

Environmental Fate of Propyzamide

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INTRODUCTION

Propyzamide was first registered as a pesticide in the United States in 1972 to use as a selective, systemic, pre- and post-emergence herbicide to control against grasses and weeds in food and feed crops (Kearney and Kaufman 1976; US EPA 1994). Propyzamide is a soil-active, systemic organochlorine herbicide with a mode of action that interferes with cell division (mitosis) in the root systems of select annual grasses and broadleaf weeds by disrupting microtubule formation (Dow 2012; Sedbrook et al. 2004; Tomlin 2000; US EPA 1994). In California, products containing propyzamide are most commonly used for the production of artichoke, endive, lettuce, and radicchio (DPR 2016a). This report contains a review of propyzamide's chemical and physical properties, environmental fate, and specific uses and product formulations in California.

CHEMICAL DESCRIPTION

Propyzamide, also known as pronamide, is the common name for 3,5-dichloro-N-(1,1-dimethyl-2-propynyl) benzamide or N-(1,1-dimethyl propynyl)-3,5-dichloro benzamide (Figure 1). The compound is an odorless, off-white solid that is formulated as wettable powders, suspension concentrates, and water-dispersible granules (Dow 2012). It is relatively stable with an observed half-life of 13 – 57 days in artificial sunlight and can remain in solution for up to 28 days (pH 5 – 9, 20°C) with a loss of less than 10% (DPR 2009; Tomlin 2000). Table 1 summarizes the chemical and physical properties of propyzamide.

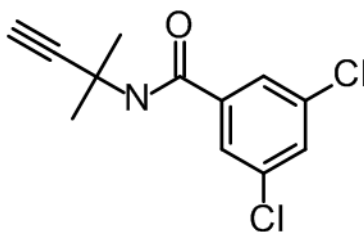


Figure 1. Structure of propyzamide.

Table 1. Chemical and physical properties of propyzamide.

Chemical Name	3,5-dichloro-N-(1,1-dimethyl-2-propynyl) benzamide or
Common Name	Propyzamide, Pronamide
CAS Registry Number	23950-58-5
Physical State	Crystalline Solid
Molecular Formula	C ₁₂ H ₁₁ Cl ₂ NO
Molecular Weight	256.13 g/mol
Chemical Family	Benzamide
Melting Point	155 - 156 °C
Vapor Pressure	8.5 x 10 ⁻⁵ mmHg
Water Solubility	1.5 x 10 ⁻⁵ g/mL at 25 °C
Henry's Law Constant	9.77 x 10 ⁻⁹ atm m ³ mol ⁻¹ at 25 °C
Log Kow	2.63 - 3.20
Log Koc	2.95
Density	1.26 g/cm ³

*Dow Propyzamide (KERB) Info.pdf, The Pesticide Manual 12th Ed., Herbicide Handbook 6th Ed., Santa Cruz Biotechnologies catalogue, US EPA.

REGULATION

In 1979 the US EPA completed a Rebuttable Presumption Against Reregistration (RPAR) or Special Review on propyzamide that was based on an 18-month mouse carcinogenicity study by Fitzgerald et al. (1974) linking propyzamide to cancer in mice (US EPA 1994). The study concluded that mice given diets containing propyzamide showed a treatment-related increase in hepatocellular carcinomas. The US EPA concluded that the cancer risk presumption had not been rebutted, and that the uses of propyzamide posed unacceptable risks of cancer to certain exposed groups. After considering risks in relation to benefits of propyzamide use, the US EPA determined that these risks could be reduced by modifying the terms and conditions of registration for some uses (US EPA 1994).

As a direct result of the RPAR, new requirements for propyzamide were enacted, including: 1) end-use products containing 50% propyzamide were classified as restricted use; 2) protective clothing must be worn by personnel when mixing and applying wettable powder formulations; 3) water-soluble packaging for the wettable powders; and 4) decreased tolerance of pesticide residues on lettuce from 2 ppm to 1 ppm (US EPA 1994). Further chronic feeding/oncogenicity studies on mice linked exposure to propyzamide to liver carcinoma (US EPA 1993, 1994). These findings resulted in additional US EPA restrictions on propyzamide use and the eventual addition of the compound to California's Proposition 65 list of chemicals, which lists chemicals known to cause cancer or birth defects or other reproductive harm. (US EPA 1994; OEHHA 2015). In 2014, based on an evaluation of new carcinogenicity study data, US EPA reclassified propyzamide as "Not likely to be Carcinogenic to Humans" (US EPA 2014).

In 1986, US EPA issued a Registration Standard requiring additional generic data on propyzamide and issued a Data Call-In in 1990 requiring additional product chemistry, plant protection and environmental fate data (US EPA 1994). The regulatory conclusion of the Data Call-In was that use of all currently registered pesticide products containing propyzamide would not pose unreasonable risks or adverse effects to humans, provided they are used in accordance with approved labeling (US EPA 1994). The Food Quality Protection Act (FQPA) of 1996 mandated the registration review program for all pesticides distributed or sold in the United States. As part of this registration review program, US EPA issued a registration review on propyzamide in September of 2009 and subsequent Data Call-In. The registration review was expected to be completed in 2015 but a decision has yet to be made by US EPA (US EPA 2009a).

Under California state law, all pesticide products sold in the state must undergo evaluation and registration by the Department of Pesticide Regulation (DPR) before sale or use in California (DPR 2011). In California, as of April 2016, four products containing propyzamide from the Dow Chemical Company's Kerb line of herbicides and two products from Willowood USA's Pronamide line of herbicides are actively registered with DPR (DPR 2016b). Product applications are limited to soil by either ground or aerial methods. Table 2 summarizes the current active products containing propyzamide as an active ingredient (a.i.) in California.

Table 2. Summary of propyzamide-containing products as an active ingredient currently registered in California.

Product Name	% a.i.	Formulation	Methods of Application	Rate of Product Application (per acre)	Application Rate (a.i. pounds/acre)
Kerb 50W	50	Wettable Powder	Aerial, Ground	1 - 8 pounds	0.5 - 4
Kerb 50WP	50	Wettable Powder	Aerial, Ground	1 - 4 pounds	0.5 - 2
Kerb SC	35.6	Liquid Suspension	Aerial, Ground	1.25 - 9.5 pints	0.5 - 4
Kerb SC T&O	35.6	Liquid Suspension	Aerial, Ground	1.25 - 5 pints	0.5 - 2
Willowood Pronamide 3.3SC	35.6	Liquid Concentrate	Aerial, Ground	1.25 - 9.5 pints	0.5 - 4
Willowood Pronamide 50WSP	50	Wettable Powder	Aerial, Ground	1 - 8 pounds	0.5 - 4

USE PROFILE

Propyzamide is used in agricultural, industrial, and commercial applications for the control of a wide range of grasses and certain broadleaf weeds. Propyzamide can be used during the production of fruits and vegetables, forage crops, nursery crops (ornamentals and forestry crops) and turf grown for seed or sod on nonresidential sites (Dow AgroSciences 2007, 2009, 2012a,b; Willowood 20015a,b). In the state of California, propyzamide-containing products are applied to the soil at a rate of 0.5 - 4 pounds of a.i. per acre (typically 20 to 50 gallons of spray per acre) and primarily by ground application with sprayers (Table 2 and Figure 2) (DPR 2016a).

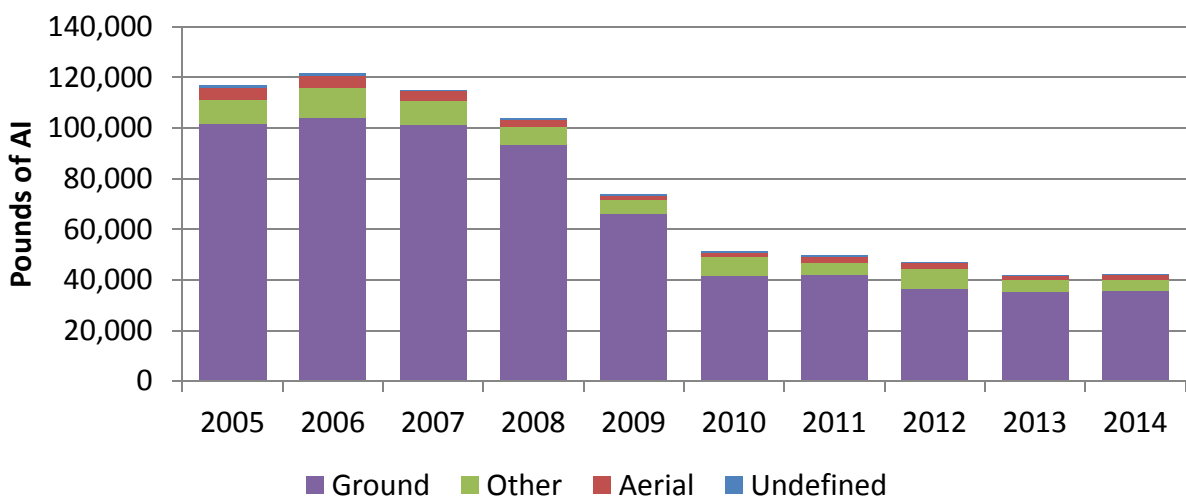


Figure 2. Comparison of application methods for propyzamide in California during 2005 – 2014 (DPR 2016a).

Domestically, it was estimated that approximately 76,000 pounds of propyzamide was applied throughout the United States during 2013 (USGS 2016). In California, use has dropped significantly over time (Figure 2), going from a peak reported use of 121,711 pounds of a.i. in 2006 to a reported use of 42,430 pounds a.i. statewide in 2014 (DPR 2016a). Monterey County consistently had the highest use from 2005 – 2014, representing 38.8% of total statewide use during this time period (Table 3).

Table 3. California counties ranked by total use of propyzamide during 2005 – 2014 (DPR 2016a).

County	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	Total	% Total
Monterey	43,431	49,083	50,249	46,766	36,550	17,640	14,842	12,156	12,699	13,120	296,537	38.8
Santa Barbara	18,299	16,225	17,224	16,225	14,840	12,139	11,622	11,375	10,870	11,440	140,258	18.4
Fresno	18,840	19,497	14,135	11,321	5,075	6,784	8,452	7,551	7,593	4,608	103,857	13.6
Imperial	11,892	14,140	12,336	11,331	7,172	7,911	8,262	10,231	5,424	7,309	96,008	12.6
San Luis Obispo	6,637	6,928	6,362	5,149	4,076	2,460	3,743	3,739	2,916	2,727	44,737	5.9
Remaining Counties	17,677	15,837	14,566	13,284	6,099	4,419	2,757	2,206	2,520	3,226	82,591	10.6
Total a.i. For Year	116,775	121,711	114,872	104,077	73,811	51,353	49,678	47,258	42,022	42,430	763,987	100.0

During 2005 – 2014, propyzamide was predominately used as an herbicide in the production of lettuce (head) crops with over 450,000 pounds of a.i. applied (Figure 3). Use for the production of lettuce (leaf) was the second largest use, with over 266,000 pounds of a.i. applied. The use of propyzamide on lettuce crops accounts for 94 percent of total use. Figure 4 displays propyzamide use spatially throughout California during 2005 – 2014. Most propyzamide applications occurred in the central coastal regions of California and the San Joaquin Valley for lettuce production.

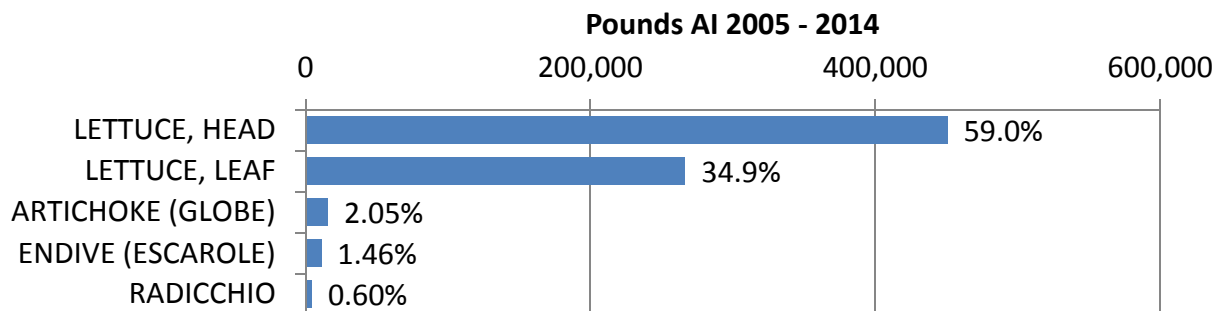


Figure 3. Reported use of propyzamide in California for the top 5 commodities during 2005 – 2014 (DPR 2016a).

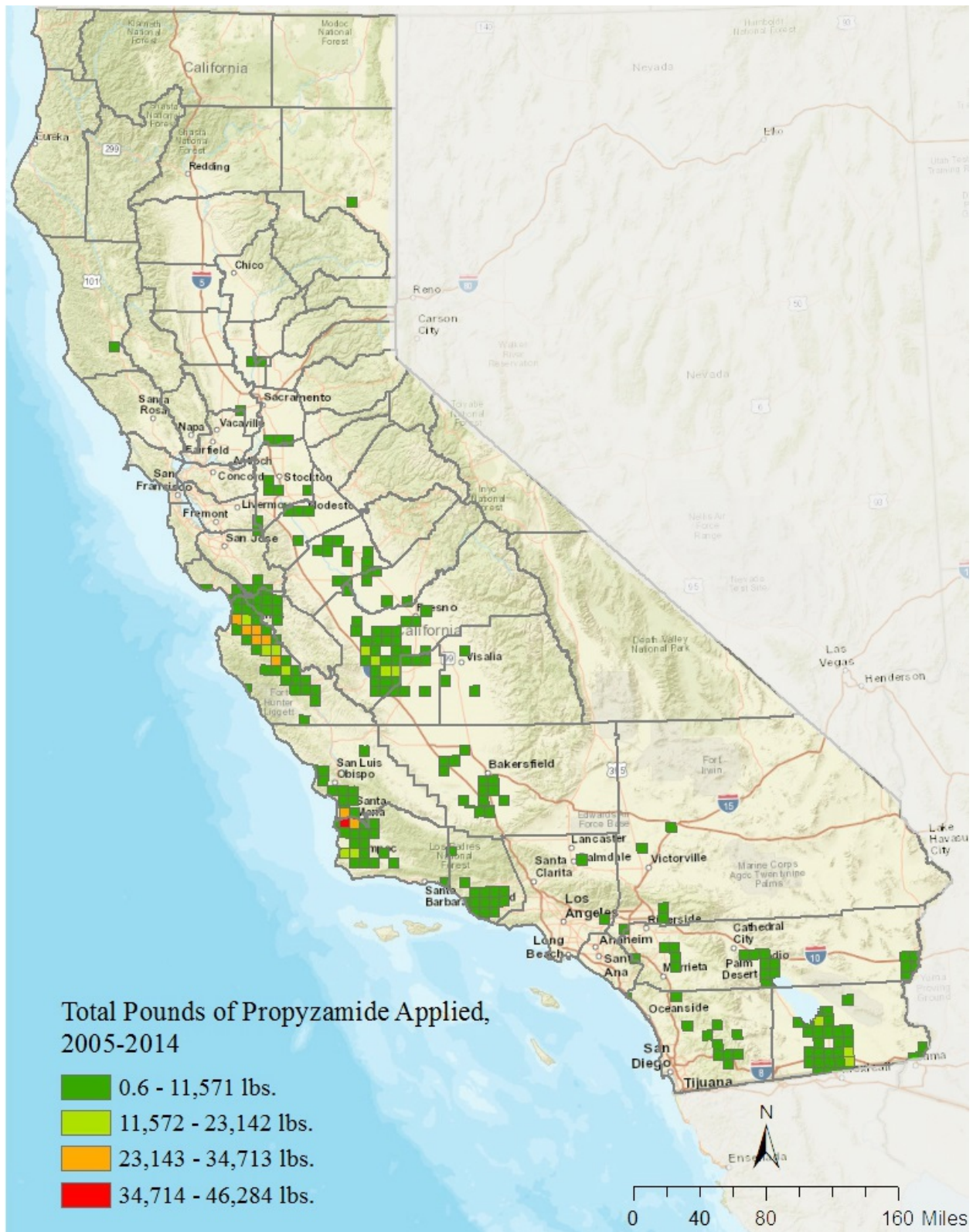


Figure 4. Use of propyzamide during 2005 – 2014 in California, data mapped by township as defined by the Public Land Survey System (DPR 2016a).

Figure 5 displays propyzamide use by crop in California from 2005 to 2014, usage was mostly steady for all crops except leaf lettuce, which by 2014 dropped to just 3% of its peak use during 2005 – 2008 due to the removal of the use for leaf lettuce from the labels in 2009 (US EPA 2009a).

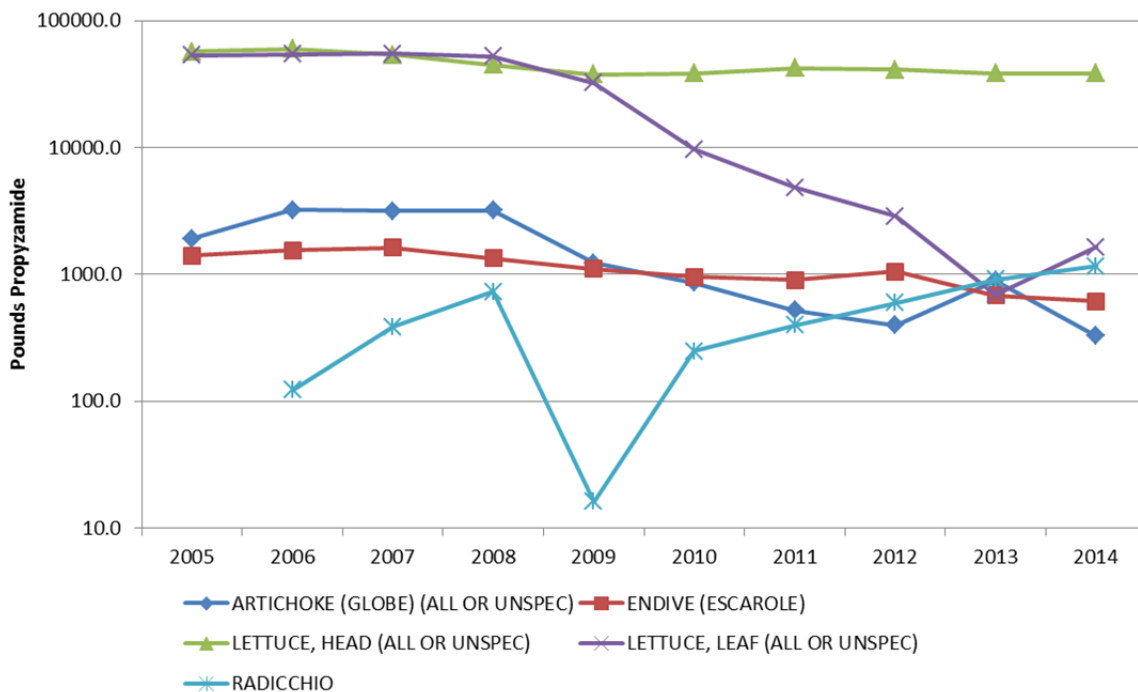


Figure 5. Propyzamide use (pounds) per top crop by year in California during 2005 – 2014, logarithmic scale (DPR 2016a).

Method of Application and Formulation

Propyzamide is formulated into products which are to be applied as a liquid (US EPA 2002). The products are sold as either wettable powders or as liquid suspensions and soluble concentrates to be mixed with water upon use. Product labels indicate that propyzamide-containing products can be applied directly to ground by spray, sprinklers, irrigation or chemigation; aerial applications are also permitted. It is typically applied as a broadcast or band application and watered in during late summer and early winter months (US EPA 2007; DPR 2016a). After application, entry to the treated site by workers is restricted for up to 24 hours (Dow AgroSciences 2007, 2009, 2012a,b; Willowood 2015a,b).

ENVIRONMENTAL FATE AND DEGRADATION IN AIR

Propyzamide has relatively low volatility (vapor pressure of 8.5×10^{-5} mmHg) and volatilization and major atmospheric transport is not expected to occur; however, possible minor transport mechanisms include spray drift and secondary drift of volatilized or soil-bound residues (US EPA 2008). Inhalation exposure to propyzamide is not expected after applications due to propyzamide's low vapor pressure and outdoor air dilution (US EPA 2002). In the atmosphere,

propyzamide may be directly photolyzed and will react with photochemically produced hydroxyl radicals with an estimated half-life of 12 hours (Howard 1991).

In 2009, the California Air Resources Board (ARB) conducted two studies to monitor airborne concentrations of propyzamide in Monterey County at the request of DPR; (1) a seasonal ambient air study, and (2) an application site study. In the seasonal ambient study, 192 24-hour air samples were collected from six separate sites in Monterey, San Benito and Santa Clara Counties over an eight-week period beginning on July 1 (Romans 2011). None of the ambient air samples contained propyzamide concentrations above the analytical method detection limit ($0.014 \mu\text{g}/\text{m}^3$ for a 24-hour sample). In the application site study, samples were collected from eight different locations around the perimeter of a 7.2 acre romaine lettuce field over the course of 3 days (Aston 2011). Propyzamide was applied by tractor at a rate of 2 pounds per acre and the field was watered immediately after. No propyzamide was detected above the method detection limit ($0.35 \mu\text{g}/\text{m}^3$ for a 24-hour sample) in any of the field samples analyzed. The results from both studies suggest that volatilization of propyzamide to the air from typical agricultural use is not significant.

ENVIRONMENTAL FATE AND DEGRADATION IN SOIL

Adsorption, Diffusion, Leaching, and Volatilization

In most soil types (clay, loam, silt, etc.), propyzamide shows little leaching and is readily adsorbed on organic matter and other colloidal exchange sites (Humburg 1989). Experimental K_{oc} values indicate that propyzamide will have low to moderate mobility in soil and adsorption increases proportionally to increases in organic matter content (Humburg 1989; Walker et al. 1977). The US EPA has stated that propyzamide has the potential to biomagnify in terrestrial habitats (US EPA 2009b).

Movement of propyzamide is greatest in coarse, textured soils; leaching is most likely to occur in loamy sand and silt loams with low organic content (US EPA 2009b). Propyzamide is moderately mobile in organic carbon-poor soils and slightly mobile in other soils. Its organic carbon-normalized Freundlich adsorption coefficients range from 548 to 1340 L/kg_{oc} in six different soils (US EPA 2008). It is known to leach through soil and into ground water when used according to the label (US EPA 2007).

Volatilization of propyzamide does occur from soil surfaces under very hot and dry conditions, but should not be an important fate process given an estimated Henry's Law constant of $9.77 \times 10^{-9} \text{ atm}\cdot\text{m}^3/\text{mol}$ and low vapor pressure of $8.5 \times 10^{-5} \text{ mmHg}$ (Budavari 1989; Howard 1991).

Degradation

The average persistence of propyzamide varies between 2 to 9 months when used at the recommended rates. Persistence depends upon soil type and organic carbon content (US EPA 2009b). Bioassays of soils treated with propyzamide demonstrated the presence of significant

residues after six to seven months (Kearney and Kaufman 1976). The degradation half-life in soil is reported to range from 9.5 to 80 days at 25 °C and 63 to 112 days at 15 °C according to published literature (Walker 1976). The major routes of degradation are thought to be by aerobic microbial degradation in soil and photolysis in water (US EPA 2007). Propyzamide is vulnerable to photodecomposition at the soil surface (Howard 1991; Kearney and Kaufman 1976) and has a reported half-life of 249 days when subjected to soil photolysis (US EPA 2007).

In soil, propyzamide primarily undergoes chemical transformation by cyclization to produce 2-(3,5-dichlorophenyl)-4,4-dimethyl-5-methyleneoxazoline which is then hydrolyzed to N-(1,1-dimethylacetyl)-3,5-dichlorobenzamide. These two transformation products and small levels of unaltered propyzamide constituted over 96% of material remaining after 90 days of soil treatment with the herbicide (Kearney and Kaufman 1976). This appears to occur both chemically and microbially, although the rate of cyclization is much higher in the presence of soil microorganisms (Howard 1991). Initial biodegradation rates increase as the number of subsequent soil treatments increases, suggesting selection for biological mediation by microorganisms. Degradation products resulting from the alterations of the terminal carbons of the propynyl side chain were present in trace amounts (Kearney and Kaufman 1976). All degradates except carbon dioxide contain the 3,5-dichlorobenzoyl moiety of propyzamide which is assumed by the US EPA to be as toxic as the parent compound and are also considered residues of concern (US EPA 2009b).

In a study on propyzamide's persistence in soil, plots of a pear tree orchard planted on sandy loam soil were treated with 1.0 - 1.25 kg of propyzamide per hectare (Rouchaud et al. 2000). In the plots not previously treated with propyzamide, soil half-life was observed to be about 30 days. In the plots treated annually for 3 or 14 years with propyzamide, the soil half-life was 12 and 10 days, respectively. These results may indicate that the accelerated biodegradation of propyzamide could reduce the effectiveness of the herbicide. Conversely, accelerated biodegradation reduces concern about the possible accumulation of these herbicides in soil.

ENVIRONMENTAL FATE AND DEGRADATION IN WATER

Based upon a water solubility of 15 milligrams per liter (15 mg/L), propyzamide is relatively insoluble in water. However, groundwater contamination can occur during the use of propyzamide in areas where soils are permeable and the water table is shallow (US EPA 2007). Products containing propyzamide can lead to surface water contamination resulting from the runoff of rainwater or irrigation (US EPA 2007). The US EPA has classified the compound as having a high potential for runoff several months or more after application and identified primary routes of transport to source water to include runoff, erosion, leaching, and spray drift (US EPA 2007). Experimental K_{oc} values ($\text{Log}_{K_{oc}} = 2.95$) indicate propyzamide may adsorb to suspend solids and sediment in the water column.

Propyzamide is stable to hydrolysis over a wide pH range and is not expected to degrade by this pathway (US EPA 2007, 2008). It may be subject to direct photolysis when present in water under direct sunlight (Méallier et al. 1980) and is moderately susceptible to aquatic photolysis

with a reported half-life of 42 days (US EPA 2007). Estimated half-lives of propyzamide for a model lake and model river are reported to be 230 and 31 days, respectively (Lyman et al. 1990). One major photodegradate by aquatic photolysis was identified as β -(3,5-dichlorobenzamino- β -methyl-butyl)butyric acid (US EPA 2007).

It is biodegraded at moderate to low rates in aerobic aquatic systems ($t_{1/2} = 69 - 119$ days) and at lower rates in anaerobic aquatic systems ($t_{1/2} = 127$ days) (US EPA 2007). Propyzamide has the potential to bioaccumulate in fish due to an octanol-water partition coefficient (K_{ow}) greater than 1,000 and its aqueous photolysis half-life. Volatilization of propyzamide from bodies of water is unlikely to be significant, with the possible exception to shallow rivers (DPR 2009; Howard 1991).

The US Geological Survey (USGS) performed studies on the occurrence of pesticides in the valley floor portion of the San Joaquin Valley in California during the 1990s. In one study, 143 surface water samples were collected from sites on the San Joaquin River and three of its tributaries near Modesto. The study determined 51% of samples collected had detectable propyzamide; however, the median concentration was less than the method detection limit and could not be confidently determined (Panshin et al. 1998). In a second study, surface water samples were collected from agricultural areas and the Modesto urban area to determine the loads of dissolved pesticides in the Tuolumne River Basin. Propyzamide was not detected at any level in any of the collected surface water samples (Kratzer 1998). The USGS conducted similar studies in 50 other major hydrologic systems across the country from 1992 - 2001 for the National Water-Quality Assessment (NAWQA) Program. The water-quality assessment concluded that propyzamide was detected in ground and surface water throughout the US, but levels never exceeded the established human-health and aquatic-life benchmarks set forth by the US EPA (Gilliom et al. 2006).

Table 4. Summary of all degradation pathways and products of propyzamide (US EPA 2008).

Study	Value (units)	Major Degradates [Minor Degradates]*	US EPA Master Record Identification #
Hydrolysis	No significant degradation at pH 4.7, 7.4, or 8.8 (20 °C)	None	107980
Aqueous Photolysis	$t_{1/2}$ = 41.7 days (parent) 217 d (TRC)	β -(3,5-dichlorobenzamino)- β -methyl-butyric acid [2-(3,5-dichlorophenyl)-4,4-dimethyl-5-methylene-2-oxazoline]* [3,5-dichlorobenzoic acid]* [N-(1,1-dimethylacetyl)-3,5-dichlorobenzamide]* [2-(3,5-dichlorophenyl)-4,4-dimethyl-5-hydroxymethyl-oxazoline]* [N-(1,1-dimethyl-3-hydroxyacetyl)-3,5-dichlorobenzamide]* [3,5-dichlorobenzamide]*	40420301, 40320601
Soil Photolysis	$t_{1/2}$ = 249 days (parent) Stable (TRC)	N-(1,1-dimethylacetyl)-3,5-dichlorobenzamide [2-(3,5-dichlorophenyl)-4,4-dimethyl-5-methylene-2-oxazoline]* [N-(1,1-dimethyl-3-hydroxyacetyl)-3,5-dichlorobenzamide]*	41913504
Aerobic Soil Metabolism	$t_{1/2}$ = 20.1, 21.5, 44.6, 392 days (parent) 64.9, 96.6, 166, 2340 days (TRC)	2-(3,5-dichlorophenyl)-4,4-dimethyl-5-methylene-2-oxazoline N-(1,1-dimethylacetyl)-3,5-dichlorobenzamide carbon dioxide [3,5-dichlorobenzoic acid]* [N-(1,1-dimethyl-2,3-dihydroxypropyl)-3,5-dichlorobenzamide]*	41568901, 46413407
Anaerobic Soil Metabolism	$t_{1/2}$ = 450 days (parent) Stable (TRC)	2-(3,5-dichlorophenyl)-4,4-dimethyl-5-methylene-2-oxazoline N-(1,1-dimethylacetyl)-3,5-dichlorobenzamide [2-(3,5-dichlorophenyl)-4,4-dimethyl-5-hydroxymethyl-oxazoline]*	41913505, 263649 (accsn. #)
Anaerobic Aquatic Metabolism	$t_{1/2}$ = 127 days (parent) 402 d (TRC)	2-(3,5-dichlorophenyl)-4,4-dimethyl-5-methylene-2-oxazoline [3,5-dichloro-N-(1,1-dimethyl-2-propenyl)benzamide]* [3,5-dichlorobenzoic acid]* [N-(1,1-dimethylacetyl)-3,5-dichlorobenzamide]* [N-(1,1-dimethyl-2,3-dihydroxypropyl)-3,5-dichlorobenzamide]* [carbon dioxide]* [Additional Unidentified Products]*	46413408
Aerobic Aquatic Metabolism	$t_{1/2}$ = 69.0, 119 days (parent) 899, 782 days (TRC)	3,5-dichloro-N-(1,1-dimethyl-2-propenyl)benzamide [2-(3,5-dichlorophenyl)-4,4-dimethyl-5-methylene-2-oxazoline]* [N-(1,1-dimethylacetyl)-3,5-dichlorobenzamide]* [N-(1,1-dimethyl-2,3-dihydroxypropyl)-3,5-dichlorobenzamide]* [Additional Unidentified Products]*	46427901
Terrestrial Field Dissipation	$t_{1/2}$ = 31 days (sandy loam), 56 days (loam)	[2-(3,5-dichlorophenyl)-4,4-dimethyl-5-methylene-2-oxazoline]* [N-(1,1-dimethylacetyl)-3,5-dichlorobenzamide]*	44078601

TRC = total residues of concern

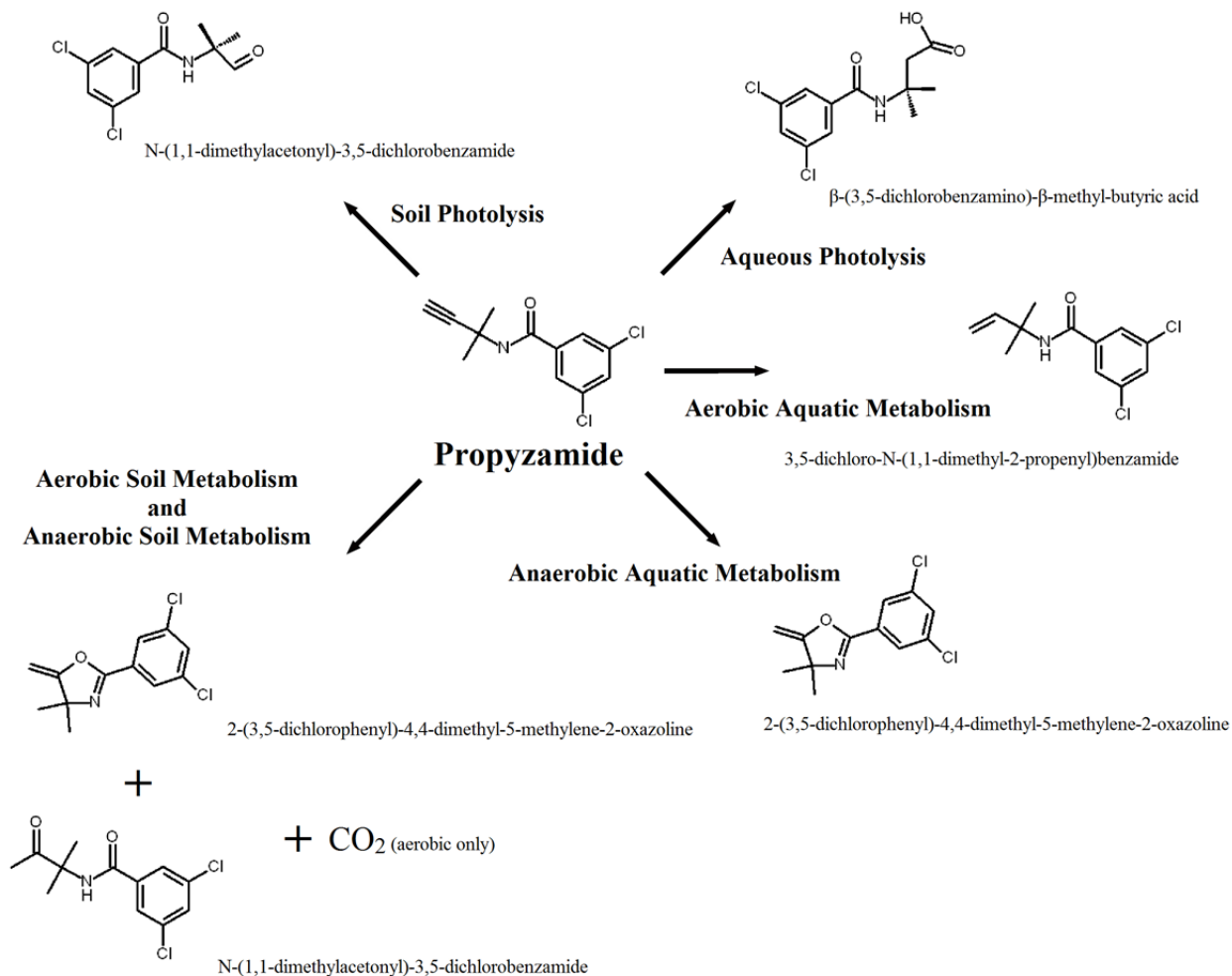


Figure 6. Diagram of major degradation pathways leading to the major degradates of propyzamide (minor degradates not shown).

TOXICITY

Mammals

Propyzamide has a relatively low order of mammal toxicity via the oral, dermal, and inhalation routes of exposure (Toxicity Category III or IV), produces mild irritation to the eyes and skin (Toxicity Category IV), and is not a dermal sensitizer (US EPA 2002). Draize tests on rabbits indicate propyzamide is slightly irritating to the eyes and skin but did not cause systemic intoxication (DPR 2009; Tomlin 2000). It has an acute oral LD₅₀ of 8,350 mg/kg and 5,620 mg/kg in male and female rats, respectively; an acute LD₅₀ greater than 10,000 mg/kg was observed in dogs (Humburg 1989; Tomlin 2000). In 2015, as part of the registration review process and to propyzamide's proposed use on leaf lettuce, US EPA established a chronic reference dose of 0.04 mg/kg/day for propyzamide which was determined be protective of non-carcinogenic and carcinogenic effects observed in mouse and rat studies (US EPA 2015b). Table 5 summarizes the acute toxicity of propyzamide in mammalian test species.

Table 5. Summary of acute toxicity properties of propyzamide in mammals.

Study Type	Species	Results	Toxicity Category
Acute Oral > 92.0% a.i.	Rat	LD ₅₀ (males and females) greater than 5,000 mg/kg	IV
Acute Oral (Limit Test) 95.7% a.i.	Rat	LD ₅₀ (males and females) greater than 5,000 mg/kg	IV
Acute Dermal (Limit Test) 95.7% a.i.	Rabbit	LD ₅₀ (males and females) greater than 2,000 mg/kg	III
Acute Inhalation 95.7% a.i.	Rat	LC ₅₀ is greater than 2.1 mg/L following a 4 hour exposure	III
Primary Eye Irritation 95.7% a.i.	Rabbit	Mild ocular irritant	IV
Primary Dermal Irritation 95.7% a.i.	Rabbit	Slight dermal irritant	IV
Dermal Sensitization > 92.0% a.i.	Guinea pig	Not a sensitizer	N/A

Propyzamide appears to be a liver toxicant and has caused liver tumors in male mice and was originally classified as a B2 “probable” carcinogen (Dow 2012; US EPA 2002). Adverse liver-related effects (increases in liver weight and/or liver-related serum enzymes and/or histopathology) were also observed in rats, rabbits, and dogs (US EPA 2002). Other target organs included the thyroid, testes, and pituitary gland in rats, and the kidneys, adrenal glands, thymus, heart, testes, and brain in dogs (US EPA 2002). No evidence of increased susceptibility in the fetuses or offspring of rats or rabbits was observed (US EPA 2002). In 2014, based on an evaluation of new carcinogenicity study data, US EPA reclassified propyzamide as “Not likely to be Carcinogenic to Humans” (US EPA 2014).

Propyzamide had been identified by the US EPA as a potential endocrine disruptor (US EPA 2002). In 2014, US EPA’s Office of Pesticide Programs conducted a weight-of-evidence analysis of the potential interaction of propyzamide with estrogen, androgen or thyroid signaling pathways. They determined that there was no convincing evidence for a potential interaction of propyzamide with the estrogen pathway (US EPA 2015a). There was evidence for potential interaction of propyzamide in the thyroid pathway in mammals based on effects on the thyroid in rats. Observation of minimal acute neurotoxicity occurred in rats following forced-feeding (gavage) administration, but US EPA determined that there was no evidence of neurotoxicity in the subchronic neurotoxicity study and that there was no concern for developmental neurotoxicity (US EPA 2015b).

Bioaccumulation was not apparent and very little un-metabolized propyzamide was recovered in the urine (US EPA 2002). A dietary risk assessment by the US EPA for chronic exposure to propyzamide shows that chronic dietary exposure is not significant. The US EPA estimates the cancer dietary risk for propyzamide is 1.06×10^{-7} for the US population, meaning a person living in the US has a 1 in 10 million chance of developing cancer in their lifetime from propyzamide's exposure in the US (US EPA 1999, 2002). Dermal exposures to propyzamide are considered to be a significant pathway of exposure; however, the US EPA estimates the potential cancer risk

from one day per year of high contact post-application dermal exposure to treated turf was 8.4×10^{-7} for the US population, or about 8 in 10 million for persons in the US.

Birds

After reviewing several studies, the US EPA has determined propyzamide is practically nontoxic to birds when exposed orally to a single dose (US EPA 1994). Also, the agency determined technical propyzamide (94.5% a.i.) to be practically nontoxic when exposure is through the diet to upland game birds (bobwhite quail) and waterfowl (mallard duck). No chronic avian toxicity data has been submitted to the US EPA by registrants and is thus unavailable (US EPA 2009b). Table 6 summarizes the acute and subacute avian toxicity of propyzamide.

Table 6. Summary of propyzamide toxicity to avian species.

Acute Oral Toxicity			
Species	% a.i.	LD₅₀ (mg/kg)	Conclusion
Japanese Quail	75	8770	Practically nontoxic
Mallard	75	20000	
Subacute Dietary Toxicity			
Species	% a.i.	LC₅₀ (ppm)	Conclusion
Bobwhite	94.5	> 4000	Practically nontoxic
Mallard	94.9	> 10000	

Fish and Aquatic Life

The US EPA determined that propyzamide was slightly toxic to coldwater and warmwater fish, and aquatic-phase amphibians, and was moderately toxic to freshwater invertebrates after the review of toxicology studies on non-target fish and aquatic invertebrates (US EPA 1994, 2009b). 96-hour LC₅₀ doses greater than 4.7 mg/liter and 5.1 mg/liter were observed for rainbow trout and carp, respectively (Tomlin 2000). An LC₅₀ greater than 5.7 mg/liter was observed for *Daphnia*, a genus of small planktonic crustaceans (Tomlin 2000). Acute toxicity studies on saltwater species were inhibited due to solubility limits of propyzamide in salt water (US EPA 2009b).

Due to low fish bioconcentration factors, ranging from 21 – 77, propyzamide is not expected to bioconcentrate in aquatic environments (US EPA 2008). No studies on the chronic toxicity of propyzamide to fish were conducted due to the low acute toxicity of the compound (US EPA 2009b). Table 7 summarizes the toxicity of propyzamide to various freshwater aquatic species.

Table 7. Summary of propyzamide toxicity to freshwater aquatic species (US EPA 1994).

Freshwater Animal Acute Toxicity			
Species	% a.i.	LC₅₀ (ppm)	Conclusion
Bluegill	50	> 100	Slightly toxic
Trout	75	72	
Catfish	75	200 – 500	
Goldfish	75	350	
Guppy	75	150	
Daphnia magna	93.8	> 5.6	Moderately toxic

Insects

Propyzamide was determined to be practically non-toxic to bees with a 48-hour acute contact LD₅₀ greater than 181 µg/bee; an LC₅₀ greater than 346 ppm was observed for earthworms (DPR 2009; Tomlin 2000; US EPA 2009b). A survey of pesticide residues found on bees and bee products (collected pollen, wax, broods, etc) during 2007 – 2008 found that less than 1% of bees and less than 5% of wax and pollen analyzed had detectable levels of propyzamide (Mullin et al. 2010). The US EPA does not consider bees to be vulnerable to propyzamide use as applications are mostly made in the fall or early winter when bees are not expected to be active (US EPA 1994).

SUMMARY

Propyzamide is a soil-active, systemic organochlorine herbicide that was first registered in 1972 for use on select annual grasses and broadleaf weeds. Due to propyzamide's low vapor pressure, volatilization and major atmospheric transport are not expected to occur at significant amounts. When introduced to the atmosphere, propyzamide can be directly photolyzed by sunlight and has an estimated half-life of 12 hours. Field studies performed by California's ARB and DPR failed to detect quantifiable levels of propyzamide after soil applications to simulate real-world use. While propyzamide can be moderately mobile in some soil types, it is readily degraded by soil microorganisms as shown by laboratory and field studies. While propyzamide's use is a greater concern for both surface and groundwater contamination resulting from the runoff of rainwater or irrigation, studies performed by the USGS failed to detect propyzamide levels exceeding the established human-health and aquatic-life benchmarks set forth by the US EPA.

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