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

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

DATE: 10/24/96

SUBJECT: ID#96AZ0012 SECTION 18 EXEMPTION FOR USE OF CHLORFENAPYR ON LETTUCE IN THE STATE OF ARIZONA.

DP Barcode: D229541 Caswell: NA
Trade Name: Alert/Pirate Chem#: 129093
Reg#: 241-EUP-136 Case#: NA
Class: Insecticide-Miticide 40 CFR: NA

TO: M. Collantes/R. Forest, PM Team 41
ERMUS/RSB/RD (7505W)

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INTRODUCTION

The Arizona Department of Agriculture is proposing a specific exemption for the use of chlorfenapyr on lettuce for control of beet armyworm. This is the first §18 request for this use. The proposed program will entail application of 32,500 gallons of Alert (65,000 lbs ai) on 65,000 acres in the counties of La Paz, Yuma, Maricopa, Pinal, Pima, and Cochise, during the period October 6, 1996 - May 31, 1997.

RECOMMENDATION

Occupational and aggregate risk estimates do not exceed HED's level of concern. This Section 18 exemption and other pending uses of chlorfenapyr should not pose an unacceptable health risk to infants and children. Therefore, HED has no objection to the issuance of this Section 18 exemption for the use of chlorfenapyr on lettuce in the State of Arizona. A time-limited tolerance for regulable

residues of chlorfenapyr at 8 ppm on head lettuce and 15 ppm on leaf lettuce should be established to support this Section 18 exemption.

CONCLUSIONS

Hazard Assessment

1. Occupational Exposure Endpoint Selection

a) Short- and Intermediate- Term Risk.

Dermal Exposure: For short-term MOE calculations, the TES [Toxicity Endpoint Selection] Committee recommended use of a 28-day dermal toxicity study [MRID#: 43492831] in rabbits. The NOEL was 100 mg/kg/day. The LEL of 400 mg/kg/day was based on increased serum cholesterol, increased relative liver weights, and unspecified histological lesions.

Inhalation Exposure (for short- , or intermediate-endpoints): As determined by the TES committee, this endpoint was based on the combined LC_{50} of 1.9 mg/L. Chlorfenapyr is placed in Toxicity Category III. Therefore, risk via the inhalation route is not a concern at this time.

b) Chronic Risk. Chronic MOE calculations were not performed since there is no chronic exposure scenario for this Section 18 use.

c) Cancer Risk. The HED Carcinogenicity Peer Review Committee met on September 25, 1996. Pirate/Alert (Chlorfenapyr) was classified as a Group D (not classifiable as to human carcinogenicity) chemical and a risk assessment was not performed.

d) Dermal Penetration.

A dermal absorption factor is not required for the short- and intermediate-term occupational exposure risk assessments since a 21-day dermal toxicity study was used for these scenarios.

2. Dietary Endpoint Selection

a) Acute Risk. 45 mg/kg/day. For acute dietary risk assessment, the TES Committee recommended use of an acute neurotoxicity study (MRID#: 43492829) in rats. The NOEL was 45 mg/kg/day. The LEL of 90 mg/kg/day was based on lethargy of the rats on the day of treatment.

b) Chronic Risk. The HED RfD Peer Review Committee (July 18, 1996) has established an RfD of 0.03 mg/kg/day, with an uncertainty factor (UF) of 100, for Pirate/Alert

(Chlorfenapyr). These findings were observed in a combined toxicity/oncogenicity study (MRID#: 43492838) in mice which included central nervous system lesions and scabbing of the skin (males).

c) Cancer Risk. The HED Carcinogenicity Peer Review Committee (CPRC) met on September 25, 1996. Pirate/Alert (Chlorfenapyr) was classified as a Group D (not classifiable as to human carcinogenicity) chemical and a risk assessment was not performed.

d) Infants and Children

i) Developmental Toxicity Studies

Rat - From the developmental toxicity study (MRID #: 42770221/428884202) in rats, the maternal (systemic) NOEL was 25 mg/kg/day. The LEL of 75 mg/kg/day was based on decreased body weight gain, decreased relative feed intake, and decreased water consumption. The developmental (pup) NOEL was ≥ 225 mg/kg/day (HDT).

Rabbit - From the developmental toxicity study (MRID #: 42770222) in rabbits, the maternal (systemic) NOEL was 5 mg/kg/day. The LEL of 15 mg/kg/day was based on decreased body weight gain. The reproductive/developmental NOEL was ≥ 30 mg/kg/day (HDT).

ii) Reproductive Toxicity Studies

Rat - From the multigeneration reproductive toxicity study (MRID #: 434292836) in the rat, the maternal (systemic) NOEL was 5 mg/kg/day. The LEL of 22 mg/kg/day was based on decreased body weight gain (pre-mating). The reproductive/developmental NOEL was 5 mg/kg/day. The LEL of 22 mg/kg/day was based on decreased weight gain during lactation.

Occupational Exposure

1. Acute data for this formulation were not provided to PIRAT. No determination can be made as to whether the work clothing and personal protective equipment (PPE) appearing on the label are in compliance with the Worker Protection Standard (WPS). The Alert Insecticide-Miticide label (EPA Reg. No. 242-EUP-136) requires applicators and handlers to wear: long-sleeved shirt, long pants, chemical-resistant gloves, and shoes plus socks. RD should insure that the appropriate WPS statements appear on the label.

2. Acute data for the technical are available. The restricted

entry interval (REI) of 12 hours appearing on the label is in compliance with the WPS.

3. Occupational exposure assumptions and estimates of exposure are summarized in Tables 1 and 2, respectively. PIRAT has conducted the estimates of exposure with workers wearing a single layer of clothing plus gloves. Pilots are not expected to wear gloves.

   The TES Committee does not consider workers to be at risk from inhalation exposure due to the low toxicity of the chemical. Consequently, an inhalation component has not been included in the estimates of exposure for workers.

Aggregate Exposure

Dietary Exposure

1. The nature of the residue of chlorfenapyr in plants is adequately understood. The residue of concern is parent compound only.

2. Adequate enforcement methodology is available to enforce the tolerance expression. A GC\ECD method by American Cyanamid, M 2216, is available in PP#3G4224 for chlorfenapyr residues in cottonseed (MRID# 427702-38).

3. An incomplete set of magnitude of the residue studies on head lettuce have been reviewed by CBRS. Residues of chlorfenapyr on head lettuce did not exceed 5 ppm (PP#5G04523 and PP#5G04548, MRID No. 43638904, G. Otakie, 3/21/96). CBRS requested additional studies of chlorfenapyr on head lettuce and a complete set of studies on leaf lettuce. With this §18 request, the registrant has submitted summary tables of the residues of chlorfenapyr on leaf and head lettuce from the additional studies. Although apparently the data has been submitted and an MRID has been assigned (MRID 43996207), the studies have not as yet been reviewed. For the purposes of this §18 use only, PIRAT will use this data summary and the previously submitted data on head lettuce to recommend temporary tolerances. **Residues of chlorfenapyr are not likely to exceed 8 ppm on head lettuce and 15 ppm on leaf lettuce as a result of this Section 18 use. Time-limited tolerances should be established at these levels.**

4. Secondary residues are not expected in animal commodities as no feed items are associated with this Section 18 use.

5. Acute Dietary Risk. The acute dietary exposure endpoint of concern for chlorfenapyr is lethargy the day of dosing which

would effect all population subgroups. The acute analysis assumed tolerance level residues for all commodities. For all the population subgroups, the calculated Margin Of Exposure (MOE) values are greater than 1125 based on high end exposure (10/3/96).

6. Chronic Dietary Risk. Chronic dietary exposure estimates (DRES) for chlorfenapyr are summarized in the Appendix. The DRES analysis assumed tolerance level residues and 100% crop treated for all commodities. The proposed Section 18 use result in a Theoretical Maximum Residue Contribution (TMRC) that is equivalent to the following percents of the RfD:

U.S. Population (48 states)	6.3%
Nursing Infants	0.0%
Non-Nursing Infants (<1 year old)	0.2%
Children (1-6 years old)	5.1%
Children (7-12 years old)	6.7%
Females 13+, Nursing	8.2%

The subgroups listed above are: (1) the U.S. population (48 states); (2) those for infants and children; and, (3) the subgroup which occupies the highest percentage of the RfD. Pirat notes that there are other subgroups with higher percentages of the RfD than the U.S. population (see attached).

7. Dietary Cancer Risk. Based on the CPRC classification of this chemical, Group D, dietary cancer risk assessment is not required.

Exposure from Water

EFED ground water data base has no information on chlorfenapyr. In the absence of data, PIRAT must assume that chlorfenapyr is persistent and mobile. There is no established Maximum Concentration Level for residues of chlorfenapyr in drinking water. No health advisories for chlorfenapyr in drinking water have been issued.

PIRAT does not have available data to perform a quantitative drinking water risk assessment for chlorfenapyr at this time. Previous experience with persistent and mobile pesticides for which there have been available data to perform quantitative risk assessments have demonstrated that drinking water exposure is typically a small percentage of the total exposure when compared to the total dietary exposure. This observation holds even for pesticides detected in wells and drinking water at levels nearing or exceeding established MCLs. Based on this experience and our best scientific judgement, HED concludes that it is not likely that the potential exposure from residues in drinking water added to the current dietary

exposure will result in an exposure which would exceed 100% of the RfD.

Non-occupational Exposure

Chlorfenapyr is not currently registered for any residential uses; therefore no significant exposure is anticipated.

Cumulative Effects

At this time, the Agency has not made a determination that chlorfenapyr and other substances that may have a common mode of toxicity would have cumulative effects.

Determination of Safety for Infants and Children

Based on current toxicological data requirements, the data base for Alert/Pirate (chlorfenapyr) relative to pre- and post-natal toxicity is complete.

PIRAT notes that the developmental toxicity NOELs of >225 mg/kg/day (HDT in rats) and >30 mg/kg/day (HDT in rabbits) demonstrate that there is no developmental (prenatal) toxicity present for Alert/Pirate (chlorfenapyr). Additionally, these developmental NOELs are 75- and 10-fold higher in the rats and rabbits, respectively, than the NOEL of 1.8 mg/kg/day from the 1-year feeding study in dogs (the basis of the RfD).

In the reproductive toxicity study in the rat, the reproductive/developmental NOEL (5 mg/kg/day) is equal to the parental NOEL (5 mg/kg/day). Both the pup LEL and the parental LEL of 22 mg/kg/day were based on decreased body weight. This finding suggests that there is no special post-natal sensitivity present in the reproduction study and that young rats have the same sensitivity to Alert/Pirate (chlorfenapyr) as adult animals.

These developmental and reproductive toxicity studies indicate that infants and children have no special sensitivity to chlorfenapyr relative to other population groups. An additional safety factor for infants and children is not necessary for this proposed use.

SUPPLEMENTAL INFORMATION

Occupational Exposure

Table 1. Occupational Exposure Assumptions	
PARAMETER	**ASSUMPTION**
Pesticide Handlers Exposure Database (PHED), Version 1.1, Unit of Exposure From Best Available Surrogate Exposure Table (BASET, 7/25/96)	Mixer/Loader (all liquid formulations, open mixing, single layer clothing plus gloves): Dermal = 43.0 µg/lb ai handled.
	Applicator (groundboom, open cab, single layer clothing no gloves): Dermal = 14.0 µg/lb ai applied.
	Applicator (aerial, single layer clothing no gloves): Dermal = 5.0 µg/lb ai applied.
Percent Absorption	Dermal: NA (Tox value-dermal toxicity study)
Application Type	Ground and air
Minimum Finish Spray	Ground: 25 gal/A Air: 3 gal/A
Maximum Application Rate	0.15 lb ai/A
Maximum Applications Per Year	3
Duration of occupational exposure	Intermediate (one week to several months)
Acres Treated/Day (Y, NG,BEAD)	Ground: 73 acres Air: 511 acres
Average Farm Size (1992 Ag Census)	Based on Yuma county, AZ 1007 acres
Worker Weight	70 kg (Tox endpoint)
Number of Farms Treated by PCO (Professional Chemical Operator)	Ground: 2 (OREB default value) Air: 10 (OREB default value)

Table 2. Occupational Exposure and Risk Assessment[a]		
Worker	Average Dermal Daily Dose[b] (ug/kg/day)	Dermal Short & Intermediate -Term MOE[c]
Ground Mixer/Loader	6.73	15,000
Ground Applicator	2.19	46,000
Aerial Mixer/loader	47.09	2,100
Aerial Applicator	5.48	18,000

[a] MOEs are expressed to two significant figures.

[b] Average Dermal Daily Dose (ADD) = PHED unit exposure x application rate x acres treated/day ÷ kg body weight.

[c] Short and Intermediate-Term Dermal Occupational Exposure MOE = NOEL/ADD (where NOEL = 100 mg/kg/day).