

US EPA ARCHIVE DOCUMENT

359C



U. S. ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA OFFICE 651

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

DATE: 7/22/97

SUBJECT: ID#97WA0022. SECTION 18 EXEMPTION FOR THE USE OF
PIRIMICARB ON VEGETABLE SEED CROPS IN WASHINGTON.

DP Barcode:	D235362	Caswell#:	359C
PRAT Case#:	288614	Chemical#:	06101
Trade Name:	Pirimor 50DF	40 CFR:	none
EPA Reg#:	10182-370	Class:	Insecticide

TO: Steven Schaible/Meredith Johnson, PM Team 41
MUIERB/RD (7505C)

FROM: William D. Wassell, Chemist
William G. Dykstra, Toxicologist
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HED (7509C)

THRU: Richard Loranger, Branch Senior Scientist
RAB2/HED (7509C)

INTRODUCTION

The Washington Department of Agriculture has proposed a specific exemption for the use of pirimicarb on vegetable seed crops (Chinese mustard; Chinese cabbage; broccoli raab; mustard; rutabaga; rape greens; collard; kale; Chinese kale; cauliflower; cabbage; brussels sprouts; spinach mustard; turnip; turnip, fodder; arrugula; radish; swiss chard; beet, table; spinach; endive; lettuce; coriander; parsnip; and parsley) for control of bean aphids, green peach aphid, turnip aphid, lettuce aphid, and melon aphid. This is the third year for this §18 request. The proposed program will entail application of 2,250 pounds of

product (1,125 lbs ai) on 6,000 acres statewide, during the period May 1, 1997 to September 15, 1997.

Tolerances are not currently established for residues of pirimicarb and/or its metabolites in/on raw agricultural commodities.

SUMMARY

Provided the rotational crop restrictions (specified below under OTHER CONSIDERATIONS) are added to the label, then:

This Section 18 use has previously been classified as a nonfood use. Thus, tolerances and a dietary (food only) risk assessment are not required.

Occupational exposure estimates do not exceed HED's level of concern. Therefore, HED has no objections to the issuance of this Section 18 exemption for the use of pirimicarb on vegetable seed crops in the State of Washington.

RD should insure that the appropriate WPS statements regarding PPE (long-sleeved shirt and long pants, waterproof gloves, and shoes plus socks) and the appropriate REI (12 hours) appears on the label intended for use on vegetable seed crops.

TOXICOLOGICAL ENDPOINTS

DIETARY

As this use has been classified as a nonfood use and tolerances are not required, dietary risk assessments are not required.

NON-DIETARY

- 1) *Short-Term Toxicity.* For short-term Margin of Exposure (MOE) calculations, the Toxic Endpoint Selection Committee (TESC) recommended (6/27/96) use of the systemic NOEL of 40 mg/kg/day from a 21-day dermal toxicity study in rats. This was based upon decreased

plasma and brain levels of cholinesterase at the LOEL of 200 mg/kg/day.

- 2) *Intermediate-Term Toxicity.* For intermediate-term MOE calculations, the TESC recommended (6/27/96) use of the NOEL of 1.8 mg/kg/day from the subchronic toxicity study in dogs [MRID#: 43641001]. The LOEL of 4 mg/kg/day was based on hematopoietic effects including bone marrow effects indicative of a compound-dependent hemolytic anemia of the "penicillin type".
- 3) *Chronic Toxicity.* As a chronic exposure scenario does not exist for this Section 18 use, this risk assessment is not required.
- 4) *Dermal Penetration.* Dermal penetration of 25% has been recommended by the TESC (6/27/96) based on a comparison of several different studies.

CANCER

The cancer status of pirimicarb has not been determined (TESC, 6/7/96) due to an inadequate database.

EXPOSURES AND RISKS

In examining aggregate exposure, FQPA directs EPA to consider available information concerning exposures from the pesticide residue in food and all other non-occupational exposures. The primary nonfood sources of exposure the Agency looks at include drinking water (whether from groundwater or surface water), and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor and/or outdoor uses). In evaluating food exposures, EPA takes into account varying consumption patterns of major identifiable subgroups of consumers, including infants and children.

1. From Food and Feed Uses:

Tolerances have not been established for residues of pirimicarb in/on raw agricultural commodities, foods and feeds and the subject Section 18 use has been classified as a nonfood use and

tolerances are not required. Thus, exposure to pirimicarb residues from food is not expected.

2. *From Drinking Water:*

Based on information in the Pesticide Environmental Fate One Line Summary (last update dated 5/6/97), pirimicarb may be persistent and mobile, but the data are inconclusive. There are no established Maximum Contaminant Levels for residues of pirimicarb in drinking water and no Health Advisory Levels in drinking water have been established for this active ingredient (personal communication, EPA Safe Drinking Water Hotline, 6/9/97).

Because the Agency lacks sufficient water-related exposure data to complete a comprehensive drinking water risk assessment for many pesticides, EPA has commenced and nearly completed a process to identify a reasonable yet conservative bounding figure for the potential contribution of water related exposure to the aggregate risk posed by a pesticide. In developing the bounding figure, EPA estimated residue levels in water for a number of specific pesticides using various data sources. The Agency then applied the estimated residue levels, in conjunction with appropriate toxicological endpoints (RfDs or acute dietary NOELs) and assumptions about body weight and consumption, to calculate, for each pesticide, the increment of aggregate risk contributed by consumption of contaminated water. While EPA has not yet pinpointed the appropriate bounding figure for consumption of contaminated water, the ranges the Agency is continuing to examine are all well below the level that would cause pirimicarb to exceed the RfD if the uses being considered in this document were granted. The Agency has therefore concluded that the potential exposures associated with pirimicarb in water, even at the higher levels the Agency is considering as a conservative upper bound, would not prevent the Agency from determining that there is a reasonable certainty of no harm if the tolerance is granted.

3. *From Non-Dietary Uses:*

A search of the Reference Files System (REFS) on 6/24/97, did not locate information for pirimicarb. According to RD (Susan Lewis, personal communication, 7/14/97), pirimicarb has no residential

uses. Thus, a comprehensive residential risk assessment is not required.

4. *From Cumulative Exposure To Substances with a Common Mechanism of Toxicity:*

Pirimicarb is a member of the carbamate class of pesticides. Other members of this class include carbaryl, methomyl, carbofuran, thiodicarb, methiocarb, aldicarb, oxamyl, aminocarb, propoxur, bendiocarb, trimethacarb, isoprocarb, cloethocarb, carbosulfan, aldoxycarb, promecarb, mexacarbate and fenoxycarb (The Pesticide Book, G. Ware, 4th ed., 1994).

Section 408(b)(2)(D)(v) of the Food Quality Protection Act requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity". As this use has been classified as a nonfood use and tolerances are not required, a cumulative risk assessment is not required.

DETERMINATION OF SAFETY FOR U.S. POPULATION

1. *Acute Aggregate Risk.* An acute dietary (food only) risk assessment was not performed as exposure to residues of pirimicarb from food is not expected. The Agency acknowledges the potential for exposure to pirimicarb in drinking water, but does not expect that exposure from drinking water would result in an MOE that would exceed the Agency's level of concern.

2. *Chronic Aggregate Risk.* A chronic (food only) risk assessment was not performed as exposure to residues of pirimicarb from food is not expected. Despite the potential for exposure to pirimicarb in drinking water, HED does not expect the exposure from drinking water to exceed HED's level of concern. Pirimicarb has no residential uses. Thus, a comprehensive residential risk assessment is not required.

3. *Short- and Intermediate-Term Aggregate Risk.* Short- and intermediate-term aggregate exposure takes into account chronic dietary food and water (considered to be a background exposure

level) plus indoor and outdoor residential uses. Exposure to pirimicarb is not expected from food. Pirimicarb has no residential uses. Thus, a comprehensive residential risk assessment is not required.

DETERMINATION OF CANCER RISK

The cancer status of pirimicarb has not been determined (TESC, 6/7/96) due to an inadequate database. Thus, a cancer risk assessment was not performed.

ENDOCRINE DISRUPTOR EFFECTS

EPA is required to develop a screening program to determine whether certain substances (including all pesticides and inerts) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect..." The Agency is currently working with interested stakeholders, including other government agencies, public interest groups, industry and research scientists in developing a screening and testing program and a priority setting scheme to implement this program. Congress has allowed 3 years from the passage of FQPA (August 3, 1999) to implement this program. At that time, EPA may require further testing of this active ingredient and end use products for endocrine disruptor effects.

DETERMINATION OF SAFETY FOR INFANTS AND CHILDREN

In assessing the potential for additional sensitivity of infants and children to residues of pirimicarb, EPA considered data from developmental toxicity studies in the rat and rabbit as well as a 2-generation reproductive toxicity study in the rat.

Developmental toxicity studies are designed to evaluate adverse effects on the developing fetus resulting from maternal pesticide exposure during gestation. Reproductive toxicity studies provide information relating to pre- and post-natal effects from exposure to the pesticide, information on the reproductive capability of mating animals, and data on systemic toxicity.

FFDCA section 408 provides that EPA shall apply an additional 10-fold margin of safety for infants and children in the case of threshold effects to account for pre-and post-natal toxicity and

the completeness of the data base unless EPA determines that a different margin of safety will be safe for infants and children. Margins of safety are incorporated into EPA risk assessments either directly through use of a margin of exposure analysis or through using uncertainty (safety) factors in calculating a dose level that poses no appreciable risk to humans. In either case, EPA generally defines the level of appreciable risk as exposure that is greater than 1/100 of the no observed effect level in the animal study appropriate to the particular risk assessment. This 100-fold uncertainty (safety) factor/margin of exposure (safety) is designed to account for inter-species extrapolation and intra-species variability. EPA believes that reliable data support using the standard 100-fold margin/factor, not the additional 10-fold margin/factor, when EPA has a complete data base under existing guidelines, and when the severity of the effect in infants or children or the potency or unusual toxic properties of a compound do not raise concerns regarding the adequacy of the standard margin/factor.

1. *Developmental Toxicity Studies.*

- a. Rats. In the developmental toxicity study (MRID#: 42796502) in rats, the maternal (systemic) NOEL was 25 mg/kg/day. The LOEL of 75 mg/kg/day was based on decreased body weight gain and decreased feed consumption. The developmental (fetal) NOEL was 25 mg/kg/day. The LOEL of 75 mg/kg/day was based on decreased mean fetal weight, increased incidence of fetal minor skeletal anomalies and an increased manus score.
- b. Rabbits. In the developmental toxicity study (MRID#: 42796501) in rabbits, the maternal (systemic) NOEL was 10 mg/kg/day. The LOEL of 60 mg/kg/day was based on reduced body weight gain and reduced feed consumption during dosing. The developmental (fetal) NOEL was >60 mg/kg/day at the highest dose tested.

2. *Reproductive Toxicity Studies.*

Rats. In the 2-generation reproductive toxicity study (MRID#: 42796503) in rats, the maternal (systemic) NOEL was 22.93 mg/kg/day. The maternal (systemic) LOEL of 88 mg/kg/day was based on decreased body weight gain, decreased food consumption,

and decreased food efficiency. [Note: The RfD Committee recommended redefining the reproductive toxicity observed in this study as developmental/systemic toxicity, 7/27/96.] The developmental/systemic (pup) NOEL was 22.93 mg/kg/day. The developmental LOEL of 88 mg/kg/day was based on decreased pup weights.

3. Pre- and Post-Natal Sensitivity.

The toxicological data base for evaluating pre- and post-natal toxicity for pirimicarb is complete with respect to current data requirements. There are no pre- or post-natal toxicity concerns for infants and children, based on the results of the rat and rabbit developmental toxicity studies as well as the 2-generation rat reproductive toxicity study. In the rat developmental toxicity study, the NOELs and LOELs for developmental and maternal endpoints, respectively, occurred at the same dose levels. Due to this and the high dose level at the LOEL, as well as the type of developmental findings, an acute dietary risk assessment was not required. In rabbits, the maternal findings occurred below the level of the developmental findings, indicating no extra-sensitivity for infants and children. There also was no pup toxicity up to the highest dose tested in the 2-generation rat reproductive toxicity study.

Based on the above, HED concludes that reliable data support use of the standard 100-fold uncertainty factor and that an additional uncertainty factor is not needed to protect infants and children.

4. Acute Aggregate Risk.

An acute dietary (food only) risk assessment was not performed as exposure to residues of pirimicarb from food is not expected. The Agency acknowledges the potential for exposure to pirimicarb in drinking water, but does not expect that exposure from drinking water would result in an MOE that would exceed the Agency's level of concern.

5. Chronic Aggregate Risk.

A chronic (food only) risk assessment was not performed as exposure to residues of pirimicarb from food is not expected.

Despite the potential for exposure to pirimicarb in drinking water, HED does not expect the exposure from drinking water to exceed HED's level of concern. Pirimicarb has no residential uses. Thus, a comprehensive residential risk assessment is not required.

DETERMINATION OF SAFETY TO OCCUPATIONALLY EXPOSED WORKERS

1. Acute data for this formulation were not provided to RAB2. The Washington State submission included two Section 18 labels. Both labels were for Pirimor 50 DF (EPA Reg. No. 10182-370). One was for use on small seeded vegetables and did not contain WPS information. The other was for use on alfalfa grown for seed in Idaho, Nevada, Oregon, and Washington. This label contained WPS statements. According to the label intended for alfalfa use applicators and other handlers must wear: long-sleeved shirt and long pants, waterproof gloves, and shoes plus socks. **RD should insure that the appropriate WPS statements regarding PPE appear on the label intended for use on vegetable seed crops.**
2. Acute data for the technical were not provided to RAB2. The label intended for alfalfa use contained WPS statements. According to the label intended for alfalfa use, the Restricted Entry Interval (REI) is 12 hours. **RD should insure that the appropriate WPS statements regarding the REI appear on the label intended for use on vegetable seed crops.**
3. Occupational exposure assumptions and estimates of exposure are summarized in Tables 1 and 2, respectively. RAB2's worker exposure estimates are based on surrogate data from the Pesticide Handlers Exposure Database (PHED), PHED Surrogate Exposure Guide (PSEG, 05/97), with workers wearing a single layer of clothing plus gloves (pilots are not expected to wear gloves). TESC did not identify inhalation exposure as a concern for workers.
4. RAB2 has calculated short-term dermal MOEs resulting from the handling and application of pirimicarb by workers ranging from 670 for aerial mixer/loaders to 10,000 for ground applicators. The intermediate-term dermal MOEs range from 120 for aerial mixer/loaders to 1,800 for ground

applicators. These MOEs do not exceed HED's level of concern for occupationally exposed workers.

OTHER CONSIDERATIONS

Proposed use

1. The letter from the State of Washington indicates this use is being pursued for the following vegetable seed crops: Chinese mustard; Chinese cabbage; broccoli raab; mustard; rutabaga; rape greens; collard; kale; Chinese kale; cauliflower; cabbage; Brussels sprouts; spinach mustard; turnip; turnip, fodder; arrugula; radish; Swiss chard; beet, table; spinach; endive; lettuce; coriander; parsnip; and parsley.

The proposed label does not list lettuce and endive as target crops. RAB2 would have no objections to including lettuce and endive in this Section 18 request.

2. The proposed label specifies applications may be made at rates of 2 to 6 oz of Pirimor per acre (1 to 3 oz ai/A) by ground or air. A maximum of 2 applications may be made. Do not apply more than 6 oz of product per acre per season.

Magnitude of the Residues

3. CBTS/HED has previously classified this use (including lettuce and endive) as a nonfood use (Memo, 2/17/95, B.A. Schneider, D212168).
4. Washington State has a program to assure that no part of the treated crop will be diverted to human food or livestock feed uses. Thus, secondary residues in animal commodities are not expected as a result of this Section 18 use.

Rotational Crop Restrictions

5. Rotational crop data are not available for pirimicarb and rotational crop restrictions are not present on the Pirimor label. RAB2 can not determine the potential for uptake of residues into crops that may be rotated into pirimicarb treated fields. In the absence of data, the following

rotational crop restriction should be added to the Pirimor Section 18 label: In order to avoid illegal residues, do not rotate treated fields to crops, other than those listed on the label for one year following application of Pirimor. One year following application of Pirimor, any crops may be rotated into treated fields.

International Residue Limits

6. As this use has been determined to be a nonfood use, tolerances are not required. Thus, harmonization with Codex, Canada and Mexico is not an issue for this Section 18 use.

SUPPLEMENTAL INFORMATION

OCCUPATIONAL EXPOSURE

Table 1. Occupational Exposure Assumptions	
PARAMETER	ASSUMPTION
Pesticide Handlers Exposure Database (PHED), Version 1.1, unit of exposure values from PHED Surrogate Exposure Guide (PSEG, 05/97)	Mixer/Loader (dry flowable, open mixing, single layer clothing plus gloves): Dermal = <u>63.3733</u> $\mu\text{g}/\text{lb}$ ai handled (medium confidence run).
	Applicator - Ground (groundboom, open cab, single layer clothing plus gloves): Dermal = <u>14.0180</u> $\mu\text{g}/\text{lb}$ ai applied (medium confidence run).
	Applicator - Air (aerial-fixed wing, open cab, single layer clothing): Dermal = <u>5.0124</u> $\mu\text{g}/\text{lb}$ ai applied (medium confidence run).

Table 1. Occupational Exposure Assumptions

PARAMETER	ASSUMPTION
Percent Absorption	Dermal: <u>25</u> % (used on intermediate exposure only based on Tox value)
Application Type	Ground and air
Minimum Finish Spray	Ground: <u>10</u> gal/A; air <u>5</u> gal/A
Maximum Application Rate	<u>0.1875</u> lb. ai/A
Maximum Applications Per Year	<u>2</u>
Acres Treated/Day (Y. NG, BEAD)	Ground: <u>104</u> ; air <u>351</u>
Worker Weight	<u>70</u> kg (based on Tox endpoint)
Number of Farms Treated by PCO	Ground: <u>2</u> , air <u>10</u> (default values)

Table 2. Occupational Exposure and Risk Assessment ^a				
Worker	ADD ^b Short-Term Dermal (ug/kg/day)	ADD ^c Intermediate- Term Dermal (ug/kg/day)	Short- Term MOE ^d	Intermediat e-Term MOE ^e
Ground Mixer/Loader	17.65	4.41	2,300	410
Ground Applicator	3.91	0.98	10,000	1,800
Aerial Mixer/Loader	59.58	14.90	670	120
Aerial Applicator	4.70	1.18	8,500	1,500

^a MOEs are expressed to two significant figures.

^b Average Daily Dose (ADD) = PHED unit exposure x % absorption x application rate x acres treated/day ÷ kg body weight.

^c Average Annual Daily Dose (AADD) = ADD x number of days to treat average field x number applications/year x number of farms treated by PCO ÷ 365 days/year.

^d Short-Term Occupational Exposure MOE = NOEL/ADD (where NOEL = 40 mg/kg/day).

^e Intermediate-Term Occupational Exposure MOE = NOEL/ADD (where NOEL = 1.8 mg/kg/day).

ADDITIONAL INFORMATION

Progress Toward Registration. The Washington Department of Agriculture in conjunction with the Washington State University and the vegetable seed industry has previously requested a 24[®] registration for this use. CBTS/HED has previously determined that this can be classified as a nonfood use (Memo, 2/17/95, B.A. Schneider, D212168).

Reregistration Status. Pirimicarb is not a FIFRA '88 reregistration active ingredient.

cc: W.D. Wassell, W.G. Dykstra, C.R. Lewis, RAB2, CBTS (Sect 18), OREB (Chem File), Caswell File.

RDI:RAB2: 07/17/97.