CALIFORNIA DEPARTMENT OF PESTICIDE REGULATION

PUBLIC REPORT 2004-01
Quinoxyfen
Tracking ID 189056 N

DESCRIPTION OF ACTION

Dow AgroSciences LLC submitted an application seeking California registration of Quintec™, U.S. EPA Reg. No. 62719-375, to control powdery mildew in grapes and hops. Quintec™ contains the new active ingredient quinoxyfen. Quintec™ was designated as a "reduced risk" pesticide by U.S. Environmental Protection Agency (U.S. EPA). The Department of Pesticide Regulation (DPR) accepted Dow AgroSciences' application for registration of Quintec™ concurrently with Dow's application to the U.S. EPA for federal registration of the product. U.S. EPA registered Quintec™ December 17, 2003.

DPR evaluated the product label and scientific data supporting registration of the product and found them to be acceptable. The acute health risks from exposure to quinoxyfen are minimal due to its low mammalian toxicity. Precautionary and first aid statements on the product label, as well as label directions requiring personal protective equipment (PPE) and other protective measures 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.

BACKGROUND

Registrant:	Dow AgroSciences LLC
Common name:	Quinoxyfen
Chemical name:	5,7-dichloro-4-(p-fluorophenoxy)quinoline
Brand name:	Quintec™
Uses:	Disease control in grapes and hops
Pests controlled:	Powdery mildew
Type of registration:	Unconditional

Quintec™ is a protectant fungicide used to control powdery mildew infections on grapes and hops. Quintec™ cannot control existing or latent infections; therefore, the pesticide must be applied before infections occur. Quintec™ is formulated as a suspension concentrate liquid with 22.6% quinoxyfen. Applications on grapes are recommended at 3-6.6 oz. per acre, with a maximum of 33 oz. applied per acre per season. Applications should be made at 14-21 day intervals depending on the disease pressure. For hops, the recommended rate is 4-8.2 oz. per acre applied at 14-day intervals. The minimum time interval between the last application and harvest is 14 days for grapes and 21 days for hops. Applications of Quintec™ should be made in accordance with the disease resistance management program outlined on the label. The product is applied as a broadcast treatment with ground boom equipment only. Aerial application and application with a irrigation system are prohibited.

SCIENTIFIC REVIEW

A. Chemistry

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

Table I. Physical and Chemical Properties of Quintec™

Properties	Values
Physical state	Liquid
Color	Opaque off-white
Odor	Faint earthy odor
Melting point*	106-107^{o} C
Density	1.097 g/ml at 20^{o} C
Solubility (water)	0.047 parts per million (ppm)
Vapor pressure*	1.2 E^{-5} at 20^{o} C
Octanol/water partition coefficient*	4.66 at 20^{o} C (LogP)
pH	7.97 (1% solution at H_20 at 22.7^{o} C)
Storage stability	Stable for 2 years

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

2. Residues in Food and Animal Feed: The submitted residue studies support the proposed use pattern and harvest limitations listed on the Quintec™ label for grapes and hops. The tolerances for quinoxyfen have been set at 0.60 ppm for grapes and 3.0 ppm for hops (dried cones). When applied in accordance with label directions, quinoxyfen residues are not expected to exceed the established tolerances. The Quintec™ label does not bear any plant-back or rotational crop restrictions. The results of a rotational crop study indicate that the likelihood of subsequent crops sequestering significant residues of quinoxyfen from a treated site is miniscule.

3. Environmental Fate: The quinoxyfen environmental fate studies which included: soil adsorption/desorption, hydrolysis, photolysis (aqueous and soil), aerobic and anaerobic soil metabolism, aerobic and anaerobic aquatic metabolism, field accumulation, terrestrial field dissipation and aged column leaching study, were found to be satisfactory. Based on the reported half-lives from the hydrolysis, soil photolysis, aerobic/anaerobic soil metabolism, and the field dissipation studies, quinoxyfen has chemical properties which imply that it may be persistent in the environment under certain conditions. However, once it is in the soil, the studies show quinoxyfen is immobile to slightly mobile depending on the soil type. Metabolism studies verify that quinoxyfen is rapidly metabolized under aquatic conditions, but more stable under terrestrial conditions. The water solubility and the Kd, K_{oc} values indicate quinoxyfen is poorly soluble and will adsorb tightly to soil particles. These properties indicate quinoxyfen residues are not easily moved by water passing through the soil profile. The field accumulation studies, conducted over a five-year period in Europe, indicate quinoxyfen can accumulate in the soil. When applied on a annual basis, residues of quinoxyfen did not dissipate from year to year in the soil horizon.

The submitted product, environmental fate and residue chemistry data support registration of the subject active ingredient. Although Quinoxyfen shows a tendency to accumulate in soil, it is not considered to be an environmental pollutant because it is immobile in soil. Compounds that are strongly absorbed to soil particles are not likely to leach, even when they are persistent. They are retained in the root zone and eventually taken up by plants or degraded. The use of quinoxyfen is expected to have minimal impact on the environment and it is not expected to leach into groundwater.

B. Toxicology

Dow AgroSciences submitted adequate toxicity studies to conduct a complete toxicological evaluation of Quintec™ . DPR evaluated the submitted data to ascertain the potential for adverse health effects. The estimated acute toxicity parameters for Quintec™ are summarized in Table II.

Table II. Estimated Acute Toxicity of Quintec™

Type of Study	Acute Toxicity Values	Acute Toxicity Category
Acute oral	LD_{50} (M/F)>2000 mg/kg	III
Acute dermal	LD_{50}(M/F) >2000 mg/kg	III
Acute inhalation	Not submitted*	IV*
Primary eye irritation	N/A	IV
Primary dermal irritation	N/A	IV
Dermal sensitization	N/A	Not a dermal sensitizer
Signal word	N/A	WARNING

*Acute inhalation study was conducted with technical quinoxyfen and the estimated LC_{50} (M/F) > 3.38 mg/L.

DPR's evaluation of the acute toxicity studies indicates that Quintec™ 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 adequate to satisfy the data requirements of the Birth Defects Prevention Act (SB 950). The results from the chronic toxicity studies indicate a possible adverse health effect was observed in the chronic dog study. A neurotoxicity study is not required at this time.

At this time, quinoxyfen has not been prioritized 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 health effects, number of species affected, 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 place in moderate or low priority. The purpose of the risk assessment will be to appraise the potential for quinoxyfen 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 quinoxyfen will also be evaluated during the risk assessment. Further toxicity information is available in DPR's Summary of Toxicology Data

for quinoxyfen, available on DPR public website at http://www.cdpr.ca.gov/docs/toxsums/pdfs/5789.pdf

C. Health & Safety

An evaluation of the medical management information on the Quintec™ label and the acute toxicity study results indicate that the product label bears all of the required statements and warnings regarding safety to handlers and other persons who may be exposed to the pesticide. The product label bears an adequate first aid statement and the required PPE are listed. The product label requires persons handling and applying Quintec™ to wear a long-sleeved shirt and long pants, chemical-resistant 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. Persons entering a treated area before the 12-hour reentry interval has elapsed must wear coveralls, chemical-resistant 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 rats, mallard duck, bobwhite quail, bluegill sunfish, rainbow trout, sheepshead minnow, Daphnia magna (water fleas), mysid shrimp, oysters, and honey bees. The studies were conducted using technical quinoxyfen as the test material. The submitted data was determined to be adequate to characterize the toxicity to wildlife and aquatic animals from environmental exposure. Table III summarizes the results of these studies.

Table III. Summary of Toxicity Studies for Wildlife

Test Animal	Type of Study	Acute Toxicity Value[a]	Relative Toxicity
Rat, female	Single acute oral dose	>5000 mg/kg (LD_{50})	Relatively non-toxic
Rat, male	Single acute oral dose	>5000 mg/kg (LD_{50})	Relatively non-toxic
Bobwhite quail	Single acute oral dose	>2,250 mg/kg (LD_{50})	Relatively non-toxic
Mallard duck	Feeding study (8 days)	>5,620 ppm (LC_{50})	Relatively non-toxic
Bobwhite quail	Feeding study (8 days)	>5,620 ppm (LC_{50})	Relatively non-toxic
Bluegill sunfish	Water exposure (96 hrs.)	284 ppb (LC_{50})	Highly toxic
Rainbow trout	Water exposure (96 hrs.)	270 ppb (LC_{50})	Highly toxic
Sheepshead minnow	Water exposure (96 hrs.)	168 ppb (LC_{50})	Highly toxic
Daphnia magna	Water exposure (48 hrs.)	90 ppb (LC_{50})	Extremely toxic
Mysid shrimp	Water exposure (96 hrs.)	79 ppb (LC_{50})	Extremely toxic
Oyster	Water exposure (96 hrs.)	72 ppb (LC_{50})	Extremely toxic
Honey bee	Dermal exposure (48 hrs.)	>100 (LD_{50})	Relatively non-toxic

a. Values expressed as; a. LD_{50}= lethal dose that will kill 50% of test population, and b. LC_{50}= lethal environmental concentration that will kill 50% of test population.

The data indicate quinoxyfen is relatively non-toxic to terrestrial wildlife, but highly toxic to freshwater fish and extremely toxic to aquatic invertebrates. However, toxic concentrations of Quinoxyfen are not expected to occur in aquatic environments due to its chemical properties and the proposed use pattern. Quinoxyfen residues from an accidental

introduction were estimated to result in an initial concentration of 100 ppm (application rate-8.2 oz product per acre). These residues will be rapidly degraded by photolysis (est. half-life-18 minutes to one day depending on pH of water). Quinoxyfen is poorly soluble and residues will be strongly bound to sediments in the water. The Quintec™ label bears a warning indicating that the product is toxic to fish and aquatic invertebrates. The label prohibits applications directly to water or when weather conditions favor runoff or drift from the target site. The label also bears directions on how to minimize the off-site movement of quinoxyfen residues into aquatic environments.

Based on the submitted data, intended use, label rates, and use restrictions, DPR does not expect toxic concentrations of quinoxyfen to occur in aquatic environments when Quintec™ is used in accordance with the label directions.

E. Efficacy & Phytoxicity

Submitted data indicate that Quintec™ provides control of powdery mildew infections in grapes and hops when applied at 21-day intervals following label directions. Quintec™ does not control existing or latent infections of powdery mildew and must be applied on a preventative schedule. The product does not appear to be phytotoxic.

ALTERNATIVES

Quinoxyfen provides a new multi-site mode of action to control powdery mildew that is different from the demethylation inhibitors (DMIs) and the strobilurins that act on a single site. The actual mode of action is yet to be fully understood, but quinoxyfen is believed to inhibit mildew infection through disruption of early cell signaling events in the fungus that control the morphological changes that lead to infection. The use of quinoxyfen does not provide an exclusive alternative fungicide to currently used fungicides for powdery mildew control, but allows better flexibility in the use of fungicides and sulfur for resistance management purposes. When used on a preventative 21-day treatment program to control powdery mildew, the use of other fungicides and sulfur can be reduced.

CONCLUSION

DPR evaluated the product label and scientific data submitted to support the registration of Quintec™ and found them acceptable to support registration. The acute health risks to humans from exposure to quinoxyfen are minimal due to its low mammalian toxicity. The precautionary and first aid statements on the product label, as well as the required PPE and other protective measures mitigate potential health risks to persons who may be exposed to the pesticide. If, a risk assessment is conducted and DPR determines that exposure to quinoxyfen may result in unacceptable margins of exposure, further restrictions will be placed on the use of quinoxyfen at that time. Submitted data also indicate that no significant adverse environmental impacts are expected to occur from the use of Quintec™. When used in accordance with label directions, the product will be effective for its intended use.