NATULAR® G30

NATURALLY DERIVED ACTIVE INGREDIENT

Larvicide for Mosquito Control

- Granular formulation
- Up to 30 days of control
- Reduced Risk active ingredient
- WHO PQ Listed – PQT/VC Ref Number: 020-003
- Unique mode of action
- Novel class of chemistry for public health
- Formulated for sustainable solutions

RESOURCE GUIDE

NATULAR® G30
A LARVICIDE WITH A NATURALLY DERIVED ACTIVE INGREDIENT

Natular larvicides are a complete portfolio of public health mosquito control larvicides developed and manufactured exclusively by Clarke. All Natular formulations contain the patented active ingredient, Qalcova® brand spinosad, a product derived from a naturally-occurring soil bacterium. Simply stated, Natular is like no other larvicide on the market.

Natular G30 is an extended-release granule formulation in the Natular portfolio that delivers up to 30 days of larval control in a wide variety of habitats.

PORTFOLIO FEATURES »

Reduced Risk active ingredient

Qalcova spinosad is registered under the U.S. EPA's Reduced Risk program, meaning it has reduced risk to human health, the environment, and non-target organisms when compared to other available alternatives.

Unique mode of action

Qalcova's unique mode of action ensures no cross-resistance with other chemistries and works on all four stages of feeding mosquito larvae.

Novel class of chemistry

Natular is the first and only public health larvicide in the IRAC Class 5 chemical classification, making it an excellent insecticide resistance management tool.

WHO PQ Listed

Multiple Natular formulations, including G30, have been evaluated and listed by the World Health Organization's Pre-Qualification Program for Vector Control Products (WHO-PQ).

Sustainable solutions

The Natular portfolio contains multiple formulations for treating a wide range of habitats, and most are Organic Material Review Institute (OMRI) Listed® for use in and around organic agriculture.

PORTFOLIO BENEFITS »

Provides the right balance of efficacy with environmental stewardship

Minimal PPE requirements for application

Excellent option for resistance management and rotational use

Lower toxicity toward mammals and other non-target organisms

All formulations of Natular were designed as sustainability solutions

Green Chemistry active lets you use with confidence in your community

Offers exceptional control of feeding larvae from the first through early 4th instar stages

WE'RE SETTING NEW BENCHMARKS WITH QALCOVA BRAND SPINOSAD

Qalcova spinosad, a product derived from a naturally ocurring soil bacterium, is the active ingredient in Natular. It provides the perfect balance of efficacy and environmental stewardship, and has an excellent safety record.

The complete Natular portfolio of larvicides includes multiple formulation types, including granules, liquids, and tablets, to fit a wide range of habitats. Each formulation type offers exceptional handling characteristics and proven, reliable efficacy.

The Structure of Qalcova

Chemical name: Saccharopolyspora spinosa
Common name: Spinosad, a patented combination of spinosyn A and spinosyn D

	SPINOSYN A	SPINOSYN D
Molecular Formula	$C_{41}H_{65}NO_{10}$	$C_{42}H_{67}NO_{10}$
Molecular Weight	731.98	746.00
Color and State	Crystalline Solid, White to Tan	Crystalline Solid, White to Tan
Vapor Pressure (25°C)	3.0×10^{-11} kPa	2.0×10^{-11} kPa
Melting Point	84—100°C	161—170°C
Water Solubility: (20°C)		
pH 5	290 mg/L	28.7 mg/L
pH 7	235 mg/L	0.332 mg/L
pH 9	16 mg/L	0.053 mg/L

The Origins of Qalcova Spinosad and Natular

In 1982, a vacationing scientist took a soil sample from a drum that was used to make rum in the Caribbean. From this sample, a new species of bacteria was identified in 1986: *Sacchrapolyspora spinosa*. (This translates into "spiny sugar.") The bacteria was later fermented in a lab and yielded spinosyns A and D, the most active metabolites of S. spinosa. Together, they comprise spinosad.

In 2002, Clarke acquired the public health development rights to Qalcova spinosad. After six years and over 35,000 hours of development and regulatory review, Natular larvicides became the first public health label for spinosad, and also the first aquatic use pattern with the active as well.

Today, Qalcova products are registered for use over 250 crops in more than 95 countries. Qalcova is also approved for non-crop uses on turfgrass and ornamental plants, for livestock pest control, fire ant control, and mosquito larva control, among other uses.

The First Reduced Risk Larvicide

In 1993, the U. S. Environmental Protection Agency created the Reduced Risk Pesticide Initiative to "encourage the development, registration and use of lower-risk pesticide products, which would therefore result in reduced risks to human health and the environment when compared to existing alternatives."

Qalcova spinosad, the active ingredient in Natular, is the only Reduced Risk larvicide for mosquito control. According to the EPA, the advantages of Reduced Risk pesticides include:

- Low impact on human health
- Lower toxicity to non-target organisms (birds, fish, plants)
- Low potential for groundwater contamination
- Low use rates
- Low pest resistance potential
- Compatibility with Integrated Pest Management (IPM) practices

https://www.epa.gov/pesticide-registration/conventional-reduced-risk-pesticide-program

Recipient of The U.S. Presidential Green Chemistry Challenge Award

Spinosad is one of less than 20 pesticide products to ever receive the Presidential Green Chemistry Challenge Award*, one of the U.S. Government's highest environmental honors.

Corteva Agriscience (formerly Dow Agrosciences) received the U.S. Green Chemistry award on the development of spinosad as an active ingredient in 1999. Clarke was also awarded a U.S. Green Chemistry award for its end-use larvicide tablet technology containing spinosad in 2010.

Green chemistry, also known as sustainable chemistry, is the design of chemical products and processes that reduce or eliminate the use or generation of hazardous substances. The benefits of green chemistry technologies include:

- Reduced waste, eliminating costly end-of-the-pipe treatments
- Safer products
- Reduced use of energy and resources

Green chemistry applies across the life cycle, including the design, manufacture, and use of a chemical product.

*www.epa.gov/greenchemistry

A REVOLUTIONARY MODE OF ACTION THAT'S IDEAL FOR ROTATIONAL USE

Delivering a Unique Mode of Action

The active ingredient in Natular G30 works like no other larvicide. Qalcova spinosad alters the function of insect nicotinic acetylcholine receptors in a unique action that causes continuous nervous impulses. This constant involuntary nervous stimulus causes paralysis and death. The action results primarily by ingestion, as well as by contact with the active.

In a Class by Itself: Group 5

Because of its unique mode of action, Qalcova spinosad is classified as a Group 5 insecticide by the Insecticide Resistance Action Committee. It's the only active ingredient classified in Group 5 used for mosquito control. Because this class is unique and distinct from all other public health larvicides, Natular is truly one of a kind.

It also makes an excellent option for resistance management. Its novel mode of action and distinct class grouping makes Natular ideal for rotational use since it shows no cross-resistance with existing products used for mosquito control.

Proven Performance

The consistent performance of Qalcova spinosad — logged and observed in testing and operational work — has demonstrated exceptional control of larvae from the first through early fourth instar stages. Qalcova spinosad begins to work immediately upon contact and ingestion; its first visible effects are seen within hours of application. Optimal control is reached within 24-72 hours, sustained at very uniform levels for the labeled control period.

Natular formulations have been very effective in a wide spectrum of habitats in more than 50 domestic tests and 15 international studies. Data has been gathered on more than 20 species and continues to be expanded with operational use.

We believe that an important part of being an environmental steward is product rotation. Our product rotation methods maximize the effectiveness of every program by preventing cross-resistance. To help select products for rotation in your program, visit https://www.clarke.com/mosquito-products/ to view our full line of product offerings.

WHO PQ Listed

Several formulations in the Natular brand portfolio, including Natular G30, have been evaluated and listed by the World Health Organization's Pre-Qualification Program for Vector Control Products (WHO PQ).

For more details visit:

https://extranet.who.int/prequal/vector-control-products

https://extranet.who.int/prequal/vector-control-products/prequalified-product-list

OMRI Listed

Most Natular larvicide formulations, including Natular G30, are Organic Material Review Institute (OMRI) Listed® for use in and around organic farms and gardens. OMRI reviews to the USDA National Organic Program Standard.

OMRI™ Listed
Organic Materials Review Institute

A Clarke NextGen Product

Natular was the first product to be ranked in the "NextGen" category on the Clarke Eco-Tier® Product Index. NextGen products represent cutting-edge, novel solutions for the most sustainable mosquito control possible.

NEXTGEN

Qalcova spinosad is a naturally derived active ingredient produced during fermentation by the soil organism, Saccharopolyspora spinosa.

NATULAR G30 FORMULATION SPOTLIGHT

About Natular G30

Natular G30 is a multi-brood, extended-release granule that contains 2.5% Qalcova spinosad and delivers 30 days of larval control in treated sites. It is well suited for use in permanent or temporary standing water areas, in open or dense vegetation habitats, fresh or brackish water types, in cold or warm water conditions, and in areas with high or low organic content and pollution. Please refer to the product label for specific application sites and rates.

Applying Natular G30

Natular G30 can be applied by hand, through conventional ground application equipment like backpacks, with air blast equipment, or by air (fixed wing airplanes, helicopters, or drones) to target standing water sites where mosquito breeding is occurring or expected. Please refer to the product label for specific application guidance and always ensure application equipment is properly calibrated for accurate dosing.

Flexible Treatment Window

Pre-treatment applications of larvicides in areas that intermittently flood and breed mosquitoes is an important larval source management practice, and larvicides that are effective on multiple broods and all four feeding instar stages offer the most flexibility to applicators. Natular G30 offers exceptional application flexibility and is labeled for pre-hatch applications. When used as a pre-treatment tool, Natular G30 will activate once wet, and begin to control mosquito breeding for 30 days. Field study work also shows that Natular G30 will continue to deliver larval control after rewetting and dry down periods.

REDUCING ENVIRONMENTAL IMPACT

The active ingredient in Natular G30, Qalcova spinosad, is a highly selective insect control product with high potency for target insects but low toxicity toward mammals and other non-target organisms.

Environmental Fate

In Soil: Spinosad is rapidly broken down by microbes in soil. Primary mechanisms of degradation are sunlight photolysis and microbial breakdown. Under field conditions, spinosad breaks down rapidly in the soil with observed half-lives of 9-17 days. It is moderately to strongly absorbed by soil particles and is considered to be "relatively immobile to immobile" with regard to leaching.

In Water: In natural water systems, spinosad degrades rapidly in sunlight. A water column half-life of less than one day has been observed in artificial pond systems in outdoor conditions.

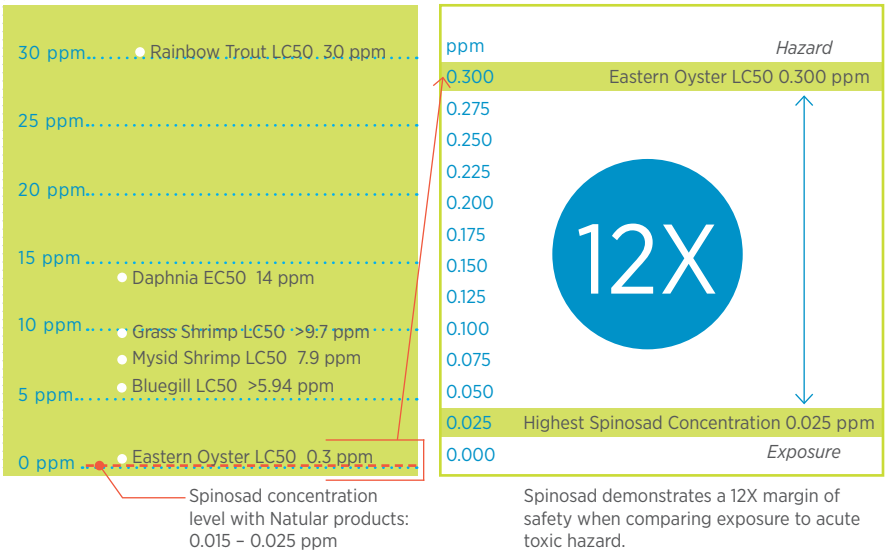
In Animals: Because of its unique mode of action, spinosad is highly selective to insects. In mammals, spinosad is not readily absorbed through the skin; any minute amounts that are absorbed or ingested are rapidly metabolized to inactive by-products, which are excreted. As a result, it has very low acute toxicity. In long term studies, no evidence of carcinogenicity, mutagenicity, or neurotoxicity has been observed.

Toxicity, Mutagencity, Genotoxicity

Spinosad is well known to present a relatively low risk to beneficial and non-target insects compared to other broad-spectrum, insecticide products. It is not acutely toxic to terrestrial birds, wildlife, or to fish and most aquatic invertebrates. Investigated in a battery of genotoxicity studies, it has been found to possess no mutagenic potential.

During the six years of development and the operational use of Natular products since introduction in 2009, there have been no observed or validated non-target effects. Many characteristics of spinosad make this possible: low dose rate, rapid breakdown by sunlight, binding to soil, rapid dissolution in water, as well as non-target location and lifecycle at time of application.

Indicator Aquatic & Invertebrate Species Sensitivity to Spinosad

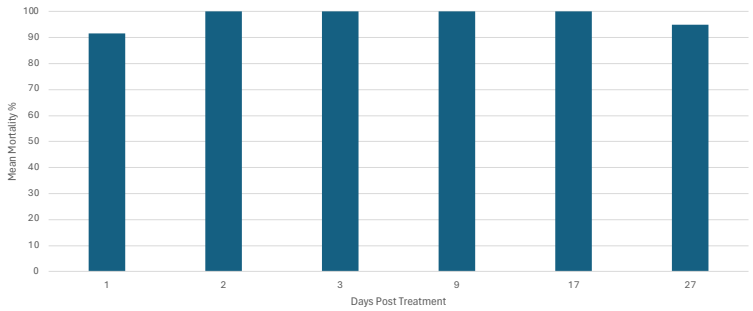


Spinosad concentration level with Natular products: 0.015 – 0.025 ppm

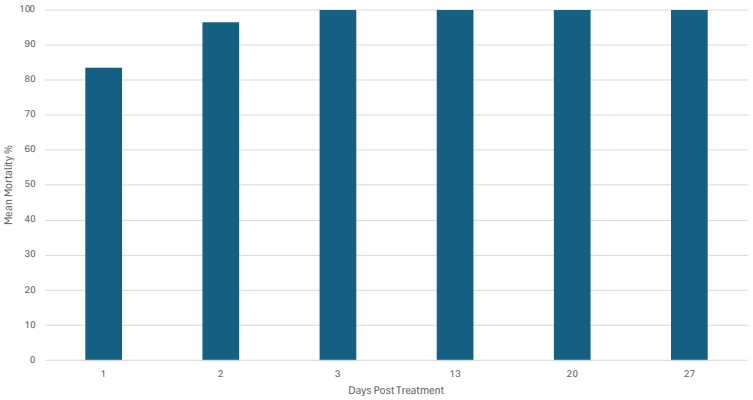
Spinosad demonstrates a 12X margin of safety when comparing exposure to acute toxic hazard.

RESULTS

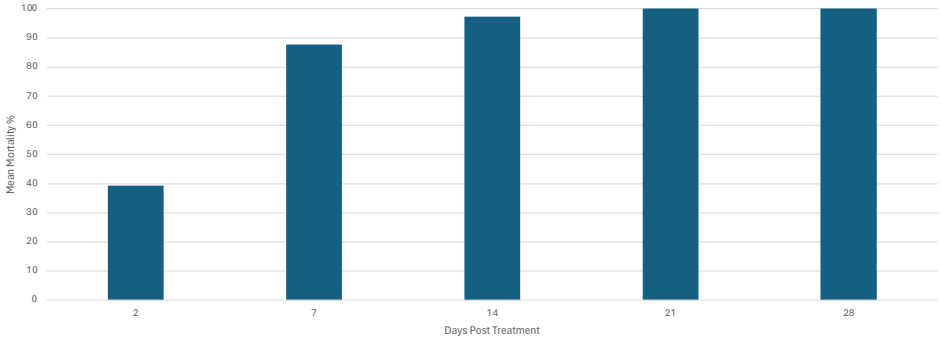
Natular G30 Efficancy on *Aedes aegypti* late instar larvae
0.058 mg/mL of Natular G30 applied in 120L plastic barrels, India



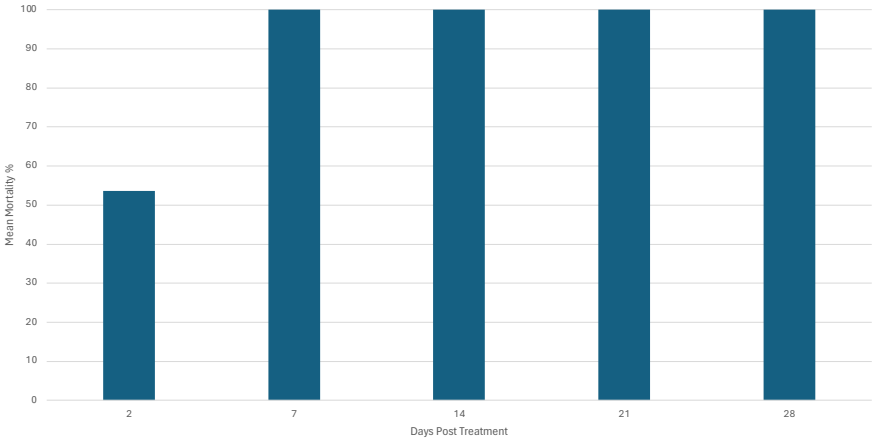
Natular G30 Efficancy on *Anopheles stephensi* late instar larvae
0.074 mg/mL of Natular G30 applied in 150L cement cisterns, India



Natular G30 Efficancy on *Anopheles arabiensis* late instar larvae
25 a.i./m^2 of Natular G30 applied to rice paddies, Kenya



Natular G30 Efficancy on *Culex quinquefasciatus* late instar larvae
25 a.i./m^2 of Natular G30 applied in septic pits, Kenya



FREQUENTLY ASKED QUESTIONS

Q: What is the active ingredient in Natular® G30?
A: Qalcova brand Spinosad. It is a naturally derived active ingredient produced during fermentation by the soil organism, *Saccharopolyspora spinosa*. The natural metabolites produced during the fermentation process were termed "spinosyns". Spinosad is the collective term for the two most prominent and most active compounds in the fermentation broth (spinosyn A and spinosyn D). Hence the name "Spinosad".

Q: How does the active ingredient in Natular formulations control mosquito larvae?
A: Spinosad has a novel mode of action; it alters the function of insect nicotinic acetylcholine receptors in a unique manner. Ultimately paralysis sets in upon ingestion and contact and the mosquito larvae don't recover.

Q: What does Group 5 Insecticide mean on the Natular label?
A: Group 5 is a designation by IRAC (Insect Resistance Action Committee), which is a global industry organization that promotes the development of insecticide resistance management strategies to maintain efficacy and support sustainable agriculture and improved public health. Each group has a distinctly different mode of action. Spinosad is the only active ingredient in Group 5 used for mosquito control. The benefit of this is that it has no cross-resistance with existing products – making Natular an excellent option for resistance management.

Q: What are the inert ingredients in Natular G30?
A: Natular G30 is a silica-based granule. All inert components in Natular G30 are non-synthetic (natural) or are synthetic components which do not contribute to mammalian or aquatic toxicity.

Q: Are Natular formulations suitable for use in organic agriculture?
A: Most formulations of Natular, including G30, are listed by the Organic Materials Review Institute (OMRI) for use in and around organic agriculture. OMRI reviews to the USDA National Organic Program standard.

Q: What types of mosquito larvae can Natular control?
A: Natular can kill the larvae of both nuisance and disease vectoring mosquitoes, including *Aedes*, *Anopheles* and *Culex* species that can carry and transmit diseases, such as West Nile Virus, Dengue, Zika and Malaria. Natular is effective on larvae from all four feeding instar stages and has been tested on twenty of the most common vector and nuisance mosquito species.

Q: What is the ecological toxicity of Natular?
A: Spinosad was registered under the U.S. EPA Reduced Risk program and has favorable environmental characteristics compared to other mosquito larvicides. The active ingredient in Natular larvicides, spinosad, is well known to present a relatively low risk to beneficial and non-target insects compared to other broad-spectrum, insecticide products. Spinosad is not acutely toxic to terrestrial birds, wildlife, or to fish and most aquatic invertebrates. Extensive field experience indicates that spinosad's overall impact on beneficial insects is generally limited and transitory, and spinosad fits well into Integrated Pest Management (IPM) programs.

Q: What impact does spinosad have on non-targets?

A: Spinosad is of low acute and chronic toxicity to a wide range of non-target species. Under laboratory conditions, spinosad is toxic to some aquatic invertebrates, primarily upon chronic exposure. The rapid degradation of spinosad in natural aquatic environments prevents the long-term exposure to levels needed for these effects to occur in real world situations. Indeed, field studies indicate that effect on non-target species is mitigated by virtue of low application rates and rapid dissipation of spinosad. Natular may be used in fish ponds at label rates.

Q: Is Natular's active ingredient toxic to mammals?
A: Mammals rapidly metabolize spinosad and any by-products are excreted. So spinosad has a very favorable mammalian toxicity profile:

- Low acute tox for both technical and end-use formulations
- No reproductive effects, not a teratogen
- Negative in genotoxicity tests
- Not a carcinogen
- No endocrine effects

Q: What about resistance?
A: The active ingredient in Natular products, spinosad, has not previously been used to control mosquitoes, hence there is no resistance to it. Spinosad is in a unique chemical class different from any other current products used in mosquito control, so there is no cross-resistance.

Q: Why is Natular G30 a good rotational product?
A: Natular formulations are the new standard in larvicide control and are excellent as rotational products because they contain a new active ingredient with a distinctly different mode of action. Natular products are a key component in rotational programs for larvicide control. Rotation will help preserve the continued use of existing products.

Q: How does Natular™ G30 perform in habitats containing high organic matter?
A: We have seen excellent results in habitats with high concentrations of organic debris with Natular, e.g. polluted water, sewage lagoons, and waters with high concentrations of leaf litter or other organic debris.

Q: How does varying amounts of sunlight affect the performance of Natular G30 products?
A: Natular formulations were developed specifically for use in natural mosquito habitats, with single or multi-brood control objectives in mind. To date we have seen very uniform control levels regardless of sunlight intensity, and consistent with the labeled control claim of each Natular formulation.

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Clarke is a global environmental products and services company. Each year, Clarke helps make communities around the world more livable, safe and comfortable by pioneering, developing and delivering environmentally responsible mosquito control solutions.

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