

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

DEC 14 1987

MEMORANDUMOFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Bifenthrin Pesticide Petition 7F3453 for a permanent tolerance for residues of (2-methyl [1,1-biphenyl]-3-yl methyl-3-(2-chloro-3,3,3-trifluoro-1-propenyl) -2,2-dimethyl cyclopropanecarboxylate in or on cottonseed/milk, meat and meat by-products; response to company letter and to Residue Chemistry Branch deferral

TO: George LaRocca
PM 15
Registration Division
(TS-767)

FROM: Margaret L. Jones *M. L. Jones 9 December 1987*
Review Section III
Toxicology Branch
Hazard Evaluation Division

THROUGH: Marcia van Gemert, Ph.D., Head
Review Section III
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and Theodore M. Farber, Ph.D., Chief
Toxicology Branch

Project No. 8-0218 Record No. 205216 Caswell No. 463F

Petitioner: FMC Petition No. 7F3453

Action Requested: Update response to petition 6F3453 for adequacy to support a permanent tolerance on cottonseed/milk, meat, and meat by-products (points 1-8, below). Respond to Residue Chemistry Branch deferral concerning BP-acid metabolite in meat and meat byproducts (point 9, below).

Conclusion: The following summary addresses the issues considered in this request.

1. Summary of selected toxicology data considered in support of the tolerance.

Acute oral LD₅₀ (rat) = 53.8 mg/kg (females), 70.1 mg/kg (males)
(category III)

Acute dermal LD₅₀ (rabbit) > 2000 mg/kg (category III)

Teratology (rat) Maternal toxicity NOEL = 1 mg/kg/day
Developmental toxicity NOEL = 1 mg/kg/day
Teratology (rabbit) Maternal toxicity NOEL = 2.67 mg/kg/day
Developmental toxicity NOEL > 8 mg/kg/day
2-generation reproduction (rat)
Maternal toxicity NOEL = 30 ppm
Reproductive toxicity NOEL > 100 ppm
Developmental toxicity NOEL > 100 ppm
90-day feeding (rat) NOEL = 50 ppm (2.5 mg/kg/day)
13-week feeding (dog) NOEL = 2.21 mg/kg/day
1-year feeding (dog) NOEL = 0.75 mg/kg/day
2-year feeding/oncogenicity (rat)
Systemic toxicity NOEL = 50 ppm (2.5 mg/kg/day)
Oncogenic toxicity LEL > 200 ppm (10 mg/kg/day)
87-week oncogenicity (mouse) Oncogenic LEL = 50 ppm (7.5 mg/kg/day)
Mutagenicity- positive assay in mouse lymphoma, forward mutation
(gene mutation)
- negative in other assays including CHO cells,
ames test, UDS up to 2.5 ul/ml, and in vivo
rat bone marrow cells (categories of gene mutation,
genotoxicity, and chromosome aberration)

2. Summary of toxicological data considered desirable but currently lacking.

Current data requirements for bifenthrin appear to be satisfied. A suggested dermal absorption study is discussed under other relevant considerations [8.b].

3. Action being taken to obtain missing data.

No action is currently warranted.

4. Summary of other tolerances granted.

No other permanent tolerances for bifenthrin are known to exist.

5. Summary of how total tolerances granted affect the maximum permissible intake (MPI).

The effect of these tolerances on the contribution to the diet and the MPI is addressed by the Residue Chemistry Branch (RCB) and the Tolerance Assessment System (TAS). The result of that assessment will be forwarded directly from RCB to Registration Division.

6. Acceptable Daily Intake (ADI) data.

The ADI (RfD) for bifenthrin was approved by the Toxicology Branch ADI Committee on 6 November, 1987. The agency-wide RfD (ADI) Committee will consider bifenthrin next month (December, 1987). The one year dog feeding study with a no observed effects level

(NOEL) of 0.75 mg/kg/day was used to calculate the ADI. The dog was apparently the most sensitive species. A safety factor of 100 was used to account for inter- and intra-species differences. The ADI is calculated to be 0.0075 mg/kg/day based on non-oncogenic considerations. Dietary exposure will be calculated by Residue Chemistry Branch, as discussed in part 5, above.

7. There are no known pending regulatory actions against the registration of bifenthrin.

8. Other relevant considerations in the setting of this tolerance.

a. As discussed in the attached documents, bifenthrin has been classified as a Category C oncogen with a quantitative risk assessment.

b. In its exposure assessment for bifenthrin, Exposure Assessment Branch made no adjustments for dermal absorption. Based on the dermal absorption study in the rat (WIL Laboratories, No. 182RATMO6, 8/15/86, EPA Accession No. 264639, Doc. No. 005731) a factor of 55.4% will be used as an upper limit for the amount remaining on skin after washing and therefore the amount potentially available for absorption. The amount measured as absorbed was less than 1.6%, which is the limit of detection for this measurement. A study measuring the portion of what remains on the skin after washing that is subsequently absorbed could be used to reduce the estimation of 55.4% absorption, which is used in the lifetime risk calculations.

c. The lifetime cancer risk to applicators from the use of bifenthrin on cotton was calculated based on 10 exposures of 0.1 lb active ingredient per acre per year as the stated label rate of application (see memorandum from Backus to LaRocca, June 3, 1987). Risk characterization is found in Table 1. The numbers have been calculated using approximate acreage for cotton farms, which was omitted in previous calculations.

As seen in Table 1, several yearly exposures would result in a lifetime risk greater than 1×10^{-5} . These include exposures for mixer/loaders using an open-loading system with liquid formulation and to mixer/loaders using wettable powder formulation, to flaggers, and to ground boom applicators with mean and high exposures.

9. Response to the Residue Chemistry Branch (RCB) deferral to Toxicology Branch concerning the BP-acid metabolite (see July 9, 1987 memorandum from Boyd to LaRocca).

The tolerance expression for Bifenthrin should include the BP-acid metabolite (2-methyl-3-phenylbenzoic acid). The proposed tolerances for Bifenthrin in meat and meat byproducts are currently high enough to account for the BP-acid metabolite and the parent compound in the residue expression, according to RCB. However,

if additional tolerances are granted, the level in meat and meat byproducts will most likely exceed the proposed amount. A search of Chemline and Medline data bases indicates there is no toxicity data on the BP-acid metabolite. Testing of this compound will not be required at present, however, toxicity testing may be required at a future date.

Table 1

Risk characterization to workers applying bifenthrin to cotton

	(1)	(2)	Upper 95% Bound on Risk $Q_1^* = 5.4 \times 10^{-2}$ (mg/kg/day ⁻¹ in human equivalents 55.4 % Dermal Absorption [(1) x $\frac{1}{365}$ x $\frac{35}{70}$] [(2) x Q_1^*] x 0.554
Mixer/Loaders			
Liquid formulation			
Open loading	16.1	2.2×10^{-2}	6.6×10^{-4}
Closed loading	4.6×10^{-2}	6.3×10^{-5}	1.9×10^{-6}
Wettable Powder	3.9	5.3×10^{-4}	1.6×10^{-5}
Pilots	4.6×10^{-2}	6.3×10^{-5}	1.9×10^{-6}
Flaggers	2.7×10^{-1}	3.7×10^{-4}	1.1×10^{-5}
Ground Boom			
Application			
Low exposure	5.9×10^{-2}	8.1×10^{-5}	2.4×10^{-6}
Mean exposure	1.1	1.5×10^{-3}	4.5×10^{-5}
High exposure	26	3.6×10^{-2}	1.1×10^{-3}

+ Based on exposure for 10 days in one year.

Attachments