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

FEB 22 1993

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM:

SUBJECT: PP#9F3724/9F03818 - Permanent Tolerance Petitions - New Chemical - Tebuconazole, Fungicide on Peanuts. Evaluation of Amendment Dated December 15, 1992. MRID Nos. 425925-01 and -02; CBTS Nos. 11170, 11171, 11172 and 11173; DP Barcodes D186731, D186738, D186726, and D186741.

FROM: Gary F. Otakie, P.E., Chemist
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Note To PM: A copy of a report on the Acute Oral Toxicity of Tebuconazole in Female Rats dated May 13, 1992 (MRID No. 425925-01) was also included in this submission and is being returned. If the study has not already been sent to TB please forward it.

Background

In a December 15, 1992 letter the petitioner indicated they had been informed that Chemistry Branch was requesting a peer review to determine whether a metabolite of tebuconazole (i.e. HWG 2061) was considered to be of toxicological significance.

In summary the petitioner chose a parent only method to measure tebuconazole residues in crops and proposed that the tolerance be established on tebuconazole only for the following reasons.

1. Tebuconazole, itself was the single, most abundant residue in any plant matrix.

2. HWG 2061 constituted only 4 to 7% of the total radioactive residue in the peanut metabolism study (of this the greatest residue occurred in a plant matrix which is only used as animal feed).

3. The acute oral toxicity values indicated that HWG 2061 was less toxic than tebuconazole (which is relatively innocuous itself).

4. At 72 hours after dosing rats with [C14] tebuconazole, HWG 2061 represented approximately one-quarter of the administered radioactivity, thereby indicating that any toxicity or lack thereof attributed to tebuconazole could be shared by HWG 2061.

5. A cost/benefit consideration definitely favors the parent only method when comparing what is gained by using an HWG 2061 + tebuconazole method vs. a parent only method.

6. Appendix I in the Agency's Standard Evaluation Procedure for Metabolism in Food Animals: Qualitative Nature of the Residue (PB90-103292) indicates that when a metabolite is not of greater toxicological significance than the parent and the metabolite does not comprise greater than 10% of the terminal residue, the metabolite should not be regulated.

Discussion

In a December 15, 1992 briefing for the HED Metabolism Committee, CBTS concluded as a worst case including residues from acid hydrolysis of peanut nutmeat solids (i.e. basing the estimate on the metabolism study) residues of HWG 2061 from 10 to 20% of the parent or 0.01 to 0.02 ppm in peanut meat may be possible.

The data reviewed were based on the third peanut metabolism study submitted to the Agency by Mobay (MRID # 419802-01). Based on this study CBTS concluded that 25% of the TRR was identified in peanut nutmeat, of which the parent accounted for 20% and the t-butylhydroxy metabolite in question (HWG 2061) 4% of the TRR or 20% of the parent level. The proposed tolerance for peanut nutmeat regulates the parent only at a level of 0.1 ppm while field trial data from the proposed use reflects parent levels in the range of <0.01 ppm to 0.05 ppm with one sample at 0.08 ppm.

Accordingly, inclusion of the metabolite in the tolerance expression based on the current data would be unlikley to require a higher tolerance level on peanut nutmeat. Available data indicate that the t-butylhydroxy metabolite will not concentrate

in peanut oil. The HWG 2061 metabolite is included in the tolerance expression for animal commodities and the available feeding studies indicate non-detectable to low residues for both the parent and the metabolite in animal commodities.

A 12/9/92 memo from Alberto Protzel evaluating the toxicity of the t-butylhydroxy metabolite concluded that a conservative assessment of the toxicity of HWG 2061 suggests that the compound should be considered to have a systemic toxicity similar to that of the parent.

Conclusion

Accordingly, the HED Metabolism Committee agreed that for the current proposed use on peanuts inclusion of the HWG 2061 metabolite in the tebuconazole tolerance expression was not required since its toxicity was expected to be similar to the parent, it accounted for less than 10% of the TRR, and it would be expected to be present at very low or non-detectable levels based on the amount of parent found in the field trials.

Therefore the tolerance expression for tebuconazole on peanuts (i.e. nutmeat, shells, forage, oil, meal and soapstock) will include the parent only.

The Committee also noted that if the t-butylhydroxy metabolite occurs at higher levels in other commodities on which use may be proposed in the future, two options could be considered.

1. Include the t-butylhydroxy metabolite in the tolerance expression for the commodity.

2. Use the parent as a marker but include the metabolite in the risk assessment.

This issue has been resolved for the proposed use on peanuts.

Attachment - Acute Oral Toxicity In Rats (MRID No 425925-01)

cc without Attachment : Reviewer-Otakie, RF, Circu, PP#9F3724, PP#9G3817, E. Haeberer

RDI: MFlood:2/11/93 RLoranger:2/19/93