Treatments for nematode infestations: novel agrochemicals and biopesticides under development.

Presentation to the Agrochemical Conference Newmarket, UK

November 2013

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Agenda

- What are nematodes?
- Nematodes cause major crop losses
- Controlling nematode infestations
- Global market for nematode control
- Nematicides in development
- Outlook

What are nematodes?

What are nematodes?
(organisms that demand a free lunch!)

Ascaris lumbricoides is a nematode (roundworm), which inhabits the intestines of 1 in 6 humans.

Pelecitus sp. a nematode that infects the human eye.

Elephantiasis, a result of chronic parasitic infection of filarial nematodes

Nematodes occur in most ecological niches. Many are parasitic on animals and plants. Around 60 species infect human beings, of which eight species can cause severe symptoms.

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What are nematodes?

Controlling human nematode infections has been mainly achieved by improved hygiene (especially in children), which is why it has become less of a problem in the developed world. Although treatments are available, avoiding infection in the first place has proved most effective.

Unfortunately, the equivalent action to control nematode infestations in agriculture (sterilisation of the soil) is not often feasible, with the exception of high-value fruits and vegetables.

Nematodes that cause significant crop losses

Infestation by root-knot nematode on a tomato root (left), with normal root for comparison (right)

Impact of root-knot nematode infestation in a field of carrots

Meloidogyne incognita, (x500) p*enetrating a tomato root*

Globodera rostochiensis, commonly known as the golden nematode golden eelworm or yellow potato cyst nematode

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Nematodes infect all crops

CROP	*Scientific Name*	Common name
Banana Nematodes	*Helicotylenchus multicinctus*	Spiral nematode
Banana Nematodes	*Hoplolaimus pararobustus*	Crown-headed/ Lance nematode
Banana Nematodes	*Meloidogyne spp*	Root Knot nematode
Banana Nematodes	*Pratylenchus coffeae*	Lesion nematode / Banana nematode
Banana Nematodes	*Pratylenchus goodeyi*	Lesion nematode / Banana nematode
Banana Nematodes	*Radopholus similis*	Burrowing nematode / Root nematode
Coffee /Tea Nematodes	*Meloidogyne exigua*	Coffee root-knot nematode
Coffee /Tea Nematodes	*Meloidogyne spp*	Root Knot Nematode/ Coffee Nematode
Coffee /Tea Nematodes	*Pratylenchus coffeae*	Coffee meadow nematode
Coffee /Tea Nematodes	*Pratylenchus coffeae*	Coffee root-lesion nematode
Cotton Nematodes	*Belonolaimus longicaudatus*	Sting nematode
Cotton Nematodes	*Meloidogyne brevicauda*	Tea root-knot nematode
Cotton Nematodes	*Meloidogyne incognita*	Root Knot Nematode
Cotton Nematodes	*Rotylenchulus reniformis*	Reniform nematode
Veg. & Ornamental Nematodes	*Aphelenchoides spp.*	Foliar nematodes
Veg. & Ornamental Nematodes	*Belonolaimus longicaudatus*	Sting nematode
Veg. & Ornamental Nematodes	*Ditylenchus dipsaci*	Stem and bulb nematode
Veg. & Ornamental Nematodes	*Meloidogyne spp.*	Root-knot nematodes
Maize / Corn Nematodes	*Belonolaimus*	The Sting Nematode
Maize / Corn Nematodes	*Criconemoides*	Ring nematodes
Maize / Corn Nematodes	*Helicotylenchus*	Spiral Nematodes
Maize / Corn Nematodes	*Heterodera zeae*	The Corn Cyst Nematode
Maize / Corn Nematodes	*Hoplolaimus*	The Lance Nematode
Maize / Corn Nematodes	*Longidorus*	The Needle Nematode
Maize / Corn Nematodes	*Meloidogyne*	The Root-Knot Nematodes
Maize / Corn Nematodes	*Paratrichodorus*	Stubby-Root Nematodes
Maize / Corn Nematodes	*Pratylenchus*	The Lesion Nematode
Maize / Corn Nematodes	*Tylenchorhynchus*	Stunt Nematodes
Maize / Corn Nematodes	*Xiphinema*	The Dagger Nematode
Peas, Beans, Peanuts	*Heterodera goettingiana*	Pea cyst nematode
Peas, Beans, Peanuts	*Heterodera goettingiana*	Pea root eelworm
Peas, Beans, Peanuts	*Heterodera goettingiana*	Pea root nematode
Peas, Beans, Peanuts	*Meloidogyne arenaria*	Peanut root-knot nematode
Potato Nematodes	*Ditylenchus destructor*	Potato Rot Nematode
Potato Nematodes	*Globodera rostochiensis*	Golden Nematode / Potato Cyst Nematode
Potato Nematodes	*Meloidogyne chitwoodi*	Columbia Root-knot Nematode
Potato Nematodes	*Meloidogyne hapla*	Northern Root Knot Nematode
Rice Nematodes	*Aphelenchoides besseyi*	White Tip Nematode
Rice Nematodes	*Ditylenchus angustus*	Rice stem nematode
Rice Nematodes	*Hirschmaniella*	Rice Root Nematode
Rice Nematodes	*Meloidogyne graminicola*	Rice root-knot nematode
Rice Nematodes	*Radopholus oryzae*	Rice-root nematode
Rice Nematodes	*Tylenchorhynchus martini*	Rice stunt nematode
Soybean Nematodes	*Belonolaimus spp.*	The Sting nematode
Soybean Nematodes	*Heterodera glycines*	Soybean cyst nematode (SCN)
Sugar Beet / Sugar Cane Nematoc	*Ditylenchus dipsaci*	Beet stem nematode
Sugar Beet / Sugar Cane Nematoc	*Heterodera sacchari*	Sugar cane cyst nematode
Sugar Beet / Sugar Cane Nematoc	*Heterodera schachtii*	Sugar beet cyst nematode
Sugar Beet / Sugar Cane Nematoc	*Heterodera schachtii*	Sugar cane cyst nematode
Sugar Beet / Sugar Cane Nematoc	*Tylenchorhynchus martini*	Sugar cane stylet nematode
Trees and Grapevines Nematodes	*Belonolaimus longicaudatus*	Sting nematode
Trees and Grapevines Nematodes	*Bursaphelenchus xylophilus*	Pine wilt nematode
Trees and Grapevines Nematodes	*Meloidogyne hapla*	Root-knot nematode
Trees and Grapevines Nematodes	*Mesocriconema xenoplax*	Ring nematode
Trees and Grapevines Nematodes	*Pratylenchus spp.*	Lesion nematode
Trees and Grapevines Nematodes	*Radopholus similis*	Burrowing nematode
Trees and Grapevines Nematodes	*Rotylenchulus spp.*	Reniform nematode
Trees and Grapevines Nematodes	*Tylenchorhynchus spp.*	Stunt nematodes
Trees and Grapevines Nematodes	*Tylenchulus semipenetrans*	The Citrus nematode
Trees and Grapevines Nematodes	*Xiphinema americanum*	The Dagger nematode
Turf Nematodes	*Belonolaimus species*	The Sting Nematodes
Turf Nematodes	*Criconemoides species*	Ring Nematode
Turf Nematodes	*Hoplolaimus galeatus*	The Lance Nematode
Turf Nematodes	*Meloidogyne species*	The Root-knot Nematodes
Wheat, Barley	*Anguina tritici*	Wheat gall nematode
Wheat, Barley	*Heterodera avenae*	Cereal cyst / Root nematode
Wheat, Barley	*Heterodera hordecalis*	Barley cyst nematode
Wheat, Barley	*Heterodera latipons*	Wheat cyst nematode
Wheat, Barley	*Heterodera major*	Cereals root eelworm
Wheat, Barley	*Meloidogyne nassi*	Barley root-knot nematode
Wheat, Barley	*Meloidogyne nassi*	Cereal root-knot nematode

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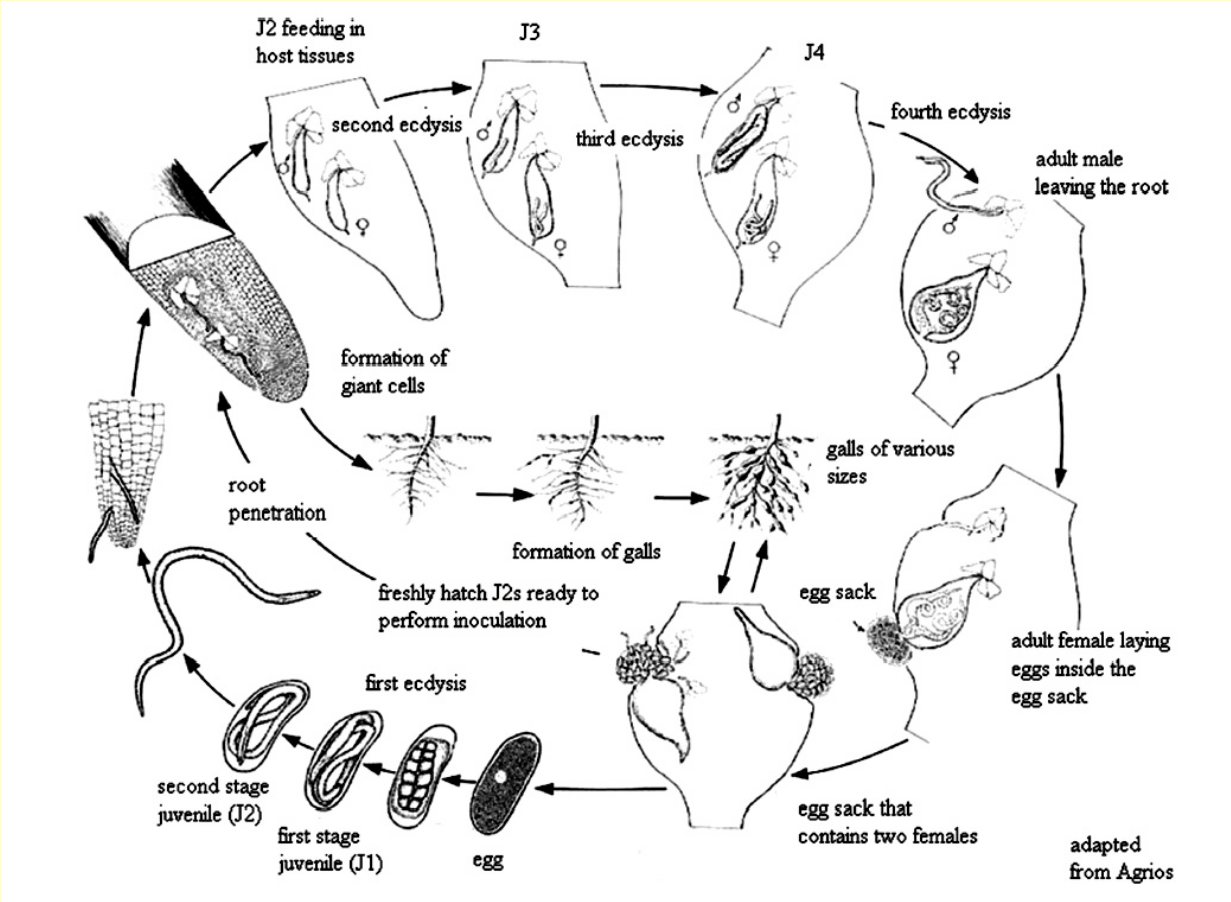
A selection of the most damaging agricultural nematodes

Life-cycle of nematodes



Source: Botanical nematicides: a review, Ntalli & Caboni, J. Agric. Food Chem.9929-9940 (Vol 60) 2012

As with many multicellular parasites, this complex life-cycle has helped to complicate the invention of effective controls.

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Crop losses caused by nematodes

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Nematodes: crop losses

Across the world, nematodes infect all crops to a greater or lesser extent.

Levels of infestation depend upon many factors, including the crop, whether it is annual or perennial and the average soil temperature.

Crop /Commodity	Global crop Infestation level (average)
Bananas	90%
Potatoes	80%
Tea	70%
Coffee	60%
Peanuts	60%
Barley	60%
Tomato	55%
Citrus	50%
Maize	50%
Sugar cane	40%
Rice	40%
Cotton	40%
Fruits	40%
Vines	40%
Tobacco	38%
Vegetables/Nurseries	33%
Sugar beet	33%
Pulses	32%
Turf, Golf courses	30%
Wheat	25%
Soybean	20%

Source: Cropnosis Ltd

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Nematodes: crop losses

Crop losses are reduced using current treatments. Maintaining control of nematode losses is more important in some crops than others.

Crop /Commodity	Yield loss due to nematodes* Average %	Treated savings USD mn
Vegetables/Nurseries	45%	4,679
Bananas	65%	1,596
Citrus	30%	1,524
Wheat	30%	1,231
Tobacco	40%	1,225
Coffee	25%	1,210
Sugar cane	30%	1,111
Rice	25%	1,029
Maize	20%	1,001
Sugar beet	36%	916
Cotton	27%	883
Potatoes	15%	745
Tomato	35%	732
Fruits	25%	649
Soybean	15%	479
Vines	20%	411
Peanuts	30%	360
Tea	15%	354
Pulses	33%	283
Turf, Golf courses	30%	262
Barley	10%	195
* with current treatments	**Total:**	**20,874**

Source: Cropnosis Ltd

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Nematodes: value of crop losses

These estimates are based upon exported crops. Other research suggests the total value of the crops lost if no treatments were applied might be as much as USD 78 bn (quoted by Monsanto in a recent patent: WO2012030887), which also noted global soybean losses at USD 3.4 bn (1994).

Commodity	Est'd losses without control *USD million*
Vegetables/Nurseries	5,495
Bananas	3,845
Citrus	1,793
Tobacco	1,441
Coffee	1,424
Wheat	1,330
Sugar cane	1,263
Rice	1,143
Maize	1,112
Sugar beet	1,039
Cotton	990
Tomato	907
Potatoes	846
Fruits	721
Soybean	494
Vines	447
Peanuts	439
Tea	396
Pulses	317
Turf, Golf courses	288
Barley	207
Global total	**25,936**

Source: Cropnosis Ltd

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Nematodes reduce the size and vigour of plants

Reduced yields created by nematode infection are certainly greatly underestimated. Crop rotation has been practised for centuries to minimize the impact of nematode parasitism.

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Nematicide Market

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Nematicide Market

Global Plant Protection Market (2012 at end-user level): USD 83bn

Crop, USD 58 bn (70%) Global

Weed control	USD 25.5 bn
Insect control	USD 13.8 bn
Disease control	USD 15.1 bn
Other	USD 2.6 bn
Nematode control	**USD 1 bn**

Source: Cropnosis - Agranova

Non-Crop, USD 25 bn (30%)

Insect control	USD 13.8 bn
Weed control	USD 7.4 bn
Disease control	USD 2.7 bn
Rodent control	USD 1.0 bn
Nematode control	**USD 0.1 bn**

Source: Rod Parker

Total sales for nematode control USD 1.1 bn

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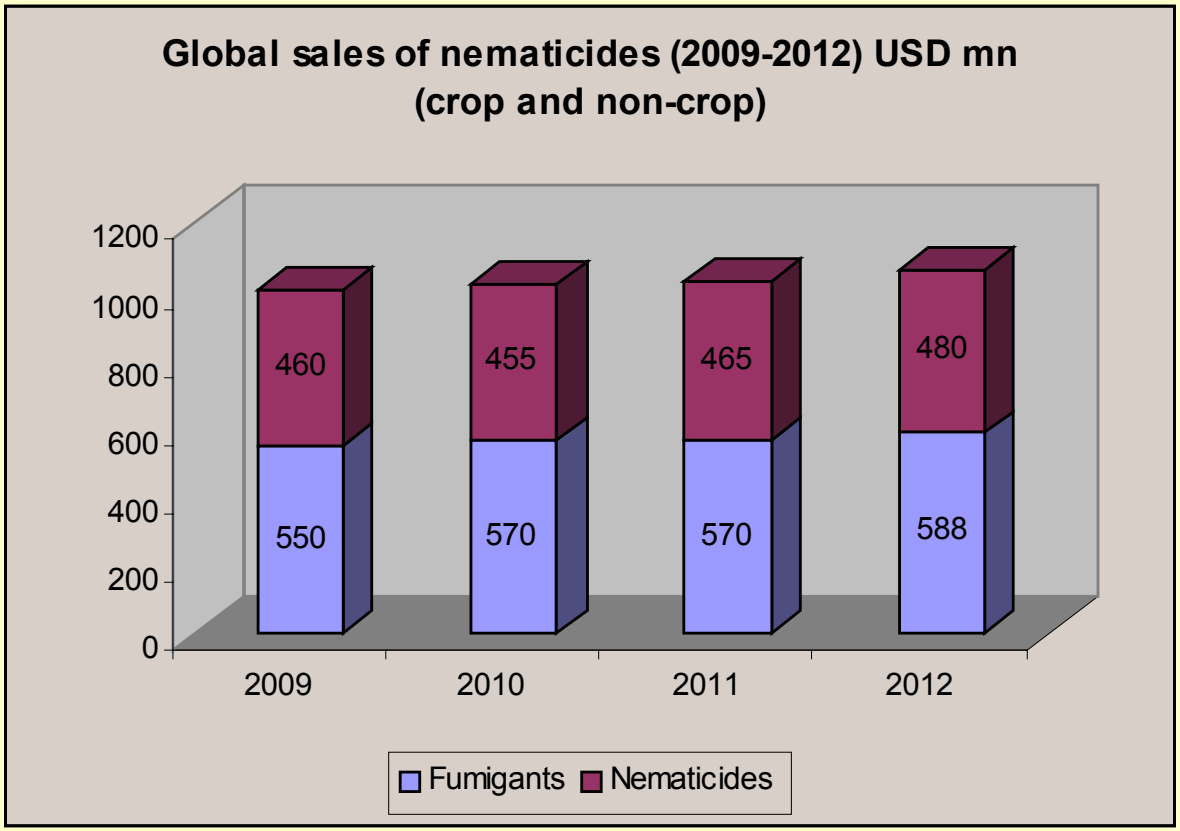
Nematicide Market

Nematode infestations can be controlled by fumigants and nematicides



Source: Cropnosis Ltd

Fumigants are, however, far more effective.
The best nematicides only remove 40-60%
and must be reapplied regularly for best results.

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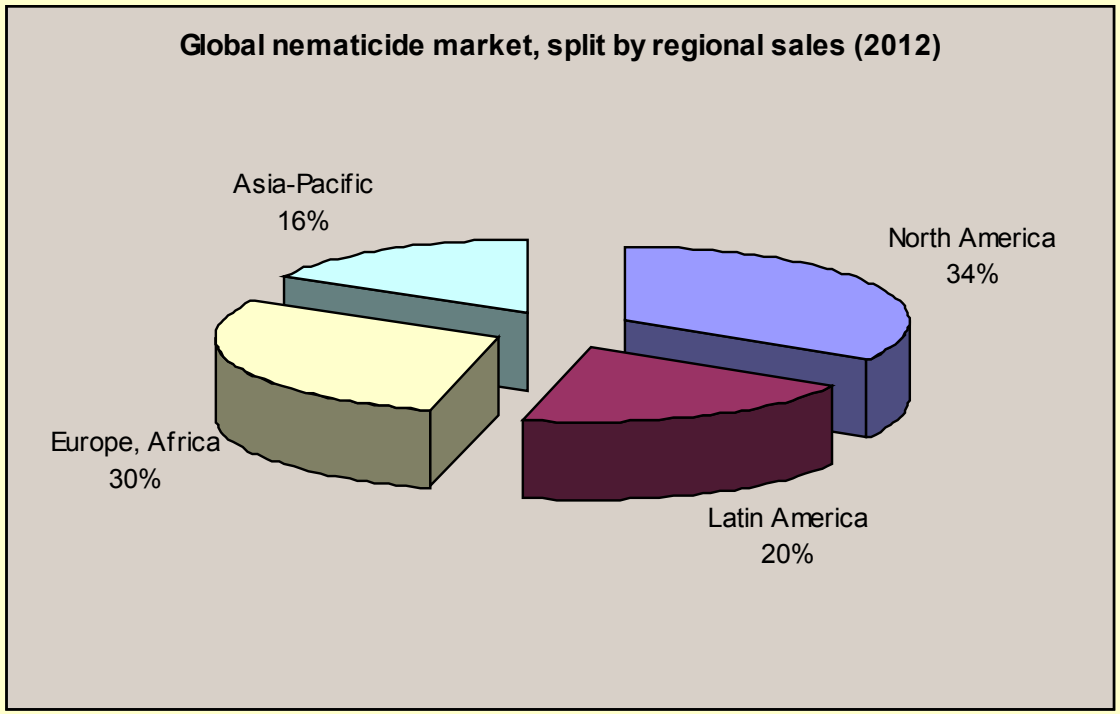
Nematicide Market



Source: Cropnosis Ltd

This graphic emphasises the fact that nematode infestation is a global problem

Regional breakdown (2012)	**USD mn**
North America	362
Latin America	213
Europe, Africa	318
Asia-Pacific	174
Global Sales	1,068

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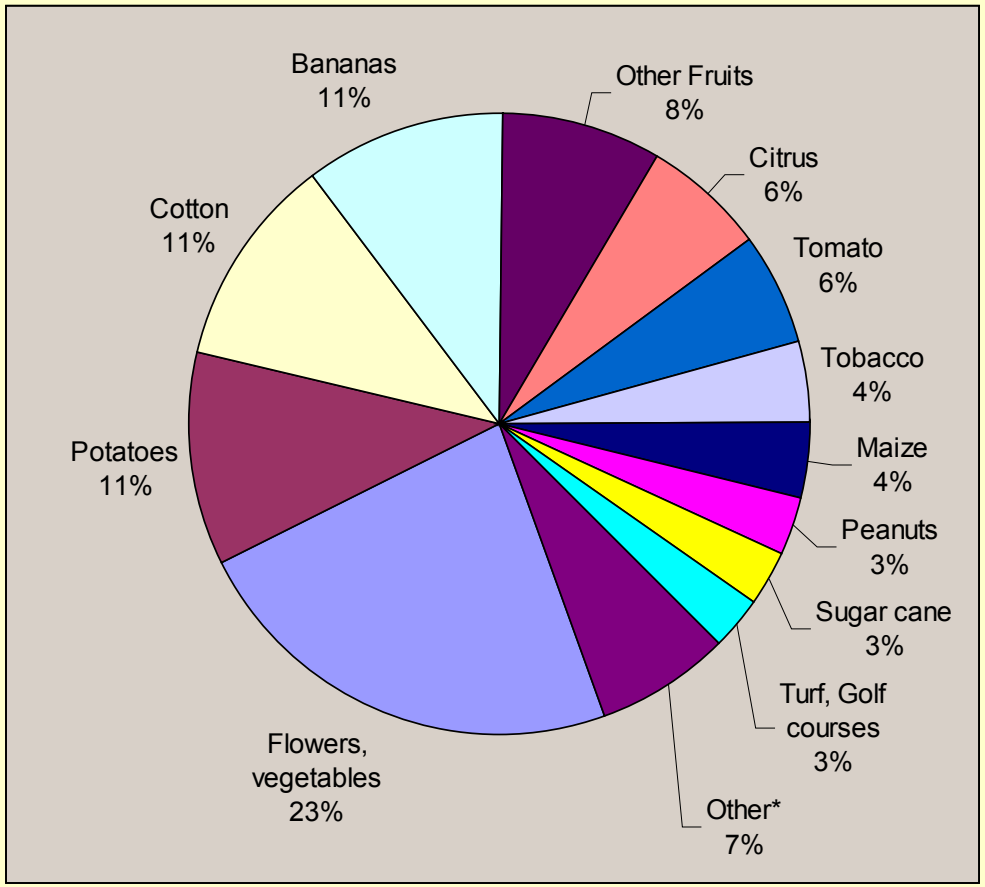
Nematicide Market



Source: Cropnosis Ltd

Crop rotation is not always feasible: for example in plantation and high-value crops.

Global Nematicide Sales (USD mn)
calculated end-user value

Flowers, vegetables	245
Potatoes	120
Cotton	119
Bananas	112
Other Fruits	88
Citrus	69
Tomato	62
Tobacco	46
Maize	42
Peanuts	33
Sugar cane	30
Turf, Golf courses	28
Other*	75

* sugar beet, vines, wheat, barley, rice, field bean, tea , soybean, coffee

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Nematicide Market

Genus	Common name of nematode
Anguina	Seed gall
Bursaphelenchus	Wilt
Criconemella	Ring
Ditylenchus	Stem and bulb
Helicotylenchus	Cyst
Globodera	Spiral
Heterodera	Cyst
Hirschmanniella	Root
Hoplolaimus	Lance
Meloidogyne	Root-knot
Pratylenchus	Lesion
Radopholus	Burrowing
Rotylenchulus	Reniform
Scutellonema	Citrus
Tylenchulus	Spiral

Source: Current nematode threats to world agriculture by Nicol et al (2011)

Cyst nematodes *(such as Globodera rostochiensis, which is a major potato pest) and* ***root-knot nematodes*** *(such as Meloidogyne spp, which infect a wide range of fruit and vegetable crops) are economically the most important.*

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Nematicide Market

active ingredient	application	key crops
NEMATICIDES		
abamectin	foliar, seed treatment	cotton
aldicarb	soil	soybeans, peanuts, potatoes, vegetables
cadusafos	soil	bananas, sugar cane
carbofuran	soil, foliar	vegetables, sunflower
ethoprofos	soil	potatoes
fenamiphos	soil	cotton, vegetables, citrus, sugar beet
fosthiazate	foliar, seed treatment	potatoes, bananas, coffee, tomatoes, peanuts
furfural	soil	tomatoes, groundnuts, other vegetables & fruit
oxamyl	foliar	cotton, vegetables
spirotetramat	foliar	vines
terbufos	soil	pineapples
FUMIGANTS		
iodomethane	soil	fruit & vegetables
chloropicrin	soil	tomatoes, strawberries
dazomet	soil	floriculture
1,3-dichloropropene	soil	vegetables
metam-sodium	soil	trees
methyl bromide	soil	post-harvest
methyl isocyanate	soil	vegetables

*These treatments are not used exclusively for **nematode** control, but cover the most widely used applications of these AIs.*

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Nematicide Market

These statistics do not show the importance of incidental nematode control by other insecticides, which when applied to control other pests also offer some activity against nematodes. Organophosphates and carbamates all offer some degree of control. Many are also being phased out.

Nematicide Market

(sales of current products)

Treatment class	*Brands*	*Active Ingredient*	*Global sales* 2011 (USD mn)*
Fumigant	Dowfume	methyl bromide	53
	Telone	1,3-dichloropropene	265
	Busan, Vapam	metam-sodium	51
	Basamid	dazomet	151
	Larvacide	chloropicrin	247
	Midas	Methyl iodide	-
	Trapex	methyl isothiocyanate	-
	Enzone	sod. tetrathiocarbonate	-
	Nemamort	DCIP	16
Organophosphate	Counter	terbufos	16
	Nemacur	fenamiphos	6
	Apache	cadusafos	-
	Thimet	phorate	41
	Hostathion	triazophos	-
	Nemakick	imicyafos	14
	Miral	isazofos	-
	Prophos	ethoprophos	-
Carbamate	Temik	aldicarb	116
	Standak	aldoxicarb	-
	Vydate	oxamyl	71
	Furadan	carbofuran	133
	Lance	cleothocarb	-
	Eclahra	fosthiazate	61
Biopesticide	Bionem	Bacillus firmus	21
	Prophyta, Nema	Paecilomyces lilacinus	-
	Ditera	Myrothecium verrocarria	-
	Nemacheck	P. lilacinus strain 251	-
	Econem	Pasteuria usgae	-

Source: Agranova

* sales include those all uses, not just for nematode treatments. They are reported at the end-use level.

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Fumigation: effective, but emotive

It has to be said that these pictures of strawberry field fumigation in California hardly evoke the type of bucolic bliss for which green campaigners yearn

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Nematicides in development

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Urgent need for new effective treatments

Suppliers of nematicides	Key products (red: will be discontinued, purple: under review)
Agro-Kanesho	dazomet, 1,3-dichloropropene, metam-sodium
Albemarle	methyl bromide
Amvac	ethoprophos, fenamiphos, terbufos, dazomet, metam-sodium
Bayer	aldicarb, fenamiphos, spirotetramat, methyl isocyanate
Certis (Europe)	dazomet
Chemtura	methyl bromide
Dead Sea Bromine	methyl bromide
Dow AgroSciences	aldicarb, 1,3-dichloropropene
Du Pont	oxamyl
FMC	cadusafos, carbofuran
Great Lakes Chemical	chloropicrin
Illovo Sugar	furfural
ISK	fosthiazate
Makhteshim-Agan	carbofuran, fenamiphos
Mitsui Chemical	chloropicrin
Nippon Kayaku	chloropicrin
Nufarm	metam-sodium
Rotam	terbufos
SDS Biotech	1,3-dichloropropene
Syngenta	abamectin, fosthiazate
Taminco	metam-sodium
United Phosphorus	terbufos

By 2018-2020, most current products will have lost their approved status in developed markets

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Nematicides in development
(synthetic chemicals)

Developer	*Active Ingredient*	*Notes*
Arkema - Certis	dimethyl disulphide (Paladin)	Fumigant commercialsed in Lebanon and Turkey in 2010.
Bayer	BCS-AR83685 (probably fluopyram)	Under test as a cotton seed treatment in USA. Granted a temporary license for testing in Brazil in 2010. Launched in Aug 2013 as **Verango** to treat bananas (Honduras)
BOC - CSIRO	cyanogen (oxalonitrile) STERIGAS	Undergoing approvals in Australasia as fumigant for strawberries and stored grain.
Devgen	Iprodione (new application)	Relaunched 2010 as a nematicide in USA
Du Pont	DPX-Q8U80	A 40% SC formulation has undergone extensive testing.
KRIBB	2-(4-adamantan-1-yl-phenoxymethyl)-1H-benzoimidazole-5-carboxylic acid (furan-2-ylmethyl)-	Antifeedant (development status uncertain)
Makhteshim-Agan, Bayer, SDS	fluensulfone	Sulphonylthiazole, useful in controlling root-knot nematodes in fruit/veg. Field testing completed in Japan in 2013.
Shandong Agricultural University	calcium phosphide	Undergoing tests in China as a fumigant for tomoto plots
Syngenta	Solvigo (probably SYN 351)	spiroindoline, with broad-spectrum control of lepidopteran and acaricidal pests. Also has nematicidal properties.
Nippon Kayaku	NK-1211	Vegetable nematicide, on test in Japan since 2012
Monsanto (acquired from	tioxazafen	oxadiazole nematicide (also has a tetrazole in early development)

Fumigants are highlighted in purple text.

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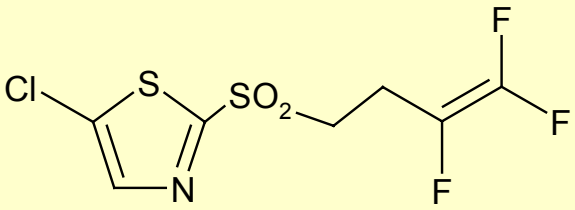
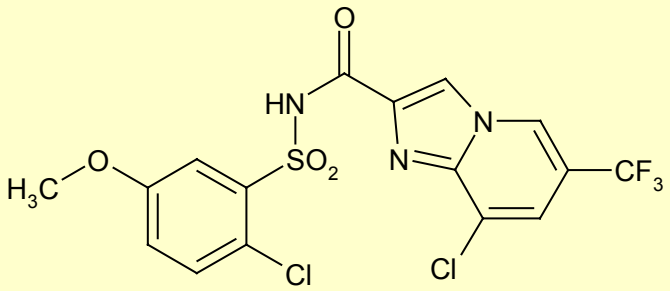
Nematicides in development

(*structures of selected compounds*)



fluensulfone



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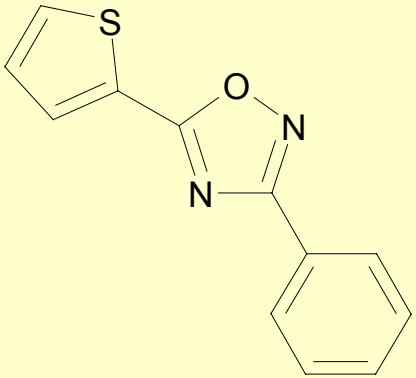
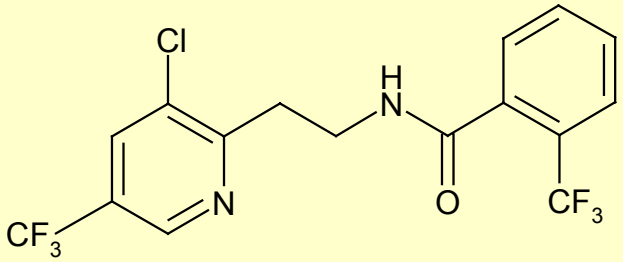


tioxazafen



Fluopyram (Verango)

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Nematicides in development
(biopesticides)

Developer	*Active Ingredient*	*Notes*
Isagro-Ricerca	IRF135	Synthetic biopesticide, with potential as a biological fumigant.
Desert King International	Quillaya saponaria extract	Biofungicide/nematicide, undergoing tests in USA.
Houbao Lun Zhijun	Verticillium chlamydosporium ZK7	Experimental
Pasteuria Bioscience	Pasteuria nishizawae strain Pn1 (Clariva)	Soybean cyst nematicide. Syngenta acquired the company in mid-2011.
Pasteuria Bioscience	Econem	Novel turf bionematicide for control of sting nematodes in turf and strawberries (commercialised in 2010)
Bayer	B. firmus strain I-1582 (Chancellor)	Votivo: seed treatment for maize, soybean and cotton Developed by Minrav, Israel, it is especially effective against Meloidogyne spp.
Chr. Hansen	Bacillus sp (Nemix)	FMC acquired rights to develop as nematicide in 2011.

Most bionematicides make only a modest impact on infestations and are best used in conjunction with more powerful control agents

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Nematicides in development
(natural products and extracts)

Developer	*Active Ingredient*	*Notes*
Boyce Thompson Institute	Ascarylose derivatives	Nematode signalling pheromones (not strictly nematicides)
Marrone Bio Innovations	MBI-302	At an early stage of development.
Tiantan Unsu (Kitasato Institute licensee)	jietacin	Streptomyces sp metabolite (development status uncertain)
EcoSpray	Extract of garlic (Nemguard)	Approved in 2009 and commercialised in Ireland.
Eden Research	Terpenes from 3-AEY Botrytis	FMC acquired Latin American rights in 2012

Bacillus firmus works a little like the yoghurts "Yakult" and "Activia" by crowding competing organisms.

outNatural products are more likely to offer clues to an improved MoA than a useful agent of control

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Outlook

Outlook

- Challenge will be to contain nematode infestations using a more restricted "toolbox"
- The rate of development of new fumigants and nematicides has been inadequate and crop losses likely to increase in the short term
- Hydroponics and use of sterile growing media in general is appropriate for high-value crops
- Improved cultivars through traditional breeding and through a deeper understanding of nematode physiology will make an important contribution, but not in the short term.

Until new treatments for lower-value crops become available, losses are likely to remain at a high level

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Acknowledgements

A number of images have been used to enliven this presentation. Agranova would like to acknowledge its indebtedness to those whose photographs were used, where space prevented a mention to be shown on individual slides.

- Cover picture: Bennett Laboratory, Nottingham University
- Sufferer of elephantiasis: J D Maclean, McGill University
- *Pelecitus* sp. a nematode that infects the human eye Centre for Disease Prevention, Clifton, USA
- *Ascaris lumbricoides*: Wikispaces, Silverscience, Tangient LLC
- Root knot nematode on tomato: University of Maryland Plant-parasitic Nematology Laboratory
- Field of infected carrots: The American Phytopathological Society
- *Globodera rostochiensis* (golden nematode): Eduardo Santz, Spain
- Larva of root-knot nematode, *Meloidogyne incognita:* Wikipedia
- Avocados: S A Sher, California Avocado Soc., 1959 Yearbook 43: 91-93
- California fumigation: Gao et al, California Agriculture 41-46 *65(1)* 2011.

Thanks also to Simon Maechling for his constructive comments during the conference, which enabled Agranova to correct two facts in the slides on development products.

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Thank you for listening

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