



# NATULAR<sup>®</sup>

## NATURALLY DERIVED ACTIVE INGREDIENT

Larvicide for Mosquito Control

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Reduced Risk active ingredient

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Unique mode of action

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Novel class of chemistry for public health

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Formulated for sustainable solutions

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# THE FIRST AND ONLY COMPLETE PORTFOLIO OF LARVICIDES WITH A NATURALLY DERIVED ACTIVE INGREDIENT

For years there have been only five active ingredient choices for larval control. Now there's a sixth, and it's found only in **Natular**<sup>®</sup>. With formulations developed and manufactured exclusively by Clarke, its patented ingredient, spinosad, is a product derived from a naturally occurring bacterium. Natular is in a chemical class different from all other larvicides and has a unique mode of action that helps fight resistance. Simply stated, Natular is like no other larvicide on the market.

## BENEFITS INCLUDE >>

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### Reduced Risk active ingredient

The active ingredient in Natular formulations is designated by the E.P.A. as Reduced Risk. This means reduced risks to human health and the environment when compared to other chemical and biochemical larvicides.

### Unique mode of action

The unique mode of action of spinosad ensures no cross resistance with other chemistries.

### Novel class of chemistry

Natular formulations are Group 5 insecticides — the first public health larvicides in this class — that provide you confident, resistance fighting performance.

### Formulated for sustainable solutions

All formulations, except Natular DT are OMRI (Organic Materials Review Institute) Listed, enabling them to be used in and around organic agriculture. The international tablet has not been submitted for review.

## What makes Natular® so unique?

Natular and its active ingredient, spinosad, offer a healthier alternative to protecting the well-being of communities.



Provides the right  
balance of efficacy  
with environmental  
stewardship

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Excellent option for  
resistance management  
and rotational use

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All formulations of  
Natular were designed as  
sustainability solutions

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Six advanced  
formulations to fit  
any habitat

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

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Minimal PPE  
requirements for  
application

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Breaks down rapidly in soil—  
spinosad degrades into  
carbon dioxide and water

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Green Chemistry active  
lets you use with confidence  
in your community

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# WE'RE SETTING NEW BENCHMARKS WITH SPINOSAD

**Spinosad**, a product derived from a naturally occurring soil bacterium, is the active ingredient in Natular®. It provides the perfect balance of efficacy and environmental stewardship. Spinosad has an excellent safety record. It breaks down quickly and does not bioaccumulate in the environment. In addition, all inert ingredients in domestic Natular formulations are included on the EPA's List of Minimal Risk Inert Ingredients.

## The Structure

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)    | $3.0 \times 10^{-11}$ kPa       | $2.0 \times 10^{-11}$ 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 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: *Saccharopolyspora 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 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.

## 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.”

Spinosad, the active ingredient in Natular, is one of only sixteen chemicals registered as a Reduced Risk pesticide and 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

## Recipient of The Presidential Green Chemistry Challenge Award

Spinosad is one of only five pesticide products to ever receive the Presidential Green Chemistry Challenge Award\*, one of the U.S. Government’s highest environmental honors.

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](http://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® works like no other larvicide. 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, 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, this makes the Natular portfolio 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 spinosad — logged and observed in testing and operational work — has demonstrated exceptional control of larvae from the first through early fourth instar stages. 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 will be expanded as usage increases.

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 [clarke.com/mosquitocontrolproducts](http://clarke.com/mosquitocontrolproducts) to view our full line of product offerings.

# FORMULATED TO MEET THE NEEDS OF ENVIRONMENTALLY SENSITIVE HABITATS

## Meets Organic and Sustainable Practice Standards

Natular® larvicides were formulated with a respect for the ever increasing number of communities with green or sustainability programs. All formulations except Natular DT have been listed by OMRI for use in organic production. Just knowing these products can be used in and around organic food production can give you confidence when using in public spaces.

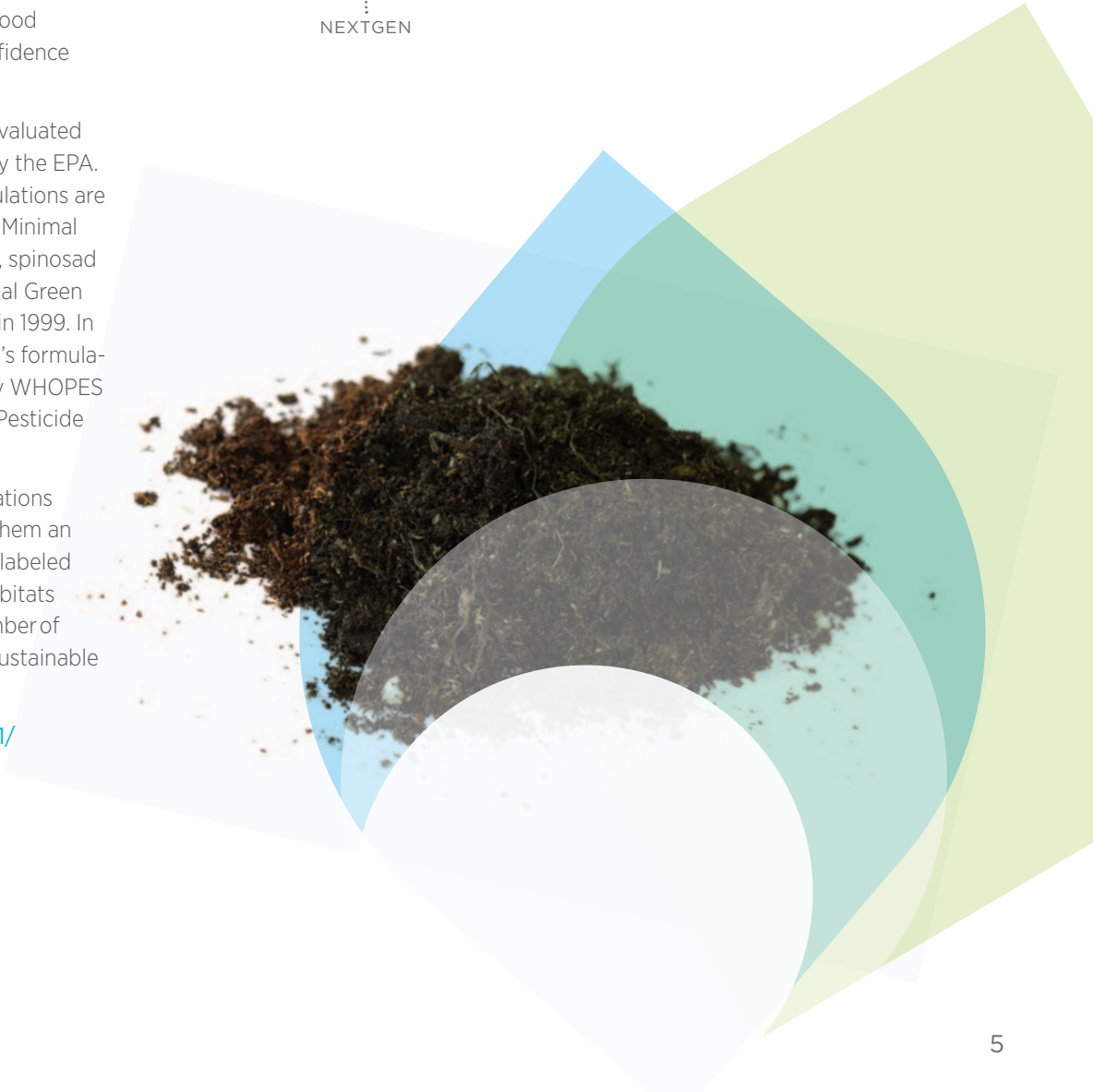
Natular is the first larvicide evaluated as a Reduced Risk product by the EPA. All ingredients in all its formulations are included on the EPA's List of Minimal Risk Inert Ingredients. In fact, spinosad received the EPA's Presidential Green Chemistry Challenge Award in 1999. In addition, two of the portfolio's formulations have been evaluated by WHOPEs (World Health Organization Pesticide Evaluation Scheme).

Bottom Line: Natular formulations meet the criteria that make them an excellent choice for not only labeled environmentally-sensitive habitats but also for the growing number of communities with green or sustainable practice guidelines.

Visit [www.epa.gov/opprd001/workplan/reducedrisk.html](http://www.epa.gov/opprd001/workplan/reducedrisk.html) for more details.

## Introducing NextGen Products

Natular is also the first product to be ranked in the "NextGen" category on the Clarke Eco-Tier™ Index of environmental impact.



# SIX DISTINCT FORMULATIONS

Natular® is available in six advanced formulations to fit the needs of any habitat. Each formulation offers exceptional handling characteristics and is labeled for only protective eyewear PPE.

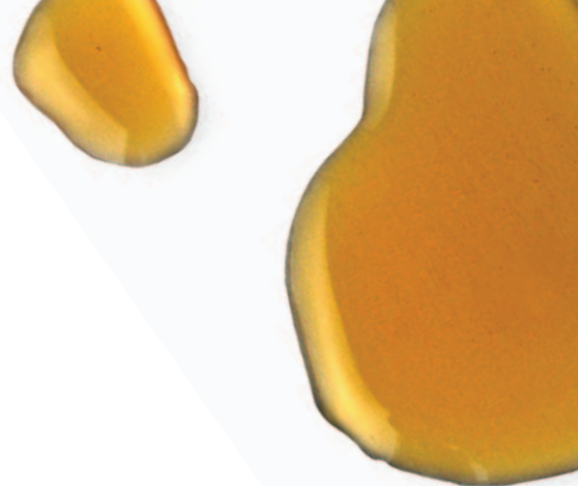
|                             | FORMULATION                                   | CARRIER & APPEARANCE                           | APPLICATION RATE*  | BULK DENSITY  |
|-----------------------------|---|--|--------------------|---------------|
| EC                          | Single-brood liquid                           | Liquid, dark and slightly cloudy in appearance | 1.1 – 2.8 fl oz/ac | 9.68 lbs/gal  |
| G                           | Single-brood granule                          | Granules made from corn cobs                   | 3.5 – 9 lbs/ac     | 33 lbs/cf     |
| T30                         | Multiple-brood 30-day tablet                  | A dust-free tablet                             | 1/100 sf           | 6 g/tablet    |
| XRT                         | Multiple-brood extended release tablet        | A dust-free tablet                             | 1/100 sf           | 40 g/tablet   |
| G30                         | Multiple-brood extended release granule       | Granules made from silica                      | 5 – 20 lbs/ac      | 85 lbs/cf     |
| DT<br>(not available in US) | Multiple-brood tablet for containerized water | Bi-layer tablet                                | 1/container        | 1.35 g/tablet |

## For International Use: Natular DT

In rural and urban areas of Latin America, the Middle East, Africa and Asia, the need to treat water barrels and other containers is crucial in the fight against Dengue, Yellow Fever and Chikungunya. To meet this need, Clarke developed the innovative bi-layer Natular DT formulation.

One layer works immediately while the second dissolves slowly. Thus, each tablet can treat a 200 liter barrel of water for more than 60 days. Successfully evaluated by WHOPEs, Natular DT has significantly reduced volume requirements, making transportation and storage much easier.

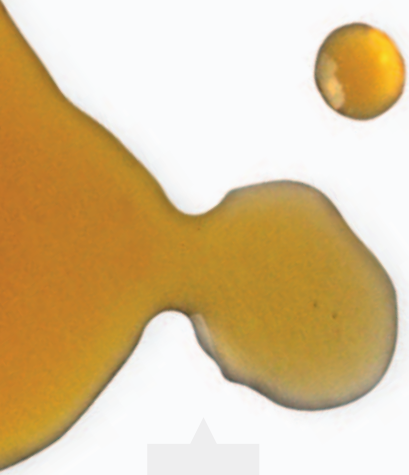
\* depending on area of treatment



DT







2EC



G30



T30



XRT



G



# REDUCING ENVIRONMENTAL IMPACT

The active ingredient in Natular® larvicides, 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 degrades readily in the soil environment and is non-persistent. 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 less than one day, degrading into carbon dioxide and water by the soil microbial community. 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.

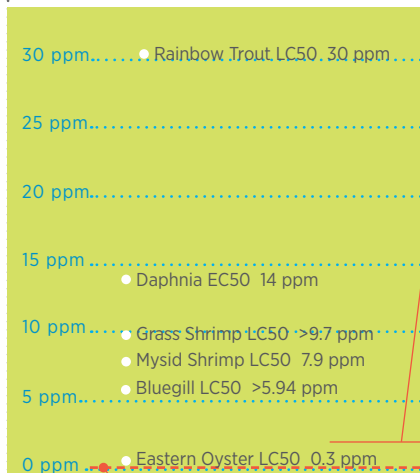
## Toxicity, Mutagenicity, Genotoxicity

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.

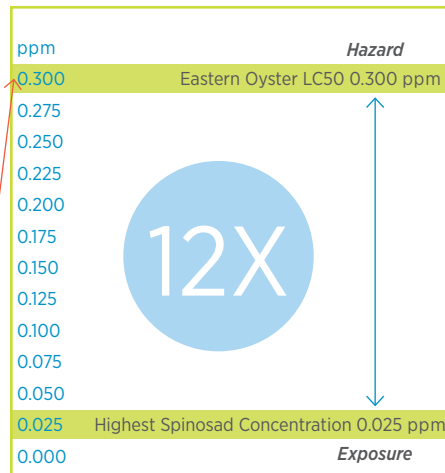
During the six years of development and the operational use of Natular products since introduction in 2009, there have been no observed or validated non-target effects. Many characteristics of spinosad make this possible: low dose rate, rapid breakdown by sunlight, binding to soil, rapid dissolution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

### Indicator Aquatic & Invertebrate Specie Sensitivity to Spinosad

#### TOXICITY CONCENTRATIONS PPM



Spinosad concentration level with Natular products: 0.015 – 0.025 ppm



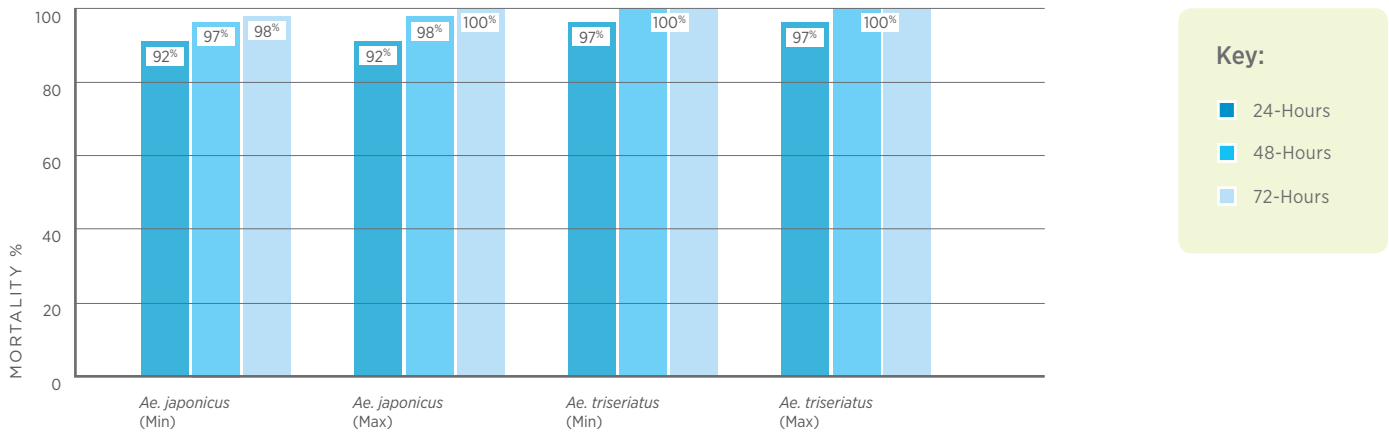
Spinosad demonstrates a 12X margin of safety when comparing exposure to acute toxic hazard.

# RESULTS

## Natular® EC

Rate: 1.1 fl oz/ac (Min), 2.8 fl oz/ac (Max)

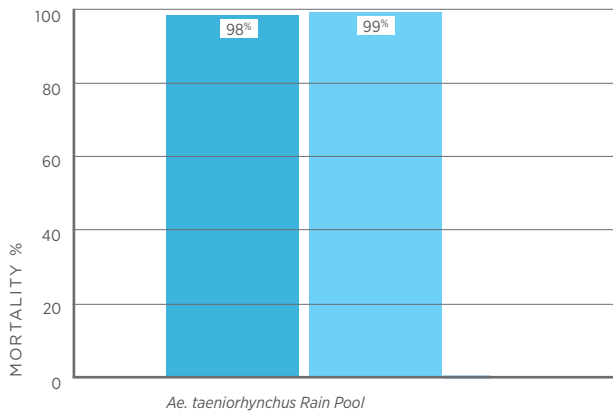
Location: Kentucky, 2008



## Natular G

Rate: 9 lb/ac (Max)

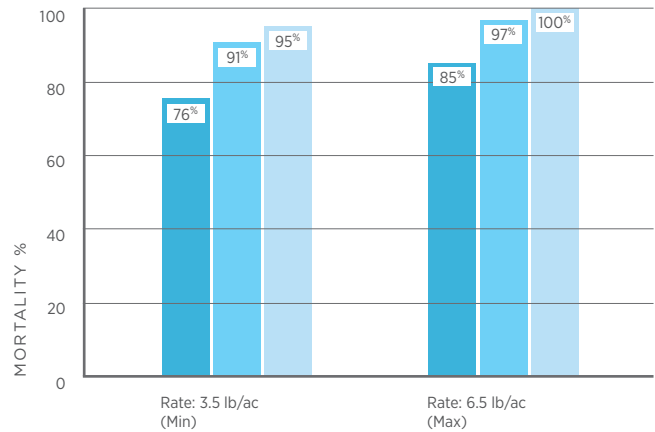
Location: Florida, 2008



## Natular G

Species: *Ae. trivittatus*

Location: Kentucky, 2008



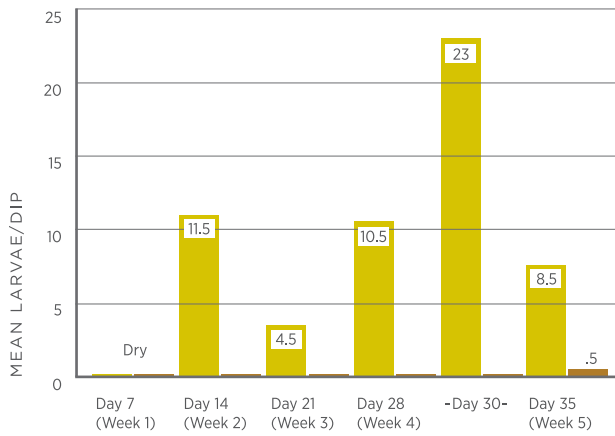
# RESULTS

## Key:

- Unt
- Trt

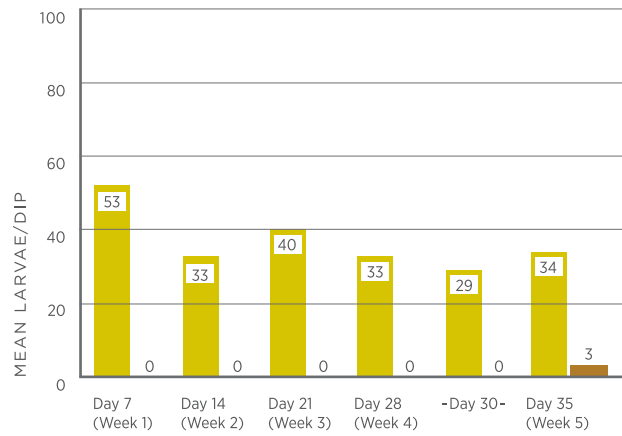
### Natular G30

Habitat: Retention Ponds/*Ae. vexans*-*Cx. pipiens*  
 Rate: 10 lb/ac (<Mid)  
 Location: Illinois, 2008



### Natular T30

Habitat: Catch Basins/*Cx. restuans* - *pipiens*  
 Location: Illinois, 2008

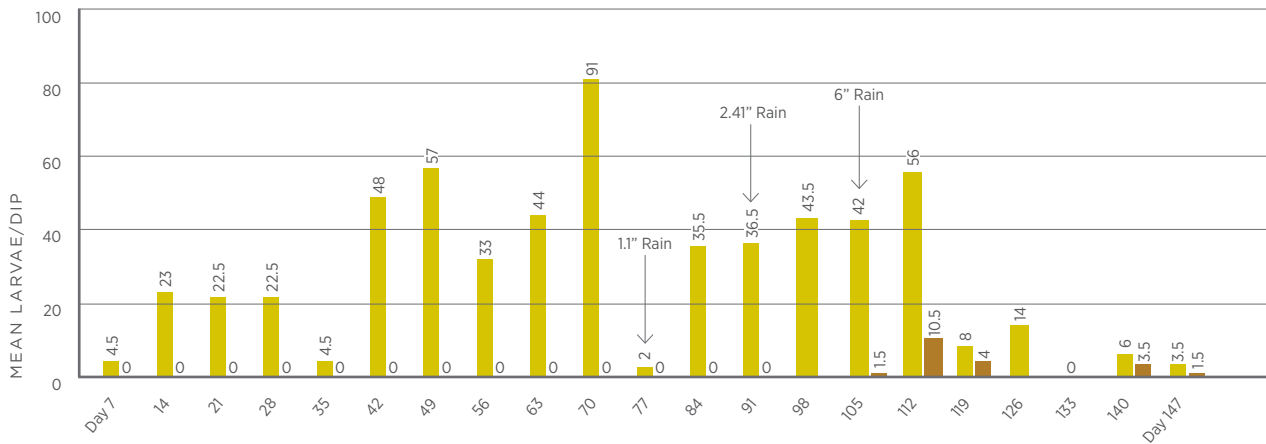


## Key:

- Unt
- Trt

### Natular XRT

Habitat: Catch Basin/*Cx. pipiens*  
 Location: Illinois, 2008



# RESULTS

## Natular G30

Habitat: Sample from Benthic Soils, Lake Monroe

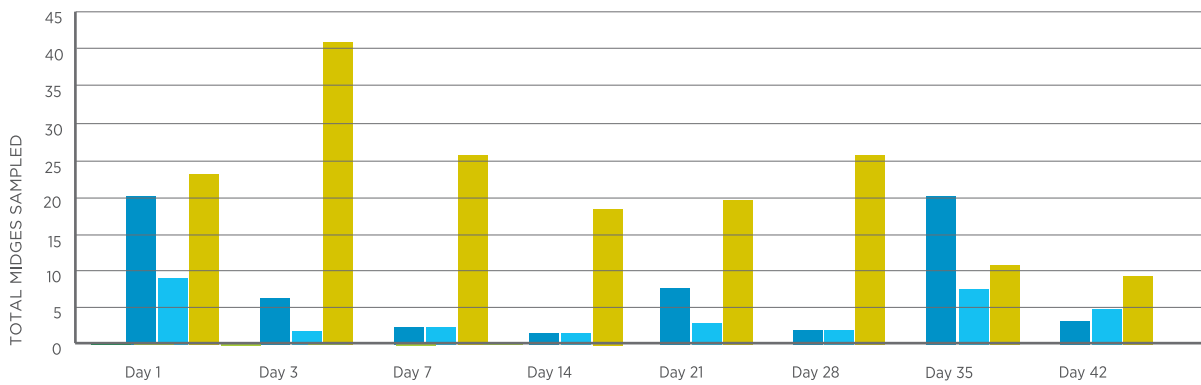
Rate: 12 lb/Acre and 12.5 lb/Acre

Location: Lake Monroe Florida, Volusia County, 2010

Species: Non-Biting Midge: *Glyptotendipes paripes* and *Chironomus crassicaudatus*

### Key:

- Natular 12 lb/Acre
- Natular 12.5 lb/Acre
- Control



\*Data provided by Edward D. Northey, Environmental Specialist, Volusia County MC, FL

### Key:

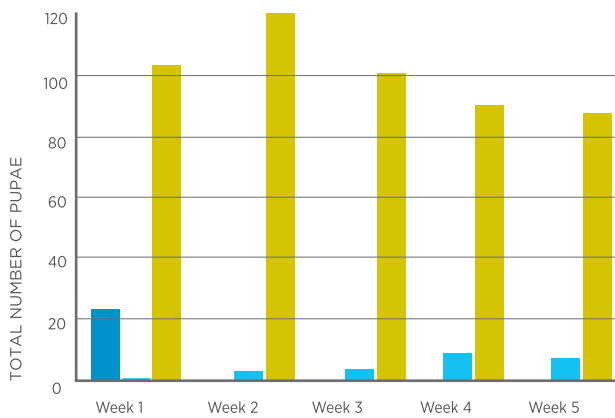
- Natular T30
- Natular G30
- Control

## Natular T30 and Natular G30

Location: Kenya Medical Research Institute, Kisumu, Kenya, 2010

Species: *Anopheles gambiae*

Large Simulated Barrow Pit Study



### Key:

- Natular 5 lb/Acre
- Natular 10 lb/Acre

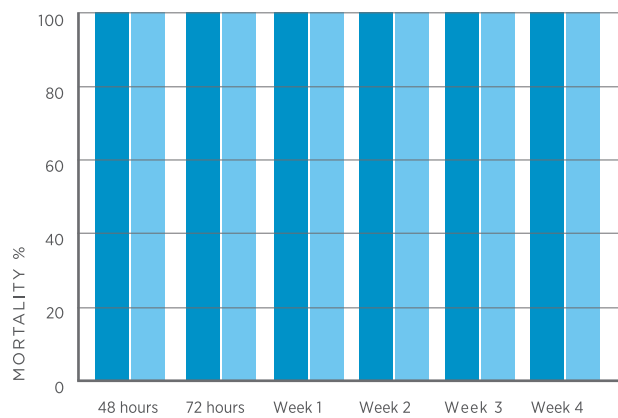
## Natular G30

Habitat: Wetlands

Rate: 10lb/A and 5lb/A

Location: Washoe County, Nevada, 2009

Species: *Cs. morsitans*, *Cx. tarsalis*



# FREQUENTLY ASKED QUESTIONS

## **Q: What is the active ingredient in Natular® larvicides?**

A: 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 is the active ingredient manufactured?**

A: Spinosad is produced in a state-of-the-art fermentation facility in the United States, using natural feed-stocks to maintain the fermentation process.

## **Q: Is spinosad new?**

A: No. Spinosad’s first global registration was in 1996. Today it’s used on more than 250 crops and in consumer and animal health uses in over 85 countries. Although Natular larvicides are the first public health usage of the active.

## **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: Are Natular formulations suitable for use in organic agriculture?**

A: All domestic formulations of Natular are listed by the Organic Materials Review Institute (OMRI) for use in and around organic agriculture.

## **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?**

A: All inert components in domestic Natular formulations are included in EPA’s list of Minimal Risk Inert Ingredients. Inerts are non-synthetic (natural) or are synthetic components which do not contribute to mammalian or aquatic toxicity.

## **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. Fortunately, the rapid degradation of spinosad in natural aquatic environments prevents the long-term exposure that would be needed for these effects to occur in real world situations.

## **Q: How effective is Natular in an open / floodwater habitats with sunlight (*Aedes vexans*)?**

A: Excellent, based on numerous cooperator and university trials.

## **Q: Do Natular larvicides control all of the important mosquito species?**

A: Natular formulations have been tested on twenty of the most common vector and nuisance mosquito species and spinosad is effective against all of them. Given the fact that spinosad is a new active ingredient and has a completely unique mode of action; we expect to see consistent performance across all species.

## **Q: How do Natular™ formulations perform in habitats containing high organic matter?**

A: We have seen excellent results in habitats with high concentrations of organic debris with Natular formulations, e.g. polluted water, sewage lagoons, and waters with high concentrations of leaf litter or other organic debris.

**Q: How have Natular products performed in catch basins?**

A: Both the 30-day Natular T30 and Natular XRT have performed exceptionally well in catch basins – even in the face of significant rain events as well as wet/dry cycles. The 30-day Natular T30 provides 30 days of control, while the XRT has consistently reached full season limits with control up to 180 days.

**Q: How does varying amounts of sunlight affect the performance of Natular 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.

**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. Clarke will implement a resistance management program. To manage resistance, Clarke will steward and monitor the applications of these products to ensure consistent use according to label directions.

**Q: What is the ecological toxicity of the Natular formulations?**

A: Spinosad was registered under the US 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 not mitigated by virtue of low application rates and rapid dissipation of spinosad.

**Q: How do Natular products affect honey bees?**

A: Field testing has demonstrated that once liquid spray residues have been allowed to dry for up to 3 hours that spinosad is not harmful to foraging honeybees and bumblebees. Spinosad has been used extensively in more than 85 countries with over 250 registered crop uses since its first launch in agriculture without any reported adverse effects on bees. This would be applicable ONLY TO THE LIQUID formulation. Granular and tablet formulations will not pose a bee hazard.

**Q: Why are Natular formulations good rotational products?**

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: 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



# Clarke

## GLOBAL HEADQUARTERS

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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 disease prevention and habitat management solutions. In 2008, Clarke founded The Clarke Cares Foundation, a non-profit created to provide disease prevention support for communities with critical needs.

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