S.F.

Propazine

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

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OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

Memorandum

Subject: Propazine. Response to Meeting (8/2/95)
Memorandum of Understanding Submitted by Griffin.

From: Michael S. Metzger, Chief
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Health Effects Division (7509C)

To: Terri Stowe, PM 22-25 Team
Fungicide-Herbicide Branch
Registration Division (7505C)

Griffin has submitted a Memorandum of Understanding for Agency comment regarding a meeting held 8/2/95. CBTS will not comment directly on the data summary submitted as part of the MOU, but will answer specific questions posed. Registrant questions are in **bold** below followed by CBTS response.

Sorghum Metabolism:

(1) What compounds will be required for setting tolerances in sorghum forage, grain, and fodder?

(2) Is additional identification work required for sorghum?

As discussed at the meeting and in a follow-up telephone conversation (11/2/95), if the metabolism of propazine is shown to be similar to the metabolism of other chloro-triazines in sorghum, and toxicity of propazine is also similar, establishment of tolerances and risk assessment would be the same as for other triazines. Tolerances would be set for residues of parent plus chloro-metabolites, and risk assessment would be done using parent plus chloro-metabolites for carcinogenic risk assessment, and hydroxy-metabolites or Total Radioactive Residues (TRR) for chronic non-cancer risk assessment. Since the registrant states that levels of chloro-metabolites, hydroxy-metabolites, and total radioactivity in each rac have been determined, and that the metabolic and toxicity profiles of propazine are very similar to other chlorotriazines, no further identification work should be required. We note that data confirming these assumptions has not yet been seen by CBTS.

Goat Metabolism:

(1) Is any further research required for metabolite identification?
(2) Since the compounds of interest for tolerance setting appear to be parent propazine and its two chloro-metabolites and given the fact that Ciba has already conducted a dairy study in which these metabolites were quantitatively determined, we are requesting the Ciba study be used to support this requirement.

As discussed previously, the residue of toxicological concern for other chloro triazine herbicides currently includes all metabolites with a triazine ring. Studies with other triazines show that the triazine ring is not significantly broken down by plants or livestock, and that the TRR therefore adequately represents total triazine ring containing residues. Therefore, if the available goat metabolism studies adequately and separately determine residues of each chlorometabolite, each hydroxymetabolite, and TRR for each commodity for which data are required, further identification work for the metabolism study in which parent propazine was fed should not be required.

However, as discussed, and as done with other triazine herbicides, radiolabel data reflecting residues in meat, milk, poultry, and eggs following dosing of livestock with propazine metabolites are required. The form of this dosing can be either dosing with a single metabolite such as hydroxy propazine serving as a surrogate for other metabolites, or dosing by feeding animals sorghum which as been treated with radiolabeled propazine as per label directions. As discussed, if propazine metabolism in plants and animals is shown to be sufficiently similar to other chlorotriazines, available data generated to support the other chlorotriazines can be referenced rather than the registrant generating new data for propazine.

A feeding study (non-radiolabel) in which livestock were dosed with parent compound, and chlorotriazine residues were determined in tissues and milk is adequate if submitted in conjunction with the other data discussed above. A copy of this study should be submitted with the petition or the study should be referenced by MRID number.

Poultry Metabolism:

Since chloro metabolites of propazine were not detected in sorghum grain and this is the only sorghum commodity fed to poultry and the highest extrapolated value of both TRR and chloro residues when propazine was fed to poultry was less than 10 ppb, we feel that the current information from the Griffin hen metabolism study and the Ciba poultry residue study provide sufficient information for estimating the exposure of propazine

residues from poultry. We are requesting comments on the need for further metabolite identification and that another poultry residue study not be a requirement for registration.

If the Agency verifies that TRR normalized to 1X are 0.001-0.006 ppm in all edible tissues, further metabolite identification and characterization is not required. However, the Agency may estimate chronic non-cancer risk for triazine herbicides based only on levels of hydroxy-metabolites. If hydroxy-metabolites levels are not separately determined, TRR values will be used in the risk assessment which could lead to risk concern. The registrant may chose to determine levels of hydroxy-metabolites to allow a more realistic risk estimate.

REVIEW OF THE RESULTS FOR SOIL METABOLISM

Soil metabolism data are under the purview of the Environmental Fate and Effects Division and questions should be addressed to them.

cc: M.Metzger; Propazine SF; RF; Circulation
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