Metabolism Committee File

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

AUG 7 1992

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Atrazine, Simazine, and Cyanazine. Results of the Metabolism Committee Meeting of 7/9/92.

FROM: Michael S. Metzger, Chemist
Chemistry Branch 2 - Reregistration Support
Health Effects Division (H7509C)

THRU: Edward Zager, Chief
Chemistry Branch 2 - Reregistration Support
Health Effects Division (H7509C)

TO: The Metabolism Committee.

A. Individuals in Attendance:

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

Karl Baetcke

Richard Loranger (Michael Flood, substituting for)

Michael Metzger - concur that maternal preg is the majority opinion of the metabolism committee

Alberto Protzel

Richard Schmitt

George Ghali (Kerry Dearfield substituting for)

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

Henry Spencer

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

B. Material Reviewed

The purpose of this metabolism committee meeting was to clarify issues related to triazine pesticides in order to proceed with Reregistration and/or Special Review.

TOX indicated that in the absence of data on the toxicity of metabolites of triazines, we would have to assume that all metabolites containing a triazine ring with a substituent have toxicity equivalent to the corresponding parent compound. Any substituent on the triazine ring would suffice. Since it is unlikely that metabolites will be found which do not have a substituent on the triazine ring, we will make the assumption that the total triazine residue includes only metabolites with substituents on the triazine ring. The residue levels used for exposure assessment should reflect total residues of all metabolites containing a triazine ring. Although structure-activity relationships indicate that the substitution on the triazine ring may affect the toxicity, the available information is not adequate to allow the Agency to conclude that a class of metabolites, such as the unchlorinated hydroxy metabolites, should not be included in the exposure assessment. The registrant has indicated that they are carrying out a chronic feeding/cancer study utilizing hydroxyatrazine. This study has not been required by the Agency in a DCI. If this study is submitted and shows that hydroxyatrazine is not carcinogenic, then the exposure assessment and tolerance expression for atrazine will include only the parent and chloro metabolites. If the study indicates that hydroxyatrazine is carcinogenic, then risk for atrazine will be calculated considering the cancer potency of both the parent and hydroxyatrazine. TOX has not made a decision on how the results of the hydroxyatrazine carcinogenicity study will affect the other subject triazine pesticides.

There are currently no analytical methods available to allow for determination of the total residues of metabolites containing

triazine rings with substituents. The Agency has issued DCIs for atrazine and simazine requiring geographically representative ^{14}C radiolabel field studies for all commodities on which atrazine and simazine are registered. The registrant currently has studies underway for representative crops for atrazine. The committee concluded that similar field radiolabel studies should also be required for ametryn. These studies will allow exposure assessment for total triazine ring residues as the total **radioactive** residue, since most of the radioactivity remains as triazine ring-containing metabolites. Field radiolabel studies will not be required for cyanazine since a small set of discreet, measurable metabolites make up a large portion of the total triazine ring residue.

Enforcement methodology which measures all metabolites containing a triazine ring is not available. Attempts to convert all triazine metabolites to a common moiety such as cyanuric acid have resulted in high background levels in untreated commodities, apparently due to conversion of naturally occurring compounds to cyanuric acid. In addition to measuring the total radioactivity in the radiolabel field studies, the registrant must identify major components of the total radioactivity in these crops. If possible, these data will be used to identify appropriate "marker" metabolites to use in developing marker-based analytical methods for enforcement purposes and for non-radiolabel field residue data.

The committee recommends that Special Review proceed utilizing the available residue and toxicity data. Risk assessments for each of these pesticides should incorporate anticipated residue estimates using the best available data to determine total residues of metabolites containing the triazine ring. The committee was made aware that estimated risks utilizing the total triazine ring with substituent residue would substantially exceed 10^{-5}, possibly by an order of magnitude or more. If only the parent and chloro metabolites are considered, this risk estimate would likely be greatly reduced for all commodities except for sugarcane treated with atrazine.

cc: M.Metzger (CBRS), Circu, Atrazine Reg. Std. File, RF, SF, CBTS, Metabolism Committee file, Signers above, W. Burnam (SACB)
H7509C:CBRS:M.Metzger:MM:CM#2:Rm816G:305-5883:8/3/92
RDI: E.Zager: 8/3/92