



United States
Environmental Protection
Agency

Office of Prevention,
Pesticides and Toxic Substances
(7501C)

PESTICIDE FACT SHEET

Name of Chemical: Pirimicarb (Pirimor®)
Reason for Issuance: New Conditional Registration
Date Issued: [REDACTED]
Fact Sheet Number: [REDACTED]

1. DESCRIPTION OF CHEMICAL

Chemical Name: 2-(Dimethylamino)-5,6-dimethyl-4-pyrimidinyl dimethylcarbamate

Common Name: Pirimicarb

Trade Names: Pirimicarb Technical; Pirimor® 50-DF Insecticide

EPA Shaughnessy Code: 106101

Chemical Abstracts Service (CAS) Number: 23103-98-2

Year of Initial Registration: 1974; however, these products were voluntarily cancelled in 1981. New registrations issued in 1997.

Pesticide Type: Insecticide

Chemical Family: Carbamate

U.S. Registrant: Zeneca Ag Products
1800 Concord Pike
Wilmington, DE 19897

2. CURRENT USE PATTERNS AND FORMULATIONS

Registered Use: Pirimicarb Technical (97% active ingredient or a.i.) is registered for formulation into end-use products labeled exclusively for terrestrial, non-food use on alfalfa grown for seed in the states of Idaho, Nevada, Oregon, and Washington only. Pirimor® 50-DF is a dry flowable formulation that contains 50% of the active ingredient and 50% inerts. The proposed label directions for alfalfa grown for seed are as follows:

*APPLICATION DIRECTIONS

ALFALFA GROWN FOR SEED: For control of aphids. Apply 2 to 6 oz of Pirimor® 50-DF per acre by ground or aerial application. The higher rate is recommended for instances of heavy infestations of aphids. Spray to wet foliage completely. Minimal application spray volume is 5 gal. per acre by air or 10 gal./acre by ground.

For the most effective and economic control, begin to apply Pirimor® 50-DF as soon as aphids appear.

PRE-HARVEST INTERVAL (PHI): A PHI of 1 day is required after application of PIRIMOR.

GENERAL USE PRECAUTIONS

- PIRIMOR® 50-DF is to be applied at a rate not to exceed 6 ounces of product per acre per season.
- Pirimor® 50-DF may be applied a maximum of twice per season not to exceed 6 ounces of product per acre per season (i.e., two applications at 3 oz. each). For a second application, reapply in no less than 7 to 10 days.
- Do not apply when weather conditions favor drift from treated areas.
- Make ground applications when the wind velocity favors on target product deposition (approximately 3-10 mph). Do not apply when wind velocity exceeds 10 mph.
- Applicators and alfalfa seed growers are required to report to EPA Headquarters, the EPA Regional Office and the State Department of Agriculture any adverse effects to birds resulting from the use of this pesticide.
- A 100-yard buffer zone is required between the border of PIRIMOR® 50-DF application sites and lakes, reservoirs, rivers, permanent streams, marshes or natural ponds, estuaries and commercial fish farm ponds.
- For aerial applications, the spray boom should be mounted on the aircraft so as to minimize drift caused by wingtip or rotor vortices. The minimum practical boom length should be used and must not exceed 75% of wing span or rotor diameter.
- Ultra Low Volume (ULV) applications are prohibited.
- The largest droplet size consistent with good pest control is required. Formation of very small droplets may be minimized by appropriate nozzle selection, by orienting nozzles away from the air stream as much as possible, and by avoiding excessive spray boom pressure.
- Spray should be released at the lowest height consistent with pest control and flight safety.
- Aerial applications should be made when the wind velocity favors on-target product deposition. Do not apply when wind velocity exceeds 10 mph. Avoid applications when wind gusts approach 10 mph.

- To avoid risk of exposure to sensitive aquatic areas, aerial applicators should avoid application when wind direction is toward aquatic areas.
- Low humidity and high temperatures increase the evaporation rate of spray droplets and therefore the likelihood of increased spray drift to aquatic areas. Avoid spraying during conditions of low humidity and/or high temperature.
- Do not make aerial applications during temperature inversions. Inversions are characterized by stable air and increasing temperatures with height above the ground. Mist or fog may indicate the presence of an inversion in humid areas. The applicator may detect the presence of an inversion by producing smoke and observing a smoke layer near the ground surface.
- For use only on fields in production of alfalfa seed. Not for use on fields producing alfalfa for livestock feed. No portion of the treated field, including seed, seed screening, hay forage or stubble, may be used for human or animal feed.
- Do not cut current years' treated alfalfa seed crop for hay or forage. Do not graze current years' treated alfalfa seed crops.
- Screening from alfalfa seed processing are prohibited from feed channels. All PIRIMOR® 50-DF treated alfalfa seed screening must be removed from the feed market.
- Treated alfalfa seed is not to be used for sprouting. All alfalfa seed treated with PIRIMOR® 50-DF is to be tagged at processing plants, NOT FOR HUMAN CONSUMPTION. It shall be the grower's responsibility to notify the processing plants of any seed crop treated with PIRIMOR® 50-DF.
- In Oregon, for use on fields of alfalfa grown for seed (operated by members of the Oregon Alfalfa Seed Growers Association, the Gardena Alfalfa Seed Growers Association, Inc., or the Josephine Growers' Cooperative Association) located in Malheur, Umatilla, Morrow, Jackson or Josephine Counties of Oregon.
- Do not apply this product through any type of irrigation system."

Target Pests: Pea Aphid, Blue Alfalfa Aphid, and Spotted Alfalfa Aphid.

3. BACKGROUND OF CHEMICAL

During the 1970's, ICI Americas (now Zeneca Inc.) had three registered products that contained the active ingredient pirimicarb. They were Pirimor 50W, 50WP, and the technical grade product. In December of 1980, the company requested that voluntary cancellation proceedings be initiated for all three products due to financial concerns associated with data requirements and the limited market for pirimicarb. The products were subsequently cancelled on 5/21/81. Prior to ICI's request, all registrations issued for the chemical were valid. The previously registered products included use of the chemical on potatoes and various ornamentals.

At the time these Section 3 registrations were active, several states (CA, ID, MT, NV, OR, and WA) issued 24(c) registrations to use Pirimor® 50W Insecticide on

alfalfa grown for seed. Originally, the Agency considered this a non-food use because labels submitted for this use contained prohibitions against the use of the treated crop for food or feed. Later, however, the Agency determined that those restrictions were not adequate assurances that the treated crop would not be diverted for food or feed use. Since no tolerance was established for pirimicarb and since the states failed to provide written assurances that the treated crop would not be diverted for feed or food use, the Agency requested immediate cancellation of the 24(c) registrations.

Section 18 exemptions have been granted in the past several years in the following states: Idaho (23,625 acres), Montana (7,000 acres), Nevada (20,000 acres), Oregon (10,000 acres), Washington (15,000 acres), and Wyoming (3,000 acres).

Pirimicarb has been found to be a useful tool in the implementation of integrated pest management programs (IPM). Pirimicarb is not toxic to beneficial insects and is not toxic to nontarget species that serve as food for the beneficial species.

4. SCIENCE FINDINGS

Summary Science Statement

Although the database for pirimicarb is limited and incomplete, a conditional registration of pirimicarb technical has been granted for terrestrial non-food use to control aphids on alfalfa grown for seed only in the states of Idaho, Nevada, Oregon and Washington. This decision was made based on the fact that this registration is for a limited use in 4 states only, on a relatively small number of acres (75,000), and a production cap for manufacture of the technical product has been established. These states have regulations in place to safeguard against any treated alfalfa commodity entering the market for human or animal consumption.

Normally, alfalfa grown for seed is considered a food use and applications to crops grown for seed can only be considered non-food uses if:

1. Subsequent to treatment, no parts of the crop will be diverted for use as human food or livestock feed; and
2. There will be no residues in crops grown from the harvested seed.

Through the implementation of specific regulations in each of the four states, these requirements have been met for pirimicarb.

As a condition of registration for this non-food use, an acute neurotoxicity study (81-8SS) and a 90-day rodent feeding study (82-1(a)) are required. Toxicology data gaps remain for pirimicarb and will impinge on any future registrations of the chemical for food or non-food uses. In addition to the acute neurotoxicity study and the 90-day rodent feeding study, the following data would be required to support any additional food uses of pirimicarb: a chronic feeding study in rodents (83-1(a)), oncogenicity in rats (83-2(a)), oncogenicity in mice (83-2(b)), and a general metabolism study (85-1). A full complement of residue chemistry data will also be needed for any future Section 3 food registrations of pirimicarb. Residential/occupational exposure data requirements will be determined on a case-by-case basis depending on the use associated with any future registration request.

Most of the available environmental fate and groundwater data on pirimicarb are either very old and/or prepared to meet European guidelines. However, based on the available data and the limited use of pirimicarb and specific environmental conditions in these states (i.e., location, amount of rainfall, type of soil, irrigation, and depth of water table), the Agency has determined that no additional data is necessary to support this limited use. However, to support any additional uses of pirimicarb, the following environmental fate data would be required: hydrolysis, photolysis, degradate mobility and terrestrial field dissipation.

The Agency has also evaluated ecological effects data for pirimicarb and has determined that the proposed use does not represent acute hazard to birds and freshwater organisms. Chronic hazard to birds could not be evaluated due to lack of avian reproduction data. Therefore, as a condition of this registration, data from two avian reproduction studies are required to support the use on seed alfalfa. There is a potential for chronic hazard to aquatic invertebrates; however, the extent cannot be fully evaluated, due to lack of environmental fate data. In order to mitigate hazard to aquatic invertebrates, the registrant has imposed buffer zones, included instructions to avoid spray drift, and limited the maximum amount of product to be applied per season to 6 ounces.

TOXICOLOGY PROFILE

Acute Toxicity (Pirimor® 50-DF)

TEST	RESULTS	TOXICITY CATEGORY
Oral LD50 - rat	LD50 (95% CI) = 379 mg/kg (M) LD50 (95% CI) = 485 mg/kg (F)	II
Dermal LD50 - rat	LD50 > 1000 mg/kg	II
Inhalation - rat	Data requirement was waived.	III
Primary Eye Irritation - rabbit	Corneal opacity in 2/3 rabbits during first 2 days. Chemosis and eye discharge resolved in 4 days; redness of conjunctivae persisted beyond day 7.	II
Primary Dermal Irritation - rabbit	Erythema and edema subsided by 72 hours.	II
Dermal Sensitizer - Guinea pig	Nonsensitizer	N/A

Subchronic Toxicity (Pirimicarb Technical)

90-Day Feeding in Dogs (82-1(b))

In a two part dietary subchronic study, beagle dogs received in Part 1 either 0, 4, 10, or 25 mg/kg/day, and in Part 2 either 0, 0.4, 1.8, or 4 mg/kg/day of pirimicarb technical (94% a.i.). Half of the dogs/dose in Part 1 were sacrificed after 90 days, while the other half was allowed 28 days for recovery. The 0, 0.4, and 1.8 mg/kg/day dose groups were sacrificed after 90 days but the 4 mg/kg/day dose group continued on the test diet for a total of 180 days. Part 2 was limited to an assessment of the hematological changes and cholinesterase effects noted in Part 1. These studies were done prior to the implementation of GLP Guidelines, and therefore, do not fall under the purview of either GLP or Quality Assurance requirements.

Test chemical effects on bone marrow cytology were evident at 4 mg/kg/day in both Parts 1 and 2. In particular in Part 2 proerythroblasts were increased in both males/females at 30, 60 and 90 days compared to controls. Other indications of bone marrow cytology and hematology also indicated effects. During the course of the study one high-dose male and female and one mid-dose female developed macrocytic anemia. The high-dose male died and the death was attributable to anemia and this dog exhibited erythropoietic hyperplasia. There was decreased body weight in males (about 4%, $p < 0.05$) at 25 mg/kg/day. The bone marrow effects were said by the study author to

be indicative of "a compound-dependent, hemolytic anemia of the 'penicillin type'". The systemic toxicity LOEL is 4 mg/kg/day, based on hematopoietic effects. The systemic toxicity NOEL is 1.8 mg/kg/day.

In part 1, plasma ChE was inhibited in 10 and 25 mg/kg/day dose males/females by approximately 24.8%/1.92% and 34.5%/18.5%, respectively, at 12 weeks; plasma ChE was significantly inhibited in both sexes by the second week. RBC acetylcholinesterase activity was inhibited in mid- and high-dose males (16.4% and 27.7%, respectively) and high-dose females (21%). In Part 2, plasma ChE and RBC AChE were not affected. The cholinesterase LOEL is 10 mg/kg/day, based on acetylcholinesterase inhibition. The ChE NOEL is 4 mg/kg/day.

21-Day Dermal Toxicity - Rat (82-2)

In a 21-day dermal toxicity study, pirimicarb (97.6% a.i.) was administered dermally to 5 male and 5 female Alpk:APfSD (Wistar derived) rats per dose group as a paste in distilled water at doses of 0, 40, 200 or 1000 mg/kg/day. A total of 15 six-hour applications were made during the 21-day test period. Animals were fitted with plastic collars to prevent oral exposure. No systemic effects were noted at any doses. The systemic toxicity LOEL is > 1,000 mg/kg and the systemic toxicity NOEL is 1,000 mg/kg/day.

In addition, reductions in plasma and brain cholinesterase were observed in males and females in a dose-related manner at all test levels. At the 1000 mg/kg dose level, brain cholinesterase was reduced 18.4% in males and 22.5% in females while at the 200 mg/kg/day dose level, reductions were 10.5% in males and 11.3% in females. Similarly, at the 1000 mg/kg/dose level plasma cholinesterase was reduced 19.6% in males and 39.7% in females while reductions were 17.6% in males and 23.4% in females at the 200 mg/kg dose level. At the low dose level (40 mg/kg) reductions were less than 5% for brain cholinesterase and less than 15% for plasma cholinesterase in both sexes. Based upon these findings, the ChE LOEL in this study is considered 200 mg/kg/day and the ChE NOEL is 40 mg/kg/day.

Chronic Toxicity (Pirimicarb Technical)

Chronic Toxicity (2-Year Dog) 83-1(b)

In a chronic feeding study, beagles received either 0, 0.4, 1.8, or 4 mg/kg/day pirimicarb (94% a.i.) in their diet for two (2) years. At 4 mg/kg/day effects were noted on bone marrow cytology as indicated by a decrease in the Myeloid:Erythroid (M:E) ratios of 64% in females and 32% males. This change resulted mainly from increases in late normoblasts ($p < 0.01$, 65%) and

proerythroblasts ($p < 0.01$, 3.5 fold) and the total erythroid mass (41%) in females with two of the four females contributing most of the change. Nonsignificant increases were noted for late normoblasts (29%) and proerythroblasts (12%) and total erythroid mass in males. Total myeloids decreased in females (49%) and males (19%). Metamyelocytes (89%, $p < 0.01$ in females and 63%, $p < 0.05$ in males) were most significantly reduced and the associated bands (56%, $p < 0.05$ in females and 39%, not significant in males) were also reduced. Myeloblasts (4 fold in females and 3 fold in males) were increased. Promyelocyte-neutrophils ($p < 0.05$, 3 fold) were increased. Metamyelocytes-neutrophils (60%, $P < 0.05$) and metamyelocytes-eosinophils (68%, $p < 0.05$) in females were decreased. The systemic toxicity LOEL is 4.0 mg/kg/day, based on changes in bone marrow cytology. The NOEL is 1.8 mg/kg/day.

Developmental and Reproduction Toxicity (Pirimicarb Technical)

Developmental Toxicity in Rats (83-3(a))

In a developmental toxicity study, 24 timed pregnant Wistar rats/group received either 0, 10, 25 or 75 mg/kg/day by oral gavage during gestation days 7 through 16, inclusive. Maternal toxicity was noted only in the high-dose group in the form of reduced body weight gain (26%; sharpest loss of 50% during 7-10 gestation days) and feed consumption (13%) during the dosing period, with a rebound post-dosing. Therefore, the Maternal LOEL is 75 mg/kg/day, based on reduced body weight gain and reduced feed consumption. The Maternal NOEL is 25 mg/kg/day.

Developmental toxicity was noted in high-dose (75 mg/kg/day) group in the form of reduced mean fetal weight, increased mean manus score and increased litter incidence of bipartite 5th sternbrae partially ossified 5th sternbrae, un-ossified odontoid, fully ossified 4th lumbar transverse process, and un-ossified calcaneum. In the 10 mg/kg/day group a significant reduction in mean fetal body weight and increased litter incidence of un-ossified 2nd centrum and un-ossified 3rd centrum were observed. However, statistical significance was eliminated when the data from the dam #48 which had all 8 fetuses undeveloped and underweight were excluded from the analysis, and therefore, the incidences were considered not related to treatment. The developmental LOEL is 75 mg/kg/day based on reduced mean fetal weight, increased incidence of minor fetal skeletal defects, and increased manus scores. The developmental NOEL is 25 mg/kg/day.

Teratology Study in Rabbits (83-3(b))

In a developmental toxicity study, pirimicarb (97.3% a.i.) was administered to

20 artificially inseminated New Zealand white rabbits per dose group, received either 0, 2, 10, or 60 mg/kg/day by gavage from gestation day 7 through 19 of gestation, inclusive. Maternal toxicity was noted in the form of a dose-related decrease in mean weight gain during gestation, and intermittently during treatment at 7 to 10 and 13 to 16 gestation days, respectively. A dose-related decrease in relative food consumption occurred during dosing at the 60 mg/kg/day group. During the post-dosing period (19-30 days), the mean body weight gain rebounded to control levels; however, food consumption lagged behind controls. The Maternal LOEL is 60 mg/kg/day based on reduced mean body weight gain and reduced food consumption during the dosing period. The Maternal NOEL is 10 mg/kg/day. No developmental effects were noted at any dosing levels. The Developmental toxicity NOEL is > 60 mg/kg/day.

Reproduction 2-Generation - Rat (83-4)

In a multigeneration reproductive study, Alpk:APfSD rats, 26 per sex per dose group, received either 0, 50, 200 or 750 ppm (the mean consumption of 0, 5.71, 22.93 or 88.0 mg/kg/day, respectively) of pirimicarb (97.3% a.i.) in the diet. The animals were mated at a one to one ratio in both generations (F0 or F1) and were given test diets for 10 weeks before mating. Selection of parents for the F1 generation was made when the pups were 29 days old and were assigned to the treatment groups.

Systemic (parental) toxicity was observed in adult males/females at the highest dose in the form of significantly decreased body weight gain, decreased food consumption, and decreased food efficiency during the study in comparison to controls. None of the aforementioned parameters were affected at the 50 or 200 ppm groups. Therefore, the LOEL for parental (systemic) toxicity is 88 mg/kg/day based on decreased body weight gain, food consumption, and food efficiency. The NOEL for parental (systemic) toxicity is 22.93 mg/kg/day.

In this reproductive study, developmental/systemic toxicity was noted in the 750 ppm (high dose) offspring in the form of reduced mean body weights at birth which became statistically significant by post natal day 29. These effects were not seen in the 50 and 200 ppm dose groups. The developmental/systemic toxicity LOEL is 88 mg/kg/day and the developmental/systemic toxicity NOEL is 22.93 mg/kg/day. There was no evidence of reproductive toxicity at any dose.

Neurotoxicity (Pirimicarb Technical)

The database lacks acute neurotoxicity information and this is a data gap. An acute neurotoxicity study (81-8SS) is required because the chemical is a neurotoxicant.

Mutagenicity (Pirimicarb Technical)

Study Type	Reported Results
Gene Mutation - Ames	No increased frequencies of reverse gene mutation from his-to-his+ were evident in any strain of <i>Salmonella typhimurium</i> (TA 1535, TA 1538, TA 98, and TA 100) treated up to the HDT, 2,500 ug/plate with S9 activation.
Reverse Gene Mutation - Ames	No increase in reverse mutation was found in replicate cultures of the Ames battery of <i>Salmonella typhimurium</i> mutant strains exposed at doses up to 2,500 ug/plate with/without S9 activation.
Chromosomal Damage in Human Lymphocytes	No chromosome aberrations were found at any dose up to the limit of solubility, 500 ug/ml, with and without S9 activation.
Chromosome Damage <u>in vivo</u> in Mice	No increased M-PCE were induced at dose levels causing cytotoxicity, 43.3 mg/kg and 69.3 mg/kg.
DNA Damage/Repair <u>in vivo</u> in Rats	There was no induced increase in NNGC at any dose up to clinically toxic MTDs (20 - 120 mg/kg).

Metabolism (Pirimicarb Technical)

The database lacks general metabolism information. A general metabolism study (85-1) would be required for a food-use, but is not required for this non-food use.

Dose Response

Reference Dose (RfD)

The studies discussed above were evaluated to determine toxicological endpoints. Toxicological endpoints for use in occupational/residential risk assessments have been established for pirimicarb. However, because of the general overall poor quality of the data and since the proposed use is a non-food use, a reference dose was not established for pirimicarb at this time.

Carcinogenicity

No oncogenicity studies are required for a non-food use (i.e., alfalfa grown for seed). For food uses, new carcinogenicity studies will be needed. The previously submitted chronic/carcinogenicity studies in rats and mice are unacceptable because of excess mortality associated with a viral infection.

Other Toxicological Endpoints

Dermal Absorption

There are no dermal absorption studies available. A comparison of LD50s of 147 mg/kg/day in the acute oral toxicity and > 500 mg/kg/day in the acute dermal toxicity study in rats suggests a dermal absorption rate of 29%. A comparison of the LOEL of 75 mg/kg/day in the developmental rat and the NOEL of 1000 mg/kg/day in the 21-day dermal toxicity study in rats suggests a dermal absorption rate of approximately 7.5%. Based on these values and the available data, the Agency will use a conservative value of no more than 25% for dermal absorption.

Acute dietary

Since this is a non-food use, an acute dietary toxicological endpoint is not applicable. The existing data base supports a non-food use only.

Short-Term Occupational and Residential

A 21-day dermal toxicity study in rats, was selected to determine the toxicological endpoint (hazard) for short term (1 to 7 days) exposure to pirimicarb. Systemic toxicity was not observed up to and including a dose of 1,000 mg/kg/day (the limit dose). The systemic toxicity LOEL is > 1000 mg/kg and the systemic toxicity NOEL is 1,000 mg/kg/day. Reductions in plasma and brain cholinesterase were observed in males and females in a dose-related manner at all test levels. The ChE LOEL is 200 mg/kg/day and the ChE NOEL is 40 mg/kg/day. The Agency will use 40 mg/kg/day for short-term occupational residential exposure based on the inhibition of brain and plasma cholinesterase.

Intermediate-Term Occupational and Residential

A 90-day dog feeding study was selected to determine the toxicological endpoint for intermediate term (1 week to several months) exposure to pirimicarb. The systemic toxicity LOEL is 4 mg/kg/day, based on hematopoietic effects. The systemic toxicity NOEL is 1.8 mg/kg/day. The ChE LOEL is 10 mg/kg/day based on plasma and RBC AChE inhibition. The ChE NOEL is 4 mg/kg/day. The Agency will use a NOEL of 1.8 mg/kg/day for intermediate occupational/residential exposure based on hematopoietic effects with adjustment for dermal absorption.

Chronic Occupational and Residential (Non-Cancer)

Two studies were selected for chronic occupational/residential (non-cancer) exposure; 1) the study described above for intermediate occupational/residential exposure, and 2) a two-year chronic dog study. For the chronic dog study, the systemic LOEL is 4 mg/kg/day, based on bone marrow cytology. The systemic toxicity NOEL is 1.8 mg/kg/day. The Agency will use a NOEL of 1.8 mg/kg/day for chronic occupational/residential exposure based on hematopoietic (bone marrow) effects with adjustment for dermal absorption.

Inhalation Exposure

Based on the LC50 of 949 $\mu\text{g/L}$ for males and 858 $\mu\text{g/L}$ for females, pirimicarb is placed in Toxicity Category III. Therefore, risk via the inhalation route is not a concern at this time.

ENVIRONMENTAL FATE AND GROUNDWATER PROFILE

Most of the available data on pirimicarb is either very old and/or prepared to meet European guidelines. Much of it is inconclusive; however, conservative interpretation of the acceptable data suggests that parent pirimicarb may be moderately persistent and mobile. Pirimicarb metabolizes into three major degradates of unknown mobility. The carbamate portion of pirimicarb and its degrade desmethyl pirimicarb (Compound III; 5,6-Dimethyl-2-methylamino-pyrimidin-4-yl dimethyl carbamate) appears to mineralize within 2-6 weeks in most soils. The other two degradates (Compound V: 5,6-Dimethyl-2-dimethylamino-4-hydroxy pyrimidine and Compound VI: 5,6-Dimethyl-2-methylamino-4-hydroxy pyrimidine) appear to be more persistent and are likely to be less toxic than pirimicarb and desmethyl pirimicarb.

Abiotic hydrolysis data are inconclusive. The submitted study suggests that pirimicarb is stable at environmental pH, with a somewhat greater tendency to hydrolyze at pH 4. However, data from an older hydrolysis study and the aerobic soil metabolism study suggests that pirimicarb may hydrolyze more rapidly at pH 7-9. It is unclear to what extent the reported hydrolysis in soil is microbiologically mediated. Pirimicarb appears to absorb light in the 315 nm range, but results of photolysis studies are uncertain. No photolytic degradates have been positively identified, but exposure of viable soil to light appeared to produce large quantities of Compound V. However, it is not certain that Compound V was produced by photolysis and not by biodegradation.

Aerobic metabolism of pirimicarb appears to degrade it first to Compound III, and then to Compounds V and VI. The carbamate portion of the molecule appears to mineralize completely to CO₂, while the ring portion of the molecule may persist for some time either as available residue or bound to the soil organic matter. Due to the clear mobility of pirimicarb in sandy soils, it may present a leaching hazard in coarse, acid soils of low biological activity, or anaerobic soils, where its persistence would be enhanced. The leaching potential of degradates is unknown. Pirimicarb's relatively high solubility (3.060 g/L) and weak adsorption to surfaces suggest that it may be washed off of leaf surfaces fairly easily and reach surface water as runoff. Although pirimicarb has been shown to dissipate from the upper soil layer in the field, its route of dissipation remains undefined.

Based on information obtained from each of the states (i.e., location, amount of rainfall, type of soil, irrigation, and depth of water table), the Agency believes that additional data is not necessary to support the limited use of pirimicarb on seed alfalfa. The reasons are as follows: pirimicarb is applied to the alfalfa foliage under drought-stress conditions and left there to dry; because there is little rain during the summer months in the use area, and because irrigation water application is restricted, pirimicarb is not likely to be washed off of the leaf surface. The water budget indicates that there is no driving force for leaching, so ground water is not at risk. The Agency had been concerned with runoff to surface water, since some alfalfa seed is cultivated on sloping land. Again, the restricted application of water precludes significant runoff. Some off-site movement of pirimicarb might occur through volatilization, which is enhanced by hot, dry conditions. However, the vapor pressure of pirimicarb is relatively low, so vapor phase concentrations of pirimicarb are expected to be low.

Any other use of pirimicarb would trigger the need for additional data.

ECOLOGICAL EFFECTS PROFILE

Terrestrial Organisms

Pirimicarb is highly to moderately toxic to waterfowl (mallard LD₅₀ = 17.2 mg/kg; mallard LC₅₀ = 740 ppm) and slightly toxic to upland game birds (bobwhite LC₅₀ = 3415 ppm). Toxicology data indicate moderate toxicity to mammals (rat LD₅₀ = 147 mg/kg).

At a rate of 0.185 lb a.i./acre, the maximum estimated residue on terrestrial food items (short grass) would be 45 ppm. This is well below 1/2 the LC₅₀ of the most sensitive species (mallard), indicating little potential for acute hazard to birds.

In the absence of avian reproduction studies at the time of registration, the Agency could not assess the potential for chronic avian hazard. Two avian studies

are required as a condition of registration.

Pirimicarb is practically nontoxic to bees and other nontarget insects; therefore, a bee toxicity statement is not required for the label.

Aquatic Organisms

Pirimicarb is slightly toxic to fish (rainbow trout $LC_{50} = 29$ mg/L; bluegill $LC_{50} = 55$ mg/L, and very highly toxic to aquatic invertebrates (Daphnia magna $LC_{50} = 19$ ppb). An aquatic invertebrate life cycle study provided an MATC > 0.9 ppb, < 1.7 ppb, for Daphnia magna.

The calculation of freshwater EEC, from runoff following ground application provides a value of 1.14 ppb. For aerial application, the EEC from drift and runoff is 1.26 ppb. These values are below the level of concern ($1/2 \times LC_{50} = 7$ ppb) for acute toxicity to aquatic organisms, indicating little potential for acute hazard.

The calculated EEC's fall within the range of values for the Daphnia MATC, indicating a potential for chronic hazard to aquatic invertebrates. The apparent persistence of pirimicarb increases the potential for chronic hazard. Certain mitigation measures have been implemented in order to reduce risk to aquatic organisms.

Endangered Species Considerations

Aquatic EEC's exceed the acute and chronic LOC's for endangered aquatic invertebrates. The only endangered species which generate any concern are six species of endangered mollusks found in Idaho. However, hazard to these mollusks is unlikely due to the following factors:

- seed alfalfa is irrigated (low probability of runoff);
- buffer zones around aquatic habitats will be established;
- all the listed mollusks require free-flowing river habitat (little likelihood of significant exposure to pirimicarb residues).

The use of pirimicarb on seed alfalfa should not present significant hazard to any other endangered species. Residues on food items will not exceed the acute LOC for birds; aquatic residues will not exceed LOC's for fish. Although chronic LOC cannot be determined, listed avian species for the subject states area are all raptors and are unlikely to be exposed via application to seed alfalfa.

SUMMARY OF REGULATORY POSITION AND RATIONALE

Pirimicarb meets the criteria specified in Section 3(c)(7)(c) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended, and is eligible for a conditional registration. The proposed pesticide products containing the new chemical, pirimicarb, are recommended for conditional registrations for use on alfalfa grown for seed in the states of Idaho, Nevada, Oregon and Washington ONLY.

Dietary Risk (Food): This use has been classified as a non-food use, therefore, there are not concerns for dietary exposure to pirimicarb. The 4 states included in this conditional Section 3 registration have all issued seed treatment regulations which contain labeling provisions and handling instructions to prevent diversion of the seed or seed screening for use has human or animal feed that should preclude any residues of pirimicarb in the human diet.

Dietary Risk (Water): Pirimicarb is expected to be mobile in a soil and water environment, and it or its degradates to be moderately persistent. Although the Agency has not yet identified an appropriate default number for the potential contribution of water related exposure posed by pesticides, including pirimicarb, the ranges we are considering are well below the level of concern.

Non-Occupational (Residential) Risks: The Agency does not expect any residential exposure scenarios to exist for uses of pirimicarb on alfalfa grown for seed. Therefore, there are no residential risks expected from the use of pirimicarb on alfalfa grown for seed. Future registrations for pirimicarb that include residential uses will require a risk estimate for those residential uses. The Agency does not have data to estimate these risks and would need to require it for any residential use registrations.

Occupational Risks: The MOEs for the short-term exposure scenarios are above 100. The Agency believes the magnitude of the occupational exposure associated with the proposed use of pirimicarb on alfalfa grown for seed is minimal.

Groundwater Risks: Based on the limited use of pirimicarb and specific environmental conditions in these 4 states (i.e., location, amount of rainfall, type of soil, irrigation, and depth of water table), the Agency has determined that ground water is not at risk and no further data is necessary to support this limited use. Any other use of pirimicarb would trigger the need for additional data.

Ecological Risks: The limited use of pirimicarb on seed alfalfa does not represent acute hazard to birds and freshwater organisms. Chronic hazard to birds cannot be evaluated due to a lack of avian reproduction data. There is a

potential for chronic hazard to aquatic invertebrates. The extent of this hazard cannot be fully evaluated due to lack of environmental fate data. Buffer zones and instructions to avoid spray drift have been added to the label to minimize exposure. Data from two avian reproduction studies are required as a condition of this registration.

FOOD QUALITY PROTECTION ACT CONSIDERATIONS

Determination of Sensitivity for Infants and Children

Based on a comparison of the NOELs for maternal effects versus developmental effects from three studies, the Agency has minimal concern for the developmental or reproduction toxicity of pirimicarb. Available data do not indicate any increased pre- or postnatal sensitivity; no additional uncertainty factor for increased sensitivity in infants and children is appropriate.

Maternal and developmental NOELs for the developmental study in rats, and the reproductivity study in rats were about the same, 25 mg/kg/day and 22.93 mg/kg/day, respectively. In the rabbit teratology study, the maternal NOEL was 10 mg/kg/day and the developmental NOEL was > 60 mg/kg/day. Although the RfD has not been established yet, the NOEL from the chronic 2-year feeding study in the dog was 1.8 mg/kg/day. This NOEL is more than 10 times lower than any of the maternal or developmental NOELs.

Cumulative Exposure to Substances with Common Mechanism of Toxicity

EPA has not yet determined whether or how to include pirimicarb in a cumulative risk assessment. This registration determination therefore does not take into account common mechanism issues. After EPA develops a methodology for applying common mechanism of toxicity issues to risk assessments, the Agency will develop a process (either as part of the periodic review of pesticides or otherwise) to reexamine those registration decisions made earlier.

DATA REQUIRED AS CONDITION OF THIS REGISTRATION

As conditions of registration for this non-food use, the following studies are required:

- 1) Acute Neurotoxicity Study (rodent: 81-8SS),
- 2) Subchronic 90-day Feeding Study (rodent: 82-1(a))
- 3) Avian Reproduction Studies (2) (71-4).

SUMMARY OF DATA GAPS REQUIRED FOR ADDITIONAL USES OF PIRIMICARB

Residue Chemistry

No data are required for a non-food use. A full complement of residue chemistry data will be required for any future food use registration requests for pirimicarb.

Toxicology

Non-Food uses:

- 1) Acute Neurotoxicity Study (rodent: 81-8SS)
- 2) Subchronic 90-day Feeding Study (rodent: 82-1(a)).

Food uses:

- 1) Chronic Feeding Study (rodent: (83-1(a))
- 2) Oncogenicity (rats: (83-2(a))
- 3) Oncogenicity (mice: (83-2(b))
- 4) General Metabolism Study (85-1)

Occupational/Residential

No data are required for the non-food use. Requirements for future Section 3 registrations will be determined on a case-by-case basis.

Environmental Fate

- 1) Hydrolysis (161-1)
- 2) Photolysis in Water (161-2)
- 3) Photolysis on Soil (161-3)
- 4) Anaerobic Soil Metabolism (162-2)
- 5) Mobility - Leaching and Adsorption/Desorption for the degradate Compounds III, V, and VI (163-1)
- 6) Terrestrial Field Dissipation (164-1)

Ecological Effects

- 1) Avian Reproduction Studies (2) (71-4) *done - acceptable.*
- 2) Additional studies based on use pattern.

OTHER REQUIREMENTS OF CONDITIONAL REGISTRATION

Production Cap and Annual Report

In order to assure that the use of pirimicarb will not be expanded beyond the terms of this limited conditional registration, the Agency has imposed a cap on the production of pirimicarb at 30,000 pounds of technical (a.i.) per year over a 3 year period (total of 90,000 pounds a.i.). This corresponds to 60,000 pounds of end-use product per year over a 3 year period (a total of 180,000 pounds of end-use product). The production cap will be reconsidered at the end of the 3 year period. It may be renewed or could be dropped depending on the results of the studies that are to be submitted. This conditional registration will be time limited with an expiration date 3 years after the date of registration. No 24(c) registrations or other section 3 registrations will be granted for this chemical until the aforementioned data requirements have been submitted to the Agency and reviewed (except as described below). Zeneca Ag Products, Inc. is required to submit annual production and sales reports to the Agency.

FUTURE USE IN TWO ADDITIONAL STATES.

Montana and Wyoming are currently working on regulations in their states and they expect final rules to be in place in time for the 1997 use season. The use of pirimicarb on alfalfa grown for seed in the states of Montana and Wyoming has been reviewed and concluded to not pose significant additional risk. However, these states will not be included in this registration until these regulations have become finalized. Registration Division will review supplemental labeling submitted by Zeneca, Inc. for each state upon receipt and acceptance of the final rules. The Agency will not consider further expansion of this use until the required data have been submitted.

CONTACT PERSON AT EPA

Dennis H. Edwards, Jr.
Product Manager (19)
Insecticide-Rodenticide Branch
Registration Division (7505C)
Office of Pesticide Programs
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460
--Office location and telephone number:
Room 207, Crystal Mall #2, (703) 305-6386
1921 Jefferson Davis Highway
Arlington, VA 22202