



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

Olinger

APR 1 1994

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: The Metabolism Committee Meetings Held on February 22 and March 1, 1994:
Captain Plant and Animal Metabolism

FROM: Christine L. Olinger, Chemist *Christine Olinger*
Reregistration Section I
Chemistry Branch II - Reregistration Support
Health Effects Division (7509C)

and

Paul Chin, Toxicologist *Paul Chin 3/29/94*
Section 2
Toxicology Branch I
Health Effects Division (7509C)

THRU: Edward Zager, Chief *E. Zager for*
Chemistry Branch II - Reregistration Support
Health Effects Division (7509C)

and

Karl Baetcke, Chief *Karl Baetcke 3/30/94*
Toxicology Branch I
Health Effects Division (7509C)

TO: The Metabolism Committee
Health Effects Division (7509C)

A. **Individuals in Attendance:**

1. Metabolism Committee: (Signatures indicate concurrence unless otherwise stated)



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Karl Baetcke


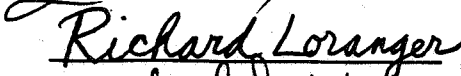
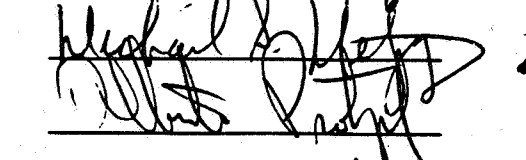
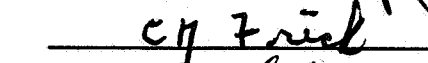

Richard Loranger

Michael Metzger

Alberto Protzel

Charles Frick



Richard Schmitt

2. Scientists: (Non-committee members responsible for data presentation; signatures indicate technical accuracy of panel report)

Christine Olinger

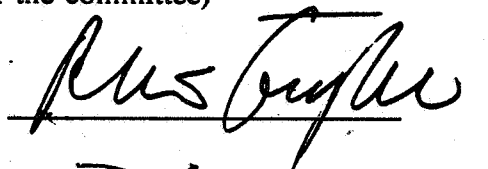

Paul Chin

3. Metabolism Committee Members in Absentia: (Committee members who were unable to attend the discussion; signatures indicate concurrence with the overall conclusions of the committee)

Reto Engler

George Ghali

B. Material Reviewed:

The Metabolism Committee considered the metabolism of captan in plants and animals to determine which, if any, metabolites should be considered in the tolerance expression for plants and animals. Captan is a B₂ carcinogen for which a Q₁* of 3.6 x 10⁻³ has been established. An RfD has been established for reproductive effects of 0.13 mg/kg/day based on one- and three-generation rat studies.

Captan has not been detected in the tissues, milk, or eggs of any animal in any metabolism study submitted to the Agency. The major metabolites in livestock include tetrahydrophthalimide (THPI) and the *cis* and *trans* isomers of 3-hydroxytetrahydrophthalimide and 5-hydroxytetrahydrophthalimide. THPI is a major rat metabolite as well.

The HED Metabolism Committee has determined that the tolerance expression for plants should include only the parent, captan, since THPI comprises less than 10% of the total captan residue (based on three plant metabolism studies). The tolerance expression for meat and milk commodities should include the parent captan and the metabolite THPI.

The risk assessment for cancer should include only the parent, captan. The Toxicology Branch does not consider, at this time, the metabolite THPI to be of cancer concern relative to the parent, due to the absence of the N-SCl₂ moiety in the structure of THPI. This conclusion is based on structure-activity relationship (SAR) considerations (personal communication with Yin Tak Woo, SAR expert, OPTS). Meat and milk commodities will therefore not be considered for the cancer risk assessment because captan is not found in animal metabolism studies and the major residue is THPI.

Both captan and THPI will be considered for the risk assessment for reproductive and developmental effects. Toxicology has no reason to exclude the metabolite THPI when considering reproductive risks and there is some preliminary indication in the scientific literature that this metabolite could be of concern for developmental effects. The RfD which has been determined for captan will cover developmental concerns which may be attributed to the metabolite THPI as well.

Poultry and ruminant metabolism studies using captan labeled at the trichloromethyl carbon are due to be submitted to the Agency within the next few months. The Committee does not have a reasonable expectation at this time that there will be a need to regulate any additional metabolites found in this study. This decision may need to be reconsidered if the new studies indicate there may be metabolites of concern.

cc: CLOlinger (CBRS); Circulate, Reg Std. File, RF, SF, Metabolism Committee File, Signers above, E. Saito (CCB)

7509C:CBRS:CLOlinger:clo:CM#2:Rm 816G:305-5406: 3/28/94

RDI: PADeschamp: 3/29/94 MMetzger: 3/29/94