CALIFORNIA DEPARTMENT OF PESTICIDE REGULATION
PUBLIC REPORT 2003-6

Flumioxazin
Tracking ID Number 191861 N

DESCRIPTION OF ACTION

Valent U.S.A. Corporation submitted an application seeking California registration of Chateau™ Herbicide SW to control certain grassy and broad-leaf weeds in various agricultural crops. This product contains the new active ingredient flumioxazin.

The Department of Pesticide Regulation (DPR) evaluated the product label and scientific data supporting registration of the product and found them to be acceptable to support a conditional registration. The acute health risks from exposure to flumioxazin are minimal due in part to its low mammalian toxicity. The precautionary and first aid statements on the product label in conjunction with the required personal protective equipment (PPE) adequately mitigate potential health risks to persons who may come in contact with the pesticide. DPR does not expect significant adverse environmental impacts to result from registration of this product.

DPR accepted Valent's application for registration of Chateau™ Herbicide SW concurrently with Valent's submission of an application to the United States Environmental Protection Agency (U.S. EPA) for federal registration. U.S. EPA conditionally registered Chateau™ Herbicide SW on April 12, 2001. The Agency required the following studies be submitted within two years or the registration will be subject to cancellation: a more specific confirmatory analytical method for plant commodities, two aqueous photolysis studies, two anaerobic soil/aqueous metabolism, and two field dissipation studies. These studies have since been completed and reviewed by DPR.

BACKGROUND

Registrant:	Valent U.S.A. Corporation
Common name:	Flumioxazin
Chemical name:	2-[7-fluro-3,4-dihydro-3-oxo-4-(2-propynyl)-2H-1,4-benzoxazin-6-yl]-4,5,6,7-tetrahydro-1H-isoindole-1,3(2H)-dione
Brand names:	Chateau™ Herbicide SW
Uses:	Weed control in peanuts and soybeans and sites to be planted to cotton, field corn, rice, sorghum, sugarcane, sunflowers, tobacco or wheat.
Pests controlled:	Certain grassy and broad-leaf weeds, such as crabgrass, Russian thistle, and velvetleaf.
Type of registration:	Conditional for two years

Chateau™ Herbicide SW is formulated as a water dispersible granule with 51% flumioxazin. Flumioxazin is a light-dependent peroxidizing herbicide that blocks

chlorophyll biosynthesis resulting in the accumulation of photo-toxic porphyrins in the plant tissues. Flumioxazin is active on a broad spectrum of broad-leaf weeds and some grassy weeds. Chateau™ Herbicide SW can be applied in peanuts and soybeans prior to crop emergence to control existing weeds. Rainfall, a light irrigation or cultivation are needed to activate flumioxazin. Chateau™ Herbicide SW can also be applied as a "burndown" treatment on sites that will later be planted with the crops listed on the product label. In California, the predominant use will probably be to "burndown" weeds before planting cotton, field corn, rice, sorghum, sunflowers, or wheat. The label recommends applying 2 to 3 ounces of product per acre (0.064-0.096 lb. active ingredient) with one application per year. Applications can be made with ground and aerial application equipment. However, application of the product through any type of irrigation system is prohibited. For aerial applications, the product label requires a 40 foot buffer zone between the target crop and non-labeled crops and plants to mitigate the potential for crop damage from drift.

SCIENTIFIC REVIEW

A. Chemistry

1. Product Chemistry: DPR evaluated the submitted chemistry studies for flumioxazin and summarized the results in the following table.

Table I. Physical and Chemical Properties of Chateau™ Herbicide SW

Properties	Values
Physical state	Light tan solid
Odor	Odorless
Density*	1.51 g/cm^3 at 20^o C
Bulk density	0.37 g/ml (22.8 lb. ft^3)
Partition Coefficient*	3.54 x 10^2 at 20^o C
Solubility (water)*	1.79 mg/L at 25^o C
pH in water	6 at 22^o C
Vapor pressure*	2.41 x 10^{-6} mm Hg at 22^o C
Stability	Stable one year in commercial pkg.

* These properties were derived using technical flumioxazin as the test substance.

DPR found the product chemistry data satisfactory to meet the regulatory data requirements to support the registration of this product.

2. Residues in Food and Animal Feed: The submitted residue studies support the harvest and use limitations listed on the Chateau™ Herbicide SW label for peanuts and soybeans. The residue levels are well within the tolerances established by the U.S. EPA for peanuts and soybeans. The established tolerances are listed in the following table.

Table II. Tolerances for Residues of Flumioxazin

Commodity	Parts Per Million
Peanuts	0.02
Soybean seed	0.02

Valent U.S.A. Corporation submitted rotational crop studies to support the "burndown" uses for the listed crop sites and the rotational crop statements for non-listed crops. DPR determined the data to be adequate.

3. Environmental Fate: The environmental fate data reviewed included studies on hydrolysis, photolysis (aqueous and soil), aerobic soil metabolism, anaerobic soil metabolism (aquatic) and terrestrial field dissipation. Flumioxazin is unstable in the environment with a half-life ranging from 0.01-5 days depending upon pH. The data indicates hydrolysis is probably the primary pathway for degradation. Flumioxazin is unstable in the presence of light with a one day half-life in water and 3-8 day half-life on soil. The aerobic soil metabolism studies observed a moderate rate of metabolism with a half-life of 5-19 days depending on the soil type. The anaerobic soil metabolism study with a saturated soil observed a half-life of less than one day. Terrestrial field dissipation of flumioxazin in loam and sandy soils ranged from 10-42 days. The high value was thought to be due to a lack of rainfall or irrigation during the sampling period. The degradation of flumioxazin on soil was too rapid to determine an adsorption/desorption coefficient. Two soil column leaching studies were conducted using various types of agricultural soils. The majority of the residues remained incorporated with the organic matter in the soil indicating flumioxazin resists leaching.

The submitted studies were found to be satisfactory to support a conditional registration of Chateau™ Herbicide SW. This product may be registered, provided the registrant conducts and submits the results of a flumioxazin metabolite study in lactating goats and a terrestrial field dissipation study (now in progress). Chateau™ Herbicide SW is expected to have minimal impact on the environment. When used in accordance with label directions, there is little potential for flumioxazin to accumulate or move into ground water.

B. Toxicology

DPR reviewed the toxicology studies submitted by Valent U.S.A. Corp. and found them adequate to conduct a complete toxicological evaluation for Chateau™ Herbicide SW. DPR evaluated the data to ascertain the potential for acute adverse health effects from exposure. The acute toxicity parameters are summarized in Table III.

Table III. Acute Toxicity of Chateau™ Herbicide SW

Type of Study	Acute Toxicity Values	Acute Toxicity Category
Acute oral (rats)	>5000 mg/kg (M/F)	IV
Acute dermal (rabbits)	>2000 mg/kg (M/F)	III
Acute inhalation (rats)	>0.969 mg/l	III
Primary eye irritation (rabbits)	N/A	IV
Primary dermal irritation (rabbits)	N/A	IV
Dermal sensitization (guinea pigs)	N/A	Not a sensitizer
Signal word	N/A	CAUTION

N/A-Not applicable.

DPR's evaluation indicates that Chateau™ Herbicide SW is low in mammalian toxicity. The precautionary language on the product label adequately identifies the acute toxicity hazards noted in the studies.

DPR found the submitted toxicology studies sufficient to satisfy the data requirements of the Birth Defects Prevention Act (Food and Agricultural Code section 13121 *et.al*.). Possible adverse health effects were observed in four of the toxicity studies. A combined chronic toxicity and oncogenicity study in rats indicated hypochronic and microcytic anemia. The subchronic dietary rat study noted adverse effects of anemia and hepatic necrosis. The two-generation rat reproduction study observed lower pup viability. The rat teratology studies observed malformations in cardiac and skeletal development. A neurotoxicity study was not submitted. The Code of Federal Regulations (CFR 40 section 158.340) does not require this study if the compound is not an organophosphate compound, or does not cause cholinesterase depression.

DPR has not yet prioritized flumioxazin for risk assessment. DPR prioritizes pesticide active ingredients for risk assessment based on the nature of the potential adverse health effects, number of potential adverse effects, number of species affected, no effect levels (NOELs), potential for human exposure, use patterns and similar factors. Based on these criteria, pesticides with the greatest potential for health problems are placed in high priority, with other chemicals being in moderate or low priority. The purpose of the risk assessment would be to appraise the potential for flumioxazin to cause adverse health effects in humans if exposed to the pesticide as the result of a legal use. The potential for exposure from eating food crops treated with flumioxazin will also be evaluated during the risk assessment. Further toxicity information is available in DPR's Summary of Toxicology Data for flumioxazin, available on DPR public website at:
http://www.cdpr.ca.gov/docs/toxsums/pdfs/5802.pdf.

C. Health & Safety

An evaluation of the medical management information on the Chateau™ Herbicide SW label and the acute toxicity study results indicate the product label bears all of the required statements and warnings regarding safety for handlers and other persons

who may be exposed to the pesticide. The product label bears an adequate First Aid Statement. In addition, the product label requires persons handling and applying Chateau™ Herbicide SW to wear long-sleeved shirt and long pants, waterproof gloves, and shoes plus socks. Workers wearing only work clothing are not allowed to enter a treated field until 12 hours after an application. The product label requires that persons entering a treated area before the 12 hour restricted-entry interval (REI) has elapsed, must wear coveralls, waterproof gloves, and shoes plus socks if they are going to contact treated plants, soil or water.

D. Fish & Wildlife

The registrant submitted fish and wildlife toxicity studies, including studies on northern bobwhite, mallard duck, rainbow trout, bluegill sunfish and daphnia magna. The submitted data are adequate to characterize the toxicity to wildlife and aquatic animals from an environmental exposure. Table IV summarizes the results of these studies.

Table IV. Summary of Toxicity Studies for Wildlife

Test Animal	Type of Study	Acute Toxicity Value[a]	Relative Toxicity
Rat (male, female)	Single acute oral dose	>5000 mg/kg(LD_{50})	Relatively non-toxic
Bluegill sunfish	Water exposure (96 hrs.)	>21 mg a.i./l (LC_{50})	Slightly toxic
Sheepshead minnow	Water exposure (96 hrs.)	4.7 mg a.i./l (LC_{50})	Moderately toxic
Rainbow trout	Water exposure (96 hrs.)	>2.3 mg a.i./l (LC_{50})	Moderately toxic
Daphnia magna	Water exposure (48 hrs.)	17 mg a.i./l (LC_{50})	Slightly toxic
Mysid shrimp	Water exposure (96 hrs.)	0.23 mg a.i./l (LC_{50})	Highly toxic
Oyster shell	Water exposure (96 hrs.)	2.8 mg a.i./l (EC_{50})	Moderately toxic
Bobwhite quail	Single oral acute dose	>2250 mg/kg (LD_{50})	Relatively non-toxic
Bobwhite quail	Feeding study (8 days)	>5620 mg/kg (LC_{50})	Relatively non-toxic
Mallard duck	Feeding study (8 days)	>5620 mg/kg (LC_{50})	Relatively non-toxic
Honeybee	Single dermal dose	105 µg/bee (LD_{50})	Relatively non-toxic

Values expressed as: 1. LD_{50}= lethal dose that will kill 50% of test population; and 2. LC_{50}= lethal environmental concentration that will kill 50% of test population. The test substance used for the studies was technical flumioxazin.

The data indicate flumioxazin is relatively non-toxic to vertebrate animals, birds and honey bees, and moderately toxic to fish. The data indicate that flumioxazin is highly toxic to some salt water invertebrates. The label bears adequate precautionary statements regarding the toxicity of the product to aquatic invertebrates. The environmental fate data indicates flumioxazin is unstable in the environment and degrades rapidly. The water solubility is low with a very low vapor pressure indicating movement off-site should be minimal. The use of Chateau™ Herbicide SW in production agricultural sites is not expected to pose a threat to wildlife when used in accordance with label directions.

E. Efficacy

The submitted field studies were adequate to demonstrate the efficacy of Chateau™ Herbicide SW to control the weeds listed on the label. The field data also indicate

that unacceptable levels of phytotoxicity do not occur when recommended rotational intervals are followed on crops grown in midwestern or southern soil types. However, no data were submitted to demonstrate that Chateau™ Herbicide SW can be safely used on crops grown under California climatic conditions and soils.

The submitted data are adequate to support a two-year conditional registration in California. Additional phytotoxicity data are needed to demonstrate the labeled preplant intervals are adequate for crops grown in California. An aerial spray drift study is also needed to support the adequacy of the required buffer zones for sensitive crops growing adjacent to treatment sites..

ALTERNATIVES

Chateau™ Herbicide SW is a contact herbicide which is active on a wide range of broad-leaf weeds and some grassy weeds. It can also be used in combination with other herbicides to broaden the spectrum of weeds controlled with a "burndown" application. With a maximum use rate of 1.5 oz of A.I. per acre, Chateau™ Herbicide SW can provide weed control at much lower use rates than most conventional contact herbicides. Its use can help to reduce the amount of herbicide needed for weed control in the labeled crops. Flumioxazin is low in mammalian toxicity and is safer for pesticide handlers to work with compared to many other contact herbicides.

CONCLUSION

DPR evaluated the product label and scientific data submitted to Chateau™ Herbicide SW and found them acceptable to support a two year conditional registration. The acute health risks to humans from exposure to flumioxazin are minimal due in part to its low mammalian toxicity. The precautionary and first aid statements on the product label, as well as the required PPE mitigate potential health risks to persons who may be exposed to the pesticide. If, after a risk assessment, DPR determines that exposure to flumioxazin may result in unacceptable margins of exposure, further restrictions will be placed on the use of flumioxazin at that time. The submitted data also indicate significant adverse environmental impacts are not expected to occur from the use of Chateau™ Herbicide SW. When used in accordance with label directions, this product should be effective for the intended use.

DPR is proposing a two-year conditional registration of Chateau™ Herbicide SW. The registrant is required to conduct and/or submit the results of the following studies: a terrestrial field dissipation study conducted in California, a metabolism study in lactating goats, field data to support the aerial application buffer zones for sensitive crops, and phytotoxicity data that demonstrates the preplant intervals for crops grown under California climatic and soil conditions are adequate.