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

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

SEP 11 1991

MEMORANDUM

SUBJECT: ICI Americas Inc.: Response to the Captan
Reregistration Standard: Plant Metabolism Studies
(MRID # 41746001, CBRS # 7583, Barcode D160608.).

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

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

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

and

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

Attached please find a review of ICI Americas response to a previous CBRS review of two captan plant metabolism studies. These data were reviewed by Dynamac Corporation under the supervision of CBRS, HED.

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



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

If you need additional input please advise.

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

cc: (Without Attachment): RF.

Final Report

**CAPTAN (CBRS No. 7583),
Task 4: Registrant's Response to
Residue Chemistry Data Requirements**

March 13, 1991

Contract No. 68-D8-0080

Submitted to:
Environmental Protection Agency
Arlington, VA 22202

Submitted by:
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CAPTAN (CBRS No. 7583)

REGISTRANT'S RESPONSE TO RESIDUE CHEMISTRY DATA REQUIREMENTS

Task - 4

BACKGROUND

The Captan Guidance Document dated 3/86 concludes that the metabolism of captan in plants is not adequately understood. In response to data requirements for plant metabolism studies, Chevron Chemical Co. submitted data (MRIDs 40658005 and 40658006) from metabolism studies on lettuce and tomatoes which were reviewed by the Agency (CBRS Memo No. 6526 dated 10/2/90 by R. Perfetti) and found insufficient because characterized/identified residue components were not quantified on a ppm basis and as a percentage of total recovered radioactivity (combustion analysis). In response to SRRD notification (11/2/90) of these deficiencies, ICI Americas, Inc. (Captan Task Force) submitted an addendum (CBRS No. 7583; MRID 41746001) containing recalculations of data included in the original reports. The current submission is reviewed here for its adequacy in upgrading the available lettuce and tomato metabolism studies.

We note that the CBRS science review (No. 6526) addresses specific data deficiencies which were not included in the Conclusions section of the review or the SRRD notification to ICI America, Inc. dated 11/2/90. For clarity, deficiencies noted in the CBRS Memo No. 6526 are itemized in this review.

CONCLUSIONS PERTAINING TO THIS REVIEW

Data presented in the current submission (MRID 41746001) as an addendum to the original submissions (MRIDs 40658005 and 40658006) are insufficient to fully upgrade the available plant metabolism data. The qualitative nature of the terminal residue in captan in plants remains inadequately understood for the following reasons:

1. The results of combustion analysis for whole tomato fruit are needed to account for any loss of ^{14}C -activity during sample extraction and workup. Table III (MRIDs 40658005 and 40658006) shows selected data for tomato leaves and stems that are consistent with data reported in Table V for these same tissues. However, the registrant must explain how the reported values of 6.9 ppm (^{14}C -TCM) and 6.72 ppm (^{14}C -CHR) captan equivalents present in whole tomato fruit were calculated/determined.

2. Additional raw data and an explanation of how the percentages of total ^{14}C -activity for identified and characterized components (see Tables VII and VIII of the original submissions) were calculated is required. The original submissions indicate that

separate samples of tomato pulp and tomato juice were worked up for residue identification, but the reported values for percentage of TRR appear to be on a whole fruit basis using 6.9 and 6.72 ppm values. The results of combustion analysis for whole tomato fruit are needed to account for any loss of ¹⁴C-activity during sample extraction and workup (see deficiency 1).

RECOMMENDATIONS PERTAINING TO THIS REVIEW

The registrant should be given a copy of this review and informed that the submitted data (MRID 41746001) are insufficient to upgrade the plant metabolism data (MRIDs 40658005 and 40658006) from studies on lettuce and tomatoes. The registrant should be encouraged to discuss protocols for additional studies with the Chemistry Branch II (CBRS) before initiating any additional experiments.

DETAILED CONSIDERATIONS

Qualitative Nature of the Residue in Plants

Plant metabolism data submitted by Chevron Chemical Co. (MRIDs 40658005 and 40658006) in response to the 3/86 Captan Guidance Document were reviewed by R. Perfetti (CBRS Memorandum No. 6526 dated 10/2/90) and found deficient for the following reasons:

1. The results of combustion analysis for whole tomato fruit were not reported, and the manner in which TRR values for whole tomato fruit were calculated/determined was unclear.
2. Data depicting soluble and insoluble total ¹⁴C-residues in tomato fruit and lettuce leaves expressed as radioactive counts or ppm were not provided.
3. Total ¹⁴C-activity in acid hydrolyzed samples of tomato pulp and lettuce leaves and the resulting fractions (carbohydrates, proteins, and lignin) were not expressed as radioactive counts or ppm.
4. The percentages of total ¹⁴C-activity for identified and characterized components listed in Tables 6, 7, and 8 of the CBRS review are apparently based on the sum of dpm found in each fraction rather than on the amount of total radioactivity in that tissue. The registrant needs to clarify how the reported percentage values for isolated components were obtained, and, if necessary, recalculate these values on the basis of the total radioactivity present in the tissue.

The registrant's responses to these deficiencies and our conclusions are addressed below. Note that the CBRS science review (CBRS Memo No. 6526 dated 10/2/90 by R. Perfetti) addresses additional specific deficiencies not covered in the SRRD notification to ICI Americas, Inc. dated 11/2/90.

Registrant's response to deficiency 1. The registrant has clarified that residue concentrations reported for tomato juice and pulp in Table V of their original submission were based on the weight of these separate fractions rather than on the weight of whole fruit. These new data are presented below.

Revised Table 3. Distribution of ¹⁴C-activity in tomato and lettuce plants following foliar applications of [TCM-¹⁴C]captan and [CHR-¹⁴C]captan.

| Component | ¹⁴ C-residues, ppm captan equivalents (% TRR) | | | |
|---------------------------|--|------------------------|------------------------|------------------------|
| | Tomato | | Lettuce | |
| | [TCM- ¹⁴ C] | [CHR- ¹⁴ C] | [TCM- ¹⁴ C] | [CHR- ¹⁴ C] |
| Leaves | 128.5(62.1) | 202.1(70.4) | 68.5(98.7) | 64.4(99.7) |
| Stems | 21.8(9.2) | 30.1(9.7) | NA ^a | NA |
| Roots | 0.2(0.2) | 0.2(0.2) | 1.3(1.3) | 0.3(0.3) |
| Fruit | 6.9(28.5) | 6.7(19.7) | NA | NA |
| Tomato Fruit ^b | | | | |
| Surface | --(79.6) | --(88.9) | NA | NA |
| Juice | 1.22(14.7) | 0.71(8.9) | NA | NA |
| Pulp | 2.94(5.7) | 1.18(2.2) | NA | NA |

^aNA = Not applicable. ^bAcetone-soluble surface residues were not expressed on a weight basis; ppm in juice is based on the weight of juice; ppm in pulp is based on the weight of pulp.

CBRS concludes that deficiency 1 is only partly resolved. The registrant must explain how the reported values of 6.9 ppm (¹⁴C-TCM) and 6.72 ppm (¹⁴C-CHR) captan equivalents present in whole tomato fruit were calculated/determined. The registrant should clarify how the calculated TRR values for tomato fruit were obtained, i.e. separate combustion of skin/pulp/juice or combustion of a sample of whole fruit. The total radioactivity remaining or on the whole edible portion at the time of sampling serves as the basis of the percentage of characterized/identified residues in that tissue.

Registrant's response to deficiency 2. The registrant has presented new data depicting soluble and insoluble ¹⁴C-residues (expressed as ppm captan equivalents), in tomato fruit, tomato foliage, and lettuce leaves.

New Table. Distribution of total radioactivity in extracts of tomato fruit, tomato foliage, and lettuce leaves following foliar treatments with [TCM-¹⁴C]captan and [CHR-¹⁴C]captan.

| <u>¹⁴C-residues, ppm captan equivalents in solvent fractions</u> | | | | | | |
|---|------------------|-------------------|-----------------------|--------|------------------|-------|
| Component | Acetone | MeOH ^a | MeOH/H ₂ O | Acidic | Insol. | Total |
| | | | | MeOH | | |
| <u>[TCM-¹⁴C]captan</u> | | | | | | |
| Tomato leaves | 109.9 | 3.0 | 4.1 | 2.8 | 8.7 | 128.5 |
| Tomato stems | 17.8 | 0.8 | 0.8 | 0.3 | 2.1 | 21.8 |
| Tomato juice | 0.2 ^b | NA ^c | NA | NA | 1.1 ^d | 1.3 |
| Tomato pulp | 0.6 | 0.1 | 0.3 | 0.2 | 1.7 | 2.9 |
| Lettuce leaves | 56.0 | 0.1 | 1.9 | 1.2 | 9.4 | 68.6 |
| <u>[CHR-¹⁴C]captan</u> | | | | | | |
| Tomato leaves | 165.3 | 7.1 | 11.9 | NA | 17.8 | 202.1 |
| Tomato stems | 25.1 | 1.0 | 1.3 | NA | 2.7 | 30.1 |
| Tomato juice | 0.3 ^b | NA | NA | NA | 0.4 ^d | 0.7 |
| Tomato pulp | 0.6 | 0.0 | 0.1 | NA | 0.5 | 1.2 |
| Lettuce leaves | 60.5 | 1.0 | 0.9 | NA | 1.9 | 64.3 |

^aMeOH = methanol. ^bTomato juice was extracted with ethyl acetate. ^cNA = not applicable. ^dRemaining juice after ethyl acetate extraction.

CBRS concludes that deficiency 2 is resolved.

Registrant's response to deficiency 3. The registrant has presented new data on the fractionation of nonextractable residues in tomato pulp and lettuce leaves. These new data are presented below.

Revised Table 5. Fractionation of insoluble residues from tomato pulp and lettuce leaves into natural plant constituents.

| Component | <u>¹⁴C-activity in insoluble residues</u> | | | | | |
|-------------------------------------|--|-----------------|-----------------------------|------|-----------------------------|------|
| | <u>Tomato Pulp</u> | | | | <u>Lettuce leaves</u> | |
| | <u>[TCM-¹⁴C]</u> | | <u>[CHR-¹⁴C]</u> | | <u>[TCM-¹⁴C]</u> | |
| | % | ppm | % | ppm | % | ppm |
| Carbohydrates | 15.3 | 0.26 | 71.2 | 0.35 | 48.0 | 4.51 |
| Proteins (amino acids) | 14.6 | 0.25 | 17.6 | 0.09 | 10.2 | 0.95 |
| Lignin | 3.7 | 0.06 | 3.3 | 0.02 | 1.7 | 0.16 |
| Remaining residue | 17.8 | 0.30 | 7.9 | 0.04 | 5.1 | 0.48 |
| Loss during hydrolysis ^a | 45.6 | -- ^b | NR ^c | NR | 35.0 | -- |
| Total | 97.0 | 0.88 | 100.0 | 0.50 | 100.0 | 6.10 |

^aA 31.9% loss of ¹⁴C-activity from tomato pulp occurred during the acid treatment, and an additional 13.7% was lost during acidification of the 20% NaOH hydrolysate. A 35% loss of ¹⁴C-activity from lettuce was also reported during acidification of the base hydrolysate. ^bResidue concentration was not reported. ^cNo losses were reported.

CBRS concludes that deficiency 3 is resolved.

Registrant's response to deficiency 4. The registrant has resubmitted data depicting identified/characterized total ¹⁴C-activity in tomatoes and lettuce without alteration explaining that their original tables presented each identified/characterized component on a ppm basis from combustion analysis and as a percentage of the total radioactivity in the tissue of fraction. The registrant also notes that ppm concentration units are not directly additive as portrayed in Table 3 on page 7 of the CBRS review.

CBRS concludes that deficiency 4 is partly resolved. We wish to clarify that the Agency concerns regarding this deficiency are not based on a misinterpretation of data presented in Table V of the registrant's original submission. CBRS requires additional clarification on the manner in which the % TRR for isolated components was determined, i.e. a percentage of the sum of dpm

found in each fraction, or of the total radioactivity determined by combustion analysis of tissue samples.

In summary, data presented in the current submission are insufficient to upgrade plant metabolism data from studies on lettuce and tomatoes submitted in response to the Captan Guidance Document dated 3/86. Data requirements for this topic remain outstanding.