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CONFIDENTIAL

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

JUL 8 1988

Memorandum

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Subject: EPA Reg. No. 299-EER; Martin's Ear-Tix-Tox (Chlorpyrifos); No MRID No.; RCB No. 3868.

From: Francis B. Suhre, Chemist
Special Registration Section II
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

Thru: Edward Zager, Section Head
Special Registration Section II
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

To: Dennis Edwards, PM-12
Insecticide-Rodenticide Branch
Hazard Evaluation Division (TS-769)

The petitioner, C. J. Martin Co., has submitted additional information in response to our previous review of their product, Martin's Ear-Tix-Tox (F. Suhre, memo of 8-6-87). Deficiencies cited in that review are restated below, followed by the petitioner's response, and any additional comments by RCB.

Deficiency 2, restated from RCB memo dated 8-6-87:

The inert ingredients identified in the Confidential Statement of Formula (CFS) for Martin's Ear-Tix-Tox are not adequately described with respect to determining whether they are covered under 40 CFR 180.1001.

Petitioner's response to deficiency 2:

The petitioner provided a revised CSF for Martin's Ear-Tix-Tox; a CAS # was provided for each component in the formulation.

RCB's comment:

The revised CSF is discussed in the Confidential Appendix to this review.

Deficiency 4 restated from memo of 8-6-87:

No residue data were provided with this submission. We can draw no conclusions concerning the adequacy of available data, to estimate residues resulting from this proposed use, until additional information is submitted, as follows:

Total amount of active ingredient applied per animal per treatment.

Maximum number of treatments per season.

% of the animal's total surface area represented by the treatment area (its ears).

Relative rate of absorption. [redacted]

Is the product intended for use on dairy cattle ?

Alternatively, if this information is not available, the registrant will be required to submit residue data reflecting the proposed use.

Petitioner's response to deficiency 4:

The petitioner responded to deficiency 4 by provided the following information:

Approximately 0.035 grams of active ingredient is to be applied per animal per treatment.

Eight treatments per season (twice per month) is considered to be the maximum dose (280 mg/animal/season).

The treatment area (cattle ears) is estimated to represent 0.085% of the total surface area.

The relative rate of absorption of chlorpyrifos is not expected to be substantially higher from application to animal ears.

The petitioner has added a restriction against treatment of dairy cattle to the product label.

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RCB' comments:

Martin's Ear-Tix-Tox is intended to control tick infestations in the ears of cattle, goats, horses, and sheep. Approximately 2 mL of product (17.5 mg chlorpyrifos a.i.) is applied to the inside of each ear (35 mg chlorpyrifos a.i. per animal). Treatment is repeated as necessary, but not more than once every 14 days. Do not use on dairy cattle. The maximum seasonal dose and preslaughter interval are not specified on the product label, however, the registrant estimates that a maximum of 8 treatments will be made per season (280 mg per animal per season). No preslaughter interval was specified.

The registrant did not provided any residue chemistry data to support this proposed use. However, since Martin's Ear-Tix-Tox is formulated by [redacted] (see Confidential Appendix), and since the proposed use closely reflect the currently registered spot treatment; we will attempt to translate available data (see Dow Chemical's letter of authorization; D. Baker, Dow Chem., to D. Edwards, EPA, dated 4-29-87) to support this proposed use. The registered use of chlorpyrifos for direct spot treatment of ruminants , and the metabolism/residue data supporting that use are discussed below:

Registered use

Spot treatment of livestock: Spot treatments utilizing a Ready-to-use formulation (3.8 lbs chlorpyrifos/gallon) are registered for cattle and sheep. The formulated product is applied directly behind the animals shoulder blades and neck junction, sheep are treated at shearing. The treatment dose is 2 mL /100 lbs animal body weight (920 mg a.i./100 lbs. body weight). Use restrictions include: do not use more than 16 mL of formulated product (7.36 g) at one time. A 14 day preslaughter interval is established for cattle. Cattle may be retreated after 45 days or after 30 days with a 30-day preslaughter interval. A 35-day preslaughter interval is required for treated sheep. Retreatment of sheep is not allowed.

Metabolism data

In response to a data gap cited in the Chlorpyrifos Registration Standard (1-25-84), Dow Chemical Co. submitted a ruminant metabolism study entitled:

Fate of ^{14}C-Chlorpyrifos Applied Dermally to Ruminants, Study No. 6148-103, Accession No. 263124.

The results of this study are summarized in table 1 below:

Table 1: Chemical identification of the radioactive components in tissue of a goat treated (direct spot application) with 1 g chlorpyrifos/100 lbs. body weight. In order to obtain maximum tissue concentration, the goat was sacrificed when analysis indicated the first drop in ^{14}C blood levels:

% of Total Radioactive Residue

Tissue	Parent	TCP	A	B	C	D	E
Liver	ND	54.1	ND	ND	ND	3.9	13.4
Kidney	8.7	59.7	ND	ND	2.6	ND	7.7
Heart	52.6	21.5	ND	ND	ND	2.9	4.9
Fat	78.4	9.2	ND	ND	ND	ND	2.2
Muscle	22.1	32.4	5.3	13.3	ND	ND	6.0

PPM Equivalent of Total Radioactive Residue

Tissue	Parent	TCP	A	B	C	D	E
Liver	ND	0.33	ND	ND	ND	0.03	0.08
Kidney	0.06	0.44	ND	ND	0.02	ND	0.06
Heart	0.25	0.10	ND	ND	ND	0.01	0.02
Fat	0.65	0.08	ND	ND	ND	ND	0.02
Muscle	0.02	0.03	0.005	0.01	ND	ND	0.005

Parent = chlorpyrifos

A,B,C,D = unknown radioactive metabolites in organic extract of tissue.

E = Unextracted radioactive residue.

In a recent review of this study (S. Willett, memo of 3-9-88), RCB questioned the registrant's interpretation of several experimental results (HPLC and TLC elucidation of tissue TRR). Pending resolution of these deficiencies, the above data indicate that chlorpyrifos and its TCP metabolite are the residues of concern in the tissue of ruminants (goats) receiving a single spot treatment at 1.0 g chlorpyrifos/100 lbs. body weight (ca. 1x the registered rate for spot treatment, and 3.5x the total proposed seasonal dose for Martin's Ear-Tix-Tox).

Residue Data

Available residue data, reflecting direct treatment of ruminants with chlorpyrifos, are discussed in the Chlorpyrifos Registration Standard. Data translatable to the proposed use of Martin's Ear-Tix-Tox are summarized below:

Cattle treated with a single spot application (2 mL/100 lbs. body weight; 920 mg) of 3.8 lbs./gal RTU along the midline were sacrificed 1 to 35 days after treatment and tissue samples were analyzed for radioactive residues. Tissue residues peaked 7 days after treatment. Combined tissue residues (chlorpyrifos plus TPC) 7 days after treatment are summarized in Table 2:

Table 2: Chlorpyrifos residues in tissue of cattle receiving a single spot treated (920 mg chlorpyrifos/100 lbs. body weight) and slaughtered 7 days after treatment.

Tissue	Chlorpyrifos (ppm)	Combined Chlorpyrifos/metabolites (ppm)
Muscle	0.01 - 0.06	<0.06 - <0.21
liver	0.01 - 0.08	0.69 - 1.58
kidney	0.09 - 0.18	0.55 - 1.58
fat	0.95 - 1.40	1.03 - 1.64

The above data indicate that direct spot treatment of beef cattle at 1.0 g chlorpyrifos/100 lbs. body weight will not produce residues in excess of established tolerances. Translating these data to the proposed use of Martin's Ear-Tix-Tox (280 mg/animal/season; 0.3x the pour-on dose) we conclude that the established tolerances for fat, meat, and meat by-products of cattle (2.0 ppm), goats (1.0 ppm), horses (1.0 ppm) and sheep (1.0 ppm) will not be exceeded.

Note to PM: Please be advised that the following conclusion is expressed in the Chlorpyrifos Registration Standard (1-26-84):

" The maximum residue which could occur from direct dips and pour-on application to beef cattle in combination with ingestion of feed items containing tolerance level residues may exceed the established tolerances for residues in cattle fat, meat, and meat by-products."

RCB's Conclusions

1. For the purpose of this registration action, we consider the metabolic nature of chlorpyrifos in ruminants to be adequately understood. The residues of concern are chlorpyrifos, per se, and its TPC metabolite.

2. Based on translating residue data form the direct spot treatment of cattle, we conclude that combined residues of chlorpyrifos and its TPC metabolite will not exceed established tolerances as a result of the proposed use of Martin's Ear-Tix-Tox.

3. The maximum seasonal rate (8 applications at 35 mg; 280 mg/animal/season) and the preslaughter interval must appear on the product label. Furthermore, since the cumulative residue level resulting from dips, pour-on treatments, and ingestion of chlorpyrifos treated feed items may result in secondary residues in fat, meat and meat by-products of livestock at levels exceeding established tolerances (see chlorpyrifos Registration Standard, 1-25-84), the product label should also contain a restriction against the use of more than one type of direct animal treatment product containing chlorpyrifos on livestock.

Recommendation

Provided the label changes cited in conclusion 3 (see above) are made, we recommend in favor of the registration of Martin's Ear-Tix-tox.

Attachment: Confidential Appendix (cc to S.F., PM-12, R.F., reviewer, and PMSD/ISB only)

cc without Confidential Appendix: Circu, RCB TAS Staff.
RDI:EZ:7/7/88:RDS:7/7/88
TS-796:FBS:fbs:557-1883:CM#2,RM814:7/7/88

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Chlorpyrifos residue chemistry review

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Pages _____ through _____ are not included in this copy.

The material not included contains the following type of information:

___ Identity of product inert ingredients

___ Identity of product impurities

___ Description of the product manufacturing process

___ Description of product quality control procedures

___ Identity of the source of product ingredients

___ Sales or other commercial/financial information

___ A draft product label

X The product confidential statement of formula

___ Information about a pending registration action

___ FIFRA registration data

___ The document is a duplicate of page(s) _____

___ The document is not responsive to the request

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.
