United States Environmental Protection Agency

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

Pesticide Fact Sheet

Name of Chemical: **Bromuconazole**
Reason for Issuance: **New Chemical**
Date Issued: **November 2002**

Description of Chemical

Chemical Name:	1-[[4-bromo-2-(2,4-dichlorophenyl) tetrahydro-2-furanyl]methyl]-1*H*-1,2,4-triazole
Common Name:	Bromuconazole
Trade Name:	CHIPCO® Bromuconazole
Chemical Class:	Triazole
EPA Chemical Code:	120503
Chemical Abstracts Service (CAS) Number:	116255-48-2
Year of Initial Registration:	2002
Pesticide Type:	Fungicide
U.S. Producer:	Bayer CropScience, Research Triangle Park, NC

Use Pattern and Formulations

CHIPCO® Bromuconazole is an emulsifiable concentrate formulation containing 20% of the active ingredient bromuconazole. CHIPCO® Bromuconazole is applied in a diluted form to roses to control black spot at rates of 1.0 to 1.5 fluid ounces of product in 100 gallons of water.

Science Findings

Summary Science Statement

EPA has concluded from the review of the supporting data that there are no risks of concern from the use of bromuconazole for use on roses. Based upon the use pattern for this product, the only toxicological concern would be related to worker exposure. Risk from exposure of workers (applicators and other handlers) was below the Agency's level of concern. Because this initial registration is for non-food use, there are no dietary exposures. The product will not be registered for residential or homeowner uses so there would be no non-occupational exposure expected, including exposure of infants or children. The Agency concluded that the use of bromuconazole on roses is unlikely to present a significant threat to non-target organisms or the environment.

Physical/Chemical Properties

Physical and Chemical Properties for Technical Grade Active Ingredient		
Requirement	**Result**	
Color	White	
Physical State	Solid	
Odor	Slightly alcoholic	
Storage Stability	Stable	
pH	5.3	
Melting Point	84ºC	
Density	1.72 g/ml	
Solubility		LS850646 / LS850647
	Acetone	31.86 g/100 ml / 21.97 g/100 ml
	Dichlormethane	49.7 g/100 ml / 35.37 g/100 ml
	Ethyl Acetate	23.19 g/100 ml / 17.30 g/100 ml
	N-Hexane	0.165 g/100 ml / 0.192 g/100 ml
	Methanol	29.54 g/100 ml / 18.85 g/100 ml
	1-Octanol	6.14 g/100 ml / 3.85 g/100 ml
	2-Propanol	5.74 g/100 ml / 3.98 g/100 ml
	Toluene	21.72 g/100 ml / 15.68 g/100 ml
	Water (Distilled)	60.9 mg/l / 20.8 mg/l
	Water (pH 5)	52.3 mg/l / 17.0 mg/l
	Water (pH 9)	59.4 mg/l / 22.1 mg/l

Toxicity Profile:

Acute Toxicity Profile of Bromuconazole				
GDLN	**Study Type**	**MRID**	**Results**	**Tox Category**
81-1	Acute Oral–Rat	429371-21	LD_{50} = 365 mg/kg (males and females, combined)	II
81-2	Acute Dermal--Rabbit	429371-22	LD_{50} > 2000 mg/kg (males and females, combined)	III
81-3	Acute Inhalation–Rat	429371-23	LC_{50} > 5.05 mg/L (males and females, combined)	IV
81-4	Primary Eye Irritation–Rabbit	430185-01	0.1 ml, mild irritant	III
81-5	Primary Skin Irritation– Rabbit	430185-02	Not an irritant	IV
81-6	Dermal Sensitization– Guinea Pig	430185-03	Not a dermal sensitizer	N/A

Toxicity Studies other than Acute Toxicity		
Guideline No./ Study Type	**MRID No. /Classification/Doses**	**Results**
870.3100 13-Week feeding - rat	429371-31 Acceptable 0, 40, 200, 1000, or 5000 ppm via the diet	**NOAEL**: 200 ppm (M: 13.8 mg/kg/day; F: 15.1 mg/kg/day) **LOAEL**: 1000 ppm (M: 68.1 mg/kg/day; F: 74.5 mg/kg/day) based on decreased body weight gains in females, changes in hematology/blood chemistry parameters and in the incidence of microscopic lesions consistent with liver toxicity, and increased liver weight gain in both sexes
870.3700 Developmental toxicity - Sprague-Dawley Rats	429371-26 & 429371-27 Acceptable 0, 10, 70, or 500 mg/kg/day by gavage	**Maternal NOAEL**: 70 mg/kg/day **Maternal LOAEL**: 500 mg/kg bw/day (significantly increased water consumption, significantly decreased body weight gain, and significantly increased absolute and relative liver weights) **Developmental NOAEL:** 10 mg/kg/day **Developmental LOAEL**:70 mg/kg/day (significant increases in placental weights and additional cervical ribs)

Toxicity Studies other than Acute Toxicity		
Guideline No./ Study Type	**MRID No. /Classification/Doses**	**Results**
870.3700 Developmental toxicity in Rabbits	429371-29 & 429371-28/Acceptable 0, 12.5, 50, or 200 mg/kg/day	**Maternal NOAEL:** 12.5 mg/kg/day **Maternal LOAEL:** 50 mg/kg/day based on increased clinical signs (lethargy/reluctance to move, increased respiration rate, ataxic/unsteady gait, aggression, lack of muscle tone and coordination, prone posture and/or vocalization); decreased body weight gain, and decreased food consumption. **Developmental NOAEL:** 50 mg/kg/day **Developmental LOAEL:** 200 mg/kg/day based on the decreased rate of live fetuses per doe, increased percentage of postimplantation loss, and slightly increased rate of resorptions.
870.3700 Developmental toxicity - Rat	430185-08 Acceptable 0, 40, 133, or 133 mg/kg/day applied dermally	**Maternal NOAEL**: 40 mg/kg/day **Maternal LOAEL**: 133 mg/kg/day based on increased clinical signs (ungroomed and unkempt coat) **Developmental NOAEL**: 40 mg/kg/day **Developmental LOAEL**: 133 mg/kg/day based on increased fetal and litter incidences of skeletal abnormalities (extra ribs or pairs of extra ribs)
870.3800 2-Generation Reproduction	430299-01 & 429371-30 Acceptable 0, 20, 200 or 2000 ppm in the diet	**Parental NOAEL**: 200 ppm **Parental LOAEL**: 2000 ppm based on decreased body weight gain, increased liver weights, and increased incidences of hepatocytic fatty vacuolation. **Offspring NOAEL:** 200 ppm **Offspring LOAEL:** 2000 ppm based on whole litter loss and decreased pup body weight gain during lactation.
870.4300 Chronic/Carcinogenicity - rat	429371-32 Acceptable 20, 150, 1000, or 2000 ppm in the diet	**NOAEL**: 20 ppm (0.88 mg/kg/day) **LOAEL**: 150 ppm (6.48 mg/kg/day) based on liver non-neoplastic lesions Not oncogenic under conditions of study.
870.4300 Carcinogenicity in Mice	430185-06 & 430185-07 Acceptable 0, 100, 1000, and 3000 ppm in the diet	NOAEL: 100 ppm (M: 12.3 mg/kg/day; F: 10.9 mg/kg/day) LOAEL: 1000 ppm (F: 134.5 mg/kg/day) based on decreased body weight gains

Toxicity Studies other than Acute Toxicity		
Guideline No./ Study Type	**MRID No. /Classification/Doses**	**Results**
870.5265 **Salmonella/microsome plate incorporate assay**	430185-09/Acceptable Strains TA98, TA100, TA1535, TA1537, and TA1538 were exposed to bromuconazole at concentrations of 50, 158, 500, 1580, and 5000 µg/plate with and without exogenous metabolic activation.	No evidence of induced revertant colonies over background at any dose tested.
870.5374 **In vitro mammalian cell cytogenetic assay**	429371-36/Acceptable Chinese hamster CHO-K1 cells were exposed to 10, 50, 100, and 250 µg/ml Bromuconazole with and without exogenous metabolic activation.	In the absence of S9 mix, statistically significant increases were seen in the mean percent of metaphases with chromosomal abserrations at 10 and 50 µg/ml when gaps were excluded from the determination. In the presence of S9 mix, statistically significant increases were seen at 10 and 50 µg/ml, whether gaps were included or excluded from the determination.
870.5395 **In vivo mouse bone marrow micronucleus assay**	429371-37/Acceptable 40, 200, or 1000 mg/kg administered by a single oral dose	Bromuconazole was tested to an adequate top dose and did not significantly increase the frequency of micronucleated polychromatic erythrocytes in mouse bone marrow.
870.5550 **In vitro cytogenetic assays**	435211-01/Acceptable	No evidence of a clastogenic response in the absence of S9 activation. However, bromuconazole was clastogenic in the presence of S9.
870.5550 **In vivo/in vitro UDS in rat hepatocytes/mammlian cells procedure**	429271-28/Acceptable 189.7 and 600 mg/kg by oral gavage	The mean net nuclear grain count was below zero for both treatment times indicating no induction of UDS as tested in the study.
870.5550 **In vitro UDS in primary rat hepatocytes/mammalian cells culture**	430185-10/Acceptable Applied at concentrations of 0.391, 1.24, 3.91, 12.4, and 39.1 µg/mL and concentrations of 0.391, 1.24, 3.91, 12.4, 39.1, and 124 µg/mL in a second assay	No evidence of UDS induction at any tested concentration as measured by incorporation of tritiated thymidine into DNA.

Summary of Toxicology Findings.

Acute Toxicity

The data for bromuconazole indicate that the acute oral toxicity is in toxicity category II and the acute dermal toxicity and primary eye irritation are in toxicity category III. Acute inhalation toxicity and primary dermal irritation is in category IV. Bromuconazole is not a dermal sensitizer.

Dermal Exposure

To evaluate potential risks associated with dermal exposure during periods of short-term and intermediate-term exposure, the Agency selected an endpoint from the dermal developmental toxicity study in rats. In this study, bromuconazole was administered to 25 Sprague-Dawley rats per dose group by the dermal route on gestational days 6-15, inclusive, at dose levels of 0, 40, 133 or 400 mg/kg/day. Compound-related maternal toxicity was ob served in a dose-related manner at 133 and 400 mg/kg/day as evidence by increased clinical signs (ungroomed and unkempt coat). The Maternal NOAEL was 40 mg/kg/day and the Maternal LOAEL was 133 mg/kg/day. Developmental toxicity was observed in this study at 133 and 400 mg/kg/day as evidenced by increased fetal and litter incidences of skeletal abnormalities (one extra rib or a pair of extra ribs) compared to concurrent and historical controls. The Developmental NOAEL was 40 mg/kg/day and the Developmental LOAEL was 133 mg/kg/day.

To evaluate potential risks posed by dermal exposure on a chronic basis, the Agency selected an endpoint from the combined chronic/carcinogenicity study in rats. The oral NOAEL in this study is 0.88 mg/kg/day based on the increase in liver non-neoplastic lesions (fatty vacuolation) at the LOAEL of 6.48 mg/kg/day.

Inhalation Exposure

To evaluate the potential risks associated with inhalation exposure resulting from short-term and intermediate term exposures, the Agency selected an endpoint from the oral developmental toxicity study in rats. The developmental NOAEL in this study is 10 mg/kg/day based on additional cervical ribs at the LOAEL of 70 mg/kg/day. To evaluate inhalation exposures resulting from chronic exposure to bromuconazole, the Agency selected the endpoint from the combined chronic/carcinogenicity study in rats (as discussed in the paragraph above on dermal exposure).

Occupational Exposure and Risk Characterization

Handlers (Commercial)

Bromuconazole is the active ingredient (20%) in the product CHIPCO®. It is a fungicide to be used primarily in enclosed commercial greenhouses to control diseases (black spot) in commercially-grown roses. The end-use product is an emulsifiable concentrate formulation that will be mixed in water at an application rate of 1-1.5 fluid ounces of product/100 gallons of water. Applications will be made using high-pressure handwands or backpack sprayers. Applications may be made at 14 day intervals. The label does not limit the number of applications.

Workers may be exposed to bromuconazole during mixing, loading, and application activities. Based on the proposed application rates and use scenarios, short- and intermediate-term dermal and inhalation exposure is expected. Chronic exposures to mixers, loaders, and applicators are not expected. The exposure scenarios assessed are: mixing/loading and applying liquid for backpack and mixing/loading and applying liquid for high pressure sprayer.

Chemical-specific data for assessing human exposures during pesticide handling activities were not submitted to the Agency in support of this Section 3 application. It is the policy of the HED to use data from the PHED Version 1.1 to assess handler exposures for regulatory actions when chemical-specific monitoring data are not available (HED Science Advisory Council for Exposure, Policy 007, "Use of Values from the Pesticide Programs," January 1999).

The unit exposure values calculated by PHED generally range from the geometric mean to the median of the selected data set. To add consistency and quality control to the values produced from this system, the PHED Task Force has evaluated all data within the system and has developed a set of grading criteria to characterize the quality of the original study data. The assessment of data quality is based on the number of observations and the available quality control data. While data from PHED provide the best available information on handler exposures, it should be noted that some aspects of the included studies (e.g., duration, acres treated, pounds of active ingredient handled) may not accurately represent labeled uses in all cases. HED has developed a series of tables of standard unit exposure values for many occupational scenarios that can be utilized to ensure consistency in exposure assessments.

The MOEs calculated for liquid application with high pressure handwand are over 3,000 for dermal with baseline PPE and over 20,000 for inhalation with baseline PPE. Liquid applications with backpack sprayer had MOEs of over 100,000 for dermal with minimum PPE and over 2 million for inhalation with baseline PPE. All MOEs exceed the target MOE of 100, indicating low worker risk concern.

The handler exposure estimates in this assessment are based on using maximum application rate, and are assumed to be representative of high-end exposures. The uncertainties associated with this assessment stem from the use of surrogate exposure data (e.g., differences in use scenario and data confidence) and assumptions regarding the amount of chemical handled. The estimated exposures are believed to be reasonable high-end estimates based on 100% dermal absorption and professional experience and judgement.

Post-Application Exposure

There is also potential dermal exposure to bromuconazole during postapplication activities. The potential for inhalation exposure from postapplication activities is low. Activities can range from low contact (e.g., scouting, irrigating, and thinning crops with low crop height and minimal foliage) to medium contact (e.g., scouting and irrigating crops with full foliage development) to high contact (e.g., pinching, pruning, and hand harvesting). All MOEs on Day 0 meet or exceed the target MOE of 100.

Ecological Effects and Environmental Fate Characteristics

Ecological Toxicity Data. The following toxicity data are available and fulfill the ecological effects data requirements for an indoor use:

1. In an acute oral study on rats using the technical grade active ingredient (TGAI), the acute oral LD_{50} was 403 for males and 328 for females, which is considered moderately toxic.

2. In a test with the TGAI fed to bobwhite quail, the dietary LC_{50} was >2150 ppm. Similar results were found in the mallard duck study. Thus, bromuconazole is practically nontoxic to avian species on an acute oral and subacute dietary basis.

3. In a test on rainbow trout using the TGAI, the 96-hour LC_{50} was 1.7 ppm which is considered to be moderately toxic. A similar result was found in the bluegill sunfish study in which the 96-hour LC_{50} was 4.2 ppm

4. In a test with *Daphnia magna* using the end-use formulation, the 48-hour EC_{50} was 0.085 ppb which is considered to be very highly toxic.

Environmental Fate Data

Given the indoor use pattern associated with the proposed use, only limited environmental fate data are typically required. Based on the use pattern for this product, this chemical will not get outdoors while being used and there is little likelihood that the mobility, persistence and degradate information obtained from these studies would be used to characterize exposure or risk.

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