gap: Data depicting residues of thiodicarb and the regulated metabolites in/on sweet corn kernels plus cobs with husks removed and forage/fodder as a result of aerial and ground application must be submitted. The aqueous and dry flowable formulations must be applied (each in separate tests) at the maximum label rate (0.75 lb a.i./A/ application), the maximum number of applications (10), the minimum retreatment interval, and a 0 day PHI should be observed. Side-by-side ground and aerial application tests must be conducted in MN/WI, WA/OR/ID, and FL which represent the major sweet corn production regions. (If a slash appears between states then either site may be chosen.)

The registrant must submit storage and retreatment interval information for samples from the existing field trial study (MRID No. 122772). If the registrant cannot determine the length and condition of sample storage, then the study may not be acceptable. The registrant should provide justification that the processing study reflects commercial practice.

Sec 24(c) registrations have been established for use on sweet corn in DE, GA, LA, MA, MD, MI, MS, NC, NJ, NY, OH, PA, AND VA. CBRS does not accept feeding or fresh market restrictions for sweet corn in states other than FL. The registrant must propose sweet corn forage tolerances to support these 24(c) registrations. Residue data for forage/fodder from aerial application of thiodicarb to sweet corn are required before consideration of a tolerance.

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Guideline #: 171-4(k/l) Description: Crop field trial/process
Commodities: Citrus, tree nuts, pome fruits, stone fruits
Is requirement applicable? (Y/N): N - see discussion
Discussion: Applications to non-bearing trees may be made. CBRS will not require residue data since the label prohibits harvest within one year of application. We reserve the need for these data.
Data Gap: Reserved pending outcome of EFGWB crop accumulation studies and any other data suggesting persistence in soil and/or accumulation in crops.

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ADDITIONAL COMMENTS:
The registrant is advised to consult the Subdivision O Residue Chemistry Guidelines, the Standard Evaluation Procedures, the Data Reporting Guidelines, and the Phase 3 Technical Guidance concerning conduct of residue chemistry studies. If the registrant has additional concerns they are advised to submit a protocol for CBRS review.

## PRODUCT CHEMISTRY

Case Name: Thiodicarb
Chemical Name(s): Thiodicarb
Registrant: Rhone-Poulenc Ag Company

| Guideline Number | Is requirement applicable? | Does summary or available information indicate MRID is a candidate for Phase 5 review? | Are additional data required? | MRID Number[a] |
|---|---|---|---|---|
| 61-1 | Y | N/A | Y[b] | N/A |
| 61-2(a) | Y | N/A | Y[b] | N/A |
| 61-2(b) | Y | N/A | Y[b] | N/A |
| 62-1 | Y | N/A | Y[b] | N/A |
| 62-2 | Y | N/A | Y[b] | N/A |
| 62-3 | Y | N/A | Y[b] | N/A |
| 63-2 | Y | N/A | Y[b] | N/A |
| 63-3 | Y | N/A | Y[b] | N/A |
| 63-4 | Y | N/A | Y[b] | N/A |
| 63-5 | Y | Y | N | 41482001[c] |
| 63-6 | N | N/A | N/A | N/A |
| 63-7 | Y | N | Y[d] | U |
| 63-8 | Y | Y | N | 41250002<br>41482002 |
| 63-9 | Y | Y | N | 41250003 |
| 63-10 | N | N/A | N/A | N/A |
| 63-11 | Y | Y | N | 41250004 |
| 63-12 | Y | N/A | Y[b] | N/A |
| 63-13 | Y | Y | N | 41250005 |

Key: Y=yes; N=no; I=a decision cannot be made at this time; N/A=not applicable; U=unsatisfactory.

[a]MRID No. is not listed if study or summary are found to be inadequate.

[b]Registrant has committed to provide a new study.

[c]The MRID number for the study summary is 92185001.

[d]Registrant has reported only the bulk density. The true density (in g/mL) must also be reported.

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