

CALIFORNIA DEPARTMENT OF PESTICIDE REGULATION

PUBLIC REPORT 2003-2 Cyhalofop Butyl Tracking ID Number 184692

DESCRIPTION OF ACTION

Dow AgroSciences LLC submitted an application seeking California registration of Clincher CA®, U.S. EPA Reg. No. 62719-356, to control various grassy weeds in rice. Clincher CA® contains the new active ingredient cyhalofop butyl.

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 conditional registration. The acute health risks from exposure to cyhalofop butyl are minimal due to its low/moderate 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 during the period of conditional registration. DPR does not expect significant adverse environmental impacts to result from registration of this product.

DPR accepted Dow's application for registration of Clincher CA® concurrently with Dow's submission of an application to the U.S. Environmental Protection Agency (U.S. EPA) for federal registration of the same product under a different brand name. U.S. EPA registered Clincher SF® on May 23, 2003. The federal registration has an expiration date of June 1, 2007, which is contingent upon the submission by Dow of additional data to U.S. EPA.

BACKGROUND

Registrant:	Dow AgroSciences LLC
Common name:	Cyhalofop butyl
Chemical name:	butyl(2R)-2-[4-(4-cyano-2-fluorophenoxy)phenoxy] propionate
Brand name:	Clincher CA®
Uses:	Weed control in rice
Pests controlled:	Grassy weeds, including barnyardgrass, johnsongrass and red sprangletop.
Type of registration:	Conditional for one year

Clincher CA® is formulated as an emulsifiable concentrate with 2.38 pounds of cyhalofop butyl per gallon of product. The product is intended to provide postemergent control of selected grassy weeds in rice. Clincher CA® does not have preemergence or soil residual activity. Cyhalofop butyl controls weeds by inhibiting acetyl Coenzyme-A carboxylase. The enzyme is responsible for the biosynthesis of fatty acids in selected grass species. This blockage of fatty acid production results in the loss of lipids and

eventual death of the dividing cells in the growing point or tip of the grass. Because this site-of-action is exclusive to certain grasses, cyhalofop butyl will not control broadleaf weeds. Clincher CA® can be applied to rice fields from the time the rice is very small (1 to 2-leaf stage) until 60 days before harvest. Application is limited to one to two treatments per season with a maximum of 0.28 pounds of cyhalofop butyl (15 ounces (oz.) of product) applied per acre per treatment. A maximum of 0.46 pounds of cyhalofop butyl (25 oz. of product) can be applied per acre per growing season. For “water-seeded rice,” a single postflood application is recommended. Fields must be partially drained prior to application to expose weeds and then reflooded within 24-48 hours for optimum weed control. Water on rice fields must be held a minimum of 7 days after the most recent treatment with Clincher CA® before being discharged. The label prohibits the removal of fish, shellfish or crustaceans from treated fields during the season of treatment. Clincher CA® is applied as a broadcast treatment with ground boom or aerial equipment. The minimum interval between application of the pesticide and harvest of the rice is 60 days. Crops other than rice cannot be planted on a treated field for a minimum of three months following a Clincher CA® treatment.

SCIENTIFIC REVIEW

A. Chemistry

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

Table I. Physical and Chemical Properties of Clincher CA®

Properties	Values
Physical state	Amber, Clear liquid
Density	0.966 g/ml
pH	7.36
Flammability	Flash point 45.4°C
Solubility (water)*	0.7, 0.44 ppm (20°C)
Vapor pressure*	8.8×10^{-9} mmHg (20°C)
Partition coefficient (Kow)*	2069, $\log_{10}Kow_3 3.32$ (25°C)
Henry's law*	9.51×10^{-4} Pa m ³ mol ⁻¹
Stability*	Stable to metals and metal ions after stored at 50°C (2 weeks)

* These properties were derived using technical cyhalofop butyl at the test substance.

2. Residues in Food and Animal Feed: The submitted residue studies support the harvest and use limitations listed on the Clincher CA® label for rice. The maximum combined residues of the parent compound and the di-acid metabolite in rice and rice straw were found to be at 0.013 ppm and 5.49 ppm, respectively. The residue levels are well within the established 0.03 part per million (ppm) tolerance for rice grain and 8.0 ppm for rice straw. The rotational crop restrictions are adequate.

3. Environmental Fate: The cyhalofop butyl environmental fate data reviewed included studies on aqueous and soil photolysis, soil adsorption/desorption, aerobic and anaerobic soil metabolism, aerobic aquatic metabolism, hydrolysis and field dissipation. The studies were found to be satisfactory.

The Koc values from the soil adsorption /desorption study ranged between 1581 and 6170 ml/g indicating that cyhalofop butyl has a low mobility in soils. The adsorption of the major soil metabolite, cyhalofop-acid on these soils was much lower than the parent ester. The hydrolysis study indicates that cyhalofop butyl was dependent on pH. Cyhalofop butyl was found to be stable at pH 5.0 but hydrolyzed quickly at pH 9.0 with a half-life of half a day. The half-life of cyhalofop butyl at pH 7.0 is 88 days. Cyhalofop butyl degraded quite rapidly under both aerobic and anaerobic conditions into several metabolites. In addition, the data show that it mineralized to a significant level under the test conditions (36-61%) suggesting that soil metabolism plays a significant role in the dissipation of cyhalofop butyl under actual use conditions. Field dissipation studies were conducted in California and Arkansas. Residues of the parent compound and its four major metabolites were analyzed in water and soil samples collected at different time intervals. The data indicate that at both locations residues were mainly found in water and remained sporadic in soil samples. Residues of two cyhalofop butyl metabolites were moderately persistent in soil. The first-order half-life of the parent compound was determined to be less than a day. No residues of the parent compound or metabolites were found in the soil lower than 15 cm deep.

The use of cyhalofop butyl is expected to have minimal impact on the environment with little potential to accumulate or move into ground water due to its physical-chemical properties when used in accordance with label directions.

The submitted product, environmental fate, and residue chemistry data support registration of the subject product with the following conditions: the applicant agrees to submit a one-year storage stability study.

B. Toxicology

The toxicology studies submitted by Dow AgroSciences LLC are not adequate to conduct a complete short and long-term toxicological evaluation of Clincher CA®. DPR evaluated the submitted data to ascertain the potential for adverse health effects. The acute toxicity parameters for Clincher CA® are summarized in Table II.

Table II. Acute Toxicity of Clincher CA®

Type of Study	Acute Toxicity Values	Acute Toxicity Category
Acute Oral	LD 50>1600 mg/kg	III
Acute Dermal	LD50>5,000 mg/kg	IV
Acute inhalation	LC50>5.19 mg/L	IV
Primary eye irritation	N/A	II
Primary dermal irritation	N/A	II
Dermal sensitization	N/A	Not a dermal sensitizer
Signal word	N/A	WARNING

DPR's evaluation of the acute toxicity studies indicates that the studies are acceptable and Clincher CA® is low to moderate in mammalian toxicity. The precautionary language on the product label adequately identifies the acute toxicity hazards noted in the studies.

Dow submitted a number of subchronic toxicology studies. Possible adverse health effects were observed in five of the studies: two dog feeding studies, three mouse feeding studies, and a rat feed study. DPR found the submitted chronic toxicology studies insufficient to support full registration of Clincher CA® in accordance with the data requirements of the Birth Defects Prevention Act (Food and Agricultural (FAC) section 13121 et al). However, the pursuant to FAC section 13126, DPR may conditionally register a pesticide product containing a new active ingredient, after consultation with the Office of Environmental Health Hazard Assessment, if one or more of the health effect studies are not adequate. DPR found a rat combined chronic toxicity/oncogenicity study to be unacceptable and inadequate to assess oncogenic risk. According to Dow, cyhalofop butyl is a member of a class of chemicals that includes numerous known peroxisome proliferators. Peroxisome proliferation is a known response in rodents that follows exposure to certain chemicals. This response does not occur in humans. As a result, most regulatory authorities do not regard the formation of tumors in rodents from peroxisome proliferation as relevant to assessment of carcinogenic risk in humans. To address the issue of whether the cancer potential is relevant to humans, Dow is conducting a 28-day mechanistic study in mice. The results of the study will be made available to DPR within one year, after which time, DPR will determine whether continued registration of Clincher CA® is warranted and if additional data are required.

DPR has not yet prioritized cyhalofop butyl for risk assessment. DPR prioritizes pesticide active ingredients for risk assessment based on the nature of the potential adverse health effects observed in laboratory studies, 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 will be to appraise the potential for cyhalofop butyl 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 cyhalofop butyl will also be evaluated during the risk assessment. Further toxicity information is available in DPR's Summary of Toxicology Data for cyhalofop butyl, available on DPR public website at: <http://www.cdpr.ca.gov/docs/toxsums/pdfs/5748.pdf>.

C. Health & Safety

An evaluation of the medical management information on the Clincher CA® 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. In addition, the product label requires persons handling and applying Clincher CA® to wear coveralls over a long-sleeved shirt and long pants, protective eyewear, chemical-resistant footwear plus socks, and chemical resistant gloves. In addition, mixers and loaders for aerial application are limited to handling no more than the amount of product needed to treat 800 acres per day. 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 over a long-sleeved shirt and long pants, protective eyewear, chemical-resistant footwear plus socks, and chemical resistant gloves 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, honeybees, rainbow trout, water fleas, and oysters. The submitted data are adequate to characterize the toxicity to wildlife and aquatic animals from an 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	>2250 mg/kg (LD ₅₀)	Relatively non-toxic
Mallard duck	Feeding study (8 days)	>5620 ppm (LC ₅₀)	Relatively non-toxic
Bobwhite quail	Feeding study (8 days)	>5620 ppm (LC ₅₀)	Relatively non-toxic
Bluegill sunfish	Water exposure (96 hrs.)	0.76 ppm (LC ₅₀)	Highly toxic
Rainbow trout	Water exposure (96 hrs.)	0.49 ppm (LC ₅₀)	Highly toxic
Daphnia magna	Water exposure (48 hrs.)	0.58 ppm (LC ₅₀)	Highly toxic
Honeybee	Contact (48 hrs.)	>100ug/bee (LD ₅₀)	Relatively non-toxic
Oyster	Water exposure (96 hrs.)	0.52 ppm (LC ₅₀)	Moderately toxic

- a. Values expressed as:
 - a. LD50= lethal dose that will kill 50% of test population, and
 - b. LC50= lethal environmental concentration that will kill 50% of test population.The test substance used for the studies was technical cyhalofop butyl.

The data indicate that cyhalofop butyl is relatively non-toxic to vertebrate animals, birds and honeybees and moderately toxic to oysters. The data indicate that cyhalofop butyl is highly toxic to fish and freshwater invertebrates. However, cyhalofop butyl, which will be applied to flooded fields is rapidly metabolized in water with an observed half-life of less than one day in soil and six to seven days in sediment water systems. In field studies, cyhalofop butyl residues were found to be below detection limits (0.5 ppb) within 10 hours after application to soil or paddy water. Cyhalofop butyl is “relatively immobile” in the soil and is only toxic to fish and aquatic invertebrates at, or exceeding its water solubility. Based on the submitted data, intended use, and low label rates for Clincher CA®, 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 efficacy and phytotoxicity studies indicate that Clincher CA® provides good control of the grassy weeds listed on the product label, with minimal phytotoxicity to rice. Phytotoxicity studies indicate that Clincher CA® is not phytotoxic to non-target aquatic plants or algae at even “worst case” levels of exposure. Non-target phytotoxicity tests also indicate that Clincher CA® is not phytotoxic to prune, cotton, safflower, and tomato crops if oversprayed at label rates. In contrast, non-target phytotoxicity tests indicate that Clincher CA® may be phytotoxic to corn at less than label rates and wheat showed some sensitivity to high rates of Clincher CA®. It has also been established that peaches and nectarines exhibit a “hypersensitive response” following exposure to Clincher CA®. The NOEL for peaches has been estimated at 0.31 gm/ha (0.15% of the 1X label rate). This NOEL is quite low and has prompted Dow to place buffer zones on the product label to mitigate the risk of exposure of peaches and nectarines to drift associated with aerial and ground applications of Clincher CA® to rice. The buffer zone for ground application of Clincher CA® is 660 feet. The buffer zone for aerial applications is 2 miles if the wind is blowing away from the peaches and nectarines and 4 miles 4 miles if the wind is blowing towards the sensitive crops. The product label also requires buffer zones for non-target cereal and grass crops. The buffer zones are 50 feet for ground applications and 450 feet for aerial applications. To address the potential for drift injury to corn, Dow is required to conduct and submit the results of a residue (deposition) vs. injury study in corn.

ALTERNATIVES

Clincher CA® would provide post-emergent control of selected grassy weeds in rice. Clincher CA® can be applied at various stages of the rice’s growth, allowing flexibility in use. The product may be applied when the rice is very young up to 60 days prior

to harvest. Clincher CA® is effective against numerous annual and seedling perennial grasses in rice, providing excellent control of the major rice weed, barnyardgrass (*Echinochloa crus-galli*), as well as an emerging weed problem, sprangletop (*Leptochloa spp.*).

Currently, the herbicides thiobencarb (Bolero) and molinate (Ordram) are used along with good water management to control early season infestations of watergrass in rice. However, the extensive use of these herbicides has led to the development of resistant weed populations. Propanil applied at 3.0-4.0 lbs. a.i./acre when rice is at the 3-6 leaf stage gave 45% less sprangletop control than did Clincher CA® applied at a rate of 0.19 lbs. a.i./acre at the same leaf stage. Whip (fenoxaprop-ethyl) applied at 0.07 lbs. a.i./acre to rice at the 6 leaf stage resulted in 30% more rice injury than did Clincher CA® applied at 0.19 lbs. a.i./acre at the same leaf stage. Cerano 5 MEG (clomazone), a newly registered herbicide is effective against several of the grassy rice weeds. However, use of Cerano 5 MEG is limited to one treatment per season and the product can only be applied before or at the time the rice emerges. In addition, Cerano 5 MEG has a 120 day pre-harvest interval.

CONCLUSION

DPR evaluated the product label and scientific data submitted to support the registration of Clincher CA® and found them acceptable to support conditional registration. The acute health risks to humans from exposure to cyhalofop butyl 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 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 cyhalofop butyl may result in unacceptable margins of exposure, further restrictions will be placed on the use of cyhalofop butyl at that time. The submitted data also indicate significant adverse environmental impacts are not expected to occur from the use of Clincher CA®. When used in accordance with label directions, the product will be effective for its intended use. DPR is proposing a one-year conditional registration of Clincher CA. The registrant is required to conduct and submit the results of the following studies: (1) a one-year storage stability study; (2) a 28-day mechanistic study in mice; and (3) a residue (deposition) vs. injury study in corn. At the end of the conditional registration, DPR will determine if continued registration of Clincher CA® is warranted and if any additional data are required.