United States
Environmental Protection
Agency

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

Pesticide Fact sheet

Name of Chemical: **Propazine**
Reason for Issuance: **New Pesticide Registration**
Date Issued: **September 1998**

DESCRIPTION OF CHEMICAL

Generic Name: 2-chloro-4,6-bis(isopropylamino)-s-triazine

Common Name: Propazine

Trade Names: Griffin Propazine Technical Propazine 4L

EPA Chemical Code:	080808
Chemical Abstracts Service (CAS) No:	139-40-2
Year of Initial Registration:	1958*/1998
Pesticide Type:	Herbicide
U.S. Producer:	Griffin Corporation

* Propazine was previously registered for use on sorghum. In December 1988 all propazine registrations and uses were canceled due to the failure of registrants to respond the April 1988 Data Call-In for a ground water monitoring study. Therefore, propazine is considered a new active ingredient by the EPA.

USE PATTERNS AND FORMULATIONS

Application Sites: Propazine is a selective herbicide that can be applied before planting, at planting and after crop emergence for preemergence control of annual broadleaf weeds in container grown ornamentals grown in greenhouses.

Formulation Types: 98.0% wettable powder technical product
43.0% flowable concentrate end-use product (4 lbs. propazine per gallon)

Application Types and Methods: Spray tank using flood or drench nozzles only.

Application Rates: Application rates for container grown ornamentals range from 3/4 to 2 1/4 tablespoons of Propazine 4L product per 1000 square feet and applied only once during the planting cycle. Application of Propazine 4L must be made before weeds emerge or after removal of existing weeds.

Carrier: Water

SCIENCE FINDINGS

Summary Science Statements

Based upon a battery of acute toxicity studies, propazine technical is classified as Toxicity Category III. The EPA determined a reference dose (RfD) of 0.017 mg/kg/day based on a 2-year chronic toxicity study in rats with a No Observable Effect Level (NOEL) of 5.2 mg/kg/day and an uncertainty factor of 300 (an additional factor of 3 was added due to the absence of a chronic dog study) based on body weight decreases at the Lowest Effect Level (LEL) of 51 mg/kg/day. Propazine has been classified as a Group "C" (possible human carcinogen) chemical based on significant increases in mammary gland adenomas and adenomas/carcinomas in female Sprague-Dawley rats. The EPA used the Q_1^* approach with $Q_1^* = 4.45 \times 10^{-2}$ based on the Multi-Stage Weib model using a 3/4 scaling factor.

The structural similarity of propazine to other triazine herbicides suggests that propazine may cause endocrine effects similar to those cause by atrazine in female rats. However, these potential endocrine effects cannot be evaluated at this time. The EPA may require further testing of propazine and the propazine end-use products for endocrine disrupter effects.

Maximum Concentration Levels have not been established for propazine in drinking water. Health Advisory levels for propazine in drinking water have been established at the following levels: 0.01 ppm - lifetime (adult), 2.0 ppm - shorter-term (adult), 0.5 ppm shorter-term (child), 1.0 ppm - 10-day (child), and 1.0 ppm - 1-day (child). With this action proprazine will be

registered for non-food uses only. Recently emergency exemptions have been granted for the use of propazine on sorghum. When the use of propazine on sorghum was considered the total oncogenic dietary risk (food only) for the U.S. population was calculated to be 5.7×10^{-8}.

Occupational exposure is the only likely potential source of exposure resulting from the greenhouse use of propazine. The EPA has estimated the Short and Intermediate Term MOEs that will result from the handling and application of propazine by greenhouse workers as 500 for

high-pressure handwand, 530 for backpack sprayer and 2800 for low-pressure handwand. The cancer risk is estimated to be 4.3×10^{-6} for high-pressure handwand, 4.0×10^{-6} for backpack sprayer, and 7.6×10^{-7} for low-pressure handwand.

There were no concerns for the container grown ornamentals greenhouse use, however based on the risk assessment for an emergency exemption for use of propazine on sorghum, the acute risk to birds, mammals, and fish appears to be minimal. Propazine is moderately persistent and mobile when used in the greenhouse to control weeds for non-food plants. If applied to an outdoor environment, propazine has a high potential to leach into ground water or reach surface waters by runoff.

Chemical Characteristics

Study	Propanil Technical	Propazine 4L
Empirical Formula	$C_9H_{16}N_3Cl$	N/A
Molecular Weight	229.71	N/A
Color	White	N/A
Physical State	Powdery solid	Liquid
Odor	Slightly waxy odor	same
Melting Point	Melts/decomposes at 217.7°C	N/A
Density	0.46 gm/ml	1.08 gm/ml
Solubility	At 25°C: Water = 3.8 ppm; Acetone = 14,252 ppm; 1-Octanol = 4,696 ppm	N/A
Vapor Pressure	2.9 x 10^{-8} Torr (20°C); <10^{-7} mm Hg at 25°C	N/A
Dissociation Constant	pKa = 1.85 at 22°C (Ref: Montgomery, 1993; p. 356)	N/A
Octanol/Water Partition Coefficient	Log K_{ow} = 2.91 (Ref: Montgomery, 1993; p. 356)	N/A
pH	5.66	6.59
Stability	DATA GAP	N/A
Oxidizing or Reducing Action	Stable to the action of hexane, mono-ammonium phosphate & zinc metal, & neutral to potassium permanganate solution	N/A
Flammability	N/A	N/A
Explodability	N/A	N/A
Storage Stability	Stable for 1-year when stored in HDPE jars under ambient warehouse conditions.	N/A
Viscosity	N/A	363 cps
Corrosion Characteristics	Non-corrosive to its commercial packaging	Non-corrosive to its commercial packaging

Toxicology Characteristics

Acute Toxicity

Acute Oral Toxicity in Rats:

Propazine Technical: LD_{50} > 5050 mg/kg/day; Tox. Category IV
Propazine 4L: Male LD_{50} > 5050 mg/kg/day, Female LD_{50} = 3922 mg/kg/day; Tox. Category III

Acute Dermal Toxicity in Rats:

Propazine Technical: LD_{50} > 5050 mg/kg/day; Tox. Category IV
Propazine 4L: LD_{50} > 5050 mg/kg/day; Tox. Category IV

Acute Inhalation Toxicity in Rats:

Propazine Technical: LC_{50} >1.22 mg/l; Tox. Category III
Propazine 4L: LC_{50} >2.13 mg/l; Tox. Category IV

Primary Eye Irritation in Rabbits:

Propazine Technical: Slight irritant; Tox. Category IV
Propazine 4L: Negative; Tox. Category IV

Primary Dermal Irritation in Rabbits:

Propazine Technical: Negative; Tox. Category IV
Propazine 4L: Negative; Tox. Category IV

Primary Dermal Sensitization in Guinea Pigs:

Propazine Technical: Negative; Tox. Category N/A
Propazine 4L: Negative; Tox. Category N/A

Chronic Toxicity

In a combined carcinogenicity toxicity study, propazine was administered to 60 (sex/dose) Sprague-Dawley rats in a diet at dose levels of 0, 3, 100, or 1000 ppm (0, 0.1, 5.2, or 51 mg/kg/day males; 0, 0.2, 6.4, or 68 mg/kg/day females for 2 years. An additional 10/sex were added to control and high-dose groups for interim sacrifice at 12 months (5/sex) and after a 4-

week recovery period (5/sex). The NOEL for systemic toxicity is 100 ppm (5.2 mg/kg/day males and 6.4 mg/kg/day females) and the LOEL is 1000 ppm (51 mg/kg/day males and 68 mg/kg/day females) based upon decreased body weight. An uncertainty factor of 100 was applied to account for both interspecies extrapolation and intraspecies variability. An additional uncertainty factory of 3 was applied to account for the lack of chronic toxicity data in a second species. A chronic dog study is needed for risk assessment purposes because the NOEL from a chronic dog study may be lower than the NOEL from the chronic rat study which was used to set the RfD for propazine.

Propazine has been classified as a Group "C" (possible human carcinogen) chemical based on significant increases in mammary gland adenomas and adenomas/carcinomas in female Sprague-Dawley rats. The EPA used the Q_1^* approach with $Q_1^* = 4.45 \times 10^{-2}$ based on the Multi-Stage Weib model using a 3/4 scaling factor.

Although there were no dermal absorption data available on propazine, dermal absorption data for closely related triazine herbicides such as atrazine and simazine are available and can be

applied to propazine because of the structural similarity of propazine and those members of the

triazine class. The 10-hour dermal absorption value for **atrazine** is 30.5% and for **simazine** is 32.07%. In both studies, the vast majority of the recovered compound was that remaining in or on the skin and considered potentially systemically available. Therefore, the EPA considered 30% absorption to be appropriate in the case of propazine.

Chronic inhalation exposure is a concern, since propazine is classified as a Group C carcinogen with a linear low dose risk assessment Q_1^*. A chronic risk assessment includes both inhalation [50% absorption] and dermal [30% absorption] exposures.

Reproductive Toxicity

A developmental toxicity study in rats at doses of 0, 10, 100 or 500 mg/kg/day from gestation days 6 through 15 with a maternal NOEL of 10 mg/kg/day and the maternal LOEL is 100 mg/kg/day based upon decreased body weights and food consumption. The developmental NOEL is 10 mg/kg/day and the developmental LOEL is 100 mg/kg/day based on decreased ossification.

A developmental toxicity study in rabbits at dose level by gavage in corn oil of 0, 2, 10 or 50 mg/kg/day from day 6 through 19 of gestation with a maternal NOEL is of 50 mg/kg/day based on decreased defecation and decreased body weight gain and food consumption during the treatment period. The maternal LOEL is 10 mg/kg/day. The developmental NOEL is >50 mg/kg/day and the developmental LOEL is $\geq$50 mg/kg/day.

A three-generation reproduction study in rats at dietary concentrations of 0, 3, 100, or 1,000 ppm (0, 0.15, 5, or 50 mg/kg/day) with a paternal/offspring NOEL of 100 ppm (5 mg/kg/ day) and the parental/offspring LOEL of 1000 ppm (50 mg/kg/day) based on body weight decrements in males and females. The reproductive NOEL is $\geq$1000 ppm based on body weight decrements in males and females.

Potential Endocrine Effects

The EPA is required to develop a screening program to determine whether certain substances may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect. The EPA is currently working with interested stakeholders in developing a screening and testing program. Congress has allowed 3 years from passage of the FQPA (08/03/99) to implement this program. The structural similarity of propazine to other triazine herbicides suggests that propazine may cause endocrine effects similar to those cause by atrazine in female rats. However, these potential endocrine effects cannot be evaluated at this time. The EPA may require further testing of propazine and the propazine end-

use products for endocrine disrupter effects.

Mutagenicity

Gene Mutation: Propazine was tested in cultured V79 Chinese hamster cells with microsomal activation and without microsomal activation. Propazine produced a dose-related positive response without metabolic activation with large increases (5-23X background) at 800 to 1000 μg/ml(Highest Dose Tested). A lesser, but positive response with activation was observed (to about 5X background up to 2000 μg/ml, nondose-related).

Structural Chromosomal Aberrations: Chinese hamsters were orally administered propazine at doses of 0, 1250, 2500, or 5000 mg/kg on 2 consecutive days. The cells displaying anomalies of nuclei in treated cells did not differ significantly from the negative controls. Propazine was considered negative in this assay.

Other Genotoxic Effects: Assays for DNA damage in primary rat hepatocytes were performed with concentrations of 0, 0.5, 2.5, 12.5, or 62.5 μg/ml. The mean number of silver grains per nucleus in the vehicle control and treated cells (at any concentration level) was not markedly different. Propazine was negative for DNA damage and repair under the conditions of the assay.

Metabolism

In a metabolism study in rats, propazine was administered as a single gavage dose of 1.0 or 100 mg/kg labeled propazine or as 14-daily doses of unlabeled 1.0 mg/kg propazine followed by a single 1.0 mg/kg labeled dose. Corn oil was the vehicle for all treatments. None of the animals died during the study and overall mass balance for all treatment groups ranged from 97.0 to

105.7%. Absorption of propazine from the gastrointestinal tract was rapid and similar for all study groups and no apparent sex-related differences were found. Based on recoveries from urine/ cage wash and tissues, absorption was $\geq$73%. Within 48 hours of treatment, 82-95% of the administered dose was recovered from excreta, predominantly the urine. No specific target organs were identified. Labeled propazine was recovered only in the feces of male and female rats in the single high-dose group and female rats in the low dose group. As presented, it cannot be determined if this represents unabsorbed material or material that underwent enterohepatic circulation. Less than 0.1% of the administered dose was detected as CO_2 during a pilot study. Thirteen metabolites were recovered; three of which were identified.

Environmental Characteristics

Propazine is moderately persistent and mobile when used in the greenhouse to control weeds for non-food plants. If applied to an outdoor environment, propazine has a high potential to leach into ground water or reach surface waters by runoff. Propazine is stable to hydrolysis in sterile aqueous pH 5, 7, and 9 buffered solutions. However, published literature on propazine and related chloro-s-triazines indicate that the chemical may be susceptible to hydrolysis after adsorption onto the surface of soil colloids (a surface catalysis effect). Propazine is moderately persistent to degradation under aerobic soil conditions, degrading with half-lives of 12 to 24 weeks (calculated 15 weeks) in a nonsterile loamy sand and 8 to 12 weeks in a sterile loamy sand soil. The major degradate in the metabolism study was hydroxy-propazine [2-hydroxy-4,6-bis(isopropylamino)-s-triazine], which comprised 14 - 16% of the applied radioactivity after 12 weeks and 31% after 1 year. Unextracted bound residues comprised 35% after 12 weeks and 58% after 1 year. Batch equilibrium studies suggest that propazine is mobile, with Freundlick K_{ads} values ranging from 0.67 to 3.19 in two separate studies involving 8 soil textures. The K_{oc} values ranged from 65 to 268 in these same studies. The major degradate, hydroxy-propazine was less mobile, with K_{ads} values of 1.13 to 106 and K_{oc} values of 276 to 2163. Volatility and air photolysis are not expected to be major routes of dissipation due to the low vapor pressure (2.9×10^{-8} Torr at 20°C).

Exposure from Drinking Water

In examining aggregate exposure, the Food Quality Protection Act (FQPA) directs the EPA to consider available information concerning exposures from the pesticide residue in food and all other non-occupational exposures. The primary non-food sources of exposure the EPA looks at include drinking water (whether from ground water or surface water), and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor and/or outdoor uses). Maximum Concentration Levels have not been established for propazine in drinking water. Health Advisory levels for propazine in drinking water have been established at the following levels: 0.01 ppm - lifetime (adult), 2.0 ppm - shorter-term (adult), 0.5 ppm shorter-term (child), 1.0 ppm - 10-day (child), and 1.0 ppm - 1-day (child). Although propazine is currently registered for non-food uses, previous emergency exemptions granted for the use of propazine on sorghum were also considered by the EPA. Therefore, the total oncogenic dietary risk (food only) for the U.S. population was calculated to be 5.7×10^{-8}.

Potential to Contaminate Ground and Surface Water

Propazine is moderately persistent and mobile when used in the greenhouse to control weeds for non-food plants. If applied to an outdoor environment, propazine has a high potential to leach into ground water or reach surface waters by runoff.

Ecological Characteristics

There were no concerns for the container grown ornamentals greenhouse use, however based on the risk assessment for an emergency exemption for use of propazine on sorghum, the acute risk to birds, mammals, and fish appears to be minimal.

SUMMARY OF REGULATORY POSITION AND RATIONALE

Available data provide adequate information to support the conditional registration of propazine as a technical product and for Propazine 4L end-use product for use on container grown ornamentals in greenhouses for preemergence control of annual broadleaf weeds.

SUMMARY OF DATA GAPS

1. 83-1(b) Chronic Feeding Toxicity - Dog Study
2. 84-2 Germinal Epithelium Cells Mutagenicity Study
3. 63-13 Stability Data

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