Fluazaindolizine

DEPARTMENT OF AGRICULTURE

CAS 1254304-22-7; EPA PC CODE 129777 | NEW ACTIVE INGREDIENT REVIEW | JAN 2024

PESTICIDE TYPE	NEMATICIDE
Chemical Class	Sulfonamide
Common Trade Names	Reklemel™ Technical, Salibro™
Major Degradate	IN-F4106, IN-VM862, IN-QEK31, IN-REG721, IN-A5760
Application Rate (lb a.i/A/year)	Max Single: 0.25 to 2.0 Max Annual: 0.75 to 4.0
Registration Status	EPA: Registered unconditionally Sept. 2023 Minnesota: 2024
Toxicity Profile for Applicators	Signal word: CAUTION Category III: Oral and dermal Category IV: Inhalation exposure
Basic Manufacturer	Corteva Agriscience
MDA Laboratory Capabilities	In discussion
HUMAN HEALTH	
Non-Cancer	Acute PAD: no value* Chronic PAD: 0.33 mg/kg/day
Cancer	Not likely to be carcinogenic to humans
Acute and chronic population adjusted doses (PAD) include all relevant uncertainty and safety factors. **A toxicological endpoint attributable to a single dose was not identified.*	
ENVIRONMENTAL AQUATIC TOXICITY	
Fish	Acute: >29,000 ppb Chronic: 11,700 ppb
Invertebrate	Acute: > 60,000 ppb Chronic: 570 ppb
Aquatic Plants (IC_{50})	Vascular: 8,500 ppb Non-vascular: 10,500 ppb
POLLINATOR TOXICITY	
Honey Bee (adult LD_{50})	Acute Contact: > 80 µg ai/bee Acute Oral: > 7.848 µg ai/bee
Level of Concern (LOC) has been applied to all values. *Toxicity values refer to the technical grade active ingredient (TGAI); however, the toxicity of the formulated product was higher in some instances.*	

INTRODUCTION

Fluazaindolizine is a new nematicide active ingredient recently registered by the United States Environmental Protection Agency (EPA) for use on various agricultural food products. Registered uses include vegetables such as carrots, squash, and potatoes, as well as select fruits, including grapes. There are no registered uses of fluazaindolizine in residential settings.

Fluazaindolizine falls within the sulfonamide chemical class and has a potential novel yet unknown mode of action. It is intended for use against plant-parasitic nematodes, including root-knot nematode, dagger nematode, sting nematode, lesion nematode, and ring nematode.

The Minnesota Department of Agriculture's (MDA) extensive review of the EPA fluazaindolizine labels and risk assessments for issues relevant to Minnesota is summarized below.

PROJECTED USE IN MINNESOTA

As a nematicide with a potentially novel mode of action, fluazaindolizine could be an important addition to Resistance Management (RM), and Integrated Pest Management (IPM) programs in Minnesota. Performance trials conducted by the product registrant across the United States and Canada suggest an equal if not better efficacy against plant-parasitic nematodes when compared to currently registered products, and a novel mode of action implies no cross resistance with current chemistries. Additional benefits include flexible application timing and methods. The MDA is not aware of any fluazaindolizine trials conducted in Minnesota by the University of Minnesota.

Application methods for fluazaindolizine are crop dependent, limited to the soil, and include broadcast incorporation, soil drench, soil spray, drip chemigation, and micro-sprinkler chemigation. Single application rates range from 0.25 to 2.0 lbs a.i. per acre and annual application rates range from 0.75 to 4.0 lbs a.i. per acre, depending on the crop/use site.

One end-use product is currently registered by the EPA and is registered for use in Minnesota.

- **Salibro™ Nematicide** (EPA Reg. No. 352-932) – Suspension concentrate containing 41.15% fluazaindolizine for use on carrots, cucurbits, fruiting vegetables, nonbearing citrus fruit, nonbearing stone fruit, nonbearing tree nut, nonbearing small fruit vine climbing, except fuzzy kiwifruit, and tuberous and corm vegetables.

LABEL ENVIRONMENTAL HAZARDS

Water Quality

- **Groundwater Advisory:** This chemical has properties and characteristics associated with chemicals detected in groundwater. This chemical may leach into groundwater if used in areas where soils are permeable, particularly where the water table is shallow.
- **Surface Water Advisory:** This product may impact surface water quality due to runoff of rainwater. This is especially true for poorly draining soils and soils with shallow ground water. This product is classified as having high potential for reaching surface water via runoff for several weeks after application. A level, well-maintained vegetative buffer strip between areas to which this product is applied and surface water features such as ponds, streams, and springs will reduce the potential loading of fluazaindolizine from runoff water and sediment. Runoff of this product will be reduced by avoiding applications when rainfall is forecasted to occur within 48 hours.

TOXICOLOGY AND EXPOSURE

EPA's screening models generate high-end, conservative exposure estimates for active ingredients and toxicologically significant degradates. Model inputs include annual usage at maximum use rates, maximum treated acres, maximum food residues, peak runoff, and drift scenarios, etc. Some proposed products, application rates, and use scenarios are not relevant to Minnesota. EPA's estimates, therefore, may not reflect future use and impacts in Minnesota.

Human Health

- **Carcinogenic Effects** – EPA classified fluazaindolizine as "not likely to be carcinogenic to humans."
- **Drinking Water Guidance** – Fluazaindolizine and its major degradates have the potential to reach surface and ground sources of drinking water. The estimated drinking water concentrations (EDWCs) for fluazaindolizine and four residues of concern (ROC) in groundwater are 1200 µg/L and 990 µg/L for acute and chronic exposure, respectively. EDWCs for a fifth ROC (IN-VM862) evaluated separately were 1780 µg/L (acute) and 1300 µg/L (chronic). Both acute and chronic dietary (food and drinking water) exposures and risk estimates are below the EPA level of concern.
- **Occupational Exposure** – Occupational handling and post-application exposures are possible; however, EPA determined risk estimates were not of concern with baseline attire, appropriate personal protective equipment, and following the label restricted-entry interval of 12 hours.

Non–target Species

- **Aquatic Life Exposure** – Fluazaindolizine is considered low risk to fish, aquatic invertebrates, and vascular and non-vascular aquatic plants on an acute exposure basis.
- **Terrestrial Life Exposure** – Fluazaindolizine acute and chronic risks to birds are expected to be low. Mammalian acute oral risk is low. Potential chronic risks exist for small to medium-sized (15 – 35 g) mammals consuming broadleaf plants treated with fluazaindolizine and exposed arthropods. Fluazaindolizine poses low risk to terrestrial plants and invertebrates; however, sublethal reproductive impacts were observed in invertebrates examined.
- **Pollinators** - Fluazaindolizine is practically non-toxic to adult honeybees on acute oral and contact bases; however, sublethal effects were noted. In chronic studies, behavioral and developmental sublethal effects and limited mortality were observed in adult and larval honeybees. Potential risks are considered low when following label-approved use patterns and application methods.

ENVIRONMENTAL FATE

Fluazaindolizine is moderately to mobile in soil and has the potential to leach to groundwater and be transported to surface water via spray drift and runoff. Fluazaindolizine and its degradates are expected to persist in groundwater due to hydrolytic stability and be less persistent in surface water.

Soil

- **Half–life** (20°C) – Aerobic: 5.8 to 729 days
  Anaerobic: 100 to 2,730 days
- **Mobility** – K_{OC} values range from 107 to 192 L/kg_{oc}
  Solubility in water (20°C, pH 7) is 56.1 mg/L
- **Photolysis Half-life** – 283.8 days (25°C, pH 7)
- **Persistence** – DT_{50} values range from 7.8 to 407 days

Aquatic

- **Half–Life** (20°C) – Aerobic: 21.6 to 51.3 days
  Anaerobic: 11.4 to 22.4 days
- **Photolysis Half–life** – 1.34 days (20°C, pH 7)
- **Hydrolysis Half–life** – 429 days (pH 4); stable at pH 7/9 (50°C)

Sediment

- **Half–Life** – Aerobic: 8.36 days, Anaerobic: 2.65 days

Air

- **Volatilization** – Nonvolatile; Vapor pressure (20°C) = 1.93×10^{-9} torr; Henry's law constant (20°C) = 2.21×10^{-9} atm-m^3 mol^{-1}

Degradates

Fluazaindolizine forms five major degradates in soil and aquatic systems: IN-QEK31, IN-F4106, IN-REG721, IN-A5760, and IN-VM862. While fluazaindolizine and its degradates do not individually persist, they can collectively persist in the environment and are moderately mobile to mobile in soil. The EPA considers the parent fluazaindolizine and degradates IN-F4106 and IN-VM86 to be ROCs for all aquatic taxa and soil-dwelling invertebrates, while the parent and IN-F4106 are ROCs for all other terrestrial taxa. Most degradates exhibited similar to lower toxicity to aquatic taxa than the parent, though IN-F4106 and IN-VM862 displayed greater toxicity to algae, and IN-VM862 exhibited greater toxicity to aquatic invertebrates than the parent. Fluazaindolizine degradates did not exhibit greater toxicity than the parent for any terrestrial taxa on a molar equivalent basis, except for soil-dwelling invertebrates.

All active ingredient technical information, risk assessment values, fate and transport data, and label hazards have been summarized from final registration documents available at www.regulations.gov Docket ID: EPA-HQ- OPP-2020-0065.