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OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: 19-AUG-1999

SUBJECT: PP# 8F04980. Chlorfenapyr (i.e. Chlorfenapyr Insecticide Cattle Ear Tag) in/on Meat & Milk. **Evaluation of Residue Data and Analytical Methods.** MRID# 445603-02. Chemical 129093. Barcodes D247483, D247491, & D247498. Cases 290113, 062365, & 044966. Submission#s S544727, S544730, & S545357.

FROM: George F. Kramer, Ph.D., Chemist *[Signature]*
RAB1/HED (7509C)

THRU: Melba Morrow, D.V.M., Branch Senior Scientist *[Signature]*
RAB1/HED (7509C)

TO: Marion Johnson/Ann Sibold
Registration Division (7505C)

American Cyanamid Company has petitioned for permanent tolerances for residues of the insecticide/miticide chlorfenapyr [4-bromo-2-(chlorophenyl)-1-(ethoxymethyl)-5-(trifluoromethyl)-1H-pyrrole-3-carbonitrile] in conjunction with the registration of Chlorfenapyr Insecticide Cattle Ear Tag as follows:

Milk	0.01 ppm
Milk Fat	0.03 ppm
Meat	0.01 ppm
Meat (Fat)	0.03 ppm
Meat Byproducts	0.30 ppm

Time-limited tolerances (in conjunction with a Section 18 registration on cotton) have been established for: cottonseed (0.5 ppm); Cotton gin byproducts (2.0 ppm); Fat* (0.10 ppm); mby* (0.3 ppm); Meat* (0.01 ppm); Milk (0.01 ppm); Milk fat (0.15 ppm) [40 CFR S180.513(b); expires 1/31/01].

*of beef, goat, swine, horse and sheep

Executive Summary of Chemistry Deficiencies

- Revised Section F.

CONCLUSIONS

OPPTS GLN 860.1200: Proposed Uses

1. The petitioner has provided an adequate set of directions for the proposed use.

OPPTS GLN 860.1300: Nature of the Residue - Plants

OPPTS GLN 860.1500: Crop Field Trials

OPPTS GLN: 860.1520: Processed Food/Feed

OPPTS GLN 860.1850 and 860.1900: Confined/Field Accumulation in Rotational Crops

2. As there are no plant commodities associated with this petition, issues pertaining to the nature and magnitude of the residue in plants (including processed commodities and rotational crops) are not germane to this petition.

OPPTS GLN 860.1300: Nature of the Residue - Animals

3. The nature of the residue in ruminants is adequately understood. Residues consist primarily of the parent in muscle, fat and milk. In the HED Metabolism Committee Meeting of 6/20/96, it was determined that for ruminant commodities the chlorfenapyr permanent tolerance expression should be in terms of parent only.

OPPTS GLN 860.1340: Residue Analytical Methods

4. Three different analytical methods for chlorfenapyr residues in milk, muscle/fat and liver/kidney are available to support the proposed permanent tolerances (MRID 43492857). A satisfactory method trial has been conducted by EPA's Analytical Chemistry Laboratory for the subject animal commodity chlorfenapyr methods (i.e. M 2405 for cattle liver, M 2398 for cattle muscle and M2395.01 for cows milk).

OPPTS GLN 860.1360: Multiresidue Method

5. Multiresidue data for chlorfenapyr were submitted. Protocols A and B were not applicable to chlorfenapyr. In Protocol C, chlorfenapyr gave a good response and a good peak with the electron capture detector on three different GC columns. In Protocol D, the 5% OV-101 column gave the greatest sensitivity at 0.05 and 0.50 ppm. In Protocol E, chlorfenapyr gave acceptable recovery.

OPPTS GLN 860.1380: Storage Stability Data

6. The samples from the residue study were stored for a maximum of 5 weeks. Residues of chlorfenapyr have been shown to be stable in animal RACs for up to 42 days of storage (Memo, G. Otakie 10/21/96). Storage stability is thus not an issue for this petition.

OPPTS GLN 860.1480: Meat, Milk, Poultry, Eggs

7. Holstein dairy cows were tagged with chlorfenapyr with 2 ear tags. Samples were analyzed with method M 2405 (LOQ = 0.05 ppm) for liver and kidney; M 2398 (LOQ = 0.01 ppm) for muscle, fat, and milkfat; and M2395.01 (LOQ = 0.01 ppm) for milk. Quantifiable residues were observed only in milkfat (0.018 ppm) and fat (0.020 ppm). Based on the results of this study, the appropriate tolerances are:

Milk	0.01 ppm
Milk Fat	0.02 ppm
Cattle Meat.	0.01 ppm
Cattle Fat	0.03 ppm
Cattle Meat Byproducts.	0.05 ppm

A revised Section F is thus required for this petition.

Other Considerations

8. There is neither a Codex proposal, nor Canadian or Mexican limits for residues of chlorfenapyr in/on meat and milk. Therefore, a compatibility issue is not relevant to the proposed tolerance. A copy of the IRLS is attached to this memorandum.

RECOMMENDATIONS

HED will recommend in favor of the proposed tolerances for chlorfenapyr in meat and milk provided that the petitioner submits revised Section F as detailed in Conclusion 7. As previous HED risk assessments have included meat and milk tolerances at higher values than those proposed in this action, a

new risk assessment will not be required for this petition.

HED notes that meat and milk tolerances which are higher than those proposed in this petition have been established on a time-limited basis under [40 CFR §180.513(b) and proposed in PP#s 6E4683, 6F4623, and 5F4456. If any of these tolerances are established on a permanent basis, then the meat and milk tolerances proposed in this petition will not be necessary.

DETAILED CONSIDERATIONS

OPPTS GLN 860.1200: Proposed Uses

Chlorfenapyr Insecticide Cattle Ear Tag (EPA Reg. No. 000241-GOT) contains 30% a.i. Chlorfenapyr Insecticide Cattle Ear Tags can be used on both beef and dairy cattle to control lice and horn flies. Two tags may be used per animal.

The petitioner has provided an adequate set of directions for the proposed use.

OPPTS GLN 860.1300: Nature of the Residue - Plants

OPPTS GLN 860.1500: Crop Field Trials

OPPTS GLN: 860.1520: Processed Food/Feed

OPPTS GLN 860.1850 and 860.1900: Confined/Field Accumulation in Rotational Crops

As there are no plant commodities associated with this petition, issues pertaining to the nature and magnitude of the residue in plants (including processed commodities and rotational crops) are not germane to this petition.

OPPTS GLN 860.1300: Nature of the Residue - Livestock

The nature of the residue in ruminants is adequately understood based on data submitted by American Cyanamid (MRID#s 42770235 and 43492855) depicting the metabolism of ¹⁴C-chlorfenapyr in lactating goats dosed orally once a day for seven days. The low and high doses represented a daily feeding level of 3.0 and 17.9 ppm for [phenyl-¹⁴C]-chlorfenapyr and 3.16 ppm and 16.4 ppm for [2-pyrrole-¹⁴C]-chlorfenapyr. These doses represent 10X and 58X the proposed maximum daily dietary burden.

The distribution of the TRR in milk and tissues from both groups

4

was similar. In the high dose group, the TRR in milk increased from 0.03 to 0.07 ppm by day 7. Radioactive residues ranged from 0.03-0.05 ppm in muscle to 1.45-1.46 ppm in liver.

Residues consist primarily of the parent in muscle, fat and milk. In addition to the parent, numerous chlorfenapyr metabolites were identified. In the liver and kidney, the metabolites CL 325,195 [i.e. 2-pyrrolidine-3-carbonitrile, 2-(p-chlorophenyl)-5-hydroxy-4-oxo-5-(trifluoromethyl)-] and CL 322,250 [i.e. Pyrrole-2-carboxylic acid, 3-bromo-5-(p-chlorophenyl)-4-cyano-] were present at the highest level as well as the parent, other metabolites and conjugates.

In the HED Metabolism Committee Meeting of 6/20/96, it was determined that for ruminant commodities the chlorfenapyr permanent tolerance expression should be in terms of parent only. Use of only parent residues is acceptable for chlorfenapyr dietary risk assessments on ruminant commodities (excluding meat byproducts). However, chlorfenapyr dietary risk assessments on ruminant meat byproducts should include the two metabolites CL 303,268, and CL 325,195 as well as the parent. The ruminant meat byproduct risk assessment will use a factor (i.e. ratio parent plus metabolites/parent) multiplied by the parent based tolerance determined from the residue levels of the three moieties in the ruminant metabolism studies.

OPPTS GLN 860.1340: Residue Analytical Methods - Animal Commodities

Three different analytical methods for chlorfenapyr residues in milk, muscle/fat and liver/kidney are available to support the proposed permanent tolerances (MRID 43492857). A satisfactory method trial has been conducted by EPA's Analytical Chemistry Laboratory for the subject animal commodity chlorfenapyr methods (i.e. M 2405 for cattle liver, M 2398 for cattle muscle and M2395.01 for cows milk).

M 2395.01 - Parent residues are isolated from milk and purified using acetone precipitation, methylene chloride partition and solid phase extraction techniques. Residues are measured using gas chromatography (GC) with electron capture detection and residues are calculated as parent by direct comparison of sample peak height to that of an external standard. The validated sensitivity of the method is 10 ppb.

M 2398.01 - Parent residues are extracted from muscle with methanol and from fat with acetonitrile. Residues are isolated by hexane partition and purified using

solid phase extraction techniques. Residues are measured using GC with electron capture detection and calculated as parent by direct comparison of sample height to that of an external standard. The validated sensitivity of the method is 10 ppb.

M 2405 - Parent residues are extracted from cattle liver and kidney tissues with acetonitrile. Residues are isolated by hexane partition and are purified using solid phase extraction techniques. Residues are measured using GC with electron capture detection and calculated as parent by direct comparison of sample height to that of an external standard. The validated sensitivity of the method is 50 ppb.

OPPTS GLN 860.1360: Multiresidue Method

Multiresidue data for chlorfenapyr were submitted. Protocols A and B were not applicable to chlorfenapyr. In Protocol C, chlorfenapyr gave a good response and a good peak with the electron capture detector on three different GC columns. In Protocol D, using pears as a nonfatty food representative, the 5% OV-101 column gave the greatest sensitivity at 0.05 and 0.50 ppm. In Protocol E, chlorfenapyr eluted well on Florisil in both the ethyl ether/petroleum ether system and the alternate hexane/acetonitrile/methylene chloride system and gave acceptable recovery.

OPPTS GLN 860.1380: Storage Stability Data

No storage stability data were submitted with this petition.

The samples from the residue study were stored for a maximum of 5 weeks. Residues of chlorfenapyr have been shown to be stable in animal RACs for up to 42 days of storage (Memo, G. Otakie 10/21/96). Storage stability is thus not an issue for this petition.

OPPTS GLN 860.1480; Meat, Milk, Poultry, Eggs

Ruminants

Submitted with this petition:

Milk and Tissue Residue Study in Lactating Dairy Cattle
Tagged with Two Ear Tags Containing 30% CL 303630
(Chlorfenapyr). MRID# 445603-02

Holstein dairy cows were treated with chlorfenapyr by application of 2 ear tags. The treated group had 4 cows. Milkfat samples were taken on days 15 and 29; milk samples, throughout the study. The cows were sacrificed on day 30. Samples were analyzed with methods M 2405 (LOQ = 0.05 ppm) for liver and kidney; M 2398 (LOQ = 0.01 ppm) for muscle, fat, and milkfat; and M2395.01 (LOQ = 0.01 ppm) for milk. The methods were validated in milk over a range of 0.01-0.05 ppm (recoveries ranged from 72-84%); in muscle, fat and milkfat over a range of 0.01-0.10 ppm (recoveries ranged from 70-103%); and in liver and kidney at 0.05 ppm (recoveries ranged from 84-93%). Quantifiable residues were observed only in milkfat (0.018 ppm) and fat (0.020 ppm).

Based on the results of this study, the appropriate tolerances are:

Milk	0.01 ppm
Milk Fat	0.02 ppm
Cattle Meat.	0.01 ppm
Cattle Fat	0.03 ppm
Cattle Meat Byproducts.	0.05 ppm

A revised Section F is thus required for this petition.

Attachment 1- IRLS Sheet

cc: PP#8F04980, Kramer, R.F.
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