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

AUG 13 1986

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Stauffer Chemical Co. Response of 6/9/86 to Residue Chemistry Data Requirements in the Captan Registration Standard, issued March 1986. (RCB No. 1132; No Accession Number)

FROM: Debra F. Edwards, Ph.D. *Debra Edwards*
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Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

THRU: Charles L. Trichilo, Chief *[Signature]*
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

TO: Henry Jacoby
Product Manager (21)
Fungicide/Herbicide Branch
Registration Division (TS-767C)

Stauffer Chemical Co., in a letter to H. Jacoby (RD), dated June 9, 1986, has requested clarification of certain residue chemistry data requirements in the Captan Registration Standard, regarding plant and animal metabolism and analytical methods. Although all of the Registrant's questions and concerns have been addressed in the Residue Chemistry chapter of the Registration Standard, RCB will reiterate our conclusions in this memorandum.

1. Stauffer Chemical Co. Questions and Concerns Regarding Residue Chemistry Data Requirements for the Nature of the Residue in Plants:

"We are not certain exactly what the Agency is requesting for postharvest use on potatoes. Is the Agency requesting two metabolism studies, one with the trichloromethyl moiety ¹⁴C-labeled and one with a carbonyl group ¹⁴C-labeled? What is the Agency's justification for this requirement? We request clarification as to the crops and number of studies that are being required by the Agency."

RCB Response:

RCB is requesting the following additional plant metabolism studies to fully elucidate the nature of the residue in plants:

<u>Commodity</u>	<u>Method of Treatment</u>	<u>Location of ¹⁴C-Label</u>
Lettuce	Foliar	Carbonyl
Lettuce	Foliar	Trichloromethylthio
Potatoes	Foliar and Postharvest	Carbonyl
Potatoes	Foliar and Postharvest	Trichloromethylthio

Application rates must be sufficiently high to permit complete identification of ¹⁴C-residues.

Although sufficient data are available regarding the metabolism of [¹⁴C-carbonyl]captan in tree fruits and of captafol (a closely related chemical) in tomatoes and corn, no data are available for any members of the Root and Tuber or Leafy Vegetable crop groups. Since captan is such a widely used pesticide on a great variety of crops, such data are needed to fully assess the nature of the residue in plants.

In addition, data specifically reflecting metabolism of the trichloromethylthio moiety are required due to TOX Branch concerns regarding this sidechain (personal communication between W. Boodee [RCB] and M. Copley [TOX] on 7/31/86). [We suggest that the Registrant schedule a meeting with representatives of the TOX Branch to resolve any further concerns pertaining to the requirement for data describing the metabolism of the trichloromethylthio sidechain.]

2. Stauffer Chemical Co. Questions and Concerns Regarding Residue Chemistry Data Requirements for the Nature of the Residue in Animals:

"As with the plant metabolism work, we request clarification and justification for this requirement. We are especially concerned that the required studies do not correspond with the studies required in the Data Call-In Notice of April, 1985. Please note that the Agency only recently (October 1985) approved the protocol for the poultry metabolism study required under the Data Call-In. When this protocol was reviewed, the Agency should have raised the questions later raised in the registration standard. We request clarification of the animal species and ¹⁴C-label sites for which the Agency is requiring data."

RCB Response:

The Agency did not approve a protocol for a proposed poultry metabolism study in October 1985, but for a proposed poultry feeding study in which unlabeled captan was to be used as the test material. To date, no poultry metabolism data or protocols have been submitted for captan. Also, although adequate data are available regarding the metabolism of [¹⁴C-carbonyl]captan in ruminants, additional metabolism data are needed regarding metabolism of [¹⁴C-trichloromethylthio]captan. [Data regarding the metabolism of the trichloromethylthio moiety are needed due to TOX Branch concerns as stated above for plant metabolism.] The following animal metabolism data are needed:

- o Metabolism studies utilizing ruminants and poultry. Poultry must be dosed with [¹⁴C-carbonyl]captan and [¹⁴C-trichloromethylthio]captan (in separate tests) and ruminants must be dosed with [¹⁴C-trichloromethylthio]captan for three days at a concentration in the total diet which will result in sufficient ¹⁴C-residues in the tissues, eggs and milk for complete characterization. Animals must be sacrificed within 24 hours of the final dose (eggs and milk must be collected twice daily). ¹⁴C-Residues must be characterized in muscle, fat, kidney, liver, eggs and milk.

3. Stauffer Chemical Co. Questions and Concerns Regarding Residue Chemistry Data Requirements for Residue Analytical Methods:

"We request that submission of additional residue methodology for plants and animal tissues be reserved pending completion of the metabolism studies required by 171-4 (Nature of Residue). We request that the Agency clarify specifically what more is required here and hold further requests in abeyance until the metabolism studies are completed."

RCB Response:

RCB required no additional residue analytical methods in the Residue Chemistry Chapter of the Registration Standard, pending receipt of the plant and animal metabolism data. For enforcement purposes, Method I in PAM, Vol. II, Pesticide Reg. Sec. 180.103 was found adequate for plant commodities. Also, it was suggested that a Chevron method, entitled "Determination of Captafol, Captan, THPI, and 3-OH THPI in Tissues and Eggs; and Determination of Captan, THPI, 3-OH THPI and 5-OH THPI in Milk and Cream", be independently validated via an EPA Method Tryout (MTO) to determine its usefulness for enforcement of tolerances for residues in animal commodities. This MTO has been requested (memo from F.D. Griffith, Jr. [RCB], dated 11/19/85, to D.A. Marlow, Chemical Operations Branch, BUD), and is currently in progress.

Although no additional enforcement methods need be submitted at this time, RCB recommends that samples from the requested metabolism studies be analyzed using available residue analytical methods which are or may in the future be used for enforcement, as well as the usual LSC procedures used in metabolism studies. This approach, in which recovery of radiolabeled residues using potential enforcement methods can be compared with analyses using LSC, provides better evidence of an analytical method's efficiency in recovering weathered residues than the usual laboratory procedures involving fortification and recovery of unlabeled materials. Presently, the established tolerances cover residues of the parent, captan, only (40 CFR 180.103). However, we recommend that all known potential residues of concern be determined in testing potential enforcement methods. In this regard, THPI, THPAM, THPI-epoxide, captan epoxide, and 3- and 5-OH THPI are known potential residues of concern in plants, and THPI, THPI-epoxide, 3-OH THPI, 5-OH THPI, and 4,5-diOH HHPI are known potential residues of concern in animals (see Attachment [Table 1 from the Residue Chemistry Chapter of the Standard] for structures and full chemical names of these metabolites). Therefore, we recommend that residue analyses include these metabolites as well as any additional, newly discovered metabolites.

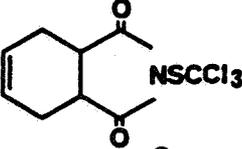
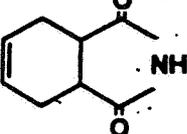
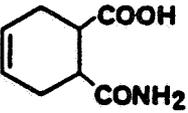
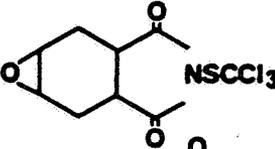
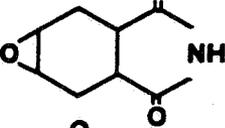
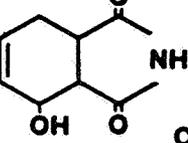
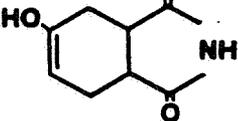
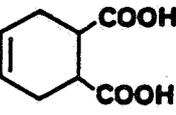
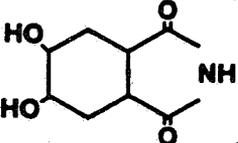
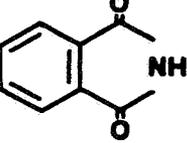
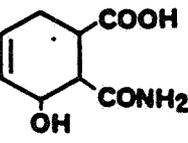
Attachment: Table 1 from the Residue Chemistry Chapter of
the Captan Registration Standard

TS-769C:RCB:Reviewer:D.Edwards:8/12/86:CM#2:Rm:812:557-4353

cc(with Attachment):A.Rispin(SIS):M.Copley(TOX):SF:RF:Reg.Standards
File:Circu:Reviewer

RDI:Section Head:W.Boodee:8/13/86:R.Schmitt:8//3/86.

Table 1. Captan and its metabolites.

CODE	STRUCTURE	CHEMICAL NAME	ABBREVIATION
I		N-(trichloromethylthio)cyclohex-4-ene-1,2-dicarboximide	Captan
II		Δ ⁴ -Tetrahydrophthalimide	THPI
III		Δ ⁴ -Tetrahydrophthalamic acid	THPAM
IV		N-(trichloromethylthio)-4,5-epoxyhexahydrophthalimide	Captan-epoxide
V		4,5-Epoxyhexahydrophthalimide	THPI-epoxide
VI		3-Hydroxy-Δ ⁴ -tetrahydrophthalimide	3-OH THPI
VII		5-Hydroxy-Δ ³ -tetrahydrophthalimide	5-OH THPI
VIII		Δ ⁴ -Tetrahydrophthalic acid	THPAL
IX		4,5-Dihydroxyhexahydrophthalimide	4,5-d10H HHPI
X		Phthalimide	PI
XI		3-Hydroxy-Δ ⁴ -tetrahydrophthalamic acid	3-OH THPAM