United States Environmental Protection Agency
Office of Pesticides and Toxic Substances (H7501C)
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EPA

Pesticide Fact Sheet

Name of Chemical: CLETHODIM
Reason for Issuance: NEW CHEMICAL
Date Issued: January 28, 1992
Fact Sheet Number: 230

Description of Chemical

Chemical Name: (E)-(+)-2-[1-[[(3-Chloro-2-Propenyl)oxy]imino]propyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexen-1-one
Common and Other Names: Clethodim
Trade Name: Select
EPA Shaughnessy Codes: 121011
Chemical Abstracts Service (CAS) No.: 99129-21-2
Year of Initial Registration: 1991
Pesticide Type: Herbicide
Chemical Family: Cyclohexanedione
U.S. and Foreign Producers: Valent U.S.A. Corporation

Use Patterns and Formulations

Application Sites: Postemergent treatment on soybeans and cotton for control of grasses
Types and Methods of Application: Foliar application by ground equipment
Application Rates: 0.094 - 0.25 lb ai/acre
Types of Formulations: 25% emulsifiable concentrate (EC)
Usual Carriers: Mix with water

Science Findings

Summary Science Statement

Review of the product chemistry, environmental fate, toxicology, ecological effects and residue chemistry data have been completed. The available data support conditional registration of Select for control of annual and perennial grasses in soybeans and cotton. Results of acute toxicity studies indicate Toxicity Category III (Caution). Chronic studies present no evidence of unacceptable health hazards resulting from the proposed uses Ecological effects data indicate that the proposed use on cotton and soybeans will result in minimal risk to avian, aquatic and mammalian species.

Clethodim and degradates do not show persistence in field dissipation studies. No significant bioaccumulation occurs in fish. Since it is easily degraded both by photolysis and aerobic microbial action, clethodim does not seem likely to threaten surface water. Under present use patterns and under most circumstances, clethodim does not appear likely to threaten groundwater.

Chemical Characteristics:

Technical

Physical State:	Viscous liquid
Molecular Weight:	359.92
Molecular Formula:	C_{17} H_{26} $CINO_3$ S
Color:	Clear amber
Melting Point	N/A
Boiling Point	N/A
Density	1.395 g/cu.cm 20 C
*Solubility	Limit, g/100 mL solvent at 25 C
Vapor pressure:	1×10^{-7} torr
Dissociation	$pK_2 = 4.47$
Octanol/water partition coefficient:	$K_{ow} = 1.5 \times 10^4$
pH	4.1 in a stirred solution or 4.2 in a standing solution 4.9 (5% aqueous solution.
Flammability:	Flashpoint 110 °C
Explodability:	N/A
Storage Stability	< 1% and < 3% degradation in glass containers and aluminum containers, respectively, after one year of storage at 21 °C
Viscosity:	100 cps at 20 °C
Miscibility	N/A

Characteristics:	N/A
Dielectric Breakdown Voltage:	N/A
Corrosiveness	N/A

Toxicology Characteristics:

Acute toxicology results: (Technical (T) 83.3% & 96.ai:)

Acute oral toxicity-(rats): 98.6%	LD_{50}(female) greater than 1.4 gm/kg category III
Acute oral toxicology-(rat): 83.3%	LD_{50}(F)=1.36 gm/kg toxicity category III LD_{50}(M) 1.63%g/kg
Acute oral LD_{50}(mice): 83.3%	LD_{50}(M)=2.57 g/kg LD_{50}(F)=2.43g/kg toxicity category III
Acute Dermal LD_{50}(rabbit) 83.3%	LD_{50}(M&F) greater than 5 g/kg toxicity category IV
Acute inhalation LD_{50} (rat): 83.3%	LC_{50} greater than 3.9/L(M&F)tox.category Ill
Primary eye irritation(rabbit) 83.3%	toxicity category III
Primary dermal irritation(rabbit)	toxicity category IV
Acute Toxicity (Select Herbicide)	26.1 and 26.0% ai)
Acute oral toxicology-(rat): 26.1%	LD_{50}(F) 2.92g/kg LD_{50}(M) 3.61%g/kg tox. category III
Acute oral LD_{50}(rat): 26.1%	LD_{50}(M)=3.61 g/kg toxicity III LD_{50}(F)2.92g/kg
Acute Dermal LD_{50}(rabbit)26.0%	LD_{50}(M&F) greater than 5 g/kg tox.category IV

Acute inhalation LC_{50}(rat): 26.1%'	LC_{50} greater than 5.4 mg/L(M&F)(0.33 mg/L)
Primary eye irritation (rabbit):26.1%	toxicity category II
Primary Dermal irritation (rabbit): 26.0%	tox.category III
Dermal sensitization:	Nonsensitizer

Subchronic Testing

21-Day Dermal (rat)- The systemic NOEL is 50 mg/kg/day. The LOEL for skin is 10 mg/kg/day (26.3%).

Chronic Testing

Carcinogenicity

In the 18-month carcinogenicity study, mice administered clethodim (83.3%) at dosages of 0, 20, 200, 1000, or 3000 ppm resulted in a systemic NOEL and LOEL of 200 and 1000 ppm (HDT) for male and female mice, respectively.

Chronic toxicity

In a 1-year feeding study, dogs were treated with clethodim (83.3%) at dose levels of 0, 1, 75, or 300 mg/kg/day. The systemic LOEL for both sexes is 75 mg/kg/day based on increased absolute and relative liver weights and alterations in hematology and clinical chemistry. The NOEL is 1 mg/kg/day.

Chronic toxicity/Carcinogenicity - (Rats)

A 2-year chronic toxicity/carcinogenicity study with rats fed clethodim (83%) at dosages of 0, 5, 20, 500, and 2500 ppm. Liver weights were not affected at study termination nor were there any compound-related histological changes noted (HDT). The systemic NOEL is 500 ppm (19 mg/kg/day), based upon the liver weights were not effected at the study termination nor were there any compound-related histological changes noted. The systemic LOEL is 2500 ppm (100 mg/kg/day).

Teratogenicity

A rat teratology study was conducted with clethodim (82.6%) using doses of 0, 10, 100, 350, and 700 mg/kg/day. Based upon reductions in body weight gain and clinical signs of toxicity,

the NOEL and LOEL for maternal toxicity are 100 and 350 mg/kg/day respectively. Based on reductions in fetal body weight and increases in skeletal anomalies the NOEL and LOEL for developmental toxicity are 100 and 350 mg/kg/day, respectively.

A rabbit teratology study was conducted using doses of 0, 25, 100, and 300 mg/kg/day (clethodim 82.6%). Maternal toxicity was manifested by clinical signs of toxicity, reduced weight gain and food consumption during treatment. The NOEL and LOEL are 25 and 100 mg/kg/day, respectively. Developmental toxicity was not observed. The NOEL for this endpoint is 300 mg/kg/day.

A rat teratology study was conducted using doses of 0, 10, 100, and 700 mg/kg/day (clethodim 98.6%). The maternal NOEL and LOEL are 10 and 100 mg/kg/day, respectively. Based upon significant reductions in fetal body weight and litter size significantly increased litter and fetal incidence of cervical rib at 700 mg/kg/day, the NOEL and LOEL for developmental toxicity are 100 and 700 mg/kg/day, respectively.

Reproduction

In a reproductive toxicity study, rats were fed doses of 0, 5, 20, 500, or 2500 ppm. The NOEL and LOEL for systemic toxicity are 500 ppm (51 mg/kg/day) and 2500 ppm (263 mg/kg/day), respectively, based on reductions in body weight, particularly in males, and decreased food consumption in both generations. No effects on fertility, length of gestation, or growth and development of offspring were observed. The NOEL for reproductive toxicity is 2500 ppm (HDT) (83.3%).

Mutagenicity

Technical material was not mutagenic in the Ames assay.

Metabolism - Rats

The requirement for a metabolism study in rats has been satisfied. Five groups of rats, 5 males and 5 females, were dosed in various sequences with either 4.5 or 450 mg/kg [^{14}C] clethodim orally.

Clethodim is readily absorbed and eliminated with essentially all of the [^{14}C] dose recovered from urine. Several days after the compound was administered, smaller amounts were recovered from feces (9-17%) and expired air. Gastrointestinal absorption was estimated at 89-96%. There was no evidence of bioconcentration following multiple exposures; the adrenal dosing had the highest concentration of radiolabel (0.07 to 0.22 ppm for low and repeated doses; 5.4 to 13 ppm for high-dose rats). Clethodim was extensively metabolized with < 1 percent eliminated

as the unchanged parent compound. The predominant metabolite recovered was clethodim sulfoxide (48 to 63% of administered label after 48 hours).

Environmental Characteristics

Hydrolysis: Propyl [^{14}C]-clethodim degraded with half-lives of 26 days (pH 5) and approximately 300 days (pH 7 and 9). Allyl-labeled clethodim degraded with half-lives of 42 days(pH 5) and 360 days (pH 7). The degrades were clethodim,oxazole, and 1-chloropropen-3-ol.

Aerobic Soil Metabolism- Under aerobic soil conditions, clethodim degrades with a half-life of 1 to 2.6 days.

Anaerobic Aquatic Metabolism - Results of the anaerobic aquatic metabolism study indicate that clethodim has a half-life of 128 days in the aqueous phase and 214 days in the sediment. The degradates formed are metabolized as rapidly as they are formed, and do not appear to accumulate.

Aqueous Photolysis - Clethodim degrades with half-lives of 1.5-9.3 days, at pH 5 and 9, respectively.

Mobility - Leaching and absorption/desorption. Clethodim and its sulfoxide, sulfone, and oxazole sulfone degradates are weakly absorbed into two sandy loam soils, clay loam, sandy clay loam, and sandy soil.

Soil Photolysis - Photolysis of clethodim on soil will not be a major pathway of degradation, since metabolism is rapid. After 7 days, less than 6.8% of parent compound remained. Little or no volatile material, organic or CO_2 was produced. The single major product was clethodim sulfoxide. Metabolism is the primary mechanism of degradation.

Terrestrial Field Dissipation - No vertical movement of the residues was observed as all measurable residues were confined to the top 20 cm of the soil.

Accumulation - In Confined Rotational Crop and in Fish - In rotational crops, some uptake and concentration were detected at an exaggerated rate of 4 X the maximum single application. Closely - related metabolites accounted for around 1/3 of the total radioactivity observed in the plants. No significant bioaccumulation occurred in fish.

Ecological Characteristics:

Available fish and wildlife data indicate that the proposed uses on cotton and soybeans will result in minimal hazard to nontarget and endangered beneficial insect, avian, freshwater

fish and mammalian species.

Clethodim is slightly to practically non-toxic to birds . The avian acute oral LD_{50} was greater than 2000 mg/kg for the bobwhite quail and the avian dietary $LC_{50's}$ were > 4270 ppm for the bobwhite quail and > 3978 ppm for the mallard duck. The mallard and avian reproduction study is acceptable and fulfills the waterfowl guideline requirement. An NOEL of 1000 ppm was reported.

Clethodim technical is slightly toxic to cold-and warm-water fish species. The fish LC_{50} for the rainbow trout is 18.0 ppm and 33.0 ppm for the bluegill sunfish. Select EC is slightly toxic to Daphnia magna. The 48 hour LC_{50} value for Daphnia magna is 20.2 mg/L; and the NOEL is 5.5 mg/L. The formulated product was tested because of a high level of a certain inert ingredient in the formulation.

Clethodim technical and Select 2 EC are practically non-toxic to honeybees,with an LD_{50} of greater than 100 ug/bee. Select 2 EC was evaluated to assess the toxicity of formulation inerts.

Tier I and II non-target plant phytotoxicity data using technical clethodim were submitted. The data demonstrate that Select 2 EC is extremely selective in its mode of action. Only grass species are at risk from off-target movement. Endangered grass in or around Select-treated fields is at risk from ground or aerial applications. Thus, Select is prohibited from use in the counties listed under "Summary of Regulatory Positions."

Tolerance Assessment - A tolerance with an expiration date is established for residue of the herbicide clethodim (ANSI), (E)-(+)-2-[1[[(3-chloro-2-propenyl)oxy]imino]-propyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexen-1-one, and its metabolites containing the 2-cyclohexen-1-one moiety in/on soybeans at 10 ppm; cottonseed at 1 ppm; meat, fat, and meat byproducts of cattle, goats, hogs, horses, poultry, and sheep at 0.2 ppm; milk at 0.05 ppm; eggs at 0.2 ppm; soybean soapstock at 15 ppm; and cottonseed meal at 2 ppm.

Summary of Regulatory Positions

Use, formulation, manufacturing process or geographical restriction: " Do not apply directly to water," "Do not apply where runoff is likely to occur." "Do not apply where weather conditions favor drift from areas treated. Do not allow Select to come in contact with desirable grass crops such as corn, rice, sorghum, small grains, or turf as these other grass crops will be injured or killed." "Minor leaf spotting may occur on soybeans and cotton under certain environmental conditions. New foliage is not affected." Do not apply a broadleaf (herbicide) within one day following application. Do not apply by air."

Select 2EC is prohibited from use in the following counties to avoid non-target injury to the endangered grass species listed: (1) Solano grass-Colusa, Contra, Costa, Fresno, Glenn, Madera, Merced, San Joaquin, Solano, Stanislaus and Tehama Counties in California, and (2) Texas wild rice - Hays county in Texas."

Summary of Major Data Gaps

Revise analytical method and have a successful independent laboratory validation conducted on the revised method.

Contact Person at EPA

Joanne I. Miller
Product Manager (23)
Fungicide-Herbicide Branch
Registration Division (H7505C)
Office of Pesticide Programs
Environmental Protection Agency
401 M Street SW.
Washington, DC 20460

Office location and telephone number:
Rm. 245, Crystal Mall #2
1921 Jefferson Davis Highway
Arlington, VA 22202
(703) 305-7830

Disclaimer: The information in this Pesticide Fact Sheet is a summary only and is not to be used to satisfy data requirements for pesticide registration and reregistration. The complete Registration Standard for the pesticide may be obtained from the contact person listed above.