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

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06 APR 1987

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Registration Standard for Captan.
Evaluation of Method Tryout Report.
(No MRID No.) [No RCB No.]

FROM: Francis D. Griffith, Jr., Chemist
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and

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THRU: Charles L. Trichilo, Chief
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Residue Chemistry Branch (RCB) has been informed by Analytical Chemistry Laboratory (ACL), Chemical Operations Branch (COB), and Benefits and Use Division (BUD) of the completion of the requested captan and its metabolites method trial. The method trial for captan and its metabolites in meat and milk was reported by King T. Zee in his memorandum dated February 20, 1987.

The method was requested for captan (cis-N-[trichloromethyl]thio)-4-cyclohexane-1,2-dicarboximide) trade named Orthocide®, and three metabolites THPI (tetrahydrophthalimide), 3-OH THPI (3-hydroxy-4-cyclohexane-1,2-dicarboximide), and 5-OH THPI (5-hydroxy-4-cyclohexene-1,2-dicarboximide) in milk and liver (see memorandum by F.D. Griffith, Jr., dated November 19, 1985, to COB/BUD). The method trial was requested for the Chevron Chemical Company procedure, Chevron file number 740.01 dated November 14, 1979. The petitioner states

this procedure is a compilation of three methods; i.e., Chevron Chemical methods RM-6G-2, and RM-1G-1, and Stauffer method RRC-75-32. No authors are identified. The title of the compiled method is "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." RCB also requested COB/BUD determine the extent of potential captafol and phaltan interference with captan determination.

The method tryout (MTO) was conducted using the petitioner's method as supplied by RCB with the minor modifications noted on the report form. No corrections were made for unspiked crop samples. RCB on reviewing the copies of ACL chromatograms determined that the captan, per se, limit of detection in liver and milk is 0.01 ppm or less. No matrix coextractives interfering with captan were noted on the ACL chromatograms.

Part of the MTO request involved determining the extent of captafol and/or phaltan potential interference with captan if either were present when captan is the suspect residue of concern. If captafol residues were present at 10X the captan residue, interference would not be a problem in this method as captafol has 2X the retention time of captan. However, if phaltan residues were present at the same time as captan residues, serious interference would occur. ACL points out that both fungicides have nearly identical GC retention times on all three suggested chromatographic systems. Since the petitioner presented no way to separate these fungicides and confirm individual residues, the method is suitable to gather residue data but cannot be an enforcement method. The petitioner should have a method that can readily separate and quantitate these closely related fungicides.

RCB requested the method be validated for captan, THPI, and 3-OH THPI in liver at 0.05 ppm (1X) and at 0.5 ppm. RCB also requested the method be validated for captan, THPI, 3-OH THPI, and 5-OH THPI in milk at 0.05 ppm (1X) and at 0.5 ppm. Captan recoveries from milk ranged from 70% to 100% (\bar{X} = 82.5% + 13.00%, coefficient of variance (CV) = 15.8%, n = 4) and in Liver ranged from 60% to 78% (\bar{X} = 66.25% + 8.1%, CV = 12.2%, n = 4). Three of the four captan recoveries from liver were less than 70 percent. For a method to be suitable to gather residue data and become an enforcement procedure recoveries should be above 70 percent. The inadequate recovery of captan is an additional reason why the method is not suitable.

The analytical reference standard for captan is available from EPA's Pesticides and Industrial Chemicals Repository at Research Triangle Park, NC. The code for Captan is 1020. Likewise, a standard for one metabolite, THPI, is available from the Repository. The code for THPI is F821 (see Analytical

Reference Standards: Federal Supplemental Index, 6th Edition, January 1987). In a telecon (F.D. Griffith, Jr., RCB to Suzanne Hart, Repository on April 6, 1987) RCB confirmed that the 3-OH THPI and the 5-OH THPI metabolites are not available from the Repository.

The petitioner has made a limited but adequate portion of these metabolites available to COB in Beltsville to facilitate running a MTO. We point out to the petitioner that making the standards available to Beltsville to run a MTO is not the same as making the standards available to the Repository at Research Triangle Park, NC. Before RCB will concur on a tolerance and the suitability of a method to enforce a tolerance, all standards of compounds to be regulated must be available from the Repository, not Beltsville, for the FDA and State enforcement work. The lack of available analytical standards for FDA and State enforcement work is a further reason why the method is not satisfactory to enforce captan tolerances.

In EPA's review of the method we observe all three metabolites are derivatized to form the N-pentafluorobenzyl derivatives. The petitioner has not provided data on the efficiency of the conversion. ACL/COB requested the petitioner provide a portion of derivatized metabolites for ACL to determine the efficiency of derivatization and thus recovery of the metabolites using the suggested method. The petitioner responded that these standards are not available. Without these standards, EPA cannot ascertain to what extent the proposed method can recover the captan metabolites. If the petitioner wishes to continue using this method to gather residue data or for the Agency to review further any data already generated by this method, then these derivatized metabolite standards should be made available to ACL to validate the method. The petitioner has been informed during the Special Review of captan that the bovine feeding study needs to be repeated. It is the petitioner's option to develop a new procedure to measure captan and its toxicologically significant metabolites or provide material to validate the existing method. While these derivatized standards are not part of the tolerance expression, EPA will expect a portion of them to be made available to the Repository for special projects, not for general enforcement work as for the 3-OH THPI and 5-OH THPI metabolite standards.

During the MTO, ACL used a 2' x 1/8" column packed with 1.5% SP-2250 plus 1.5% SP-2401 in an oven at 180 °C. The GC column needs to be conditioned with injections of standards plus crop extracts for maximum sensitivity; i.e., to repeatedly reach the limit of detection. These minor modifications do not affect the method's performance. The petitioner should incorporate them in any future revision of the method.

The method, as written, places an unnecessary burden on regulatory chemists in its use of three different determination steps. The method needs to be revised to have only one determination step to determine captan (separately from phaltan) and its toxicologically significant metabolites, and a confirmatory step. ACL states that the use of three determinative steps makes the method impractical for enforcement. While the method as written takes 2 days to run a set of 6 samples, RCB feels a revision can shorten this time factor.

RCB Conclusion

There has not been a successful MTO for recovery of captan and its metabolites from milk and liver. The method is not suitable to enforce tolerances for the following reasons:

1. The method cannot distinguish between captan or phaltan, per se.
2. The recovery of captan from liver is too low for regulatory work.
3. The metabolite analytical standards for 3-OH THPI and 5-OH THPI are not available from EPA's Repository for Pesticides and Industrial Chemicals.
4. EPA cannot determine the efficiency of the derivatization step and therefore the recovery of the three captan metabolites through the method without a known derivatized analytical standard.
5. The method as written, places an unnecessary burden on regulatory chemists having to use three determination steps. The method should be revised to have one determination and one confirmation step/procedure.

RCB Recommendations

The analytical method for captan residues in meat, milk, poultry, and eggs should not be forwarded to either FDA's Technical Editing Group nor to ISB/PMSD for general distribution. For further consideration, the petitioner has the option of correcting the deficiencies noted above, or rerun the captan bovine feeding study with a new method incorporating the concerns detailed in our conclusions.

TS-769C:RCB:Reviewer (FDG):CM#2:RM 814B:557-0826:KENCO: NeeCee:
4/13/87: vo:tar:edited:fdg:4/17/87

cc:Circu, R.F. Reviewer, Captan S.F., Captan Sp. Rev. File (see L. Bradley), TB, FDA PAM-II Editor, EEB, EAB, D.Hill (NEIC-Den) M. Bradley (MTO-File), R.F. Thompson (RepositoryRTP-NC), D.A. Marlow (COB/BUD), ISB/PMSD).

RDI:Section Head:R.S. Quick: 4/8/87:R.D. Schmitt: 4/8/87.