United States
Environmental Protection
Agency

Office of Prevention, Pesticides
and Toxic Substances
(7505C)

Pesticide Fact Sheet

Name of Chemical: **Ipconazole**
Reason for Issuance: **Conditional Registration**
Date Issued: **September, 2004**

DESCRIPTION OF CHEMICAL

Generic Name:	2-[(4-chlorophenyl)methyl]-5-(1-methylethyl)-1-(1*H*-1,2,4-triazol-1-ylmethyl) cyclopentanol
Common Name:	Ipconazole
Trade Name:	Vortex
EPA Chemical Code:	125618
Chemical Abstracts Service (CAS) Number:	125225-28-7
Year of Initial Registration:	2004
Pesticide Type:	Fungicide
Chemical Family:	Triazole
U.S. and Foreign Producers:	Crompton Corporation

Ipconazole is a new chemical registered for use as a seed treatment on various crops, turfgrass, ornamental flowers and conifers. It is a systemic, broad-spectrum fungicide seed dressing used to protect plants from soil borne and seed borne disease. Ipconazole is structurally similar to many other triazole compounds used as pesticides. Ipconazole exerts its effect by inhibiting sterol synthesis in fungi. No tolerances have been proposed or established for ipconazole residues of concern in/on plant and animal commodities. Based on the radiotracer studies, residues on crops are non-existent or low enough to be registered as a non-food use pesticide for the current seed uses:

ROOT VEGETABLES
Beet (garden), burdock (edible), carrot, celeriac, chervil (turnip-rooted), chicory (roots), chufa, dandelion (roots), ginseng, parsley (turnip-rooted), parsnip, radish, radish (oriental), rutabaga, salsify, salsify (black), salsify (Spanish), skirret, turnip and yam bean.

LEAFY VEGETABLES (Except Brassica Vegetables)
Amaranth (leafy, Chinese spinach, tampala), arugula, cardoon, celery (including Chinese), celtuce, chervil, chrysanthemum (edible-leaved and garland), corn salad, cress (garden and upland), dandelion, dock, endive, fennel (Florence, finochio), lettuce (head and leaf), orach, parsley, purslane (garden and winter), radicchio, rhubarb, spinach, spinach (New Zealand), spinach (vine), and Swiss chard.

BRASSICA (COLE) LEAFY VEGETABLE GROUP
Broccoli, broccoli (Chinese), broccoli (raab), Brussels sprouts, cabbage (including Chinese bok choy, Chinese napa, and Chinese mustard), cauliflower, cavalo broccolo, collards, kale, kohlrabi, mizuna, mustard greens, mustard spinach, and rape greens.

CUCURBIT VEGETABLES
Chayote, Chinese waxgourd, citron melon, cucumber, gherkin, gourd edible (includes hyotan, cucuzza, hechima, Chinese okra), momordica, all muskmelon, pumpkin, squash and watermelon.

CEREAL GRAINS (Includes Forage And Silage)
Corn (field corn, popcorn, and sweet corn) and sorghum only.

Cotton, sunflower, mustard, rape, canola, ornamental flowers, conifers, turf grass (seed treatments).

USE PATTERNS AND FORMULATIONS

Ipconazole is a non-food use, seed treatment fungicide that is for control of soil borne pathogens that attack seeds. Ipconazole is effective in controlling the *Zygomycetes, Ascomycetes, Basidiomycetes*, and *Deuteromycetes* fungal classes at application rates from 0.021 to 0.16 oz ipconazole/100 lb seed (use rate on corn is lower).

The manufacturer of the technical material is Crompton Corporation, Bethany, CT. The

formulated product, Vortex, contains 40.7% ipconazole and is an end-use product distributed by Gustafson LLC, Plano, TX. It is registered for use as a seed treatment on root vegetables (does not include potato, sweet potato or yam, true); leafy vegetables (Brassica and non-Brassica); cucurbit vegetables; corn (field, pop, sweet); sorghum; cotton; sunflower; canola; rape; mustard; turfgrass; ornamental flowers; and conifers. Vortex is a flowable concentrate containing 3.77 lbs ipconazole/gallon. Application of Vortex Seed Treatment Fungicide may be made as a water-based slurry with other registered seed treatment insecticides and fungicides through standard slurry or mist-type commercial seed treatment equipment. Vortex is effective in controlling the *Zygomycetes, Ascomycetes, Basidiomycetes*, and *Deuteromycetes* fungal classes. It is not active against *Pythium* or *Phytophthora* species (systemic downy mildews). The label for Vortex™ recommends it be applied in a tank mixture with Allegiance-FL®, which contains the active ingredient metalaxyl. Both fungicides are applied to the seeds prior to planting.

SCIENCE FINDINGS

CHEMICAL CHARACTERISTICS

Ipconazole consists of a 9:1 *cis-,cis-,:cis-,trans-* mixture of isomers that have significantly different physical properties. The physical properties of the isomers are different enough that they will move through the environment at different rates.

The following physical and chemical properties of technical ipconazole were submitted by the registrant as part of the product chemistry data.

TABLE 1. Physicochemical Properties of the Technical Grade Test Compound.

Parameter	Value	
Melting point/range	85-88°C	
pH	5.35 (1% Suspension at 25°C)	
Density	1.2 g/mL at 20°C	
Water solubility	cis-cis isomer: 9 ppm cis-trans isomer: 5 ppm	
Solvent solubility in g/L	Acetone	570
	1,2 Dichloroethane	420
	Dichloromethane	580
	Ethyl Acetate	430
	Heptane	1.9
	Methanol	680
	n-Octanol	230
	Toluene	160
	Xylenes	150

TABLE 1. Physicochemical Properties of the Technical Grade Test Compound.	
Parameter	Value
Vapor pressure	<5.0 x 10^{-5} Pa (at both 20 and 30°C)
Dissociation constant, pK_a	Could not be measured
Octanol/water partition coefficient, Log(K_{OW})	cis-cis isomer: 4.6 cis-trans isomer: 4.4
UV/visible absorption spectrum	222 nm: 0.74541 (Absorption AUS) 268 nm: 0.02653 (Absorption AUS)

TOXICOLOGY CHARACTERISTICS

Based on information provided by the registrant, it is unknown whether just one or both isomers that are present in technical grade ipconazole are biologically active, or the extent to which they differ in biological activity. The toxicity data were developed on tests performed with technical grade ipconazole.

Acute Toxicity: Technical grade ipconazole has minimal to moderate acute toxicity in acute oral, dermal and inhalation tests. It is moderately irritating to the eyes and skin. Ipconazole is not a dermal sensitizer.

TABLE 2: Summary of Acute Toxicity Data - Technical Grade Material		
Study Type	Results	Toxicity Category
Acute Oral (rat)	LD_{50} M: 1338 mg/kg F: 888 mg/kg	III
Acute Dermal (rat)	LD_{50} > 2000 mg/kg (both sexes)	III
Acute Inhalation (rat)	LD_{50} > 1.88 mg/L (both sexes)	III
Primary Eye Irritation (rabbit)	eye irritation present at 24 hours, cleared by day 7	III
Primary Skin Irritation (rabbit)	primary irritation index = 0.08	IV
Dermal Sensitization (guinea pig)		Non-sensitizer

Acute Toxicity: Technical grade ipconazole has minimal to moderate acute toxicity in acute oral, dermal and inhalation tests, is moderately irritating to the eyes and skin and is not a dermal sensitizer.

Subchronic Toxicity: Subchronic oral toxicity study in rats indicated increased incidences of erosion, hyperkeratosis, and hyperplasia of the mucosal epithelium of the non-glandular portion of the stomach in males at the LOAEL of 29.89 mg/kg/day.

Chronic Toxicity/Carcinogenicity: Combined chronic toxicity/carcinogenic studies in rats and mice were not included as part of the registration submission for ipconazole. However, Ipconazole belongs to the class of chemicals known as triazoles and several chemicals in this class have induced liver tumors in mice. Consequently, the Agency is using a low-dose extrapolation method (i.e, use of a Q1*) for quantification of human cancer risk for ipconazole. The most potent Q1* value of $1.6x10^{-1}$ established for a triazole compound, cyproconazole, is used for quantification of risk for ipconazole.

Developmental Toxicity: The developmental toxicity LOAEL for ipconazole in rats is 30 mg/kg/day based on decreased fetal body weight and increased incidences of visceral and skeletal variations. The developmental toxicity NOAEL is 10 mg/kg/day.

Reproductive Toxicity: Not required since registration is limited to non-food uses.

Neurotoxicity: Not required since registration is limited to non-food uses.

Mutagenicity: Ipconazole testing indicate is not mutagenic. In addition, ipconazole did not induce DNA damage/repair in spot tests with strains of *Bacillus subtilis* up to cytotoxic concentrations.

Metabolism: Radiotracer studies were submitted for canola, carrots, corn. cotton, cucumber, leaf lettuce, sorghum, soybean and wheat. The studies indicate that canola, carrot, cotton, cucumber, leaf lettuce, and sorghum are non-food use as defined in the Agency's seed treatment policy. The study for corn indicates it can be considered non-food use if the use rate is limited to an application rate of 0.0013 lb ai/100 lbs seed. The studies for soybean and wheat indicate that use on these commodities is a food use and would require tolerances. Use on soybean and wheat has been withdrawn by the registrant and have been removed from the proposed label.

TOXICOLOGY ENDPOINT SELECTION

Table 3. Summary of Toxicological Doses and Endpoints for ipconazole

Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA SF*/Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary	An acute dietary RfD was not established since the proposed registration is for a non-food use.		
Chronic Dietary	A chronic dietary RfD was not established since the proposed registration is for a non-food use.		
Short- and Intermediate-Term Incidental Oral	Endpoints of concern were not selected for incidental oral exposure scenarios (short and intermediate terms), since there are no proposed residential uses and the current registration is for a non-food use.		
Short- and Intermediate-Term Dermal	Oral NOAEL= 10 mg/kg/day (50% Dermal Absorption)	**Residential** LOC for MOE = NA **Occupational** LOC for MOE = 100	Developmental studies in rats and rabbits: Decreases in body weight gain and food consumption at 30 mg/kg/day in rats and 50 mg/kg/day in rabbits
Long-Term Dermal	Oral NOAEL= 10 mg/kg/day (50% Dermal Absorption)	**Residential** LOC for MOE = NA **Occupational** LOC for MOE = 1000	Developmental studies in rats and rabbits: Decreases in body weight gain and food consumption at 30 mg/kg/day in rats and 50 mg/kg/day in rabbits
Short- and Intermediate-Term Inhalation	Oral NOAEL = 7.22 mg/kg/day (100% Inhalation Absorption)	**Residential** LOC for MOE = NA **Occupational** LOC for MOE = 100	Subchronic oral toxicity study in rats: Increased incidences of erosion, hyperkeratosis, and hyperplasia of the mucosal epithelium of the non-glandular portion of the stomach in males at the LOAEL of 29.89 mg/kg/day.
Long-Term Inhalation	Oral NOAEL = 7.22 mg/kg/day (100% Inhalation Absorption)	**Residential** LOC for MOE = NA **Occupational** LOC for MOE = 1000	Subchronic oral toxicity study in rats: Increased incidences of erosion, hyperkeratosis, and hyperplasia of the mucosal epithelium of the non-glandular portion of the stomach in males at the LOAEL of 29.89 mg/kg/day.
Cancer (oral, dermal, inhalation)	A low-dose extrapolation method (i.e, use of a Q1*) for quantification of human cancer risk for ipconazole due to SAR with the triazoles. The most potent Q1* value of 1.6×10^{-1} established for cyproconazole was used for quantification of risk for ipconazole.		

UF = uncertainty factor, FQPA SF = Special FQPA safety factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, MOE = margin of exposure, LOC = level of concern, NA = Not Applicable

RESIDUE CHEMISTRY

The Agency's seed treatment policy (OPPTS Series 860 Guidelines, Section 1000) does not specify in quantitative terms what is meant by "no uptake of residues." In a memo dated 10/28/99, the Agency concluded that this phrase means that the total radioactive residue (TRR) needs to be 5 ppb (0.005 ppm) or lower to establish "no uptake of residues," and thus have the use be considered non-food.

In support of the registration application, Gustafson submitted radiotracer studies for the following crops: canola, carrots, corn, cotton, cucumbers, leaf lettuce, sorghum, soybean, and wheat. These data submissions were screened for residues found, and only those uses that can be classified as non-food, based on the current seed treatment policy, were reviewed. The radiotracer studies for canola, carrot, cotton, cucumber, leaf lettuce, and sorghum are adequate to classify the proposed seed treatment uses of ipconazole on these crops as non-food uses. In addition, the study for corn is adequate to classify the proposed seed treatment use as a non-food use provided the label specifies a maximum application rate of 0.0013 lb ipconazole/100 lbs of seed.

In wheat and soybean radiotracer studies, uptake of total radioactivity was greater than 5 ppb in wheat forage/hay/straw and soybean hay. As a result, cereal grain uses are limited to just corn and sorghum. With the exception of turfgrass (which is not a food or feed crop), the uses on the grass forage, fodder, and hay group are not allowed.

The Agency concludes that the following ipconazole seed treatment uses are non-food: root and tuber vegetables (except potato, sweet potato or yam, true); leafy vegetables (Brassica and non-Brassica); cucurbit vegetables; corn (field, pop, sweet); sorghum; cotton; sunflower; canola; rape; mustard; turfgrass; ornamental flowers; and conifers. No tolerances are required for residues of ipconazole for these seed treatment uses.

Worker Exposure/Risk

No chemical-specific data were submitted to support the registration of ipconazole. Due to the seasonal nature of seed treatment operation, the Agency has assumed that handlers involved in applications would be exposed for less than 6 months per year. Thus, handler's exposures are expected to be short-/intermediate- term in duration. Long-term exposures (> 6 months) are not expected for either handlers and/or farmers and thus were not considered in the risk assessment.

The dermal absorption rate used for this assessment was 50 percent (based on the data from tebuconazole, which is structurally related to ipconazole) and the inhalation absorption rate was assumed to be 100%. The dermal endpoint is based on decreases in body weight gain and food consumption from developmental toxicity studies in rats/rabbits. The inhalation endpoint is based on increased incidences of erosion, hyperkeratosis, and hyperplasia of the mucosal epithelium of the non-glandular portion of the stomach in males in a subchronic oral toxicity study in rats. Daily dermal and inhalation doses were compared to a dermal NOAEL of 10 mg/kg/day (all durations) and inhalation NOAEL of 7.2 mg/ kg/day (all durations) respectively

to determine the level of risks. The target margin of exposure (MOE) for dermal and inhalation risk is 100.

Since no chemical-specific data for assessing human exposures during pesticide handling activities were submitted to the Agency in support of the registration of ipconazole, the Agency occupational handler assessments were based on the unit exposure data from the Science Advisory Council for Exposure (Exposure SAC) Policy #14: Standard Operating Procedures (SOP) for Seed Treatment (May 1, 2003).

For occupational exposure: An MOE of 100 is adequate for dermal and inhalation routes for short and intermediate term exposure risk assessments. This is based on the conventional uncertainty factor of 100 (10X for inter-species extrapolation and 10X for intra-species variations). All MOEs calculated for the seed treatment handlers are greater than the target of 100 (ranging from 800 to 160,000,000). The post-application MOEs for seed planters also exceeded the target MOE of 100 (ranging from 960 to 150,000,000).

Most cancer risks calculated for seed treatment handlers are below 1E-4 (ranging from 1.8 E-4 to 1.4 E-8). The one exception is multiple activity workers involved in treating sorghum seeds (risk 1.8 E-4). The original characterization of the estimated cancer risk was based on the assumption of 718,000 lbs of seed treated/day and reflects an overestimate when multiple activities are considered. The Agency concurred with the registrant's contention that it would be unreasonable to expect a single worker to treat and bag 718,000 lbs of seed in a day. Furthermore, it was assumed that a worker would be involved in multiple activities for 60 days per year, and for 35 years of a 70-year lifetime. Finally, in the absence of a cancer potency factor for ipconazole, the cyproconazole cancer potency factor was used for upper bound quantification of cancer risk. Therefore, the estimated cancer risk for occupational handlers treating sorghum seed is highly conservative; the Agency agrees with the registrant's contention that risks for workers in a typical commercial treatment facility would likely be much lower, and certainly below the Agency's level of concern for cancer risk. Cancer risks for post-application seed planters are also below 1E-4. The cancer risks were calculated using the maximum application rates because no adequate data regarding typical rates were provided to the Agency by the registrant. In addition to the use of maximum application rates, the Q1* value used to estimate cancer risks was based on the most potent Q1* value of 1.6×10^{-1} established for cyproconazole. Therefore, the cancer risk estimates are believed to be very conservative.

Cancer Risk for Seed-Treatment Handlers.

Exposure Scenario (Scenario #)	**Mitigation Level/Unit Exposure (mg/lb ai)**	**Seed Category--Representative Seed Species**	**Application Rate (lb ai per lb seed)**	**Amount Treated (lb seed treated per day)**	**Cancer Risk**
Loader/Applicator					
Loading/Applying Liquids for Seed Treatment (1)	Single Layer, Gloves Dermal Unit Exposure =0.023 Inhalation Unit Exposure =0.00034	Radish	0.000025	88000	5.6 E-6
		Collars	0.0001	88000	2.2 E-5
		Beet	0.000025	8000	5.1 E-7
		Corn	0.000015	550000	2.1 E-5
		Sorghum	0.00005	718000	9.3 E-5
		Millet	0.00005	88000	1.1 E-5
		Grasses	0.000025	96000	6.2 E-6
		Alfalfa	0.000025	288000	1.9 E-5
		Safflower (cotton/ sunflower)	0.000025	718000	4.6 E-5
		Canola	0.0001	105600	2.7 E-5
		Orn, Flowers	0.0001	200	5.1 E-8
		Conifers	0.0001	3000	7.8 E-7
Sower					
		Radish	0.000025	88000	1.5 E-6
		Collards	0.0001	88000	6.2 E-6
		Beet	0.000025	8000	1.4 E-7
		Corn	0.000015	550000	6.1 E-6
		Sorghum	0.00005	718000	2.7 E-5
		Millet	0.00005	88000	3.2 E-6

Exposure Scenario (Scenario #)	**Mitigation Level/Unit Exposure (mg/lb ai)**	**Seed Category--Representative Seed Species**	**Application Rate (lb ai per lb seed)**	**Amount Treated (lb seed treated per day)**	**Cancer Risk**
		Grasses	0.000025	96000	1.8 E-6
		Alfalfa	0.000025	288000	5.1 E-6
		Safflower	0.000025	718000	1.3 E-5
		Canola	0.0001	105600	7.7 E-6
		Orn. Flowers	0.0001	200	1.4 E-8
		Conifers	0.0001	3000	2.2 E-7
Bagger					
Bagging Seeds after Seed treatment (3)	Single Layer, **No Gloves*** Dermal Unit Exposure =0.0091 Inhalation Unit Exposure =0.00016 * Screening level assessment - label requires gloves	Radish	0.000025	88000	2.2 E-6
		Collards	0.0001	88000	9.1 E-6
		Beet	0.000025	8000	2.1 E-7
		Corn	0.000015	550000	8.5 E-6
		Sorghum	0.00005	718000	3.7 E-5
		Millet	0.00005	88000	4.5 E-6
		Grasses	0.000025	96000	2.4 E-6
		Alfalfa	0.000025	288000	7.5 E-6
		Safflower	0.000025	718000	1.9 E-5
		Canola	0.0001	105600	1.1 E-5
		Orn. Flowers	0.0001	200	2.1 E-8
		Conifers	0.0001	3000	3.0 E-7
Multiple Activities Worker					
		Radish	0.000025	88000	1.1 E-5
		Collards	0.0001	88000	4.3 E-5

Exposure Scenario (Scenario #)	Mitigation Level/Unit Exposure (mg/lb ai)	Seed Category--Representative Seed Species	Application Rate (lb ai per lb seed)	Amount Treated (lb seed treated per day)	Cancer Risk
		Beet	0.000025	8000	9.8 E-7
		Corn	0.000015	550000	4.0 E-5
		Sorghum*	**0.00005**	**718000**	**1.8 E-4**
		Millet	0.00005	88000	2.1 E-5
		Grasses	0.000025	96000	1.2 E-5
		Alfalfa	0.000025	288000	3.5 E-5
		Safflower	0.000025	718000	8.8 E-5
		Canola	0.0001	105600	5.1 E-5
		Orn. Flowers	0.0001	200	9.8 E-8
		Conifers	0.0001	3000	1.5 E-6

Note: Lifetime Average Daily Dose = Combined Daily Dose (mg/kg/day) x 60 exposure days / 365 days x 35 work yrs/70 yr life expectancy. *** See risk characterization discussion just prior to the table.**

Post-application Exposure and Risk

All non-cancer post-application MOEs for seed planters are acceptable, i.e., the MOEs range from 960 to 150,000,000. Post-application cancer risks are below the Agency's level of concern (cancer risk>1 E-4) for all uses on the revised label (a few commodities have been withdrawn by the registrant based on a screening level risk assessment).

AGGREGATE EXPOSURE AND RISK CHARACTERIZATION

The currently proposed uses for ipconazole encompass only non-food uses. Therefore, no aggregate dietary exposure analysis was performed. Since the triazole contribution to groundwater from ipconazole will be insignificant due to the very low use rate for a seed treatment, the Agency concludes that no surfacewater or groundwater risk assessment is required for ipconazole.

ENVIRONMENTAL FATE AND ECOLOGICAL CHARACTERISTICS

The following data were developed for the technical grade ipconazole.

Hydrolysis

Ipconazole degraded with half-lives of 330 days in pH 5 buffer, 495 days in pH 7 buffer, and 257 days in a buffered pH 9 solution at 25° C.

Aqueous Photolysis

The half-life for ipconazole at 3 µg/ml in a buffered (pH 5) solution under a continuous Xenon lamp irradiated (pH 5) solution is 32 days (equivalent to ca. 64 days of natural sunlight). No degradation was detected in dark control samples.

Aerobic Soil Metabolism

Ipconazole, applied at 0.1 kg a.i./ha, had a first-order half-life of 330 days (r^2= 0.8745) in North Dakota sandy loam soil at 25° C in the dark. The only major degradation product (>10% applied radioactivity) was 1-H-1,2,4-triazole (triazole). It reached a maximum concentration of 11.85% of applied at 31 days post-treatment and ranged from 5.55-9.23% from 59 and 365 days. The estimated half-life for triazole was 495 days (r^2= 0.4349). No minor degradation products were identified. Extractable residues decreased from an average of 99.9% of applied at 0 days to 48.5% at 365 days. Non-extractable residues at 301 days post-treatment were characterized as 2.49% of applied in the fulvic acid fraction, 5.04% in the humic acid fraction, and 15.8% of applied in the humin fraction. The $^{14}CO_2$ at 365 days post-treatment accounted for 18.6% of applied radioactivity. No organic volatiles were detected.

Ipconazole, at 0.11 kg a.i./ha, had a first-order half-life of 1386 days (r^2=0.518) in non-sterile and sterile sandy loam soil (Mutchler sandy loam) in the dark at 25° C. No degradation products were identified. Non-extractable radiolabeled residues accounted for 17.6 to 21.7% of applied. Total $^{14}CO_2$ accounted for 0.6% of applied and not detectable in non-sterile and sterile soils, respectively.

The registrant also submitted several non-GLP metabolism studies for ipconazole in aerobic, submerged, and rice paddy Japanese soils. First-order half-lives for the ipconazole 9:1 cc:ct isomer mixture ranged from 136 to 210 days in aerobic soils, 107 to 131 days in submerged soils, and 89 to 121 days in rice field soils. Half-lives of individual ipconazole isomers were similar to half-lives for the 9:1 cc:ct ipconazole mixture. These data were not used in the risk assessment due to their non-Good Laboratory Practice (GLP) status.

Adsorption-Desorption

Ipconazole, at soil concentrations from 0.9 to 90 mg a.i./kg, had Freundlich adsorption coefficients of 90 (1/n= 0.78; K_{oc}=3214) in a Dock Road sandy loam soil, 107 (1/n=0.81;

K_{oc}=1911) in a EL7 sandy loam soil, 108 (1/n=0.80; K_{oc}=2512) in Hatzenbeler clay loam soil, 45 (1/n=0.81; K_{oc}=2513) in a Mutchler sandy loam soil, and 47 (1/n=0.86; K_{oc}=2813) in a Oregon silt loam soil (MRID 45542225). Freundlich desorption coefficients were 113 (1/n= 0.80; K_{oc}=4036) in a Dock Road sandy loam soil, 118 (1/n=0.78; K_{oc}=2107) in a EL7 sandy loam soil, 146 (1/n=0.83; K_{oc}=3938) in Hatzenbeler clay loam soil, 63 (1/n=0.84; K_{oc}=3938) in a Mutchler sandy loam soil, and 59 (1/n=0.86; K_{oc}=3026) in a Oregon silt loam soil. Simple adsorption K_ds for ipconazole ranged from 67 to 213. No adsorption/desorption coefficients were available for sand textured soils (sand or loamy sand).

Residues of ipconazole, at a nominal concentration of 0.1 µg/g, were incubated in sandy loam soil for 30 days. No radiolabeled residues were identified during the incubation period. After incubation, aged residues were placed on a 30 cm column of sandy loam soil and then leached at rate of 0.8 mL/hour with 0.01 M $CaCl_2$ over a 2 day period. Aged radiolabeled residues in the soil column were identified as ipconazole. Radiolabeled residues were predominately detected (>96.6% of applied) in the 0-5 cm soil column segment. Radioactivity in leachate and volatility traps account for <0.01% of applied.

Spray drift

No ipconazole-specific studies were reviewed or required. Droplet size spectrum (201-1) and drift field evaluation (201-2) studies are not required since ipconazole is a seed treatment and will not be applied aerially.

Environmental Fate Summary

Ipconazole is persistent and bioaccumulative. The log K_{ow} is >3, thus it can be considered potentially bioaccumulative, but the bioconcentration factor calculated using pbtprofiler (www.pbtprofiler.net) is 350, significantly below the EPA criteria of 1000 for bioaccumulative compounds. Ipconazole is persistent ($t_{1/2}$= 330 days to 1386 days) and relatively immobile (K_f=45 to 108 ml/g) in terrestrial and aquatic environments. Triazole was identified as the only major aerobic soil degradation product (>10%) of ipconazole.

ECOLOGICAL CHARACTERISTICS

Aquatic

Acute Freshwater Fish

Bluegill	96-hr LC_{50} = >0.73 - 1.8 ppm	LOAEC = 1.8 ppm*
Rainbow trout	96-hr LC_{50} = 0.76 - 2.1 ppm	LOAEC = 0.76 ppm

* Sub lethal effects.

Acute Freshwater Invertebrates

Daphnia magna 48-hr EC_{50} = 1.7 ppm NOAEC = 0.13 ppm

Avian

Avian Acute Single Oral Dose

Bobwhite quail	LD_{50} > 962 mg/kg-bw	NOAEC = 31.3 ppm

Avian Acute Dietary

Bobwhite quail	LC_{50} > 5710 mg/kg-diet	NOAEC = <169 ppm
Mallard duck	LC_{50} > 5710 mg/kg-diet	NOAEC = 587 ppm

Avian Chronic

Bobwhite quail	NOAEC = 48.5 ppm	LOAEC = 97.6 ppm
Mallard duck	NOAEC = 97.6 ppm	LOAEC = 97.6 ppm

Mammal

Acute Oral

Mouse	LD_{50} = 468 mg/kg bw/day (females); 537 mg/kg bw/day (males) NOAEC = 10 mg/kg bw/day LOAEC = 30 mg/kg bw/day
Rat	LD_{50} = 888 mg/kg bw/day (females); 1388 mg/kg bw/day (males) NOAEC = 10 mg/kg bw/day LOAEC = 30 mg/kg bw/day

Chronic Oral

Rat Developmental	NOAEC = 10 mg/kg bw/day LOAEC = 30 mg/kg bw/day

Environmental Risk Summary:

Agency analysis indicates that because only low levels of ipconazole will be found in the environment following its use as a seed treatment, there is no direct acute or chronic risk to endangered or non-endangered terrestrial vertebrate species of any phyla. Food chain effects and indirect effects have been considered, and appear also to be below levels of concern. Although no toxicity tests have been performed on non-target insects, triazoles are generally non-toxic to bees. The risk to non-target insects and to terrestrial plants is expected to be below levels of concern.

The Agency has conducted a screening level analysis to assess potential ecological risks posed by ipconazole. This analysis was performed using the physical properties and biological activity data for technical grade ipconazole. However, the two isomers may differ in biological activity and the rate at which they move through the environment.

The exceedence of an RQ does not necessarily indicate “high risk” to a species as the RQ is not an absolute estimate of the likelihood, magnitude, or severity of risk. Inputs into this screening level assessment were designed to overestimate likely exposures and effects of ipconazole. Because of the very low concentrations of ipconazole expected from a seed

treatment application, both acute and chronic risk quotients were very low ($\leq 5.20 \times 10^{-4}$ for birds and $\leq 4.86 \times 10^{-4}$ for mammals.) There were no exceedences of acute, chronic, or endangered species LOCs for any terrestrial animals. Based on this analysis, the Agency believes that potential ecological risks are very low.

SUMMARY OF DATA GAPS

EPA review of the product chemistry, residue chemistry, acute toxicity data, and toxicity database has been completed. In general, the studies provided enough information to perform an adequate human health, environmental fate and ecological risk assessment; however, to confirm these assessments, the following studies will be required as a condition of registration. In particular, the 90-day inhalation toxicity study in rats and the 28-day dermal toxicity study in rats would provide route specific toxicity data.

An additional soil adsorption/desorption study conducted in a low organic matter soil. (Guideline No. 163-1)
In vivo cytogenic assay. (Guideline No. 870.5395)
A 90-day inhalation toxicity study in rats. (Guideline No. 82-4)
A 28-day dermal toxicity study in rats. (Guideline No. 82-2)

PUBLIC INTEREST FINDING

Due to its activity and lower application rates, the registrant believes that ipconazole can replace a significant portion of the market share held by the old chemicals captan, carboxin, PCNB, and thiram–therefore, it has requested that ipconazole's registration be considered in the public interest. The Agency has previously denied the registrant's request for reduced risk status since triazole fungicides, as a group, have yet to be evaluated in the reregistration eligibility decision (RED) process.

The registration of a new pesticide ingredient is presumed to be in the public interest if one or more of the following criteria are applicable: 1) the pesticide is a replacement for another pesticide that is of concern to the Agency; 2) the pesticide has a use for which a Section 18 emergency exemption has been granted because of the lack of a suitable alternative; and 3) the pesticide is to be used against a pest of public health significance. If any of the these criteria do not apply, then one of the following three criteria must be met: 1) there is a need for the new pesticide that is not being met by currently registered pesticides; 2) the new pesticide is less risky than currently registered pesticides; 3) the benefits from the new pesticide are greater than those from currently registered pesticides or non-chemical control measures. The Agency believes that a public interest finding recommending for registration is appropriate, based on agricultural need and the likely benefits.

Fungicide treatments help to speed seedling emergence and improve the uniformity of the stand, thus optimizing yields. Fungicide seed treatments can provide a means of encouraging optimal plant stands and healthy seedling growth. While there is no substitute for using high quality seed, for many crops, fungicide seed treatments can reduce the effects of soil-borne or

seed-borne pathogens, such as those that cause damping-off diseases (e.g., *Rhizoctonia solani*, *Fusarium* spp., *Sclerotinia* spp., *Pythium* spp., and *Phytophthora* spp.). *Rhizoctonia*, *Fusarium*, and *Phomopsis* are the targeted major soil and seed borne pathogens, which are responsible for important damping-off diseases. In addition, *Mucor*, *Rhizopus*, *Aspergillus*, *Penicillium*, *Alternaria*, and *Cladosporium* would likely be inhibited. Ipconazole is not active against *Phytophthora* spp. or *Pythium* spp., but would be used in combination with metalaxyl or mefanoxam where applicable.

There are two relatively new fungicide seed treatments currently available for the crops targeted by the ipconazole product. These products are used at approximately the same range of low use rates that are proposed for ipconazole. The registrant of the ipconazole product intends to market their product as an additional chemistry to the reduced risk products. In addition, with another chemical having a different mode of action, overall disease management can be improved on many crops since seed treatment fungicides are commonly used in combination to provide a broader range of pest control.

The registrant supports ipconazole as an alternative to (or for some crops a replacement for) several "old chemicals" that are currently used as fungicide seed treatments for some of the proposed target crops. Both IR-4 and several seed industry users submitted letters of support for registering ipconazole. The old chemicals, captan, carboxin, PCNB, and thiram are among the most used seed treatments, and are generally used at significantly higher rates than the newer generation of fungicides [for example, a product containing a mix of carboxin + PCNB (Vitavax®-PCNB) is a standard used on cotton seed at a minimum rate of 65.5 g/100 kg seed for *each* of the active ingredients]. For cotton, the registrant considers ipconazole a replacement for the PCNB component of a carboxin-PCNB treatment. The registrant believes ipconazole can replace thiram for cotton seed currently treated with triadimenol and thiram. In addition, the registrant believes that ipconazole can replace captan for corn and sorghum seed treatments.

The Agency has determined that request for registration of ipconazole in the public interest has merit. Agriculture would benefit for growers to have a low use rate product that would be effective, and of a different chemistry, than is currently available. Fludioxonil and azoxystrobin are both relatively new seed treatment fungicides, which are used at a relatively low rates. However, captan, carboxin, PCNB, and thiram are "old chemicals", and labeling of an additional active ingredient could replace some of their uses. A fungicide with a new mode of action could improve disease management, by increased choices for the most effective products to manage specific pest concerns.

GOVERMENT PERFORMANCE AND RESULTS ACT

Registering ipconazole will meet objectives of GPRA title 3.1.1 by assuring new pesticides entering the market are safe for humans and the environment.

CONTACT PERSON AT USEPA

Cynthia Giles-Parker

Mailing Address:

Office of Pesticide Programs
Registration Division (7505C)
US EPA
Ariel Rios Building
1200 Pennsylvania Ave.
Washington, DC 20460

Office Location and Telephone Number:

Room 213, Crystal Mall Building #2
1801 South Bell Street
Arlington, VA 22202
(703) 305-7740

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The information presented in this Pesticide Fact Sheet is for informational purposes only and may not be used to fill data requirements for pesticide registration and reregistration.