

# New York State Department of Environmental Conservation

## Division of Solid & Hazardous Materials

Bureau of Pesticides Management

Pesticide Product Registration Section

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February 11, 2005

### **CERTIFIED MAIL** **RETURN RECEIPT REQUESTED**

Ms. Leslie Garcia  
Registration Submission Specialist  
Registration & Regulatory Affairs  
Valent U.S.A. Corporation  
P.O. Box 8025  
Walnut Creek, California 94596-8025

Dear Ms. Garcia:

**Re: Registration of Two New Pesticide Products, TetraSan 5 WDG (EPA Reg. No. 59639-108) and ZEAL Miticide (EPA Reg. No. 59639-123), Which Contain the New Active Ingredient Etoxazole**

The New York State Department of Environmental Conservation (Department) has completed its review of your application, received February 25, 2004, and additional information, received May 10, 2004 and July 19, 2004, to register the new products **TetraSan 5 WDG** (EPA Reg. No. 59639-108) and **ZEAL Miticide** (EPA Reg. No. 59639-123) in New York State. The products contain the new active ingredient **etoxazole** (chemical code 107091).

The application was deemed complete for purposes of review on September 14, 2004 and a registration decision is due by **February 11, 2005**.

The active ingredient, etoxazole, is a miticide/ovicide for use in controlling the major tetranychid (spider) mite species in egg and nymph stages of growth. Etoxazole exhibits strong translaminar movement within plant leaves. Spray contacting the upper surface of leaves will absorb into the leaves and locally translocate within the leaf. Thus, mites feeding on the undersides of leaves will be controlled.

TetraSan 5 WDG is labeled for use on indoor (green, shade and lath houses) and outdoor ornamentals, including flowering and foliage crops, ground covers, shrubs and ornamental trees, and non-bearing fruit and nut trees. The maximum application rate is 16 ounces of product per 100 gallons of water which is applied foliarly to provide uniform coverage. The maximum application rate per acre is 0.1 to 0.2 pounds active ingredient per acre per year.

ZEAL Miticide is labeled for use on cotton, pome fruit, non-bearing tree fruits and nuts, and strawberries. The label allows one foliar application of one ounce of product per acre for cotton, and of three ounces of product per acre for the other uses. The maximum application rate is 0.135 pounds of active ingredient per acre per season.

The Department has reviewed the information supplied to date in support of registration of the new products **TetraSan 5 WDG** (EPA Reg. No. 59639-108) and **ZEAL Miticide** (EPA Reg. No. 59639-123).

### **HEALTH EFFECTS:**

The New York State Department of Health (DOH) stated that neither the active ingredient etoxazole nor the two formulated products TetraSan 5 WDG and ZEAL Miticide were very toxic in acute oral, dermal and inhalation toxicity studies. In dermal irritation studies (tested on rabbits), neither the active ingredient nor the formulated products were very irritating to the skin. In eye irritation studies, the active ingredient was not an eye irritant (tested on rabbits), whereas the formulated products were moderately irritating. The active ingredient as well as the formulated products were not skin sensitizers (tested on guinea pigs).

Ettoxazole caused some toxicity in chronic animal feeding studies. In a chronic feeding/oncogenicity study in rats, ettoxazole caused an increase in absolute and relative liver weights and dental defects including abnormal formation of tooth enamel at a dose of 187 milligrams per kilogram body weight per day (mg/kg/day) in males and 216 mg/kg/day in females. The respective no-observed-effect levels (NOELs) were 1.8 and 2.1 mg/kg/day. In mice, slight changes in liver morphology were observed at 484 and 482 mg/kg/day for males and females, respectively; the respective NOELs were 242 and 243 mg/kg/day. In dogs, an increase in alkaline phosphatase activity and liver effects (increase in liver weight and incidences of hepatocellular swelling) were reported at a dose of 23.5 for males and 23.8 for females, with respective NOELs of 4.6 and 4.8 mg/kg/day. The United States Environmental Protection Agency (USEPA) Office of Pesticide Programs established a reference dose (RfD) of 0.046 mg/kg/day based on the NOEL of 4.6 mg/kg/day in the chronic feeding study in dogs and an uncertainty factor of 100. This RfD has not yet been adopted by the USEPA's Integrated Risk Information System (IRIS). Although using the NOEL of 1.8 mg/kg/day from the chronic rat study would yield a lower RfD value, USEPA chose to use the NOEL from the dog study for determining an RfD because the NOEL in the rat study was believed to be an artifact of dose selection, and based on all rat data combined, an actual NOEL for rats was likely to be above the NOEL of 4.6 mg/kg/day from the dog study.

Ettoxazole caused some developmental toxicity in the offspring of rabbits, but not rats. In a rabbit oral developmental toxicity study, an increased incidence in skeletal variations of pre-sacral vertebrae and extra ribs in the fetuses was observed at 1,000 mg/kg/day; the NOEL was 200 mg/kg/day. In this study maternal toxicity, characterized by liver enlargement and decreased body weight gains and food consumption, was reported at 1,000 mg/kg/day with a NOEL of 200 mg/kg/day. In a rat oral developmental toxicity study, no developmental effects or maternal toxicity were reported at the highest dose tested which was 1,000 mg/kg/day. In a multi-generation reproduction study in rats, ettoxazole caused an increase in rat pup mortality at a dose of 100 mg/kg/day; the NOEL was 20 mg/kg/day. Parental toxicity, which was characterized by an increase in liver weights in males and adrenal weights in females, was observed at 100 mg/kg/day with a NOEL of 20 mg/kg/day.

Ettoxazole did not cause oncogenic effects in either rat or mouse chronic feeding studies. This chemical also was negative in a number of genotoxicity studies. The USEPA classified ettoxazole as "not likely to be carcinogenic to humans."

The USEPA established tolerances for etoxazole residues in or on pome fruit at 0.2 parts per million (ppm); strawberries (0.5 ppm) and wet apple pomace (0.5 ppm). The chronic population adjusted dose (cPAD) for etoxazole is 0.046 mg/kg/day and has the same basis as the RfD. The USEPA estimated that chronic dietary exposure to etoxazole residues would be one percent of the cPAD for the general U.S. population, three percent for all infants less than one year old, five percent for children one to two years old and three percent for children three to five years old. This chronic exposure analysis is based on the conservative assumptions that 100 percent of the crops would be treated with etoxazole and that all treated crops had etoxazole residues at the respective tolerance levels.

The USEPA conducted a risk assessment for exposure of workers to etoxazole from its use on ornamental plants (using TetraSan 5 WDG) and on pome fruit and strawberries (using ZEAL Miticide). Because no toxicity to laboratory animals has been observed from dermal exposure to etoxazole up to the limit dose of 1,000 mg/kg/day, margins of exposure (MOEs) were only estimated for inhalation exposures. Depending on worker activity (i.e., mixer/loader versus applicator) the MOEs ranged from 1,700 to 2,700,000 in the treatment of ornamental plants and from 13,000 to 42,000 in the treatment of edible crops. For inhalation exposure, the USEPA assumed 100 percent absorption. The NOEL used for estimating these MOEs was 4.6 mg/kg/day from the chronic feeding study in dogs. Generally, the USEPA considers MOEs of 100-fold or greater to provide adequate worker protection. Because dermal toxicological endpoints for etoxazole were not identified, no risk assessment for post-application occupational activities was conducted.

There are no chemical specific federal or State drinking water/groundwater standards for etoxazole. Based on its chemical structure, this chemical falls under the 50 microgram per liter New York State drinking water standard for “unspecified organic contaminants” (10 NYCRR Part 5, Public Water Systems).

The available information on etoxazole and the two formulated products, TetraSan 5 WDG and ZEAL Miticide, indicates that overall the active ingredient and these formulated products are not very acutely toxic in laboratory animal studies. While both formulated products caused moderate eye irritation, they are granular formulations packaged in water-soluble packets and thus are unlikely to get into the eyes of workers during mixing and loading operations. Moreover, the labels of both products state “Causes moderate eye irritation. Avoid contact with eyes, skin or clothing.” which provides some warning to workers. Although data from chronic and developmental/reproductive studies on etoxazole also indicate that this chemical has the potential to cause some toxicity, the expected exposure from the labeled uses of these two etoxazole-containing pesticide products should not pose a significant risks to workers or the general public. In addition, etoxazole has a low vapor pressure ( $5 \times 10^{-8}$  millimeters mercury at 25 degrees Celsius) so the potential for inhalation exposure following application in confined spaces (e.g., greenhouses) appears minimal. Also, neither product contains volatile organic compounds that would pose a risk of inhalation exposure in confined spaces. Because the labeled uses of TetraSan 5 WDG and ZEAL Miticide do not seem to pose significant risks to workers or the general public, we do not object to the registration of these products in New York State.

### **ECOLOGICAL EFFECTS:**

The Department's Division of Fish, Wildlife & Marine Resources' Bureau of Habitat (BOH) reviewed the information submitted in support of the registration of TetraSan 5 WDG and ZEAL Miticide. The BOH stated that etoxazole is a diphenyl oxazoline that has activity against juvenile stages of spider mites, eggs to nymphs, but is not toxic to adults. Adults that are treated, however, will not produce viable eggs.

Etoxazole is practically non-toxic to birds and mammals on an acute basis and also exhibits low toxicity with chronic exposures. It is highly to very highly toxic to all aquatic organisms for which study results were submitted.

Screening modeling was conducted to estimate non-target organism exposures when TetraSan and ZEAL are used as labeled. Etoxazole residues, calculated using the maximum seasonal application rate and utilizing the highest likely residue levels immediately following application, were well below mammalian and avian toxicity thresholds for all food categories.

Runoff modeling was conducted using the seasonal maximum application rate. For a chemical with etoxazole's  $K_{OW}$ , the BOH uses 0.25, 0.5, and 1.0 percent runoff rates to evaluate potential impacts in receiving waters. At the highest runoff rate, immediately following application using standard pome orchard parameters (50% target plant deposition and 60% of runoff reaching the receiving water), the acute  $LC_{50}$  for the oyster and the chronic LOEL for the mysid shrimp is exceeded in the 1 foot water depth. At the middle, 0.5%, rate the predicted concentration is below the oyster  $LC_{50}$ , and only the Mysid LOEL is exceeded.

No direct effects to birds or mammals are anticipated from labeled use of TetraSan 5 WDG and ZEAL Miticide. Impacts to aquatic invertebrates are possible from etoxazole use if heavy rain is received immediately following application. Standard agricultural practices include avoiding pesticide applications immediately prior to rainstorms so the highest exposures estimated are not likely to occur. The limited applications, relatively low application rates, immobility, and low persistence make significant widespread impacts to fish or wildlife resources unlikely.

### **ENVIRONMENTAL FATE AND GROUNDWATER IMPACTS:**

The Department's groundwater staff stated the following:

#### **Ettoxazole has the following degradates:**

- R-3 N-(2,6-difluorobenzoyl)-4-*tert*-butyl-2-ethoxybenzamine
- R-4 N-(2,6-difluorobenzoyl)-2 amino-2-(4-*tert*-butyl-2-ethoxyphenyl)ethanol
- R-7 2 amino-2-(4-*tert*-butyl-2-ethoxyphenyl)ethyl 2',6'-difluorobenzoate hydrochloride
- R-8 2 amino-2-(4-*tert*-butyl-2-ethoxyphenyl)ethanol
- R-13 4-(4-*tert*-butyl-2-ethoxyphenyl)-2-(2,6-difluorophenyl)oxazole

**Solubility:** The solubility is 0.075 ppm.

**Hydrolysis:** In a study that the USEPA found to be supplemental, the hydrolysis of etoxazole was relatively stable. At 20°C, the half-life was 9.59 days at pH 5 (major degradate R-7), 99.02 days at pH 7 (major degradates R-4 and R-7), and 97.63 days at pH 9 (major degradates R-4 and R-7).

**Aqueous Photolysis:** In an unacceptable study, the half-life was 10-11.6 days. R-11 was the only major degradate at 64% at 288 hours.

**Soil Photolysis:** In a supplemental study, the half-life was 19.25 days in a clay loam with no major degradates

**Aerobic Soil Metabolism:**

Soil Type	T <sub>1/2</sub>	Degradates	Percent degradate	pH	% OC
sand <sup>S</sup>	12.74 days	R-4 R-8	11.9 44.2	6.7	0.6
loamy sand <sup>S</sup>		R-8	38.5	6.7	2.1
clay loam <sup>S</sup>	44.72	R-3 R-8 R-13	10.4 14.6 19.1	7.4	1.3
sandy loam <sup>S</sup> at 10°C	26.16	R-4 R-7 R-8	10 15 43.3	5.1	2.4
sandy loam <sup>S</sup> at 30°C	2.31	R-7 R-8	24 38.9	5.1	2.4
sandy loam <sup>A</sup>	19.4	R-13	26.6	8.8	1.5 OM
sandy loam <sup>A</sup>	23.2	R-13	30	8.8	1.5 OM
sandy loam <sup>A</sup>	12.0	R-7 R-8 R-13	11.5 44.8 11.7	5.6	2.0
sandy loam <sup>A</sup>	10.2	R-7 R-13	21.6 10.9	5.6	2.0

<sup>A</sup>-Study found to be acceptable

<sup>S</sup>-Study found to be supplemental

**Aerobic Soil Metabolism of Degradates:** According to the USEPA Section 3 Risk Assessment dated August 14, 2003, page 13, the mean estimated aerobic metabolism half-life for R-8 is 377 days, for R-13 it is 265 days and for R-7 it was about 60 days.

**Anaerobic Soil Metabolism:** In a supplemental study, the half-life in a water/clay system was <5 days in the water (pH 8.2), and 139 and 157 days in the soil (pH 5.7 and 3.6% OM). The total system had half-lives of 155 and 138 days.

**Adsorption/Desorption:**

Soil Type	Adsorption K <sub>oc</sub>	Desorption K <sub>oc</sub>	pH	%OC
sandy loam <sup>S</sup>	18,000		8.8	0.87
sandy loam <sup>S</sup>	23,100		6.1	1.45
sandy loam <sup>S</sup>	55,300		6.4	0.35
sandy loam <sup>S</sup>	14,200		6.7	1.10
sandy loam <sup>S</sup>	5,460	40,750	5.1	2.4
clay loam <sup>S</sup>	5,230	11,850	7.4	1.3
sand <sup>S</sup>	11,000	23,500	6.7	0.6
loamy sand <sup>S</sup>	4,910	19,950	6.7	2.1

**Adsorption/Desorption of Degradates:** The following data was taken from studies supplied by the company. No DERs were submitted for these studies.

Soil Type	Adsorption $K_{oc}$	Desorption $K_{oc}$	pH	%OC
R-7 sandy loam	1125	3500	5.1	2.4
R-7 clay loam	7540	22000	7.4	1.3
R-7 sand	2330	13170	6.7	0.6
R-8 sandy loam	103	38	5.1	2.4
R-8 clay loam	351	376	7.4	1.3
R-8 sand	207	NA	6.7	0.6
R-13 sandy loam	36540	25790	5.1	2.4
R-13 clay loam	83230	271850	7.4	1.3
R-13 sand	13670	25670	6.7	0.6
R-13 sandy loam		18,000	8.8	1.5 OM
R-13 sandy loam		23,100	6.1	2.5 OM
R-13 sandy loam		55,300	6.4	0.6 OM
R-13 sandy loam		14,200	6.7	1.9 OM

<sup>A</sup>-Study found to be acceptable

<sup>S</sup>-Study found to be supplemental

**Field Dissipation:** In an acceptable study, using a sandy loam soil, the half-life was 7.0 days with major degradate R-7 found at about 30% of applied. In an acceptable study, using a silt loam soil, the half-life was less than one day with major degradate R-7 found at about 24% of applied. In an acceptable study using a sandy loam soil, the half-life was 11.7 days with major degradate R-7 found at 16% of applied. Neither the parent nor R-7 were detected below the 7.5 cm depth.

**Computer Modeling:** Computer modeling was not run on the parent because chemicals with  $K_{oc}$ s in this range do not leach. Modeling was performed on degradate R-8, the only one with a  $K_{oc}$  low enough to leach, using Riverhead sand, an application rate of 45% of Tetrasan rate of 0.2 lb ai/a/yr (because the degradate was found at 45% of applied), a  $K_{oc}$  of 207, and an aerobic half-life of 377 days. These parameters assume the worst case scenario of 100% of the applied product reaching the soil and all of it degrading aerobically to yield the R-8 degradate at 45%. The model projected breakthrough at about 18 months, with a continuous concentration between 2 and 3.5 ppb through the ten year modeling cycle. Modeling was again run using an application rate of 45 % of the ZEAL rate, and the model projected breakthrough at about 18 months and a continuous concentration of about 1.8 to 2 ppb through the ten year modeling cycle.

Since the products are applied foliarly and have to contact the leaves and be absorbed to be effective, the probability that the above-modeled concentrations of the R-8 degradate will be even approached and impact groundwater is quite negligible when the products are applied according to label directions.

The Department concludes that TetraSan 5 WDG and ZEAL Miticide should not have an adverse effect on the health of workers or the general public, the fish and wildlife resources, or the ground and surface water when used as labeled.

Therefore, the Department hereby accepts for registration the new products **TetraSan 5 WDG** (EPA Reg. No. 59639-108) and **ZEAL Miticide** (EPA Reg. No. 59639-123).

The Certificate of Pesticide Registration and a copy of the New York State stamped "ACCEPTED" labeling for TetraSan 5 WDG (EPA Reg. No. 59639-108) and ZEAL Miticide (EPA Reg. No. 59639-123) are enclosed for your records.

Valent U.S.A. Corporation is reminded that if New York State registration is requested for TetraSan 5 WDG, ZEAL Miticide or for any other product which contains etoxazole with an increased application rate, different application method and/or expanded use sites, the product will be considered **a Major Change in Labeling and the Department will require an extensive review.**

If you have any questions, please contact Mr. Samuel Jackling, Chief of our Pesticide Product Registration Section, at (518) 402-8768.

Sincerely,

Maureen P. Serafini  
Director  
Bureau of Pesticides Management

Enclosures

cc: w/enc. - N. Kim/D. Luttinger - NYS Dept. of Health  
R. Zimmerman/ R. Mungari - NYS Dept. of Ag. & Markets  
G. Good/W. Smith - Cornell University, PMEP