

# CALIFORNIA DEPARTMENT OF PESTICIDE REGULATION

## PUBLIC REPORT 2003-4

### Fenamidone

### Tracking ID 191097N

#### DESCRIPTION OF ACTION

Aventis Crop Science submitted an application seeking a California registration of Reason<sup>®</sup> 500 SC Fungicide, US EPA Reg. No. 264-xxx to control certain plant diseases in vegetable crops. Reason<sup>®</sup> 500 SC Fungicide contains the new active ingredient, fenamidone. DPR accepted Aventis Crop Science's application for registration of Reason<sup>®</sup> 500 SC Fungicide concurrently with their application to the U.S. Environmental Protection Agency (U.S. EPA) for federal registration of the product. U.S. EPA has not yet completed its review of the product. Therefore, Reason<sup>®</sup> 500 SC Fungicide is not yet federally registered. Pesticide products must be federally registered before they can be registered for use in the State of California. DPR will not register Reason<sup>®</sup> 500 SC Fungicide until the product is registered with the U.S. EPA.

The Department of Pesticide Regulation (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 fenamidone 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:	Aventis Crop Science
Common name:	Fenamidone
Chemical name:	[(5s)-3,5-dihydro-5-methyl-2-(methylthio)-5-phenyl-3-(phenylamino)-4H-imidazol-4-one]
Brand name:	Reason <sup>®</sup> 500 SC Fungicide
Uses:	Disease control in potatoes, tomatoes, bulb vegetables, lettuce, and cucurbit vegetables
Pests controlled:	Early and late blight, Downy mildew, Alternaria leaf spot, and Purple blotch
Type of registration:	Unconditional

Reason<sup>®</sup> 500 SC Fungicide is formulated as a flowable concentrate with 44% fenamidone. The product is intended to provide broad-spectrum control of early and late blight in potatoes and tomatoes, downy mildew in bulb and cucurbit vegetables, and head and leaf lettuce. The product is also intended to control purple blotch in bulb vegetables and Alternaria leaf spot in cucurbit vegetables. As specified on the product label, application rates and frequency of application vary based on the crop, the amount of disease pressure present, and weather conditions. Reason<sup>®</sup> 500

SC Fungicide should be integrated with other fungicides into a resistance management program. The product is applied as a broadcast treatment with ground boom or aerial equipment. The minimum time interval between application and harvest is two days for crops harvested for human consumption. There are no rotational crop restrictions.

## SCIENTIFIC REVIEW

### **A. Chemistry**

1. Product Chemistry: DPR evaluated the submitted chemistry studies for the formulated product Reason<sup>®</sup> 500 SC Fungicide and summarized the results in the following table.

**Table I. Physical and Chemical Properties of Reason<sup>®</sup> 500 SC Fungicide**

Properties	Values
Physical state	Liquid
Color	White opaque
Odor	No odor
Melting point*	135° C
Density	1.12 g/ml
Solubility (water)*	7.8 mg/L at 20° C
Vapor pressure*	2.6 x 10 <sup>-9</sup> mm Hg at 25° C
Octanol/water partition coefficient*	Log Pow = 2.8
pH	7.2
Storage stability	Stable at accelerated temp. 54°C for 14 days

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

2. Residues in Food and Animal Feed: The submitted residue studies support the harvest and use limitations listed on the Reason<sup>®</sup> 500 SC Fungicide label for bulb and cucurbit vegetables, lettuce, potatoes and tomatoes. The proposed tolerances for the label crops include the combined food residues of fenamidone and three metabolites. The submitted data indicate the residues of fenamidone and the three metabolites are not likely to exceed the proposed tolerance levels, with the exception of cucurbit vegetables. DPR chemists have recommended that the proposed tolerance for this crop group be increased to 0.15 ppm or higher to avoid any occurrence that fenamidone residues on harvested crops will exceed the proposed tolerance. In response Aventis Crop Science has petitioned US EPA to increase the proposed tolerance level for residues of fenamidone and its metabolites in/on cucurbit crops from 0.10 ppm to 0.15 ppm. US EPA has recently established fenamidone tolerances for head and leaf lettuce.

3. Environmental Fate: The fenamidone environmental fate studies which included : soil adsorption/desorption, hydrolysis, photolysis (aqueous and soil), aerobic soil metabolism, and terrestrial field dissipation have been found to be satisfactory. The results of these studies indicate fenamidone is stable regarding hydrolysis at pHs 5 and 7, but degraded under more acidic and basic conditions (pHs 4 and 9) with half-lives of 42 and 28 days, respectively. Under aqueous photolytic conditions it degrades rapidly indicating that aqueous photolysis may be a

significant role in dissipation. However, the photolysis on soil was not significant. The soil adsorption/desorption studies were conducted with four soil types and one aquatic sediment. The soil adsorption coefficients ranged from 2.4-8.9 indicating fenamidone has the potential for moderate to high mobility in the soil depending on environmental conditions. Aerobic soil metabolism of fenamidone was investigated in two US soils and the observed half-lives ranged from 6-8 days. The results from the terrestrial field dissipation studies suggest fenamidone is more stable in soil. These studies were conducted in four different states including California. The observed half-lives ranged from 0.3-2 months with a vertical movement of 0.15-0.75 meters over the monitoring periods. For California, the observed half-life was 2 months with a movement of 0.3 meters in a loamy sand soil. A second study was conducted in California at the same site with the fenamidone applied under a different application regime. A similar half-life of 1.4 months was observed with a vertical movement in the soil of 0.3 meters. Although the laboratory conducted environmental fate studies imply fenamidone is stable in soil and has moderate to high mobility, the terrestrial field dissipation studies observed fenamidone does degrade with minimal movement in the soil. The use of fenamidone is expected to have minimal impact on the environment with little potential to accumulate or move into ground water.

## B. Toxicology

Aventis Crop Science submitted adequate toxicology studies to conduct a complete toxicological evaluation of fenamidone. DPR evaluated the submitted data to ascertain the potential for adverse health effects. The acute toxicity parameters for Reason<sup>®</sup> 500 SC Fungicide are summarized in Table III

**Table III. Acute Toxicity of Reason<sup>®</sup> 500 SC Fungicide**

Type of Study	Acute Toxicity Values	Acute Toxicity Category
Acute oral	LD <sub>50</sub> >5000 mg/kg	IV
Acute dermal	LD <sub>50</sub> >5000 mg/kg	IV
Acute inhalation	LC <sub>50</sub> >0.9 mg/l	III
Primary eye irritation	N/A	III
Primary dermal irritation	N/A	IV
Dermal sensitization	N/A	Not a dermal sensitizer
Signal word	N/A	WARNING

DPR's evaluation of the acute toxicity studies indicates that Reason<sup>®</sup> 500 SC Fungicide 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 (SB 950). The results from the chronic toxicity studies and genotoxicity studies indicate possible adverse health effects in laboratory animals. As a result of these findings, DPR has placed fenamidone in "low" priority for conducting a 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 placed in moderate or low priority. The purpose of the risk assessment will be to appraise the potential for fenamidone 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 fenamidone will also be evaluated during the risk assessment. Further toxicity information is available in DPR's Summary of Toxicology Data for fenamidone, available on DPR public website at <http://www.cdpr.ca.gov/docs/toxsums/pdfs/5791.pdf>

### C. Health & Safety

An evaluation of the medical management information on the Reason<sup>®</sup> 500 SC Fungicide label and the acute toxicity study results indicate 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. In addition, the product label requires persons handling and applying Reason<sup>®</sup> 500 SC Fungicide to wear long-sleeved shirt and long pants, waterproof gloves, shoes plus socks, and protective eyewear. 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 waterproof gloves, shoes plus socks and protective eyewear 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, and oysters. The submitted data are adequate to characterize the toxicity to wildlife and aquatic animals from 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 <sup>a</sup>	Relative Toxicity
Rat, female	Single acute oral dose	2028 mg/kg (LD <sub>50</sub> )	Relatively non-toxic
Rat, male	Single acute oral dose	>5000 mg/kg (LD <sub>50</sub> )	Relatively non-toxic
Bobwhite quail	Single acute oral dose	>2000 mg/kg (LD <sub>50</sub> )	Relatively non-toxic
Mallard duck	Feeding study (8 days)	>5,200 ppm (LC <sub>50</sub> )	Relatively non-toxic
Bobwhite quail	Feeding study (8 days)	>5,200 ppm (LC <sub>50</sub> )	Relatively non-toxic
Bluegill sunfish	Water exposure (96 hrs.)	0.74 ppm (LC <sub>50</sub> )	Highly toxic
Rainbow trout	Water exposure (96 hrs.)	0.74 ppm (LC <sub>50</sub> )	Highly toxic
Sheepshead minnow	Water exposure (96 hrs.)	2.5 ppm (LC <sub>50</sub> )	Moderately toxic
<i>Daphnia magna</i>	Water exposure (48 hrs.)	0.19 ppm (LC <sub>50</sub> )	Highly toxic
Mysid shrimp	Water exposure (96 hrs.)	69 ppb (LC <sub>50</sub> )	Extremely toxic
Oyster	Water exposure (96 hrs.)	120 ppb (LC <sub>50</sub> )	Highly toxic

a. Values expressed as; a. LD<sub>50</sub>= lethal dose that will kill 50% of test population, and b. LC<sub>50</sub>= lethal environmental concentration that will kill 50% of test population.

The results indicate fenamidone is relatively non-toxic to terrestrial wildlife, but highly toxic to freshwater fish and aquatic invertebrates. Fenamidone undergoes microbial degradation in the soil (average half-life of 7.9 days) and photolytic degradation in water (half-life of 5 to 5.8 days.) Soil dissipation half lives vary from 0.3 to 2 months. Fenamidone is hydrolytically stable at pH 5 and 7 but degrades under more acidic or basic conditions. Label directions bear a warning indicating that the product is moderately to highly toxic to fish and aquatic organisms and prohibit application of the product directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark.

Based on the submitted data, registered uses, label rates, and use restrictions for Reason<sup>®</sup> 500 SC Fungicide, DPR does not expect toxic concentrations to occur in aquatic environments from use of the product in accordance with label directions.

### **E. Efficacy & Phytotoxicity**

Submitted data indicate that Reason<sup>®</sup> 500 SC Fungicide provides broad-spectrum control of early and late blight in potatoes and tomatoes, control of downy mildew in bulb and cucurbit vegetables, and head and leaf lettuce. The product also controls purple blotch in bulb vegetables and Alternaria leaf spot in cucurbit vegetables when applied according to label directions. The product does not appear to be phytotoxic.

### ALTERNATIVES

Fenamidone is the first commercial member of a new class of fungicides called the imidazolinones. U.S. EPA has designated the proposed uses of fenamidone as “reduced risk.” Fenamidone works by inhibiting mitochondrial respiration in several Phycomycete fungi, including the downy mildews and diseases caused by Alternaria and Pythium. Fenamidone is active on multiple stages in the lifecycle of these pathogenic fungi providing control over a range of environmental conditions. Important diseases caused by these pathogenic fungi include early and late blight in potatoes and tomatoes. Currently, the ethylene bis dithio carbamate (EBDC) fungicides (mancozeb, maneb, metiram) and chlorothalonil are the primary fungicides used to control early and late blight in potatoes and tomatoes. These fungicides must be applied at substantially higher rates than fenamidone to control early and late blight. Therefore, the use of fenamidone to control these diseases can reduce the amount of pesticide residues present in the environment.

Repeated use of the same fungicide or fungicides with similar modes of action can result in the failure to control plant pathogenic fungi, allowing them to reproduce and generate resistant fungi populations. The registration of fenamidone provides an alternative fungicide that can be used in resistance management programs with other fungicides that have other alternative modes of action. Fenamidone has not exhibited any known cross-resistance to sterol-inhibitor, dicarboximide, benzimidazole, anilinopyridine or phenylamide type fungicides. However, cross-resistance has been observed in plant pathogenic fungi that have been exposed to certain strobilurin fungicides, like azoxystrobin and trifloxystrobin. Since fenamidone has a similar

mode of action as azoxystrobin and trifloxystrobin, these three pesticides should not be used together in a resistance management program.

## CONCLUSION

DPR evaluated the product label and scientific data submitted to support the registration of Reason<sup>®</sup> 500 SC Fungicide and found them acceptable to support registration. The acute health risks to humans from exposure to fenamidone 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, after the risk assessment, DPR determines that exposure to fenamidone may result in unacceptable margins of exposure, further restrictions will be placed on the use of fenamidone at that time. Submitted data also indicate that no significant adverse environmental impacts are expected to occur from the use of Reason<sup>®</sup> 500 SC Fungicide and that when used in accordance with label directions, the product will be effective for its intended use.

Before the product will be registered for use in California, the applicant must provide proof of federal registration and a copy of the U.S. EPA accepted Reason<sup>®</sup> 500 SC Fungicide label. In addition, the applicant must provide evidence that U.S. EPA has established acceptable tolerances for the residues of fenamidone and its metabolites in/on the crops allowed on the label.