MEMORANDUM

Subject: Propazine (PC Code: 80808, CAS#: 139-40-2). Review of the Proposed Protocols for Conducting the Following Studies Using ^{14}C-Labeled Propazine:
Nature of the Residue in Sorghum
Nature of the Residue in Lactating Goats
Nature of the Residue in Laying Hens
Confined Rotational Crops

(No MRID#, DP Barcode# D196214, CBTS# 12729).

From: G. Jeffrey Herndon, Chemist
Tolerance Petition Section II
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Health Effects Division (H7509C)

Through: Debra Edwards, Ph.D., Chief
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and

Albin Kocialski, Head
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Griffin Corporation has submitted a series of draft protocols for conducting various studies on propazine, or 2-chloro-4,6-bis(isopropylamino)-s-triazine (see Attachment I):

^{14}C Propazine: Metabolism, Fate, and Distribution in Grain

Sorghum
^{14}C Propazine: Metabolism in a Lactating Goat Following Oral Adminimistration for 3 Consecutive Days
^{14}C Propazine: Metabolism in Laying Hens Following Oral Adminimistration for 3 Consecutive Days
^{14}C Propazine: A Confined Rotational Crop Study

Propazine was previously registered and had negligible residue tolerances established on various sorghum products at 0.25 ppm. Previously cited residue chemistry deficiencies include:

- nature of the residue in plants and animals are not adequately understood
- data on storage stability are unavailable
- processing studies are required for grain sorghum and sweet sorghum

DCI Notices were issued in 1983, 1984, and 1988 for various issues not related to residue chemistry. In response to the 1988 DCI Notice, the manufacturer of propazine, Ciba-Geigy, elected to cancel its registrations of propazine. No other registrant had committed to generate data required by that Notice and all products were either cancelled or suspended.

With their current submission, Griffin Corporation has shown an interest in supporting the previously cancelled uses of propazine on grain sorghum.

On 3/14/94, Vernon White (Director of Regulatory Affairs for Griffin Corp.) and Bill Tweedy (Director of PTRL South Inc., the testing facility performing the protocols) met with Elizabeth Haeberer and Jeff Herndon to discuss the protocols and registration of propazine on grain (and possibly sweet) sorghum. The review of the protocols and pertainent points discussed in the 3/14/94 meeting are addressed below.

Conclusions and Recommendations

The 4 proposed protocols are in line with the current CBTS/CBRS guidelines. However, CBTS would like to provide the following additional guidance/recommendations:

Metabolism

1. The Agency considers the 3 day dosing period for performing nature of the residue in animal studies to be a minimum. If the petitioner expects that, based on the properties of propazine (i.e. low transfer of residues to tissue, milk, and eggs), they will ask for a waiver from conducting cold livestock (cow and hen) feeding studies, then a longer dosing period (≥7 days) would provide more support for such a waiver. (min. of 7 day for eggs)

2. In the 3/14/94 meeting, CBTS clarified the point that the

metabolism studies should be performed using a high enough rate to result in sufficiently high radioactivity levels to allow for characterization/identification of the residue. In the case of oral livestock metabolism studies, the dose should, at a minimum, approximate the maximum anticipated dietary burden, but in no instance should the level be less than 10 ppm in the diet. CBTS explained that we do not discourage the use of exaggerated rates necessary to provide sufficient radioactivity for delineation of the residue. However, in cases where there has been little or no characterization/identification of the residue due to low levels of activity, CBTS may ask that the study be repeated using higher rates. Enclosed as Attachment II is a copy of Residue Chemistry's most recent guidance document for conducting plant and animal metabolism studies.

3. In the 3/14/94 meeting, CBTS reminded the petitioner to save some of the radiolabeled matrices from the metabolism studies to perform future radiovalidation of the analytical methods.

Confined Rotational Crop

4. In performing the confined rotational crop study, the sponsor should instruct the testing facility to leave the plant thinnings (Section 9.5 of proposed protocol) and any weeds that are pulled (Section 10.2.4) on the soil surface (i.e. do not discard them).

Note to P.M.: Please forward Attachment II to the petitioner. Also, CBTS recommends that the petitioner receive a copy of this complete review.

Attachment I: Proposed Protocols (4) for Conducting New Studies Using ^{14}C-Labeled Propazine:
Nature of the Residue in Sorghum (16 pgs)
Nature of the Residue in Lactating Goats (14 pgs)
Nature of the Residue in Laying Hens (15 pgs)
Confined Rotational Crops (18 pgs)

Attachment II: memo of 7/16/92 "Additional Guidance for Conducting Plant and Livestock Metabolism Studies"

cc (with Attachment I): RF, Propazine Reg.Std. files, G.J. Herndon.

cc (with Attachment II): Robert Taylor/Wesley Allen, PM Team 25 only (2 copies)

cc (without Attachments): circu., E. Haeberer (section head).

RDI: Acting Section Head: M. Flood: 3/23/94.
Branch Senior Scientist: R. A. Loranger: 3/23/94.
Branch Chief: D. Edwards: 3/24/94.

H7509C: CBTS: G. Herndon: 305-6362: CM#2: Rm 804C: 3/16/94.