Dow AgroSciences

Clopyralid

a North American technical profile

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CLOPYRALID HERBICIDE PROFILE OVERVIEW

Products Containing Clopyralid
Confront, Curtail, Fieldstar, Hornet, Lontrel, Prevail, Reclaim, Scorpion III, Stinger, Striker, Transline

Example Uses
Asparagus, barley, blueberry, cole crops, corn, flax, grasses, mint, non-cropland, oats, pasture, rights-of-way, strawberry, sugar beets, turf, wheat

Biological Activity

Major Weed Families Controlled:
Asteraceae
Fabaceae
Solanaceae
Polygonaceae

PROPERTIES

Environmental Fate

Soil:
Weakly adsorbed
K_{oc}: 0.4-30 mL/g
Surface photolysis: stable
Aerobic half-life: 25 days
Low to moderate potential for mobility

Water:
Solubility: 7850 ppm
Hydrolysis: stable
Photolysis: stable
Acid dissociation constant: 2.0

Air:
Low volatility
Vapor pressure = 1.02×10^{-5} mm Hg

Ecotoxicity

Birds:
Low acute toxicity
No effect on reproduction

Aquatic Animal Life:
Practically non-toxic

Bees and Other Insects:
Non-toxic

Earthworms:
Non-toxic

Soil Microorganisms:
No significant effect

Aquatic Plants:
Slight to moderate toxicity to some aquatic plants

Toxicity

Acute oral LD_{50} in rats: >2500 mg/kg
Acute dermal LD_{50} in rabbits: >2000mg/kg
Acute inhalation LC_{50} in rats: >0.38 mg/liter of air (highest attainable concentration)
Non-irritant to skin: Irritant to eyes
Not a skin sensitizer
Chronic NOEL: 50 mg/kg/day in 2 year chronic rat study
Not carcinogenic
Not mutagenic
Not teratogenic
Not a reproductive toxin

Dietary Residues

Acceptable Daily Intake (ADI) or Reference Dose (RfD): 0.5 mg/kg/day

Theoretical Max Residue Contribution (TMRC): Worst case uses <2.5% of RfD

CONCLUSIONS

Active Ingredient Classification:
Relatively non-toxic
Consumer Exposure:
Large margin of safety
Environmental Impact:
Minimal under normal use conditions
Environmental Fate:
Low to moderate potential for mobility
Operator Exposure:
Large margin of safety

1. IDENTITY OF ACTIVE INGREDIENT

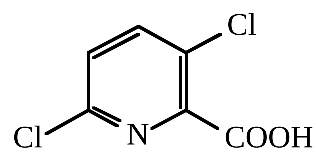
Chemical Name:
3,6-dichloro-2-pyridinecarboxylic acid (CAS)
3,6-dichloropyridine-2-carboxylic acid (IUPAC)
3,6-dichloropicolinic acid

Common Name: clopyralid (*BSI, ANSI, and ISO)*

Molecular Weight: 192.0

Empirical Formula: $C_6H_3Cl_2NO_2$

Structural formula:



CAS Registry Number: 001702-17-6

Chemical Family: pyridinecarboxylic acid

2 PHYSICAL AND CHEMICAL PROPERTIES

State:	Crystalline Solid
Color:	Off-white
Odor:	Odorless to Musty/Moldy
Boiling Point:	Not applicable to a solid
Melting Point:	151 to 152°C
Density:	Bulk Density = 0.46 g/mL at 25°C Relative Density = 1.575 at 20°C
Solubility:	a) In water

Solvent	g/100mL (20°C)
Distilled water	0.785
Water, buffered pH 5	11.8
Water, buffered pH 7	14.3
Water, buffered pH 9	15.7

b) In organic solvents

Solvent	Weight Percent (20°C)
Acetonitrile	12.1
Hexane	0.6
Methanol	10.4
N-Methyl Pyrrolidinone	39.3
Octanol (25°C)	14.0

Vapor Pressure:	1.02×10^{-5} mm Hg at 25°C 2.0×10^{-7} mm Hg at 25°C (Monoethanolamine salt)
Dissociation Constant:	pK_a = 2.0 (exists in anion form)
Octanol/Water Partition Coefficient:	

Buffer	Log 10 K_{ow} (20°C)
pH 5	-1.81
pH 7	-2.63
pH 9	-2.55

pH: 1.8 (10% solution in water)

Stability: Clopyralid is considered stable under normal conditions and at 122°F when in contact with certain metals and metal ions.

Ox/Reducing Activity: No oxidizing or reducing potential

Flammability: Not applicable to a solid

Explodability: No evidence of explodability

Storage stability: Stable

Viscosity: Not applicable to a solid

Miscibility: Not applicable to a solid

Corrosion Characteristics: Not corrosive to standard manufacturing materials

3 Biological Activity and Use

3.1 Purpose

Clopyralid is a growth regulator herbicide discovered in 1961. Since its initial launch in Europe in the mid to late 1970's, clopyralid has been used effectively for control of annual and perennial broadleaf weeds in certain crops and turf. Clopyralid also provides effective control of certain brush species on rangeland and pastures.

3.2 General Information

Clopyralid is active when applied preemergence, preplant incorporated or post emergence. The activity of clopyralid on weeds (annuals and perennials) may vary by type of application. For instance, only post emergence applications of clopyralid provide effective control of perennials. It has a relatively narrow spectrum of activity being particularly effective against members of four specific broadleaf weed families:

- *Asteraceae* (such as sunflower, cocklebur, ragweed, chicory, scentless chamomile, sagebrush, Canada thistle, knapweed, dandelion, and perennial sow-thistle);
- *Fabaceae* (such as clover, black medic, vetch, mesquite);
- *Solanaceae* (such as nightshade, jimsonweed);
- *Polygonaceae* (Buckwheat).
  -clopyralid control of *Polygonaceae* species can vary:
    - wild buckwheat (excellent control)
    - smartweed (fair to good control)

3.3 Field Biological Activity

Ornamental Turf

Clopyralid is available for use in turf as a package mix combination with triclopyr amine in a 1 to 3 ratio of clopyralid to triclopyr. The product is marketed under the name Confront and is available as 3 lb ae/gallon liquid or impregnated on fertilizer. The application rates for clopyralid in the premix range from 0.09 to 0.18 lb ae/acre (100-200 g/ha). The Confront product label lists over 40 susceptible weeds. Confront shows a greater level of control and broader spectrum than would be expected by examining the activity of the single active ingredients. Greatest activity is observed when applications are made to actively growing plants in the 4 to 6 leaf stage of growth. Weed control is primarily from foliar activity although clopyralid does have soil residual activity at higher application rates. Both warm and cool season grasses are quite tolerant to applications of clopyralid at rates higher than typical use rates. Any phytotoxicity that may be seen on warm season turf from applications of Confront is due to the triclopyr component.

Range & Pasture

Clopyralid products that are registered for use in rangeland and permanent grass pastures include Curtail, Reclaim, Stinger and Transline. Clopyralid is foliar applied at rates ranging from 0.125 to 0.5 lb ae/acre (140 - 560 g/ha) as a broadcast, spot or individual plant treatment for selective control of certain woody plants and broadleaf weeds. The primary woody plants that are controlled with clopyralid are mesquite and other associated woody legumes, while the key broadleaf weeds that are controlled include spotted knapweed, diffuse knapweed, yellow starthistle, musk thistle and Canada thistle.

Non-Crop

Clopyralid products registered for use on non-cropland areas include Curtail, Stinger and Transline. These products are foliar applied as a broadcast or spot treatment for selective control of certain broadleaf weeds or woody plants on rights-of-way, wildlife openings and other non-crop areas. The application rates range from 0.09 to 0.5 lb ae/acre (100 - 560 g/ha). The primary broadleaf weeds on non-crop areas that can be controlled with clopyralid include Canada thistle, musk thistle, bull thistle, kudzu, yellow starthistle, diffuse knapweed and spotted knapweed while mesquite is the primary woody plant targeted for control.

Crops

(These crops are listed as a general guide to the user. Be sure to refer to a current product label for complete use directions and precautions. Always read and follow label directions.)

Asparagus - Stinger is registered for post emergence control of Canada thistle and certain other broadleaf weeds in asparagus. Application rates range from 0.19 to 0.25 lb ae/acre (212 - 280 g/ha). Treatments are applied broadcast with ground equipment.

Blueberry, highbush (Canada) - Lontrel is registered for post emergence control of certain broadleaf weeds at 150 - 300 g ae/ha. Treatments may be applied broadcast using ground equipment.

Canola (Canada) - Lontrel is registered for post emergence control of certain broadleaf weeds in all varieties of canola and rapeseed. Lontrel may be applied as a broadcast or spot treatment with ground equipment. Application rates range from 150 to 300 g ae/ha.

Cereal Grains: (Wheat, Barley and Oats) - Curtail, Curtail M, Stinger, Lontrel (Canada) and Prevail (Canada) are registered for post emergence control of certain broadleaf weeds in wheat, barley and oats. The application rates for clopyralid range from 0.09 to 0.125 lb ae/acre (100 to 140 g/ha) in the US. In Canada, the rate range for Lontrel is 150 to 300 g/ha and for Curtail M and Prevail the rate range is 75 to 100 g/ha.

Christmas Tree Plantations - Stinger and Lontrel (Canada) are registered for post emergence control of certain broadleaf weeds in Christmas tree plantations. Christmas tree species that have shown tolerance to Stinger include balsam fir, blue spruce, Douglas fir, Fraser fir, grand fir, lodgepole pine, noble fir, ponderosa pine, and white pine. The application rates for clopyralid range from 0.09 to 0.25 lb ae/acre (100 - 280 g/ha). Treatments may be applied broadcast or in a band with ground equipment.

Field Corn - Hornet and Fieldstar (Canada), combination products containing flumetsulam and clopyralid, may be applied as a soil or post emergence treatment for control of a wide spectrum of broadleaf weeds. Hornet and Fieldstar may be applied as a broadcast or band treatment. The application rates for the clopyralid portion of the product range from 0.125 to 0.19 lb ae/acre (140 - 210 g/ha) for soil applied treatments and from 0.06 to 0.16 lb ae/acre (70 to 175 g/ha) for post emergence treatments.

Scorpion III and Striker (Canada), premixes of flumetsulam, clopyralid and 2,4-D, may be applied as a post emergence treatment to corn for control of a wide spectrum of broadleaf weeds. The application rate for the clopyralid portion of the product is 0.06 lb ae/acre (70 g/ha).

Stinger may also be applied as a post emergence treatment to corn for control of certain broadleaf weeds. The application rates range from 0.125 to 0.25 lb ae/acre (140 - 280 g/ha). Treatments may be applied broadcast, spot or in a band.

Flax (Canada) - Lontrel and Curtail F are registered for post emergence control of certain broadleaf weeds in flax. The application rates of clopyralid range from 100 to 300 g/ha.

Grasses Grown for Seed - Clopyralid products that are registered for use on grasses grown for seed include Curtail, Curtail M, and Stinger. These products are applied post emergence in either a broadcast or spot treatment for control of certain broadleaf weeds. The application rates for clopyralid range from 0.09 to 0.25 lb ae/acre (100 - 280 g/ha). Stinger may be applied with ground equipment. Curtail or Curtail M may be applied with either aerial or ground equipment.

Mint - Stinger is registered for post emergence control of certain broadleaf weeds in spearmint and peppermint. Application rates range from 0.125 to 0.25 lb ae/acre (140 to 280 g/ha).

Rutabagas (Canada) - Lontrel is registered for post emergence control of certain broadleaf weeds at 200 g ae/ha. Treatments may be applied broadcast using ground equipment.

Strawberry (Canada) - Lontrel is registered for post emergence control of certain broadleaf weeds at 200 - 300 g ae/ha. Treatments may be applied broadcast using ground equipment.

Sugar Beets - Stinger and Lontrel (Canada) are registered for post emergence control of certain broadleaf weeds, including Canada thistle, in sugar beets. The application rates for clopyralid range from 0.09 to 0.25 lb ae/acre (100 - 280 g/ha). Treatments may be applied broadcast or in a band with ground equipment.

3.4 Mode of Action and Symptomology

Clopyralid is a synthetic form of natural plant growth hormones called auxins. It disrupts plant growth processes by binding at the receptor sites normally used by the plant's natural growth hormones. This binding causes unproductive and abnormal plant growth resulting in plant death. Plants may die in a few days or, in the case of some perennial weeds, the process may continue for a longer period. Plant uptake of clopyralid occurs through both roots and leaves.

Whether clopyralid enters the plant through leaves or roots has only a slight impact on the resulting plant symptomology. The symptoms shown by annual and perennial weeds are similar, but the degree of control may differ. For example, established Canada thistle plants intercept enough foliar applied clopyralid to result in the death of top-growth and roots. However, when clopyralid is soil applied, the roots of Canada thistle intercept only enough clopyralid to cause some symptoms but not death. In contrast, however, clopyralid applied preemergence sometimes kills germinating seedlings before emergence.

The symptoms of clopyralid activity include:

- root and shoot inhibition
- thickened roots and inhibited root hair production
- thickened, curved, and twisted shoots, stems and leaves
- parallel venation (narrow leaves with callus tissue)
- cupping and crinkling of leaves
- callus (hardened) growth on stems
- stem cracking
- proliferated growth

Since clopyralid has systemic rather than contact activity, control can be achieved with less than total foliar coverage. Applied preemergence, the systemic activity of clopyralid can provide “reachback” or residual control if weeds do emerge.

3.5 Uptake (Absorption) and Translocation Characteristics

Uptake

As a soil-applied preemergence compound, clopyralid becomes a component of the soil solution and enters the plant primarily through plant roots although some clopyralid may also enter the plant through emerging shoots. As a foliar treatment, clopyralid is rapidly absorbed through leaves. As a result, clopyralid typically needs only a brief (2 hours) rain-free period after foliar application.

Foliar uptake of clopyralid is influenced by relative humidity as well as the stage of the weeds at application. Rate of foliar absorption is increased under higher humidity conditions and when applied to vegetative as opposed to flowering plants.

Translocation

Once absorbed, clopyralid moves readily throughout the plant via both the xylem (water-transporting) and phloem (nutrient-transporting) systems of the plant. Clopyralid is distributed throughout the entire plant to the meristems (growing points) and other developing plant parts. Eventually, lethal amounts of clopyralid accumulate in the meristems and result in plant death.

Uptake of clopyralid through roots continues even after emergence providing residual control of weed seedlings that may germinate after treatment. Foliar applied clopyralid translocates rapidly from treated leaves to the shoot apex and the roots. The chemical accumulates primarily in shoot meristems, especially the upper shoot. Rapid translocation through the phloem to roots enables foliar applications of clopyralid to control deep-rooted perennials like Canada thistle.

Factors that impact plant growth also impact the translocation of clopyralid and thus, clopyralid performance. Disruption of the plant's metabolism will reduce the amount of herbicide translocated to meristems. Environmental conditions that are not conducive to active plant growth may reduce translocation and result in reduced herbicidal activity, while normal growing conditions result in optimum control. However, the rapid translocation of clopyralid can mean better performance under certain conditions. For instance, its rapid translocation enables clopyralid to reach the roots of perennials and continue working even if the shoot is killed by frost, mowing or cultivation.

3.6 Plant Selectivity and Weed Sensitivity

The fate of clopyralid in plants varies between crop and weed species thus determining crop tolerance and/or weed control effectiveness. Plant selectivity to clopyralid appears to be determined by the sum of a plant's morphological features (such as tissue structure) and its physiological reaction to the herbicide (such as conjugation or excretion of the compound). Since clopyralid is not readily degraded even in tolerant plants, other factors are likely involved in the ability of tolerant crops to prevent the growth regulator activity of clopyralid, including:

- tissue structures in grasses -- the arrangement of vascular tissues and meristems in grasses may restrict movement of growth regulators via phloem to meristematic tissue;
- physical differences -- narrow-leafed grasses simply do not absorb as much of the compound as broadleaf plants;
- conjugation of the compound -- tolerant species may have enzymes that can bind to or "complex" plant substrates with clopyralid molecules, thus inactivating the compound;
- excretion of the compound -- some plants have the ability to release growth regulator herbicides through their root systems.

Weed sensitivity to clopyralid depends on the weed species and the application rate.

Weeds susceptible to clopyralid at 105 to 210 g ae/ha (1.5 to 3.0 oz ae/A) include:

Clover	Jerusalem artichoke	Pineappleweed
Cocklebur	Jimsonweed	Coffeeweed
Sunflower	Marshelder	Mayweed
Ragweed	Vetch	Sicklepod

Weeds susceptible to clopyralid at 210 to 280 g ae/ha (3 to 4 oz ae/A) include:

Scentless chamomile	Nightshade	Sow thistle, annual
Common groundsel	Buffalobur	Smartweed (suppression)
Wild buckwheat	Canada thistle	Perennial sow thistle (suppression)

Weeds susceptible to clopyralid at 280 to 560 g ae/ha (4 to 8 oz ae/A) include:

Knapweed, diffuse	Mesquite	Chickweed
Knapweed, spotted	Acacia	Dandelion
Knapweed, Russian (suppression)		

The timing of clopyralid application (preemergence versus post emergence) impacts weed sensitivity. For example, Canada thistle, a perennial, is not well controlled by preemergence applications of clopyralid but is controlled effectively by post emergence applications at the proper growth (vegetative) stage. The control of some annual weeds is also influenced by application timing. For instance, giant ragweed is slightly more sensitive to post-applied clopyralid than is common ragweed. However, common ragweed is more sensitive than giant ragweed when clopyralid is applied preemergence.

As with crops, growing conditions play an important role in determining a weed's ability to detoxify most herbicides. Adverse growing conditions may reduce weed control because weed growth may be slowed or stopped, rendering the herbicide ineffective until active growth resumes. While the weed's growth rate is suppressed, uptake and translocation decrease, allowing herbicides to bind to cell constituents or partition into surrounding tissues, thus decreasing the amount of herbicide that reaches meristems. Under these circumstances, weeds may be temporarily stunted but may resume growth when environmental conditions improve.

Plant Residues and Crop Rotation

Analysis of crops treated with clopyralid indicates that residues of clopyralid may remain in treated plants through the growing season. The amount of clopyralid residue in plants varies by species, application timing, period after application and environmental conditions. Since clopyralid is not readily degraded, clopyralid residues in one crop could impact a sensitive rotational crop. For instance, a large clump of decomposing wheat straw or corn stalks might occasionally release enough clopyralid to cause herbicidal effects in a sensitive rotational crop. As the crop residue decomposes in the soil, clopyralid is released and is degraded by soil microorganisms. Labels for clopyralid products provide guidance on proper rotational intervals to avoid injury to the following crop.

3.7 End Use Products and their Uses

Clopyralid and clopyralid combinations are available in different countries/markets under different trade names (for example, see Table 1). Before using a product containing clopyralid, be sure to check the appropriate label for approved crops and follow label use directions.

Table 1. End Use Products Containing Clopyralid

Selected Trade Names	Country	Active Ingredient(s)	Markets
Hornet Fieldstar	USA Canada	clopyralid (acid) + flumetsulam	field corn
Confront	USA	clopyralid (triethylamine salt) + triclopyr (triethylamine salt)	ornamental turf
Curtail	USA	clopyralid (monoethanolamine salt) + 2,4-D (triisopropanolamine salt)	wheat, barley, grasses grown for seed, rangeland and pasture
Curtail M	USA and Canada	clopyralid (acid) + MCPA 2-ethylhexyl ester	wheat, oats, barley, grasses grown for seed
Curtail F	Canada	clopyralid (acid) + MCPA 2-ethylhexyl ester	flax
Lontrel	Canada	clopyralid (monoethanolamine salt)	canola, small grains, sugar beets, flax, forage grasses, rutabagas, strawberry, highbush blueberry, balsam fir Christmas trees
Prevail	Canada	clopyralid (acid) + MCPA 2-ethylhexyl ester + tralkoxydim	wheat, barley
Reclaim	USA	clopyralid (monoethanolamine salt)	rangeland and pastures
Scorpion III Striker	USA Canada	clopyralid (acid) + flumetsulam + 2,4-D (acid)	field corn
Stinger	USA	clopyralid (monoethanolamine salt)	sugar beets, field corn, mint, asparagus, small grains, rangeland, pastures, and non-crop uses
Transline	USA and Canada	clopyralid (monoethanolamine salt)	non-cropland areas, industrial sites, rights-of-way, wildlife openings

4 FATE AND BEHAVIOR IN THE ENVIRONMENT

4.1 Environmental Properties of the Molecule

Use Rates:	250-280 g ae/ha (approx. 100-300 ppb in soil) 120 g ae/ha (approx. 50-150 ppb in soil)
Water Solubility:	S_W = 7850 ppm (20 °C) (Soluble)
Sorption Coefficient:	K_d = 0.01 - 0.21 mL/g (Low soil sorption)
Soil Organic Carbon Sorption Coefficient:	K_{oc} = 0.4 - 29.8 mL/g (Increased soil sorption with time)
Octanol/Water Partition Coefficient:	log K_{ow} = -2.63 at pH 7 (Favors water, hydrophilic)
Dissociation Constant:	pK_a = 2.0 (25 °C) (Dissociates rapidly to the anion)
Vapor Pressure:	$V_p = 1.02 \times 10^{-5}$ mm Hg (25 °C) (Low volatility; exists as anion in the environment)
Henry's Law Constant:	$K_H = 3.28 \times 10^{-10}$ atm m^3/mol (20 °C) (Low air-water partitioning)
Hydrolysis:	Stable in water at 25 °C (pH 5-9)
Aqueous Photolysis:	$t_{1/2}$ = 261 days at 25 °C (No significant degradation from sunlight)
Soil Photolysis	Stable (No significant degradation from sunlight)
Aerobic Soil Metabolism:	Typical soil, average half-life = 25 days Range = 8-250 days (19 soils) Less than 69 days in 95% of the soils Shorter half-life in warm, moist soils and lower application rates
Aerobic Aquatic Metabolism:	No significant degradation
Anaerobic Aquatic & Soil Metabolism:	No significant degradation
Field Aquatic Dissipation:	Field half-life: 9-22 days in natural freshwater lake
Field Soil Dissipation:	Average half-life = 25 days Range = 8-66 days (20 sites)
Lysimeter Tests (Undisturbed soil columns):	Center of mass movement: 6-18 inch soil depth Leached: 0.1-0.6% applied
Major Degradation through Microbial Action:	Degradation enhanced with lower application rates, higher soil moisture and temperature.

4.2 Fate in Soil

Clopyralid degradation in soil is driven by microbial processes. Therefore, environmental factors that affect microbial activity, such as soil moisture and temperature, also affect the degradation of clopyralid.

The rate of aerobic soil degradation increases in moist, warm soils, and with lower application rates. The only significant metabolite is CO_2. In early studies (pre-1980), where acetone solutions were used as the carrier to treat samples, aerobic soil half-life averaged 36 days in 13 US soils. In all but two of the soils tested, average half-life was 25 days. In more recent US studies conducted with aqueous solutions of test substance, and under typical US temperature and moisture conditions (25 °C, 0.3 bar moisture), aerobic soil half-life averaged 28 days in 10 US soils. Under a typical Canadian and European temperature (20 °C) and moisture conditions at 40% Water Holding Capacity (WHC), aerobic soil half-life averaged 25 days (3 Canadian, 6 European soils). Under dryer soil conditions (15 bar or 10% WHC), half-life averaged 43 days (5 US, 3 European soils). Under more moist soil conditions (0.3 bar or 60% WHC), half-life averaged 11 days (3 US, 3 European soils).

Decreased degradation is expected in waterlogged or anaerobic conditions. In an early (1977) US anaerobic soil degradation study, two soils were treated at 0.16 ppm, under waterlogged conditions at 25 °C. Degradation over 300 days was not significant enough to calculate in the Commerce loam waterlogged soil. In a waterlogged Flannagan silty clay loam soil, a half-life of about 693 days (R^2=71%) was observed. In a more recent (1995) anaerobic aquatic degradation study, samples of natural water/silt loam sediment were treated at an initial water concentration of 0.36 ppm. Clopyralid distributed preferentially into the water phase (68% of applied), versus sediment (22% of applied). Over the 365-day, anaerobic test period, no significant degradation occurred in either water or sediment. The laboratory tests discussed above demonstrate that clopyralid degradation is significantly limited under cold, dry or anaerobic soil conditions, and most rapid under warm, moist aerobic soil conditions.

The effect of temperature on degradation was demonstrated in Canadian, US and European studies. At about 250 g ae/ha and under cooler temperature conditions (10 °C), average half-life was 64 days (3 Canadian, 3 European soils). Under warmer conditions (30-35 °C), average half-life was 19 days (3 Canadian, 3 US soils).

The effect of application rate (and associated starting soil concentration) on degradation was demonstrated in various US and European laboratory studies. At lower starting soil concentrations (0.025 - 0.05 ppm in soil), average half-life was 14 days (5 US, 3 European soils). At a higher starting concentration of 1 ppm in soil, average half life was 88 days (3 European soils). At the higher concentration of 2.5 ppm in soil, average half-life was 572 days (5 US soils).

The degradation of clopyralid under actual field conditions agrees well with laboratory degradation observations. At 120-250 g ae/ha, the average field half-life at 20 sites globally was 25 days with a range of 8 to 66 days. Observations in laboratory environmental fate studies (application rate, moisture, temperature) have been confirmed in field studies. At 750 g ae/ha, and in either cold or dry conditions, average half-life was 83 days; whereas, at 120-280 g ae/ha in mid-US and European latitudes, average field half-life was 20 days. Downward movement through the soil profile was generally confined to the upper 18 inches of the soil profile.

Clopyralid is soluble in water, dissociating rapidly to the anionic form with its associated negative charge. It has low volatility and is not susceptible to breakdown by sunlight and hydrolysis. Binding to organic matter (sorptivity, K_{oc}) increases over time and ranges from 0.4 to 29.8 mL/g. Based solely on physical and chemical characteristics such as acidity, water solubility and stability to hydrolysis and photolysis, clopyralid has potential for downward movement through the soil profile. However, the behavior of the compound under field conditions demonstrates fairly rapid degradation and limited downward movement.

Because preliminary assessments based on physical/chemical properties indicate a potential for downward movement, lysimeter studies were conducted using clopyralid. In an early (1977) US study, undisturbed soil columns (lysimeters), 8 inches in diameter and 3 feet deep, were treated with 950 g ae/ha under actual field conditions. Residues of clopyralid in soil and soil-water (leachate) were collected in the closed system. The average depth of movement for the majority of clopyralid (center of mass) was 11 inches, and no detectable residues were observed in the leachate during the 9-week test period.

In a 1991 European study, lysimeters, 1 - 3 ft. in diameter and 3 ft. deep containing either degraded loess or silty sand soil, were treated with 120 and 240 g ae/ha of clopyralid under actual field conditions. The average center of mass was 12 inches. The amount of ^{14}C in leachate accumulated over 2 years in the degraded loess and silty sand lysimeters, was only 0.6% and 0.3% of applied, respectively. The leachate concentrations of ^{14}C-labeled clopyralid in degraded loess and silty sand throughout the first 10-16 months of the study ranged from 0.002-0.14 μg/L (ppb) and 0.003-0.02 ppb, respectively. A more recent (1994) European lysimeter study with silty sand lysimeters treated with 120 g ae/ha revealed a 2-year cumulative clopyralid leachate of only 0.1% of applied (0.04 ppb). These studies demonstrate that in lysimeter test systems, under actual field environmental conditions, clopyralid rapidly dissipates. Also, the very low levels observed in leachate demonstrate that there is very little potential for clopyralid to leach through soil and contaminate ground water.

Computer modeling (EPA's PRZM) was used to assess the dissipation and movement of clopyralid in five highly permeable soils, representative of rangeland conditions in Texas. After the model was validated, runs were conducted using higher than normal rainfall events (1 in 10 yr. occurrences), and an application rate of 560 g ae/ha. Predictions demonstrated that maximum depth of residues was 18-inches, 73 days after application in a highly permeable fine sand, with no residue detections throughout the entire profile of all soils by 6 months after application.

Field dissipation studies, lysimeter studies, and validated computer model simulations demonstrate, that under typical use patterns, potential for downward movement of clopyralid through the soil profile is not as high as simple physical and chemical characteristics would predict.

4.3 Fate in Aquatic Environments

Although clopyralid resists hydrolysis and photolysis in sterile water at pH 7, dissipation has been demonstrated in actual pond water and sediment systems. In southern Ontario, clopyralid was applied at 20 and 200 g ae/ha directly to the surface of intact columns of water and sediment in an actual pond (limnochorrals). The average field half-life in the water was 9 days, and no detections were observed in the sediment, suggesting some degree of microbial degradation. In another limnochorral study in a colder climate (Alberta), the average field half-life in water was 22 days, and residues in sediment declined from 29 ppb to 7 ppb in 84 days (half-life = 40 days). Hence, there is evidence that clopyralid dissipates in aquatic environments.

Surface water run-off

As with most herbicides, run-off of clopyralid is most likely to occur as a result of heavy rainfall immediately after application. In a 1985 Australia field study, clopyralid was monitored in streamwater (adjacent to the treatment area and 13 km downstream) after a helicopter application of 1.0 kg ae/ha to a 56-ha pine tree plantation. A 20- to 90-m-wide vegetated buffer strip (native and improved pasture) separated the treatment area from the stream. Seven rainfall events totaling 5.6 inches occurred during the first 19 days after treatment, including 3 inches within 3 days. During that time period, the highest clopyralid concentration in streamwater (0.017 mg/L) was observed at the adjacent location 3.5 hours after the first rainfall event, 35 hours after application. Clopyralid concentrations at the adjacent location declined to 0.003 mg/L over the next 12 hours. The highest concentration at the 13-km-downstream location was 0.001 mg/L, observed in association with the third rainfall event, 60 hours after application. These concentrations were well below the maximum allowable residue limit of 1.0 mg/L in potable water, as recommended by Australia's National Health and Medical Research Council. During run-off events, after leaving the edge of a treated field, residues in surface water become diluted. Also, the aquatic dissipation half-life (9 and 22 days, as noted above) of clopyralid indicates that surface water residues are not persistent.

Potential to bioaccumulate

The potential for clopyralid to bioaccumulate in or on aquatic organisms is low based on the low octanol/water partitioning coefficient (log K_{ow} = -2.63), a measurement simulating water-to-fish partitioning. The Bioconcentration Factor (BCF), is calculated from the equation:

$$\log BCF = 0.76 \log K_{ow} - 0.23$$

Based on the low octanol/water partitioning coefficients, the BCF values are 0.01 to 0.42, indicating a very low potential to bioaccumulate in or on aquatic organisms.

5 CLOPYRALID RESIDUES IN FOOD

5.1 Analytical Methods

Analytical methods have been developed for the determination of clopyralid in support of crop tolerances and environmental dissipation studies. Examples of matrices for which methods are available include sugar beets, corn, soil and animal tissues as well as associated processed fractions of sugar beets and corn. These methods utilize either GC with electron capture detection or mass selective detection dependent upon method limit of quantitation (LOQ) and detection (LOD) levels. Limits of quantitation range from 50 ng/g (50 ppb) for sugar beets and corn to 5 ng/g (5 ppb) in soil. A method for determination of clopyralid in water is available with limits of detection down to 0.05 ppb.

5.2 Residues in Plants

The amount of residue on plants treated with clopyralid varies by species, application timing, period after application, and environmental conditions. The only residue of significance is clopyralid. Residue concentration within plants declines with time, probably as the result of a dilution effect due to plant growth rather than degradation.

Residues in sugar beets (roots and leaves) treated at 0.25 lb ae/A (280 g/ha) have not exceeded 1 ppm at preharvest intervals (PHIs) of 85-90 days. Residues do not concentrate in pulp or sugar, but have a concentration factor of 8.1 in molasses.

Residues in field corn, sweet corn, and popcorn grain, forage, and fodder treated at 0.25 lb ae/A have not exceeded 1 ppm in grain, 3 ppm in forage, and 9 ppm in fodder. Residues do not concentrate in the corn milling products of starch, flour, meal, crude or refined oil, and have only slight concentration factors of 1.1 in grits and grain dust. Cannery waste from sweet corn processing contains no detectable residues of clopyralid.

Wheat, barley, and oats treated at 0.125 lb ae/A (140 g/ha) contained residues of clopyralid that did not exceed 3 ppm in grain or 9 ppm in forage and straw. Residues do not concentrate in flour but do concentrate to some extent in the other milled fractions of wheat and barley. In Canada, the maximum rate of clopyralid on cereal grains is 300 g/ha and requires a Maximum Residue Limit (MRL) of 2 ppm in whole grain and 7 ppm in milled fractions of cereal grains, excluding flour.

Grass treated at 0.5 lb ae/acre, (560 g/ha), the maximum use rate for rangeland and permanent grass pastures, contained residues of clopyralid of 23-86 ppm at 0 days after treatment (DAT) while residues in hay were 32-225 ppm. Residues declined steadily for 42 days. Half-lives calculated for clopyralid residues were 7 and 8 days for grass and hay, respectively.

Residues of clopyralid in mint treated at 0.25 lb ae/acre (fall) followed by 0.125 lb ae/acre (spring) were less than 3 ppm in foliage. No residue was detected in mint oil. Multiple applications of clopyralid to growing asparagus at 0.25 lb ae/acre resulted in residues that did not exceed 1 ppm.

In Canada, residues in strawberries and flax (whole seed) at harvest following applications of clopyralid did not exceed 1 and 0.2 ppm respectively.

5.3 Residues in Rotational Crops

Because of the decline pattern of clopyralid residues in the soil, the representative confined rotational crops were planted at 10½ months after clopyralid residues were aged in the soil. The total radioactive residues in the tested rotational crops were below

0.01 ppm. Since levels of clopyralid were well below the 0.01 ppm, rotational crop tolerances are not required when using the 10½ month plant-back interval.

5.4 Residues in Animals

Metabolism studies conducted in ruminants and poultry found that clopyralid was rapidly excreted primarily unchanged in the urine with low residues found in the tissues. Magnitude of residue studies verified these results. When cattle, chickens, and swine were dosed with clopyralid, the highest residues were found in kidney tissue rather than liver, muscle or fat. Lowest residues were found in milk and eggs. There was no tendency for residues to accumulate in the fat tissues.

5.5 Frozen Storage Stability

Clopyralid residues have been shown to be stable in a variety of crops stored frozen for 4 years.

5.6 Residue Tolerances - US

US Tolerances are established for residues of clopyralid in or on the following raw and processed agricultural commodities:

Table 2. US Tolerances for clopyralid

Commodity	**Parts per million**
Asparagus	1.0
Barley, forage	9.0
Barley, grain	3.0
Barley, straw	9.0
Barley, milled fractions (except flour)	12.0
Field corn, grain	1.0
Field corn, fodder	10.0
Field corn, forage	3.0
Field corn, milled fractions	1.5
Cattle, fat	1.0
Cattle, kidney	12.0
Cattle, meat	1.0
Cattle, mbyp (except kidney)	1.0
Eggs	0.1
Goats, fat	1.0
Goats, kidney	12.0
Goats, meat	1.0
Goats, mbyp (except kidney)	1.0
Grasses, forage and hay	500.0
Hogs, fat	0.2
Hogs, meat	0.2
Hogs, mbyp	0.2
Horses, fat	1.0
Horses, kidney	12.0

Horses, meat	1.0
Horses, mbyp (except kidney)	1.0
Commodity	**Parts per million**
Milk	0.1
Mint hay	3.0
Oats, forage	9.0
Oats, grain	3.0
Oats, straw	9.0
Oats, milled fractions (except flour)	12.0
Poultry, fat	0.2
Poultry, meat	0.2
Poultry, mbyp	0.2
Sheep, fat	1.0
Sheep, kidney	12.0
Sheep, meat	1.0
Sheep, mbyp (except kidney)	1.0
Sugar beet roots	1.0*
Sugar beet tops	1.0*
Sugar Beet, molasses	8.0*
Wheat, forage	9.0
Wheat, grain	3.0
Wheat, straw	9.0
Wheat, milled fractions (except flour)	12.0

mbyp is meat by-products
*Tolerance revisions requested by and in review at US EPA

6 ANIMAL AND PLANT METABOLISM

In rats, nearly all of the radiolabeled clopyralid, given as a 5 mg/kg intravenous or a 150 mg/kg oral dose, was rapidly absorbed and excreted from the body, with the majority being rapidly excreted in the urine (half-life of 3 hours) during the first 24 hours (79 to 96% of the dose). Only clopyralid was recovered from the urine; no metabolites were apparent. The predominant fecal radioactive residue was also clopyralid. There were no apparent differences between doses with respect to tissue distribution, except that the carcass residues were higher at the high dose. Multiple treatments did not change tissue distribution or elimination patterns. At 72 hours after clopyralid administration, tissue residues were low, with values less than 0.01% of the total dose in all cases. There were no apparent differences between sexes with respect to tissue residues, carcass residues or excretion routes and rates. The data indicate that clopyralid was well absorbed and rapidly excreted in the urine as unchanged clopyralid. There were no significant differences in the absorption, disposition or metabolism of clopyralid based on sex, dose or prior exposure.

A metabolism study with radiolabeled clopyralid administered to laying hens at an exaggerated rate equivalent to 100 ppm in feed also demonstrated that clopyralid was not metabolized. The clopyralid was recovered unchanged in the droppings indicating that the chicken does not metabolize or otherwise degrade the compound. Residues rapidly reached plateaus of 0.15 ppm in egg white and 0.02 ppm in egg yolk and were shown to be only unchanged clopyralid. Samples of tissue taken after 5 and 6 days of dosing showed residues ranging from 0.02 ppm in fat to 1 ppm in kidney. Only unchanged clopyralid was found in kidney, liver and leg muscle tissues.

Two goats were fed radiolabeled clopyralid at rates equivalent to 230 and 69 ppm in feed for 7 days. Again, essentially all of the chemical was rapidly excreted primarily in the urine. The radioactivity recovered in the urine was unchanged clopyralid (97%) and a minor (3%) metabolite identified as the conjugate of clopyralid with the amino acid glycine. Milk and tissues contained 0.04% and less than 1% of the dose, respectively. The milk residue averaged approximately 0.03 ppm and was shown to consist of approximately equal amounts of clopyralid and its glycine conjugate. The residues in liver (approx. 0.04 ppm) and kidney (approx. 0.6 ppm) tissues were shown to be unchanged clopyralid. Residues in muscle and fat were too low (less than 0.02 ppm) to isolate.

A series of studies with clopyralid applied to pasture grass, corn, spring wheat and cabbage indicated that clopyralid did not significantly metabolize or otherwise degrade in those plants.

7 TOXICITY OF THE TECHNICAL ACTIVE INGREDIENT

Clopyralid can be produced by two different manufacturing routes each delivering a slightly different ingredient profile. Both routes are approved by and are on file at the US EPA. The older method is commonly referred to as the "penta" process and the more recent method is called the "electrochemical" process. The resulting acute toxicology profile is very similar resulting in no changes in required precautionary label language. However, the data point values may differ slightly and are indicated below.

7.1 Acute Oral Toxicity -- Rat (Fischer 344) LD_{50}

Penta process:	male and female > 5000 mg/kg	
Electrochemical process:	males:	3738 mg/kg
	females:	2675 mg/kg

7.2 Acute Dermal Toxicity -- Rabbit (New Zealand White) LD_{50}

Penta process: male and female > 2000 mg/kg
Electrochemical process: male and female > 2000 mg/kg

7.3 Acute Inhalation Toxicity -- Rat (Fischer 344) LC_{50} (4-hour "nose only")

Penta process: male and female 1.0 mg/L of air (highest attainable concentration)
Electrochemical process: male and female 0.38 mg/L of air (highest attainable concentration)

7.4 Skin Irritation -- Rabbit (New Zealand White)

Penta process: not an irritant
Electrochemical process: not an irritant

7.5 Eye Irritation -- Rabbit (New Zealand White)

Penta and Electrochemical process:

Slight to marked redness and chemosis were present after treatment with undiluted material. Reddening of the iris and corneal opacity were observed in all animals. Signs of irritation were present in all animals 21 days post-treatment.

7.6 Skin Sensitization -- Hartley Albino Guinea Pig

Penta process: 10% solution negative
Electrochemical process: 10% solution negative

7.7 Sub-chronic Toxicity

Rat (90-day oral):

Fischer 344 rat were fed diets containing clopyralid at doses of 5, 15, 50 or 150 mg/kg/day with no adverse effects attributed to treatment.

In a second study, Fischer 344 rats were fed diets containing clopyralid at doses of 300, 1500 and 2500 mg/kg/day. Effects at the highest doses were decreased food consumption accompanied by decreased body weights and weight gains in both males and females. Slightly increased mean relative liver and kidney weights were noted in males of all 3 doses and in females at the top 2 doses. Because there were no other effects, the kidney and liver weight effects were judged as being adaptive rather than directly toxic. The no-observed-adverse effect level (NOAEL) was 1500 mg/kg/day for males and females. The no-observed-effect level (NOEL) was 300 mg/kg/day for females.

Mouse (90-day oral):

$B_6C_3F_1$ mice were fed on diets containing clopyralid at doses of 200, 750, 2000 or 5000 mg/kg/day. A slight decrease in body weight occurred at the high dose in both sexes. The liver was identified as target organ based on slight increases in liver weights and minimal microscopic alterations at the higher dose levels. The liver changes were considered to be reversible and adaptive. The NOEL for males was 2000 mg/kg/day and for females was 750 mg/kg/day.

Dog (180-day oral):

Beagle dogs were fed diets containing clopyralid at doses of 15, 50 or 150 mg/kg/day; there were no adverse effects. In a second dietary study, dogs also were fed diets containing clopyralid at doses of 15, 50 or 150 mg/kg/day; the only effect was an increase in the mean relative liver weight in females at the 150 mg/kg/day.

Dog (one-year oral):

Dietary administration of clopyralid to beagles at doses of 100, 320 or 1000 mg/kg/day for 1 year resulted in minimal effects at 320 and 1000 mg/kg/day. Red blood cell parameters were reduced at these levels, but were within a normal range for dogs. Serum proteins also were slightly reduced at these mid- and high-dose levels. Relative liver weights were increased in mid- and high-dose dogs. The NOEL in this study was 100 mg/kg/day.

Rabbit (21-day dermal):

Clopyralid was applied by repeated dermal application to New Zealand White rabbits at dose levels up to 1000 mg/kg/day. Treatment produced no systemic effects.

7.8 Chronic Toxicity

Rat (two-year oral):

In a chronic toxicity and oncogenicity study, Sprague-Dawley rats were fed diets containing clopyralid at doses of 5, 15, 50 or 150 mg/kg/day. With a NOEL of 50 mg/kg/day, the only effect was a trend toward a decreased body weight of female rats receiving the 150 mg/kg/day dose. In a second study clopyralid was fed to Fischer 344 rats in the diet at doses of 15, 150 or 1500 mg/kg/day. The effects were confined almost entirely to the 1500 mg/kg/day dose groups and included slightly decreased food consumption and body weights, slightly increased liver and kidney weights and (non-tumorigenic) macroscopic and microscopic changes in the stomach (also seen in the stomachs of a few of the rats dosed at 150 mg/kg/day). No tumorigenic response was present and the NOEL for this study was 15 mg/kg/day. Overall, the most appropriate NOEL for both studies is 50 mg/kg/day.

Mouse (two-year oral):

$B_6C_3F_1$ mice were maintained for 2 years on diets formulated to provide targeted dose levels of 100, 500 or 2000 mg/kg/day. The only evidence of toxicity was body weight depression in males dosed at 2000 mg/kg/day. There was no evidence of tumorigenic response at any dose level.

7.9 Reproductive Toxicity

Rat Teratology:

Clopyralid was not teratogenic in a study using Fischer 344 rats administered daily average doses of clopyralid at 15, 75 or 250 mg/kg/day on days 6-15 of gestation. Maternal toxicity, as evidenced by decreased body weight gain, was observed among pregnant rats in the 250 mg/kg/day group. The maternal NOEL was 75 mg/kg/day and the developmental NOEL was >250 mg/kg/day (a maternally toxic dose).

Rabbit Teratology:

New Zealand White rabbits were dosed with 110 or 250 mg/kg/day of clopyralid on days 6-18 of gestation. No evidence of maternal toxicity or teratogenic effects was present. In a second teratology study, pregnant New Zealand White rabbits were given clopyralid at dose levels of 0, 50, 110 or 250 mg/kg/day on days 7-19 of gestation. Several maternal effects were reported at 250 mg/kg/day including mortality, morbidity, weight loss and clinical signs of labored breathing. Developmental effects were seen in the litters of some animals given 250 mg/kg/day: these effects were attributed to severe maternal toxicity. No maternal or developmental effects were seen at 50 or 110 mg/kg/day.

Rat Multigeneration:

In a two-generation reproductive study, Fischer 344 rats were fed clopyralid in the diet at targeted dose levels of 150, 500 or 1500 mg/kg/day over two successive generations with two litters per generation. A slight reduction in pup body weight during lactation and an increase in liver weights in 1500 mg/kg/day F1a and F1b weanlings were considered treatment related. There were no adverse effects on mating, fertility or reproductive performance of either parental generation or on the morphology, growth or viability of their offspring; thus, the reproductive NOEL was >1500 mg/kg/day.

7.10 Genotoxicity

a) Ames bacterial mutagenicity assay (with and without exogenous metabolic activation): **Negative**
b) Host-Mediated assay: **Negative**
c) *In vivo* cytogenetic test, rat: **Negative**
d) *In vivo* cytogenetic test, mouse: **Negative**
e) *In vivo* dominant lethal test, rat: **Negative**
f) *In vitro* unscheduled DNA synthesis assay in primary rat hepatocyte cultures: **Negative**
g) *In vitro* mammalian cell gene mutations assay in Chinese hamster ovary cell cultures (with and without exogenous metabolic activation): **Negative**

7.11 Neurotoxicity

The molecular structure of clopyralid does not suggest that any neurotoxicity is likely to occur as a result of exposure to the compound. There is no evidence from the battery of toxicity studies with clopyralid to suggest that it is likely to cause a neurotoxic effect.

8 HUMAN EXPOSURE, AND RISK INFORMATION

8.1 Consumer Exposure and Risk

Clopyralid is registered for use in the US and Canada on a number of crops including corn, sugarbeets, wheat, barley, and oats. Tolerances exist on commodities of these crops, and on meat, milk, poultry and eggs.

An exposure analysis system was used to estimate dietary exposure to US populations resulting from the use of clopyralid. This program is similar to the Dietary Residue Evaluation System (DRES) that is used by the US EPA. It estimates the percent of the reference dose (RfD) that is utilized by the input residue values. The RfD for clopyralid is established by the EPA at 0.5 mg/kg body weight (BW)/day based on a NOEL of 50 mg/kg BW/day from the 2-year feeding study in rats and an uncertainty factor of 100. The residue data that is input in a Tier 1 assessment are the existing raw agricultural commodity tolerances. Tolerance level residues are used in the dietary risk analysis for all commodities. No allowance is made in a Tier 1 assessment for the percent of the acreage treated, that is, it assumes 100% of the crop is treated: so the analysis is a very conservative one and is often termed “worst case”.

The total Tier 1 dietary exposure, assuming all existing, temporary, and proposed tolerances for residues of clopyralid, to the general population in the United States is calculated to be 0.010 mg/kgBW/day, which is 2% of the RfD of 0.5 mg/kgBW/day. The most sensitive population subgroup is Children (1-6 years). The total exposure for this subgroup is calculated to be 0.024 mg/kgBW/day, which accounts for 4.9% of the RfD. No other subgroup exceeds 3.2% of the RfD. The total exposure for the subgroup, females (13+/pregnant/not nursing), consumes only 1.6% of the RfD, which is less than that for the general population. Hence, existing and proposed uses of clopyralid on various agricultural crops do not present a significant dietary hazard to any population subgroup in the US.

8.2 Occupational Exposure and Risk

An occupational exposure assessment has not been needed because of the low order of toxicity of clopyralid and because it is not regarded as an oncogen, teratogen, mutagen or reproductive toxicant.

8.3 Aggregate Exposure and Risk

When assessing aggregate non-occupational risks to the US population, only exposures attributed to re-entry upon treated turf and dietary intake are considered. Potential exposures to children and adults re-entering turf treated with clopyralid were estimated by using data derived from a re-entry study previously conducted by Dow AgroSciences with a surrogate compound. Based upon these results, clopyralid exposures were determined by simply adjusting the estimated absorbed dose from this study to reflect chemical-specific differences in the percutaneous absorption and application rate of clopyralid and the surrogate compound.

As a result, estimated clopyralid exposures for a young child or infant were calculated to be 0.048 mg/kgBW/day. Similarly, exposures were calculated for sub-populations representing both the general US and pregnant female populations. Consistent with the previous calculation, exposures to these populations were extrapolated from the turf re-entry study performed with a surrogate compound. Based upon this calculation, exposures resulting from contact with residues on treated lawns are approximately 0.034 mg/kgBW/day for members of either the general US population or pregnant females.

The labeled uses of clopyralid should not add any additional dietary exposure to humans due to drinking water. Field studies using lysimeters have shown that residues of clopyralid are not likely to be found in groundwater. Studies monitoring spray drift and runoff have shown that clopyralid readily dissipates in water. If these rare events should occur, they would result in insignificant residue intake. Therefore, dietary exposure calculations for clopyralid when including residues from drinking water are not significantly increased.

Aggregate or total exposures were determined by summing the likely exposures resulting from turf re-entry and ingestion of water and food commodities containing clopyralid. Based upon the preceding DRES analysis and turf re-entry exposure evaluations, calculated aggregate exposures were 0.072 mg/kgBW/day, 0.042 mg/kgBW/day and 0.044 mg/kgBW/day for the child, pregnant female and general populations, respectively. These levels correspond to levels that are approximately 694X, 1190X, and 1136X less than the lowest toxicological no-observed-effect level (NOEL) of 50 mg/kgBW/day following chronic exposures.

Based on these assessments, it is unlikely that aggregate exposures attributed to the uses of clopyralid will adversely affect either young children, pregnant women, members of the general population, or any other population subgroup.

9 WILDLIFE AND OTHER NON-TARGET SPECIES

9.1 General Summary

Clopyralid and clopyralid containing products have a very favorable ecotoxicology profile. Laboratory studies indicate low toxicity to birds, fish, terrestrial and aquatic invertebrates, soil microorganisms and algae. Consequently, based on its low toxicity and estimates of expected residues in or on vegetation, soil and water, clopyralid poses insignificant risk to fish and wildlife. However, as a herbicide, it is not unexpected that clopyralid exhibits toxicity to some non-target terrestrial plant species. The following is a summary of the ecotoxicological properties of clopyralid. The qualitative statements characterizing toxicity are standard US EPA terminology.

9.2 Avian Species

Clopyralid technical is slightly toxic to the mallard duck *(Anas platyrhynchos*) and practically non-toxic to the bobwhite quail *(Colinus virginianus*) when administered as a single oral dose. In addition, it is practically non-toxic when fed to both the mallard and bobwhite in avian food. A one-generation reproductive study with clopyralid in the mallard showed no effects on reproductive parameters (eggs laid, eggs cracked, viable first generation embryos, and 14-day survival of offspring), body weight, or feed consumption. The NOEC for the mallard was 1000 ppm in the food. Formulations containing clopyralid are also characterized as practically non-toxic to avian species. Oral LD_{50} and dietary LC_{50} values range from >2000 mg/kg for the mallard to >5620 ppm in feed for the mallard and bobwhite.

Study	Species	Value
Clopyralid technical		
Acute Oral LD_{50} (mg/kg body weight)	Mallard Duck	1465
	Bobwhite Quail	>2000
5-day Dietary LC_{50} (ppm in food)	Mallard Duck	>4640
	Bobwhite Quail	>4640
One-generation Reproductive NOEC (ppm in food)	Mallard Duck	1000
Clopyralid (as monoethanolamine salt 35% ae)		
Acute Oral LD_{50} (mg a.i./kg body weight)	Mallard Duck	> 2000
5-day Dietary LC_{50} (ppm a.i. in food)	Mallard Duck	>5620
	Bobwhite Quail	>5620

9.3 Aquatic Species

Clopyralid technical is practically non-toxic to fish and invertebrate species. LC_{50} values range from 103.5 mg/L for the rainbow trout *(Oncorhynchus mykiss)* to 232 mg/L for *Daphnia magna*. Formulations containing clopyralid are also non-toxic to fish and invertebrates with LC_{50} values ranging from 1100 mg/L for *D. magna* to 4700 mg/L for the Bluegill sunfish *(Lepomis macrochirus)*.

Study	Species	Value
Clopyralid technical		
Acute 96-hour LC_{50} (mg/L)	Rainbow Trout	103
	Bluegill Sunfish	125
Acute 48-hour LC_{50} (mg/L)	*Daphnia magna*	232
Clopyralid (as monoethanolamine salt 35% ae)		
Acute 96-hour LC_{50} (mg/L)	Rainbow Trout	2000
	Fathead Minnow	>2900
	Bluegill Sunfish	4700
Acute 48-hour LC_{50} (mg/L)	*Daphnia magna*	1100
Clopyralid (100 g/L as monoethanolamine salt)		
Acute 96-hour LC_{50} (mg/L)	Rainbow Trout	500
Prolonged 21-day LC_{50} (mg/L)	Rainbow Trout	321
Prolonged 21-day NOEC (mg/L)	Rainbow Trout	125
Acute 48-hour EC_{50} (mg/L)	*Daphnia magna*	1029
Reproduction Test NOEC (mg/L)	*Daphnia magna*	66

9.4 Soil Microorganisms

The effect of clopyralid on soil microorganisms was evaluated by assessing glucose-stimulated respiration and nitrogen mineralization in different soils at varying test concentrations. Test concentrations of 1 and 10 ppm clopyralid technical and five different soil types were used to assess potential effects upon nitrification, nitrogen fixation and respiration. The results showed that at 1 and 10 ppm clopyralid, there is no effect on nitrification, nitrogen fixation or degradation of carbonaceous material by soil microbes. Under normal use conditions, it is not expected that clopyralid would have an effect on soil microbial functions.

In a separate study, clopyralid was tested at 1X (91.6 μL/kg soil) and 5X (8.0 μL/kg soil) field concentrations using a sandy soil and a loamy soil. The effects on long-term respiration were short-lived, with the experiment terminated after 42 days of exposure. In both soils tested, nitrification was very rapid, being essentially complete after two weeks. Based on studies conducted to date, clopyralid does not appear to have lasting effects on soil respiration or nitrification.

9.5 Non-Target Aquatic Plants

Clopyralid is slightly toxic to duckweed (*Lemna gibba*) with an EC_{50} of 89 mg/L and a NOEC of 7.2 mg/L, and is moderately toxic to green algae (*Selenastrum capricornutum*) with an EC_{50} of 6.9 mg/L.

Study	Species	Value
Clopyralid technical		
Acute 5-day EC_{50} (mg/L)	Green Alga	6.9
Acute 14-day EC_{50} (mg/L)	Vascular Plant - Duckweed	89
Clopyralid (100 g/L as monoethanolamine salt)		
Acute 72-hour EC_{50} (mg/L)	Green Alga	449
Clopyralid (200 g/L as monoethanolamine salt)		
Acute 5-day EC_{50} (mg/L)	Green Alga	61

9.6 Other Non-Target Organisms

Clopyralid technical and its formulations are practically non-toxic to beneficial non-target terrestrial organisms. Results showed that technical clopyralid and formulations containing clopyralid are practically non-toxic to the earthworm *(Eisenia foetida*) and the honey bee *(Apis mellifera*). Studies also showed that clopyralid and its formulations have no effect upon beneficial arthropods, such as the wolf spider *(Paradosa spp.),* the carabid beetle *(Poecilus cupreus)* and the rove beetle *(Aleochara bilineata).* No effects on survival, feeding behavior, or reproductive success (rove beetle) were noted at a dose level of 1.2 L/ha, the highest concentration tested.

Study	Species	Value
Clopyralid technical		
Acute 14-day Static LC_{50} (mg/kg of soil)	Earthworm	>1000
Acute 48-hour Contact LD_{50} (µg a.i./bee)	Honey Bee	>100

9.7 Non-Target Terrestrial Plants

Laboratory studies were conducted to measure effects on growth of terrestrial plants. No-Observed-Effect Concentrations (NOEC) were determined for 10 test species.

Test Species	Topical Treatment NOEC (lb/A)	Soil Treatment NOEC (lb/A)
Corn	>0.5	0.5
Soybeans	0.0005	<0.0063*
Radish	>0.5	0.5
Tomato	0.0005	0.031*
Snap Bean	0.0005	<0.0031*

Canola	>0.5	0.5
Sunflower	0.0005	0.031*
Barley	>0.5	0.5
Wheat	0.05	0.5
Onion	0.05	0.13

* Phytotoxic symptoms on growth at these NOECs

9.8 Environmental Risk

As mentioned, according to EPA methodology used to identify potential environmental risk, clopyralid has little likelihood of negatively impacting birds, mammals, fish, and aquatic and terrestrial invertebrates. There may be potential risk to terrestrial plants, which is not unexpected since clopyralid was selected for its herbicidal properties.

For risk to terrestrial plant life, a "worst case" Tier 1 exposure assessment as conducted by the US EPA was used to assess potential risk to plants. This analysis suggests potential impact can occur to non-target plants near the edge of treatment areas since the no-effect endpoints for soybean, tomato, snapbean, and sunflower exceed estimated worst case concentrations. Care should be taken when applying this and any pesticide to prevent drift and run off.

10 CLOPYRALID AND ITS METABOLITES

Residues of clopyralid in plants occur as the unmetabolized parent acid. In animals, clopyralid is rapidly excreted as the parent acid. No metabolites were found in tissues of rats, hens, or goats. One minor metabolite (3%) was identified in goat urine as a glycine conjugate of clopyralid. Goat milk contained approximately equal amounts of clopyralid and its glycine conjugate. A single hydrolysis product (<3% of applied clopyralid) was found in the aerobic soil metabolism study. In soil, the only significant metabolite is CO_2.

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