Reklemel™ active

Technical Bulletin

CORTEVA™ agriscience

The Importance of a Healthy, Productive Soil

Healthy soils are the foundation for successful farming and sustained food production. They are rich in beneficial soil organisms that help improve soil quality. The balanced coexistence of beneficial organisms helps plants improve water and nutrient use, enhancing their tolerance to pests, diseases and environmental stresses (Figure 1). But when the soil balance is altered, often unintentionally by changes in land and crop management, detrimental organisms such as plant-parasitic nematodes and other natural antagonists take over. Plant-parasitic nematodes are a threat to food production. Unlike their beneficial free-living counterparts, plant-parasitic nematodes feed upon and destroy plant roots, affecting plant metabolism and lowering plant defenses. In their weakened condition, plants become susceptible to diseases and other stresses, leading to reduced yield quality and quantity.

Corteva Agriscience introduces Reklemel™ active, a new way to manage plant-parasitic nematodes. Reklemel helps preserve healthy soils by controlling damaging nematode species while being highly compatible with beneficial organisms. Reklemel provides targeted protection against plant-parasitic nematodes, enabling root establishment and contributing to healthy crops and high quality harvests.

Figure 1. Healthy soils contain abundant and balanced populations of beneficial organisms.

Plant-Parasitic Nematodes - A Significant Threat to Food Security

Plant-parasitic nematodes need to feed on plant tissue to grow and reproduce. Most species live hidden beneath the soil, feeding in or on plant roots. A few species invade leaf and stem tissue above the ground. Plant-parasitic nematodes are often overlooked as soil pests due to their near microscopic size and concealed living habits. However, they can lead to severe crop damage, increasing production costs and causing significant yield loss (Figure 2). Economic losses to agricultural production are estimated as more than 100 billion U.S. dollars worldwide.

Plant-parasitic nematodes cause direct and indirect injury to plants. Direct mechanical injury occurs by inserting their needle-like mouthpart into plant cells. Some species cause root mass reduction, destroying fine feeder roots and leading to a disruption of nutrient and water uptake. They also cause indirect injury, including physiological and metabolic changes in host plants and transmission of plant viruses by some species. Affected plants become weak and cannot function properly, exhibiting non-specific above-ground symptoms such as stunting, wilting, yellowing and even plant death. These symptoms often are mistakenly attributed to many other biotic and abiotic factors including drought, nutrient deficiency, bacterial, fungal or viral diseases, etc.

Plant-parasitic nematodes typically complete their life cycle from egg to adults in 20 to 40 days. Some species can slow down their metabolism and survive several years in their egg or cyst stage in a dormant state. Young nematodes hatching from eggs are worm-shaped and are called juveniles. They resemble small adults and move in water films through soil pores in search of host plant roots (Figure 3). Nematodes normally shed their skin four times before becoming adults. In the presence of host plants and favorable environmental conditions, plant-parasitic nematodes reproduce rapidly, with several generations occurring in a crop cycle. Their specialized survival skills make them difficult to manage and almost impossible to eradicate once established in a field.

Figure 2. Injury caused by the root-knot nematode, *Meloidogyne incognita*. Left: Above-ground symptoms in cucurbits after severe below-ground root infestation, leading to plant death. Right: Below-ground injury, severe galling and forking on carrot roots.

Figure 3. Plant-parasitic nematodes: Root-knot nematode, *Meloidogyne incognita*, infective, J2-stage juvenile (upper left); reniform nematode, *Rotylenchus reniformis*, young female (upper right); dagger nematode, *Xiphinema* sp. (lower left); and root-lesion nematode, *Pratylenchus* sp. (lower right).

Cucurbit (gourd) roots 91 days after seeding, treated with Reklemel™ active (left) and untreated (right) showing severe galling caused by root-knot nematodes, *Meloidogyne incognita*.

Reklemel™ Active – A New Solution for Nematode Management

Reklemel™ active (fluazaindolizine[1]) is a novel, non-fumigant, chemical nematicide discovered and developed by Corteva Agriscience. Reklemel is the first sulfonamide nematicide, a chemical group different from other commercial nematicides. It's mode of action (MoA) while mechanistically unknown, has been extensively studied and appears different from all other currently available nematicides, including the traditional fumigants, organophosphates and carbamates and the newer active ingredients, such as abamectin, fluopyram, fluensulfone and tioxazafen. Reklemel has excellent activity on root-knot nematodes and many other important plant-parasitic nematode species. It has a very favorable environmental profile and is biologically compatible with beneficial insects, including pollinators and a wide range of beneficial soil organisms.

History and Discovery of Reklemel™ Active

Many conventional nematicides are under increasing regulatory pressure due to their toxicological and environmental profiles, underscoring the need for new, low-toxicity, and highly effective alternatives to meet farmer's needs. In response, Corteva Agriscience initiated an intensive effort to discover and develop a new nematicide with favorable attributes. Reklemel™ active is the result of years of diligent multidisciplinary scientific research to develop a novel solution for targeted plant-parasitic nematode control. The development process involved a series of substitutions around the sulfonamide functional group. Patented analogs demonstrated excellent activity on root-knot nematodes, *Meloidogyne* spp., with significant reduction of root gall formation at very low concentrations. Analogs with the highest potency on root-knot nematodes and suitable plant safety were advanced to field trials and tested against a range of plant-parasitic nematode species, while undergoing rigorous toxicological and environmental evaluations. During early screening, the lead analog, Reklemel, was selected for its consistent and superior efficacy on root-knot nematode species and extremely favorable toxicological and environmental attributes.

[1] Fluazaindolizine is the common name assigned to Reklemel™ active by the International Organization for Standardization (ISO) and is the name recognized by the Insecticide Resistance Action Committee (IRAC).

Key Features of Reklemel™ Active

- New and unique mode of action.
- Effective, true nematicide - Reduces motility and infectivity quickly and irreversibly.
- Highly selective against plant-parasitic nematodes, no insecticidal or fungicidal activity.
- Excellent, long-lasting (rate-dependent) control of damaging plant-parasitic nematodes.
- Favorable toxicological and ecotoxicological profile - Low impact on beneficial insects, pollinators and beneficial soil organisms.
- Effective at low-use rates – Less amount of active ingredient needed for nematode control compared to many alternative nematicides.
- Fits a broad range of application technologies and precision application methods.
- Compatible with Integrated Pest Management (IPM) and crop soil health management programs, including soil-applied biologicals.
- A core component of Integrated Nematode Management (INM) programs in multiple crops.

Unique Mode of Action

Reklemel™ active is highly selective to plant-parasitic nematodes and does not have activity against insects or fungi. IRAC assigned Reklemel into the N-UN (unknown) mode of action (MoA) classification group.[2] Numerous scientific studies, including advanced biochemical techniques, showed Reklemel's action on plant-parasitic nematodes is unique from those observed in currently known commercial nematicides including organophosphates, carbamates, avermectins, fluensulfone, fluopyram or tioxazafen. Reklemel did not show activity on acetylcholinesterase, mitochondrial electron transport, glutamate-gated chloride channels and nicotinic acetylcholine receptors (Table 1).

[2] For more information on MoA classification, visit the IRAC website at www.irac-online.com.

Table 1. Reklemel™ active proved inactive against other known modes of action for nematicides.

Target	Reklemel™ active	Nematicidal Chemistry
General biocide	Inactive[1]	Fumigants (1,3-dichloropropene)
AChE	Inactive[1,4]	Carbamates (oxamyl, aldicarb)
NAChR	Inactive[1,2,4]	Imidazothiazoles* (levamisole) AADs* (monepantel)
Vesicular ACh transport	Inactive[1]	Spiroindolines*
Glutamate-gated chloride channel	Inactive[1,4]	Macrocyclic lactones* (abamectin)
SDHI (Complex II)	Inactive[1,3,4]	Benzamide (fluopyram)
MET (Complex I/III/IV) (Mitochondria)	Inactive[1,3,4]	METIs (rotenone, antimycin A)
Oxidative phosphorylation	Inactive[1,2,4]	Pyrroles (chlorfenapyr)
Undefined MoA new nematicides	Indicative data exists to show MoA is different	Fluensulfone, Tioxazafen

[1] Nematicidal symptomology; [2] *Caenorhabditis elegans* in vivo study; [3] *C. elegans* in vitro study; [4] Insect in vitro study;
*Non-plant parasitic anthelmintic activity.

True Nematicide with Irreversible Symptoms

Reklemel™ active causes a rapid reduction in fitness of sensitive plant-parasitic nematodes by contact, resulting in irreversible nematicidal action. Several important plant-parasitic nematode species treated with Reklemel, at rates from 1 to 250 parts per million (ppm), showed symptoms of slow movement or decreased motility within a few hours after contact exposure. A few hours later, they continued to exhibit progressive symptoms described as coiling, J- or Z-shape, and reversed sinusoidal movement (Figure 4). These symptoms drastically impair their motility and ability to move in soil pore water to locate and infect roots (Figure 5). Once symptoms become visible, they are irreversible even after removing exposure and transferring nematodes into freshwater for recovery. Many plant-parasitic nematodes exposed to Reklemel typically die within a few days.

Reklemel does not induce significant direct ovicidal effects or stop egg hatching at typical soil concentrations. Thus, in treated soils, target nematodes hatch and infective juveniles get exposure to Reklemel as they move in films of water within the soil micropores in search for a host root.

Figure 4. Symptoms of intoxication by Reklemel™ active on root-knot nematode, *Meloidogyne incognita* (upper row), and on root-lesion nematode, *Pratylenchus brachyurus* (lower row).

Comparative efficacy studies based solely on nematode mortality are not appropriate to assess the true efficacy of Reklemel™ active. In aqueous exposure studies, many known nematicides show both a fast knock-down activity (within minutes) and high toxicity (LD_{50} values ≤10 ppm), allowing a rapid kill or paralysis of a broad range of nematodes. In contrast, Reklemel shows low acute toxicity to vermiform stages of target nematodes, which does not allow for reasonable toxicity estimation values during the first 24 hours of exposure, requiring LD_{50} values > 1000 ppm. LD_{50} values ranged from 25 to 30 ppm of Reklemel even after seven days of continuous exposure. However, in second level tests, Reklemel consistently demonstrated that these apparent "sub-lethal" effects are progressive and non-reversible, and are, in fact, extremely efficacious on reducing nematode fitness by impairing soil mobility, host-finding and root infectivity behaviors at EC_{50} values of ≤ 5 ppm (Figure 5).

The irreversible toxicological effects of Reklemel were observed both at low (4 to 10 °C) and high (25 to >35 °C) temperatures (39 to 50 °F and 77 to >95 °F, respectively).

Figure 5. Impaired ability of J2 plant-parasitic root-knot nematode, *Meloidogyne incognita,* to locate and penetrate plant root tips after exposure to Reklemel™ active. Top: Nematodes exposed to 5 ppm of Reklemel for 24 hours, juveniles dead or showing intoxication symptoms and unable to reach and penetrate the root tip. Bottom: Untreated, juveniles successfully locating and penetrating the root tip.

Targeted Selectivity

Reklemel™ active is effective and selective on plant-parasitic nematodes and shows high compatibility with beneficial non-target species that play an important role in healthy soils. Numerous internal and external laboratory studies on a broad range of plant-parasitic and free-living nematode species demonstrated high compatibility with many beneficial nematode species including bacteriophagous, fungivorous and entomopathogenic nematode species (Figure 6). Differences in sensitivity to Reklemel are observed depending on nematode species (Table 2). Differences in species sensitivity to any given compound have been reported for many nematicides and anthelmintics due to several factors including differences in morphological structures and different capacities to metabolize and detoxify compounds. This is important because it separates general biocides and broad spectrum nematicides from selective nematicides such as Reklemel, which selectively targets parasitic species while demonstrating high compatibility with beneficial, non-target nematode species.

Table 2. Effects of Reklemel™ active (formulated as 500 g a.i. /L SC) on the activity/motility, mobility through soil, infectivity and reproduction of plant-parasitic nematode species (in vitro laboratory and in vivo greenhouse pot studies).

Common name (Genus)	Activity[a,b]	Mobility[a,c]	Infectivity/ Reproduction[a,d]
Root-knot nematodes (*Meloidogyne*)	++++	+++++	+++++
Root-lesion nematodes (*Pratylenchus*)[e]	++	++	+++
Reniform nematode (*Rotylenchulus*)	++++	++++	++++
Potato cyst nematodes (*Globodera*)	++	++	+++
Sugarbeet/Soybean cyst nematodes (*Heterodera*)	+	+	NT
Spiral nematodes (*Helicotylenchus*)	++++	++++	++++
Sting nematode (*Belonolaimus*)	+++	+++	++
Citrus nematodes (*Tylenchulus*)	+++	+++	NT
Dagger nematodes (*Xiphinema*)	+++	NT	NT
Stem nematodes (*Ditylenchus*)	0	0	NT
Stubby-root nematodes (*Trichodorus*)	+	+	NT
Stunt nematode (*Tylenchorhynchus*)	0	NT	NT
Pin nematode (*Paratylenchus*)	+	+	++
Needle nematodes (*Longidorus*)	+++	NT	NT
Lance nematode (*Hoplolaimus*)	++	++	++
Ring nematode (*Mesocriconema*)	+	+	++

[a] +++++ = Effects visible at <1-5 ppm (a.i.); ++++ = Effects visible at <5-25 ppm; +++ = Effects visible at <25-50 ppm; ++ = Effects visible at <50-100 ppm; + = Effects visible at <100-250 ppm; 0 = no effects observed; NT= Not tested; Time course (24–72 h of exposure).

[b] Based on aqueous in vitro assays evaluating activity (normal/affected/dead) of vermiform life-stages exposed to Reklemel at 500 g/L SC.

[c] Based on in vitro assays evaluating mobility (ability to pass filter paper/sand layer, etc.) of vermiform life-stages after pre-exposure to Reklemel at 500 g/L SC followed by rinsing in fresh water.

[d] Based on in vivo assays evaluating infectivity (root infestation – endoparasitic nematodes) and/or reproduction (ectoparasitic species) after previous exposure of vermiform stages to Reklemel at 500 g/L SC.

[e] Some species of root-lesion nematodes (e.g. P. *brachyurus* or P. *coffeae*) show higher sensitivity than others (e.g. P. *penetrans*).

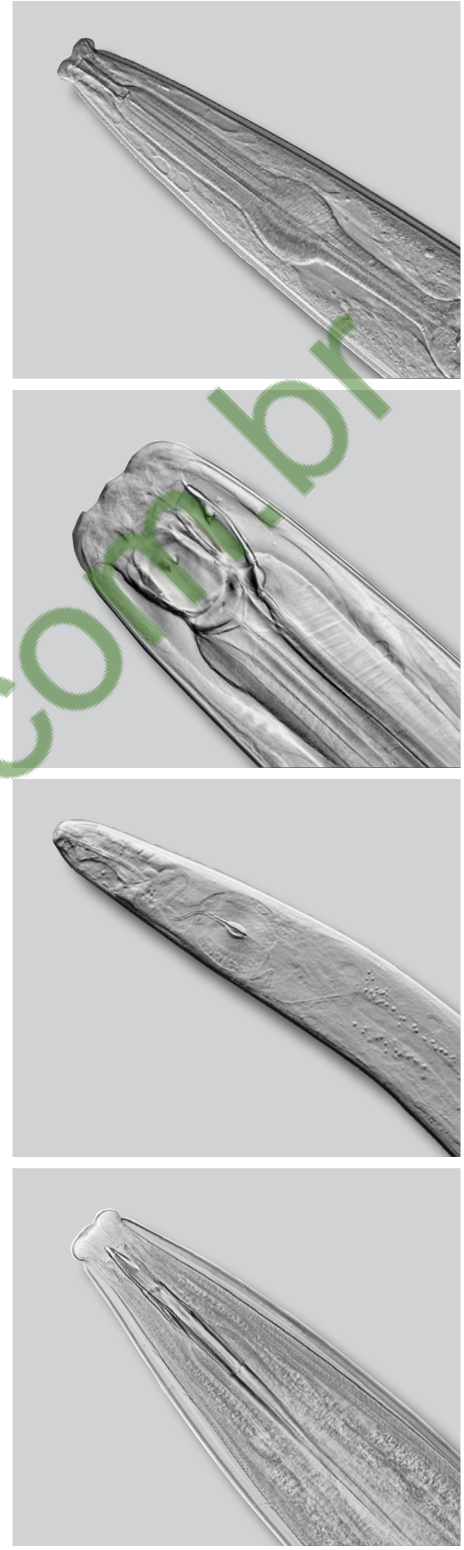


Figure 6. Beneficial nematodes. Mouthparts closeup in bacterial feeding nematode (top); carnivorous nematode (top middle); fungivorous nematode (bottom middle); and omnivorous nematode (bottom).

General Crop Groups for Reklemel™ Active

Reklemel™ active has been developed for use on a wide range of annual and perennial crop groups including fruiting vegetables, cucurbits, root and tuber vegetables, fruits and nuts, herbs and spices, plantation crops, field row crops, small fruits and berries, etc. Crop registrations differ around the world and further new registrations are sought to serve nematode management needs. Approved country registration labels will provide detailed guidance on application methods, rates and labelled crops.

Soil and Plant Mobility

The physical and chemical properties of Reklemel™ active enable a well-balanced soil mobility and residual profile, permitting good distribution in the crop root zone, and providing effective, rapid and extended root protection. The duration of root protection typically ranges between 20 to 50 days and depends upon several factors including soil type, application rate, application method and nematode pressure. Reklemel shows limited plant uptake and is not considered biologically active by systemic routes.

Field Efficacy

Reklemel™ active has been tested extensively in laboratory, greenhouse, field micro-plot studies and multiple field trials under different environmental conditions across North America, Latin America, Europe, Middle East, Africa and Asian countries. Research data show that Reklemel applied once shortly before or at planting or in sequential applications in the crop, reduces root damage and provides yield protection from plant-parasitic nematodes comparable or superior to current commercial nematicides. Under field conditions, Reklemel at rates[3] of 250 to 2400 grams a.i./ha is effective against a wide range of root-knot nematodes (*Meloidogyne* spp.), and other important plant-parasitic nematodes, including reniform (*Rotylenchulus reniformis*), dagger (*Xiphinema* spp.), spiral (*Helicotylenchus* spp.), some root-lesion (*Pratylenchus* spp.), and some cyst nematode species (*Heterodera* spp., *Globodera* spp.)

Field efficacy is expressed as root protection, allowing better water and nutrient uptake, maintaining vegetative vigor, and leading to a potential increase in crop quality and overall yields. Increases in quantity or marketable yield vary considerably depending upon nematode pressure and crop type. However, they may range from 10 to 30% and can be much higher where nematode pressure is extreme. Factors that affect efficacy include soil type, nematode species, synchronization between nematode life-stage and Reklemel application, and effectiveness of the application method. Excellent results have been observed with recommended Reklemel application methods in various soil types, under medium to high pest pressure around the world. Figures 7 to 12 show summaries of the efficacy of Reklemel expressed as root galling control and marketable yields compared to untreated checks and to farmers' programs in multiple trials across the globe. Refer to approved country-specific labels for more information on labeled crops and target plant-parasitic nematode species.

[3] Actual rates depend upon application method, crop type, volume of soil to be treated, nematode population density, level and duration of required root protection and size of root zone requiring protection (which is crop specific). Country registration labels will provide detailed guidance on crop-specific rates and approved application methods.

Root Galling Control with Reklemel™ active vs. the Untreated Control

Reklemel™ active provides consistent residual control of root-knot nematodes.

Figure 7. Field carrot trial in California, U.S.A. Root galling in carrots caused by the root-knot nematode *Meloidogyne incognita*. Top: Control with Reklemel™ active incorporated in the seed bed at 2 lb a.i. per acre; Center: Farmer's program; Bottom: Untreated control (Photo credits ©Ole Becker, UC Riverside)

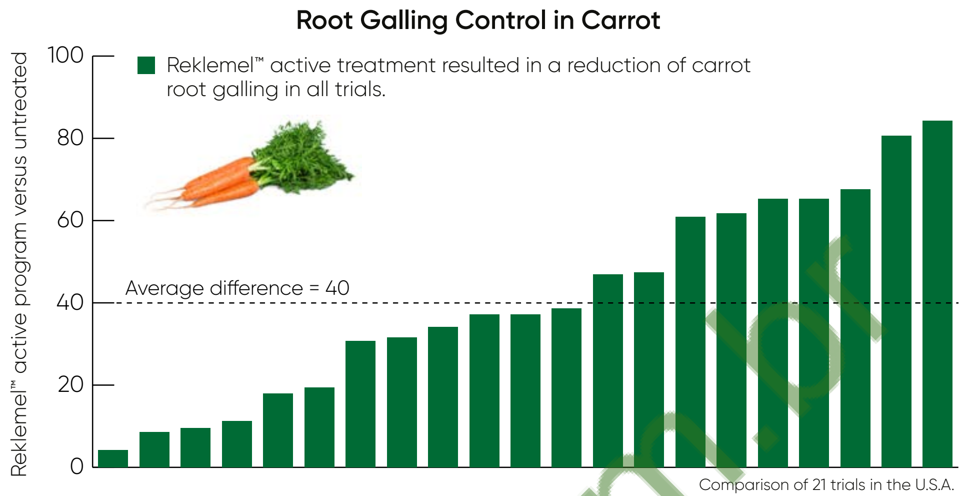


Figure 8A. Percent reduction in root gall rating in carrots for Reklemel incorporated in the seed bed at rates of 1-2 lb a.i. per acre versus the untreated. All trials conducted under a range of natural nematode field pressures in the U.S.A. from 2014 to 2019.

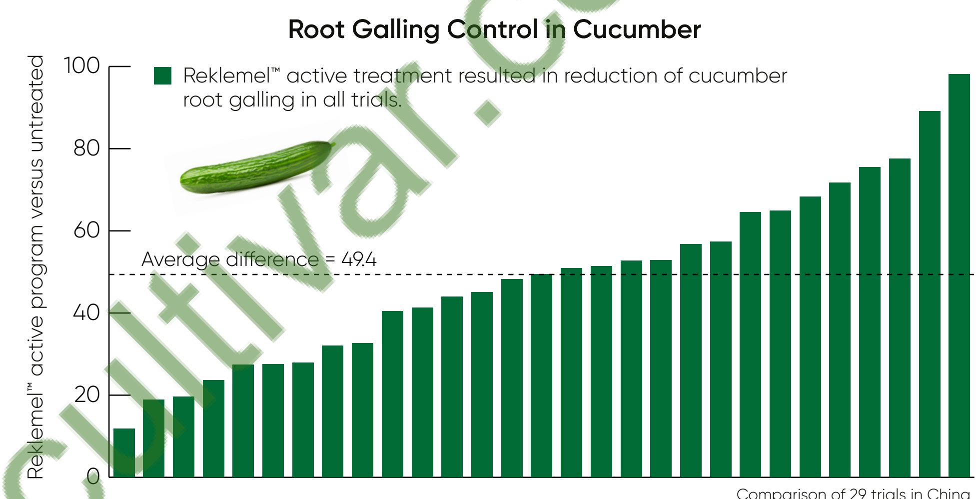


Figure 8B. Percent reduction in root gall rating in cucumbers at 58-64 days for Reklemel applied by hole-drench at 40 mg a.i. per plant versus the untreated. All trials conducted under a range of natural nematode pressures in greenhouses in China from 2014 to 2019 .

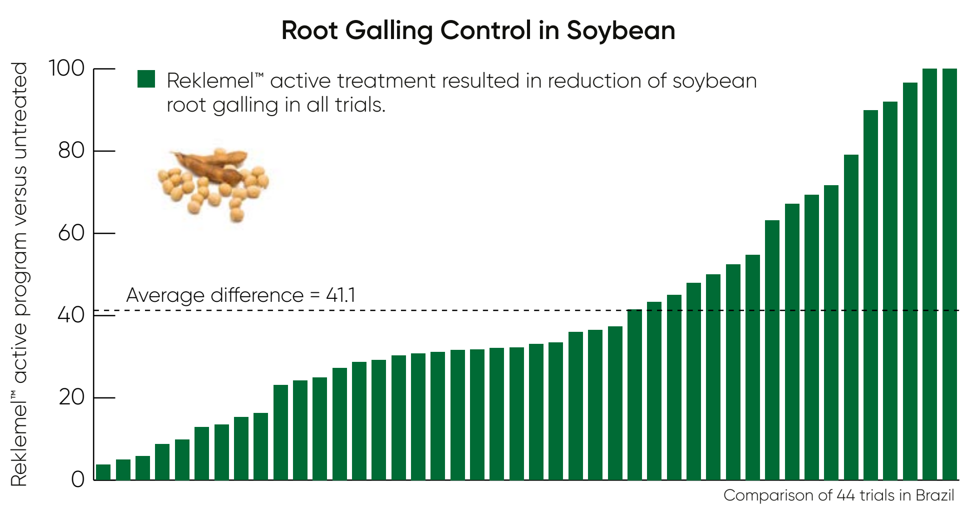


Figure 8C. Percent reduction in root gall rating 45 days after crop emergence in soybean for Reklemel applied in furrow at planting at rates of 250 to 500 g a.i. per ha versus the untreated. All trials conducted under a range of natural nematode field pressures in Brazil from 2014 to 2019.

Marketable Yields with Reklemel™ active vs. the Untreated Control

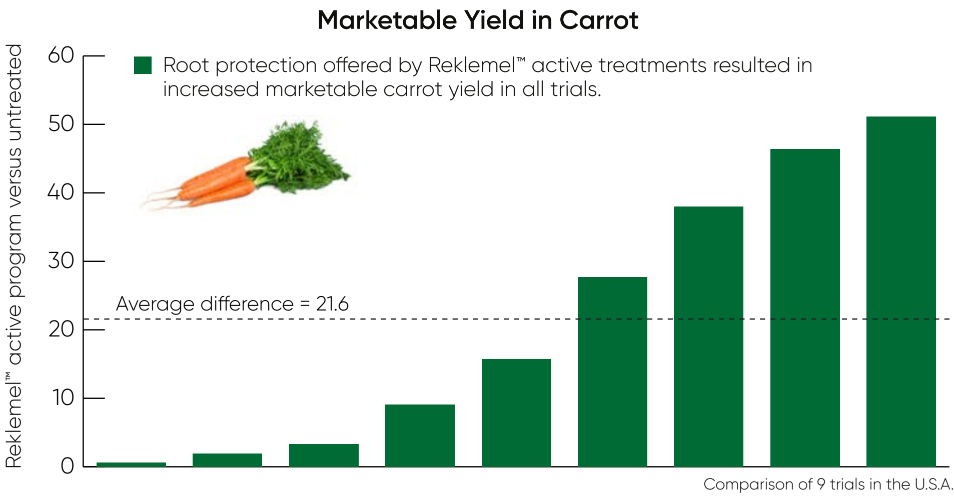


Figure 9A. Percent change in total marketable carrot yield for Reklemel incorporated in the seed bed at rates of 1-2 lb a.i. per acre versus the untreated. All trials conducted under a range of natural nematode field pressures in the U.S.A. from 2014 to 2019.

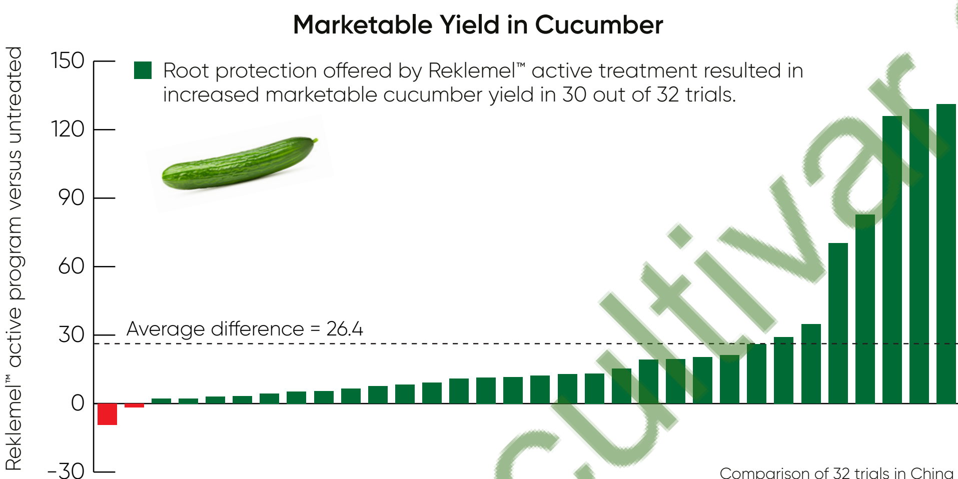


Figure 9B. Percent change in total marketable cucumber yield for Reklemel applied by hole-drench at 40 mg a.i. per plant versus the untreated. All trials conducted under a range of natural nematode pressures in greenhouses in China from 2014 to 2019.

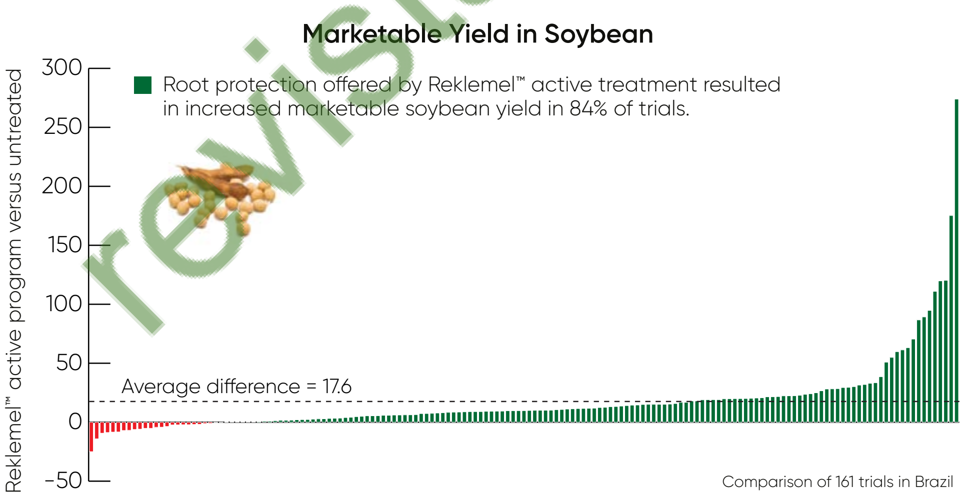


Figure 9C. Percent change in total soybean yield for Reklemel applied in furrow at planting at rates of 250 to 500 g a.i. per ha versus the untreated. All trials conducted under a range of natural nematode field pressures in Brazil from 2014 to 2019.

By protecting crop roots, Reklemel™ active provides the grower the opportunity for better yields or more marketable produce. Using Reklemel pays off.

Figure 10. Greenhouse cucumber trial in China. Root gall assessment 90 days after transplanting the crop into soil infested with high population densities of root-knot nematodes, *Meloidogyne incognita*. Treatments top to bottom: Untreated control; Reklemel™ active applied as a hole drench application at 40 mg a.i. per target; Farmer's program 1; Farmer's program 2; Farmer's program 3.

Reklemel™ active Program vs. Farmers' Program

Using Reklemel™ active in your Integrated Nematicide Management (INM) program can make the difference to improve your yield versus your current approaches.

Figure 11. Soybean root health and plant vigor 60 days after crop emergence in Brazil. Root health and plant vigor are important factors for increased yield potential. Top: Reklemel™ active applied in-furrow at planting at 500 g ai/ha; Bottom: Untreated control.

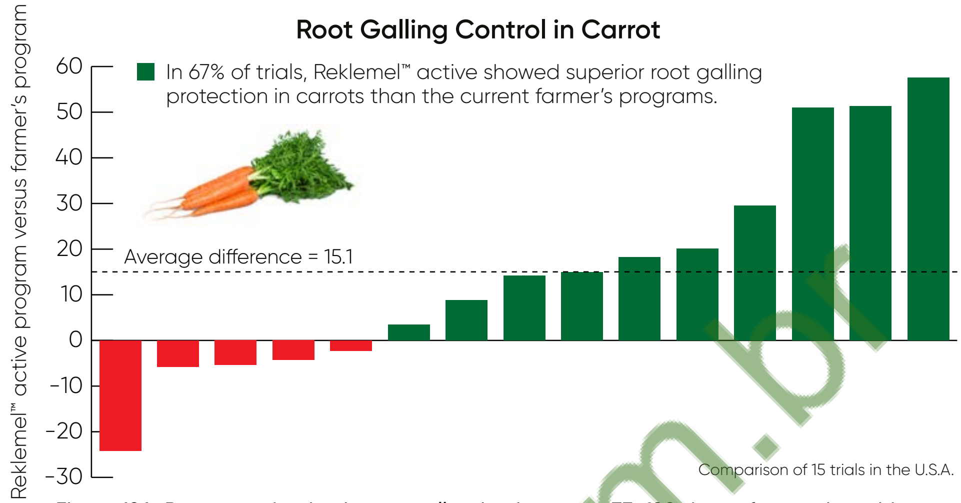


Figure 12A. Percent reduction in root gall rating in carrots 73-120 days after sowing with Reklemel incorporated in the seed bed at rates of 1-2 lb a.i. per acre versus farmers' current nematode control practices. All trials conducted under a range of natural nematode field pressures in the U.S.A. from 2014 to 2019.

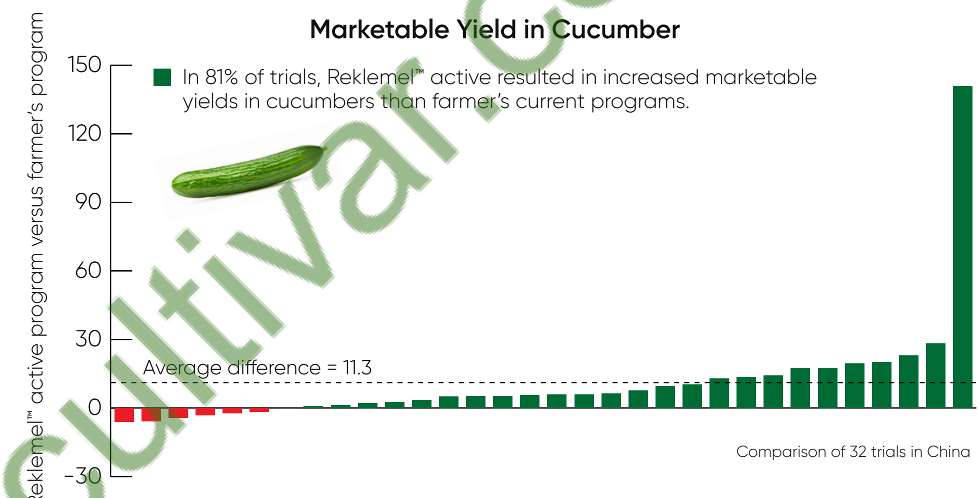


Figure 12B. Percent change in total marketable cucumber yield for Reklemel applied by hole-drench at 40 mg a.i. per plant versus farmers' current nematode control practices. All trials conducted under a range of natural nematode pressures in greenhouses in China from 2014 to 2019.

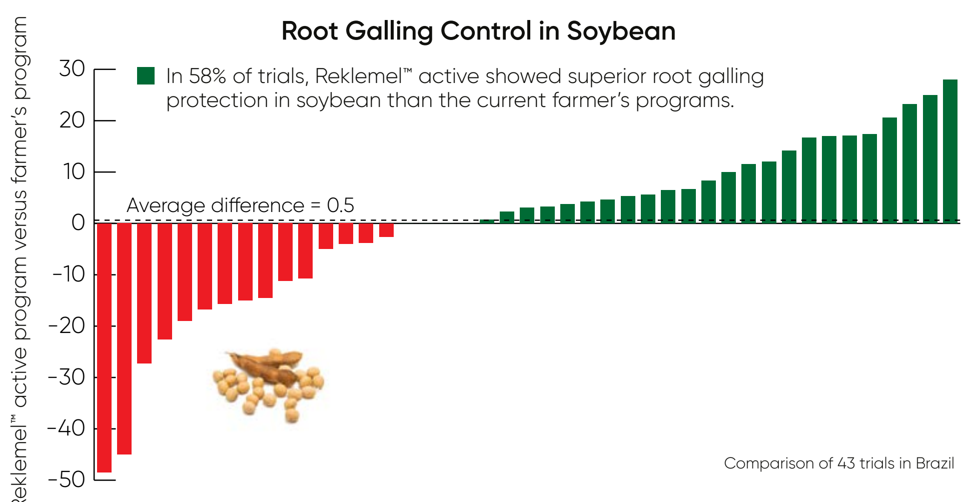


Figure 12C. Percent reduction in root gall rating in soybean 45 days after crop emergence for Reklemel applied in furrow at planting at rates of 250 to 500 g a.i. per ha versus farmers' current nematode control practices. All trials conducted under a range of natural nematode field pressures in Brazil from 2014 to 2019.

Flexibility of Timing and Application Methods

Reklemel™ active offers farmers excellent flexibility in its application timing and application methods while maintaining crop safety. Reklemel can be applied before planting the crop (pre-plant), at planting, and offers the option to follow up with in-crop treatments depending on country labels. Application methods developed in various countries around the world for Reklemel include drip irrigation, bed or soil directed sprays, micro-jets/sprinklers, chemigation, pre-plant hole drench, in-furrow applications with or without soil incorporation, etc. The excellent application timing flexibility and broad range of application methods represent a remarkable fit for a variety of crop production systems and nematode management needs. Reklemel will be most frequently applied shortly before or at planting in many annual crops, and during seasonal root flush periods in perennial crops.

Excellent Fit within Integrated Nematode Management (INM) and Integrated Pest Management (IPM) Programs

Reklemel™ active is compatible with cultural, mechanical, and biological tactics in local INM and IPM strategies. Its excellent fit with these practices will help support soil health, protect crop yields and quality, and enhance environmental benefits compared to many alternative nematicides.

Excellent Fit in Soil Health Programs

Modern nematicides should be effective on plant-parasitic nematode species while contributing to sustain healthy soils, which are critical for high and sustained crop production.

The proper balance of beneficial soil organisms in healthy soils helps promote strong root systems for enhanced water and nutrient absorption, and improved tolerance to biological and environmental stress. Thus, modern and sustainable farming requires tools and practices that target the enemies of plant roots and support beneficials that improve and sustain soil health (Figure 13).

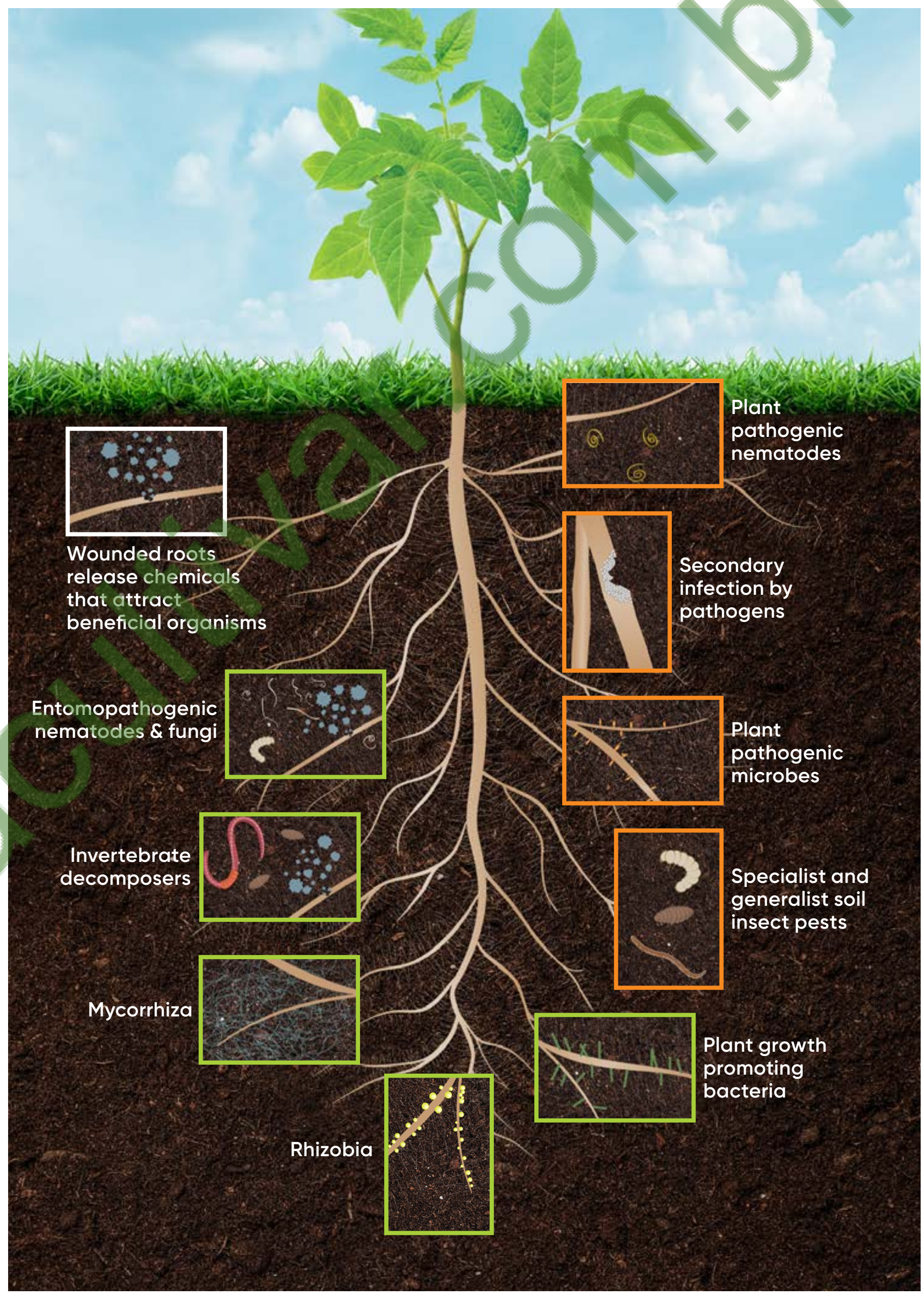


Figure 13.* Modern and sustainable farming requires tools and practices that target the enemies of plant roots (bordered in orange) and support beneficials (bordered in green) that improve and sustain soil health.

*Adapted from Pedobiologia - Journal of Soil Ecology Vol. 65, Tomonori Tsunoda and Nicole M. van Dam. Root chemical traits and their roles in belowground biotic interactions (A Review). Pages 58-67. Copyright (2017), with permission from Elsevier.

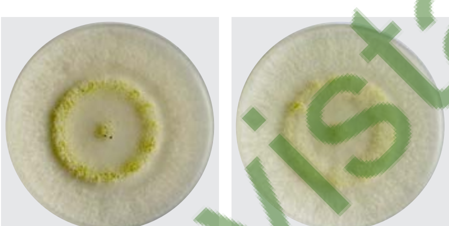
Reklemel™ active has excellent compatibility with naturally existing soil beneficial organisms and with soil-applied biologicals (Figure 14). Numerous laboratory studies demonstrate high compatibility of Reklemel with important soil organisms, including beneficial fungi, beneficial bacteria, and non-target beneficial nematodes (Table 3).

These beneficial soil organisms contribute to a healthy soil around the root zone (rhizosphere), help suppress soil pests and diseases and play important roles in the food web surrounding plant roots.

Table 3. Reklemel™ active compatibility shown in tests with a range of soil microbes that play an important role in soil rhizosphere health through pest and disease suppression.

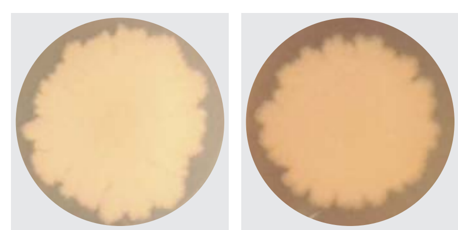
SPECIES	RHIZOSPHERE FUNCTION	COMPATIBILITY
Beauveria bassiana	Entomoparasitic fungus	Yes
Dactylella oviparasitica	Nematophagous fungus	Yes
Trichoderma hamatum	Disease suppressive fungus	Yes
Trichoderma asperellum	Disease suppressive fungus	Yes
Trichoderma harzianum	Disease suppressive fungus	Yes
Trichoderma virens	Disease suppressive fungus	Yes
Arthrobotrys oligospora	Nematophagous fungus	Yes
Harposporium anguillulae	Nematophagous fungus	Yes
Monacrosporium sinensis	Nematophagous fungus	Yes
Pochonia chlamydosporia	Nematophagous fungus	Yes
Purpureocillium (=Paecilomyces) lilacinus	Nematophagous fungus	Yes
Rhizophagus irregularis	Arbuscular mycorrhizal fungus	Yes
Bacillus subtilis	Beneficial bacterium	Yes
Bacillus firmus	Beneficial bacterium	Yes
Pseudomonas fluoresence	Beneficial bacterium	Yes

Figure 14. Excellent compatibility between Reklemel™ active with beneficial soil-applied biologicals.



Trichoderma harzianum: Reklemel at 100 ppm (left) versus untreated control (right).

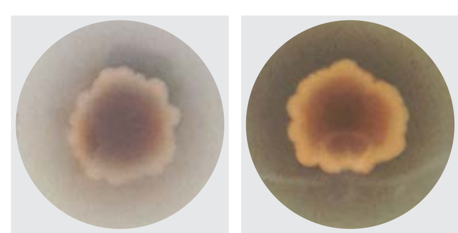
Trichoderma viride: Reklemel at 100 ppm (left) versus untreated control (right).



Bacillus firmus: Reklemel at 250 ppm (left) versus untreated control (right).

Purpureocillium (=Paecilomyces) lilacinus: Reklemel at 50 ppm (left) versus untreated control (right).

Beauveria bassiana: Reklemel at 50 ppm (left) versus untreated control (right).



Bacillus subtilis: Reklemel at 250 ppm (left) versus untreated control (right).

Nematicide Resistance Management

The risk of plant-parasitic nematodes developing resistance to an individual nematicide has proven to be low so far. Nonetheless, it is always recommended that an Integrated Nematode Management (INM) program be used in cases where populations of plant-parasitic nematodes occur at crop damaging levels, employing multiple tactics to provide effective plant-parasitic nematode control. These programs may include cultural practices, such as crop rotations or fallow periods, solarization, nematode resistant or tolerant varieties, and the use of effective chemical and biological nematicides.

Mammalian and Environmental Safety

Reklemel™ active has favorable environmental fate, toxicological, and eco-toxicological profiles, ensuring minimal impact to non-target organisms and the environment. In addition, Reklemel will be applied by methods such as drip irrigation, chemigation, directed soil spray, drench application or incorporation, which limits any potential for drift or movement from the target treatment zone. Application rates of Reklemel are relatively low compared to most alternative nematicides. Detailed best practices and guidance is provided on labels and supplementary materials for all types of Reklemel applications. Reklemel demonstrates a favorable profile compared to current standards. A summary of toxicological endpoints to non-target organisms is presented in Table 4.

Key points for the favorable mammalian toxicological profile of Reklemel™ active:

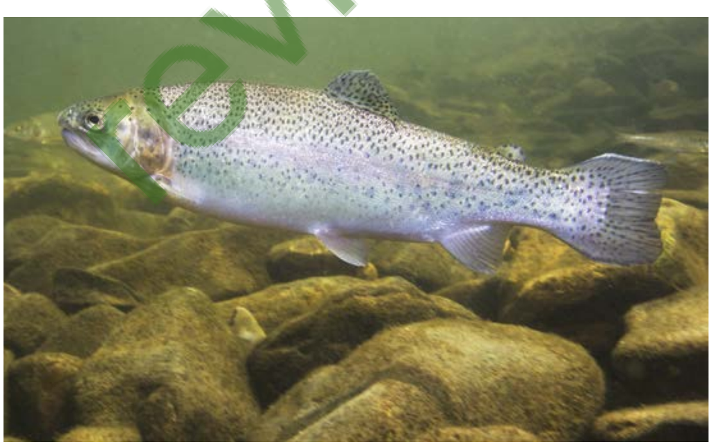
- Low acute toxicity.
- Not carcinogenic.
- Not genotoxic.
- Not immunotoxic.
- Not neurotoxic.
- No indication of reproductive or developmental toxicity.
- No evidence of endocrine toxicity.

Reklemel has an exceptionally favorable eco-toxicological profile including:

- Low toxicity to birds.
- Low toxicity to fish.
- Low toxicity to aquatic invertebrates.
- Low toxicity to algae.
- Does not bioaccumulate.

Northern bobwhite quail

Honey bee



Rainbow trout

Earthworm

Environmental Fate

The degradation rates observed in the soil and aquatic systems conducted in a variety of guideline studies for Reklemel™ active present a very favorable environmental profile and a low risk for groundwater.

Fate in Soil

Reklemel™ active degrades readily in soil under aerobic and anaerobic conditions. The rate of degradation does not show a pH dependence. The rate of aerobic degradation measured in laboratory soils showed low persistence. Degradation in soil was entirely microbial. Photolysis in soil does not contribute significantly to the degradation of Reklemel.

Reklemel has moderate mobility in soil (average K_{foc} for five types of soil = 198 mL/g). The K_d value correlates with percent organic carbon but not with soil pH. In addition, Reklemel shows enhanced sorption over time. Moderate mobility coupled with a low persistence in soil result in the projection of a low leaching potential for Reklemel. With a high solubility (2,147 mg/L) and a low Octanol-water coefficient (-0.16) at pH 7, this product has low potential to accumulate in the environment.

Fate in Water

Reklemel™ active is stable to hydrolysis and no meaningful degradation is likely at any pH due to hydrolysis reactions. However, when water solutions are exposed to sunlight, Reklemel degradation is quick, resulting in dozens of small molecule degradates over a short period of time. In natural water, the route of degradation was the same as in sterile buffers. In water-sediment systems, persistence is low under both aerobic and anaerobic conditions.

Fate in Air

Reklemel™ active has low volatility. The vapor pressure of Reklemel was 2.04×10^{-7} Pa and Henry's law constant of Reklemel is less than 3×10^{-2} Pa-m3/mol, suggesting little potential for volatilization in the environment.

The physical and chemical properties of Reklemel are summarized in Table 5.

Table 4. Toxicological endpoints of Reklemel™ active to non-target organisms.

Birds and mammals	
Mammalian acute oral, LD_{50} (mg/kg-bw)	1187
Mammalian chronic dietary, NOEL (mg/kg/d)	37.91
Avian Acute oral, LD_{50}, bobwhite quail (mg/kg-bw)	> 2250
Avian Dietary, LC_{50} (mg/kg-diet)	1414
Avian Reproduction, NOEL (mg/kg bw/d)	51.1
Avian Reproduction, NOEC (mg/kg-feed, ppm)	625

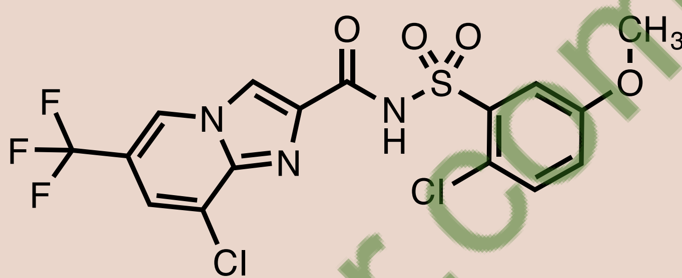
Terrestrial invertebrates	
Acute oral honey bee, LD_{50} (µg/bee)	>19.62
Acute contact honey bee, LD_{50} (µg/bee)	>200
Collembola, *Folsomia candida*, NOEC (mg/kg soil)	500
Soil mite, *Hypoaspis aculeifer*, NOEC (mg/kg soil)	1000
Earthworm, *Eisenia fetida*,acute 14 d, LC_{50} (mg/kg)	>1000
Earthworm, *Eisenia fetida*, chronic 56 d, NOEC (mg/kg)	100

Aquatic fish and invertebrates	
Acute freshwater fish, LC_{50} (mg/L)	>60
Chronic freshwater fish, NOEC (mg/L)	12
Acute saltwater fish, LC_{50} (mg/L)	>26
Chronic saltwater fish, NOEC (mg/L)	1.5
Acute freshwater invertebrate, EC_{50} (mg/L)	>120
Chronic freshwater invertebrate, NOEC (mg/L)	1.2
Acute saltwater invertebrate, EC_{50} (mg/L)	>30
Oyster, EC_{50} (mg/L)	>10
Log Kow	-0.16

Algae and aquatic plants	
Algae, Green EC_{50} (mg/L)	24 ($EC_{50\text{-yield}}$)
Algae, *Navicula pelliculosa*, EC_{50} (mg/L)	71 ($EC_{50\text{-biomass \& yield}}$)
Algae, *Skeletonema costatum*, EC_{50} (mg/L)	>48
Algae, *Anabaena flos-aquae*, EC_{50} (mg/L)	31 ($EC_{50\text{-yield}}$)
Aquatic plants, *Lemna* EC_{50} (mg/L)	16.4 ($EC_{50\text{-frond count yield}}$)
Aquatic plants, *Lemna* NOEC (mg/L)	7.2

Terrestrial plants	
Vegetative vigor, monocots, ER25 (lb/A)	> 1.794
Vegetative vigor, monocots, NOER (lb/A)	0.4485
Vegetative vigor, dicots, ER25 (lb/A)	> 1.794
Vegetative vigor, dicots, NOER (lb/A)	0.897
Seedling emergence, monocots, ER25 (lb/A)	> 1.794
Seedling emergence, monocots, NOER (lb/A)	1.794
Seedling emergence, dicots, ER25 (lb/A)	> 1.794
Seedling emergence, dicots, NOER (lb/A)	1.794

Table 5. Physical and chemical properties of Reklemel™ active.

Common Name	Fluazaindolizine (ISO)
Trade Name	Reklemel™ active
Code Number	DPX-Q8U80
Chemical Class	Sulfonamide
IUPAC:	8-Chloro-N-[(2-chloro-5-methoxyphenyl)sulfonyl]-6-(trifluoromethyl)-imidazo[1,2-a]pyridine-2-carboxamide
CAS:	8-Chloro-N-[(2-chloro-5-methoxyphenyl)sulfonyl]-6-(trifluoromethyl)imidazo[1,2-a]pyridine-2-carboxamide
CAS Registry Number	1254304-22-7
CIPAC number	986
Molecular Formula	$C_{16}H_{10}Cl_2F_3N_3O_4S$
Molecular Mass	468.24 g/mole
Chemical Structure	
Relative Density	1.6818
Physical State	Odorless solid. Pure active ingredient color was off-white, but the technical grade active ingredient manufacturing batches from different sources can vary in color from off-white to light yellowish-grey, reddish brown, beige, or brown, although all of them were confirmed with quite high purities.
Global Formulated Product (Main Trademark)	Salibro™ nematicide (500 g a.i./L SC)
Melting Point	218.5°C
Boiling Point	Decomposition at 260 °C
Flammability	Not highly flammable
Vapor Pressure (20°C)	2.04 x 10^{-7} Pa
Henry's Law Constant (20°C)	pH 4: 0.45 x 10-4 bar*m3/mol pH 7: 0.46 x 10-6 bar*m3/mol pH 9: 0.35 x 10-6 bar*m3/mol
Octanol/Water Partition Coefficient (25°C)	pH 4: 2.24 pH 7: -0.16 pH 9: -0.71 Distilled H_2O: 0.81
Dissociation Constant (pKa, 20 °C)	5.60
Hydrolytic Stability (DT_{50})	Stable
Aqueous Photostability (DT_{50})	1.6 days in natural water
Soil Photolysis (DT_{50})	Stable
Aqueous Solubility (20 °C)	Distilled H_2O: 0.0561 g/L (pH 6.4) pH 4: 0.0221 g/L pH 7: 2.1479 g/L pH 9: 2.8455 g/L
Solubility in various solvents (20°C)	Acetonitrile: 35.05 g/L Methanol: 3.47 g/L Acetone: 99.76 g/L Ethyl acetate: 27.62 g/L 1,2-Dichloroethane: 19.29 g/L o-Xylene: 1.247 g/L n-Octanol: 2.00 g/L n-Hexane: 0.002 g/L

Formulations and Worker Safety

Reklemel™ active will be marketed mainly under the global branded name Salibro™ SC nematicide, a suspension concentrate containing 500 grams of active ingredient per liter of product. Other branded formulation names may be developed for some specific countries. The United States Environmental Protection Agency assigned the signal word 'CAUTION' based on the Toxicity Category III for Reklemel.

Refer to country-specific labels for information about application and handling, including personal protective equipment (PPE), product mixers, loaders and applicators, and re-entry intervals (REI).

US EPA Reduced Risk Designation

The Reklemel™ new active ingredient application was accepted for review under the US EPA Office of Pesticide Program's Conventional Reduced Risk Pesticide Program.

Regulatory Information

Regulatory registrations are pursued to serve the agricultural needs for environmentally responsible plant-parasitic nematode management. Consult your local Corteva Agriscience representative for current information on Reklemel registration status for your country or territory and for additional regulatory information on Maximum Residue Levels (MRLs), Import Tolerances and product Stewardship Plans.

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