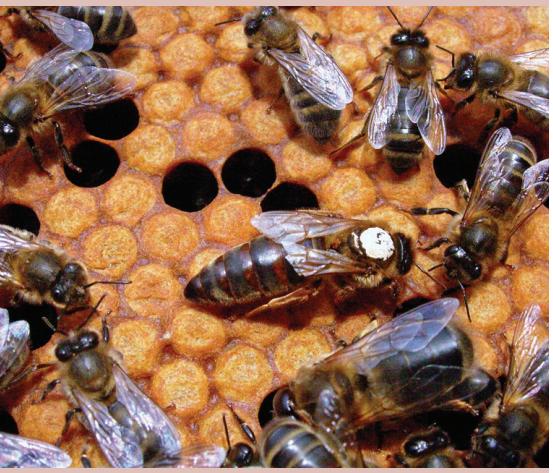
A PAN AP Factsheet Series

HIGHLY HAZARDOUS PESTICIDES

# Neonicotinoids



(Photo courtesy of Graham White)

*The mass death of bees threaten pollination and food production. In areas where neonicotinoids have been banned, bee populations have been recovering.*

Neonicotinoids are a relatively new class of insecticides, launched in 1991. They are synthetic derivatives of nicotine, the tobacco toxin.

Nicotine has been used as a pesticide for over 200 years but it degrades very rapidly, so the neonicotinoids are designed to be persistent (with the exception of dinotefuran, they are chlorinated). They target the insect's nervous system, binding with its nicotinic receptors and interrupting the sending of nerve impulses.

There are 7 different active ingredients: *acetamiprid, clothianidin, dinotefuran, imidacloprid, nitenpyram, thiacloprid,* and *thiamethoxam*.

In 2006, these were being marketed in 530 products in 123 countries.

The most common of these are *imidacloprid, clothianidin,* and *thiamethoxam*. *Thiamethoxam* breaks down into *clothianidin*.

*Imidacloprid* was the first neonicotinoid to be introduced. It is used on more than 140 crops in more than 120 countries, and is one of the fastest growing insecticides in terms of sales.

It is highly toxic to bees, as are most of the neonicotinoids, and is implicated in honeybee Colony Collapse Disorder, and in potential ecological collapse. Several of the neonicotinoids also pose human health concerns.

## Trade names

*acetamiprid* – Adjust, Assail, Chipco, Epik, Gazel, Intruder, Kadan, Matsu Green, Mospilan, Pristine, Profil, Rescate, Supreme, Tristar, Yielder

*clothianidin* – Elado, Poncho, Votivo, Prosper, Redigo Deter (seeds); Dantotsu (soil applied); Dantop (foliar)

*dinotefuran* – Albarin, Bonfram, Starkle, Safari, Scorpion, Venom, Zylam

*imidacloprid* – Antarc, Confidor, Admire, Gaucho, Chinook, Faibel, Premise, and others; Advantage (cat and dog fleas); Avenge, Zapp (sheep louse treatment); Maxforce Quantum (ant bait), Maxforce (fly bait)

*nitenpyram* – Bestguard, Capstar (cat fleas)

*thiacloprid* – Bariard, Calypso, Eco-one, Winbariard

*thiamethoxam* – Actara (foliar); Cruiser, Helix (seed treatments), Veridian, Platinum (soil)

## Uses

Broad-spectrum, systemic insecticides with stomach and contact action, and residual activity.

Some formulations are sprayed on foliage; some are used as seed treatments to control pests and vectors of viruses; some are incorporated into the soil by drenching, use of granules, injection, drip irrigation, spraying and tablets; some are painted onto or injected into trunks of trees; some are used for veterinary medicine (fleas); and others for household fly control. They are ineffective against spider mites and nematodes.

When applied into the soil or as seed treatments, they are taken up via the roots and translocated throughout the plant. Applied to the top surface of a leaf, they penetrate the leaf and kill insects on the lower side.

Seed treatment use mainly involves *imidacloprid, clothianidin,* or *thiamethoxam,* used on cotton, corn, sunflower, cereals, sugar beet, oilseed rape, vegetables, and grass seed.

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| Active ingredient | Crop/use | Pest |
|---|---|---|
| imidacloprid | cotton, sugar, oilseed rape, cereals, rice, fruit, vegetables, ornamentals; pets, houses, home gardens and lawns | jassids, aphids, thrips, mealybugs, leafminers, termites, planthoppers, whitefly, shoot fly, mustard sawfly |
| clothianidin | rice, cotton, cereals, corn, oilseed rape, fruit, potatoes, sugar beets, vegetables, maize | brown planthopper, jassids, whitefly, woolly aphid, oriental fruit moth, corn rootworm |
| thiamethoxam | vegetables, potatoes, rice, cotton, fruit, tobacco, cereals, sorghum, tea, ornamentals, maize | mealybug, leafminer, termites, aphids, jassids, whitefly, leaf folder, gall midge, plant hoppers, tea mosquito bug |
| thiacloprid | apples, pears, cotton, vegetables, oilseed rape, cereals, potato, rice, ornamentals | aphids, whiteflies, thrips, jassids, stemborer, bollworms, codling moth diamondback moth, pollen beetle, shoot and fruit borer |
| acetamiprid | cotton, vegetables, potato, apples, vines, citrus, tea, grapes, ornamentals, termites, house pests | codling moth, diamondback moth, aphids, jassids, whitefly |
| dinotefuran | vegetables, apples, sugar beets, rice, fruit, cotton, potato, turf, ornamentals, residential and commercial buildings, home gardens, pets | soft scales, thrips, mealybugs, aphids, whiteflies, crickets, leafhopper, leafminer, sawfly, various bugs and beetles, cockroaches |
| nitenpyram | rice, fruit, tea, vegetables, field crops; cat fleas | |

## Classifications

*WHO:* Class II, moderately hazardous (*imidacloprid, thiacloprid;* others are not listed)

*US EPA:*

- *imidacloprid:* moderately toxic by ingestion, variable toxicity by inhalation, very low toxicity by dermal contact: Toxicity Categories - oral II, dermal IV, inhalation I (aerosol), IV (dust)
- *clothianidin:* Toxicity Categories - oral III, dermal III, inhalation III
- *acetamiprid:* Toxicity Categories - oral II, dermal III, inhalation III
- *dinotefuran*: Toxicity Categories - oral III, dermal III, inhalation IV; moderate eye irritation (II)
- *thiacloprid:* Toxicity Categories - oral II, dermal III, inhalation III, eye IV

## Regulatory status

### International

No international action has been taken against any of the neonicotinoids.

### National

***France***

*Imidacloprid:* Use of Gaucho on sunflower seeds was banned in 1999 after 1/3rd of bees died following its widespread use; in 2004 use on sweetcorn seeds was also banned. Bee populations are reported to have increased again after the ban.

*Clothianidin* use was not approved in France.

***Germany***

In 2008, Germany suspended use of some seed treatments containing *clothianidin, imidacloprid* or *thiamethoxam* because of mass bee deaths caused by contaminated dust arising from seed drilling operations which drifted onto neighbouring crops where bees were feeding.

***Italy***

In 2009, Italy suspended neonicotinoid seed treatments as a precautionary measure relating to bees.

***US***

*Imidacloprid* voluntarily withdrawn in 2011, under pressure from state government of California, from use on almonds, a major crop for bees.

## International standards

*Clothianidin, dinotefuran, imidacloprid, nitenpyram,* and *thiamethoxam* are on PAN International's list of Highly Hazardous Pesticides (2010) for global phase-out, because of toxicity to bees; and *thiacloprid* is on the list because it is classified by the US EPA as a likely carcinogen.

## Manufacture

*imidacloprid:* Bayer. It came off patent in 2006 so there are also generic versions manufactured in China, India, and possibly other countries

*clothianidin:* Sumitomo, Bayer

*thiamethoxam:* Syngenta

*acetamiprid:* Nippon Soda, Aventis; partially off-patent

*dinotefuran:* Mitsui Chemicals

*nitenpyram:* Sumitomo, Novartis

*thiacloprid:* Bayer

## Residues in food

As they are systemic insecticides, neonicotinoids will occur as residues in foods and will not wash off. For example *imidacloprid* has been found in many foods including chestnuts, ginger, vegetables, potatoes, tea, wine, fruit, and fruit juices. The residues do not breakdown rapidly and are unchanged by processing. In the US, residues were found in 80% of bananas, 76% of cauliflower and 72% of spinach.

## Health effects

### Mechanism of toxicity

Neonicotinoids disturb the normal function of acetylcholine which plays an important role in the nervous system; they act as false neurotransmitters which bind with the acetylcholine receptor. They make neural transmission stay switched on, causing abnormal excitability.

### Poisonings

Poisonings, including a low level of fatalities, following ingestion of *imidacloprid* have been reported in a number of countries including China, India, Iran, Portugal, Sri Lanka, Taiwan, and Turkey. Signs and symptoms of poisoning include vomiting, headache, sluggishness, tachycardia, hypertension, loss of consciousness, respiratory failure, liver and kidney dysfunction, coma and death. Poisonings from inhalation and/or dermal contact have been reported from Poland and Sri Lanka. There were no deaths amongst the 68 poisonings (61 ingestions, 7 dermal) presenting to 3 hospitals in Sri Lanka. There were reported deaths in Iran and Taiwan.

Two cases of acute poisoning by *acetamiprid* in Japan involved severe nausea and vomiting, muscle weakness, hypothermia, convulsions, tachycardia, hypotension, and thirst.

A metabolite of *neonicotinoid* insecticides was found in the urine of 6 patients presenting at a clinic in Japan with the following range of symptoms: headache, general fatigue, finger tremor, short term memory disturbance, fever, cough, palpitation, chest pain, stomach ache, muscle spasm/weakness, heart rate abnormality. Symptoms were thought to be caused by high intake of fruit and tea containing neonicotinoid residues.

### Acute toxicity

***Imidacloprid:***

High acute oral toxicity, may have high inhalation toxicity, but not by skin contact (little absorption through skin).

Symptoms following exposure to agricultural formulations have included reduced activity, lack of coordination, tremors, diarrhoea and weight loss. Nausea, vomiting, dizziness, disorientation, agitation, incoherence, breathlessness, and excessive sweating have resulted from inhalation and dermal exposure.

Symptoms following ingestion include drowsiness, dizziness, disorientation, fever, vomiting, sweating, increased heart and respiratory rates.

Mild cases of dermatitis from veterinary use of imidacloprid.

***Clothianidin:***

Symptoms of poisoning include increased restlessness followed by violent convulsions and death.

### Chronic toxicity

***Imidacloprid:***

*General:* reduced weight gain, liver damage, reduced blood clotting, binds to haemoglobin.

*Neurotoxicity:* gestational exposure can result in neurobehavioural effects with long term adverse health effects in the offspring. Synergistic neurotoxic effects can occur with concomitant exposure to organophosphates.

*Genotoxicity:* regarded as being not genotoxic by most regulatory bodies; however, imidacloprid, and especially the commercial formulations, has been shown to cause DNA damage in human lymphocytes and chromosomal aberration in rat bone marrow; mutagenic in some tests.

*Cancer:* classified by the US EPA as Group E, 'no evidence of carcinogenicity'; however this is based mainly on limited data submitted by the manufacturer. Taking into account all evidence, including formulations that contain carcinogenic excipients, it can be considered potentially carcinogenic.

*Endocrine disruption:* the thyroid is especially sensitive to imidacloprid (lesions are formed). It has altered levels of luteinizing hormone, follicle-stimulating hormone and progesterone, and also altered structure of follicles.

*Reproductive and developmental toxicity:* regarded by regulators as not being a reproductive toxin, but in tests on animals it caused miscarriages, smaller offspring, and abnormal skeletons.

*Immunotoxicity:* metabolite causes increased lymphocyte count and decreased polymorphonuclear cells (a type of white blood cell).

***Clothianidin:***

*Genotoxicity:* mutagenic, clastogenic in some studies but not others.

*Cancer:* US classification 'not likely'; however this is based on limited data submitted by the manufacturer (see note on imidacloprid above).

*Reproductive and developmental toxicity:* in animals it caused stillbirths, premature births, missing lung lobes, decreased and deformed sperm, and delayed sexual maturity in males.

***Acetamiprid:***

*Neurotoxicity:* can adversely affect the brain, especially in the developmental stage.

*Genotoxicity:* clastogenic in some studies.

*Cancer:* mammary tumours in one study but regarded by regulators as not statistically significant.

*Reproductive and developmental toxicity:* at high doses caused skeletal abnormality, delayed female maturation.

***Dinotefuran:***

*General:* targets nervous and

immune systems (decreased spleen and thymus weights).

*Cancer:* US classification 'not likely'; however this is based on limited data submitted by the manufacturer.

*Endocrine disruption:* causes decrease in follicles, changes in ovary weight, changes in vagina, and altered oestrus cycles in females; abnormal sperm, decreased sperm count and motility, and decreased testes weight in males.

***Thiacloprid:***

*General:* damage to liver and thyroid.

*Cancer:* thyroid adenomas in males, and uterine tumours in females; US classification 'likely carcinogen'.

*Endocrine disruption:* changes to adrenal glands, thyroid hormone, prostate glands.

*Reproductive and developmental toxicity:* delayed sexual maturation in males.

***Thiamethoxam:***

*General:* damage to liver, kidney, testes.

*Neurotoxicity:* developmental neurotoxic effects in rats.

*Cancer:* liver tumours, but classified by US EPA as 'not likely' in humans.

## Environmental and agroecological effects

### Toxicity

UNEP reports that certain fungicides have synergised with neonicotinoids to increase their environmental toxicity up to 1,000 times; and other studies show that potentially synergistic fungicides have been found together with the neonicotinoids in pollen.

Neonicotinoids are regarded as having drastically reduced insect life in Europe including moths and butterflies, with a consequent decline in insect-eating birds.

Scientists propose that there is no safe level of exposure to these systemic pesticides, as over time very small quantities of neonicotinoid insecticides in surface waters and groundwater may cause cumulative damage to terrestrial and aquatic insect life leading to ecological collapse.

***Imidacloprid:***

*Aquatic:* very toxic to some aquatic organisms and there is a high risk for aquatic invertebrates from runoff and spray drift; extremely toxic at low concentrations to some species of crustaceans including shrimps; toxic to fish especially juveniles; can reduce the abundance of invertebrates in ponds; sublethal effects in Daphnia include reduced feeding, failure to respond to predators, slower maturity, fewer young.

*Birds:* toxicity to birds varies widely; highly toxic to certain species including house sparrow, Japanese quails, canaries and pigeons, and exceeds US EPA level of concern for songbirds; causes abnormal behaviour such as lack of coordination, lack of responsiveness and inability to fly, even in birds for which it is not highly toxic; other problems include eggshell thinning, decreased weight, and reduced egg production and hatching success.

High levels in surface water in Netherlands have been linked to insect decline and a dramatic decline in common grassland birds.

*Terrestrial invertebrates:* severe impacts on nontarget insects in field and off-field areas. Residues need to age at least 273 days before they become non-hazardous to native ground beetles in Europe.

*Plants:* can be toxic to plants, including citrus and brassica seedlings, blue-green algae and diatoms.

*Pets:* adverse reactions in dogs on which it has been used as a flea treatment include nerve inflammation, skin irritations, vomiting, seizures and difficulty in walking.

***Clothianidin:***

*Aquatic:* very highly toxic to aquatic invertebrates which are important in nutrient cycling, and uses which results in runoff or spray drift to water bodies can compromise ecological integrity; very highly toxic to shrimps.

*Terrestrial:* use of treated seeds poses acute and chronic risks to small birds and mammals.

***Dinotefuran:***

*Aquatic:* highly toxic to aquatic invertebrates including shrimp; risk from spray drift or run-off.

### Agroecological disruption

All are harmful to bees except for *thiacloprid* and *acetamiprid* (although *thiacloprid* produces sublethal effects at higher concentrations). *Imidacloprid* and *clothianidin* in particular are implicated in honeybee Colony Collapse Disorder and mass bee deaths.

Honeybees pollinate 1/3rd of the world's crops, including fruits and vegetables. Neonicotinoids are taken into the plant and translocated to all parts, including pollen, nectar and guttation drops, the droplets of water that form on the edges of leaves at night and in the early hours after sunrise. Bees can drink from these droplets, especially in areas where access to other water sources is limited, and the sugar expressed in the droplets may also be attractive to bees.

In one field experiment using treated maize seed, the levels of neonicotinoids found in guttation droplets were 254 times the $LD_{50}$ for *imidacloprid*, 280 times the $LD_{50}$ for *clothianidin* and 48 times the $LD_{50}$ for *thiamethoxam*.

Neonicotinoids have irreversible effects on the nervous system of bees, and continual exposure even to very, very small amounts results in cumulative effects eventually breaking down the nervous and immune systems.

***Imidacloprid:***

*Bees:* very acutely toxic to honeybees; high risk to bees from spray applications, including through spray drift; residues found in bees, pollen collected by bees, and beeswax; residues found in depopulated hives in Uruguay but not in populated hives; low levels of residues have been found in a high percentage of plants of crops sown with treated seed including maize, sunflower and canola.

Sublethal effects include disorientation, disrupted navigation, impaired memory and

learning, diminished foraging and returning to hive, and decreased hive activity; minute doses suppress the immune system and bees become more susceptible to diseases such as Nosema. It is suspected that sublethal exposure to imidacloprid may also reduce honeybees' ability to groom themselves which is important for removing the Varroa mite.

It is currently proposed that Colony Collapse Disorder results from the unique combination of the sublethal effects of imidacloprid on bees, together with the presence of Varroa mites and diseases such as Nosema. Mass bee die-offs have occurred in several countries coinciding with the introduction of imidacloprid and/or clothianidin.

On Canada's Prince Edward Island, beekeepers reported serious losses of bees since 1995 linked to soil applications of imidacloprid on potato crops to control Colorado potato beetle. It is believed that the rotational clover and canola crops have sublethal residues of imidacloprid in the pollen and nectar, the cumulative effects of which cause slow death of bee colonies.

Very toxic to bumblebees with sublethal effects including impaired foraging behaviour, lower reproduction and colony mortality due to a lack of food, as well as decreased pollination of plants.

*Beneficial insects:* acutely toxic to a variety of parasitic and predatory insects including mirid bugs, ladybirds and lacewings; sublethal effects include disrupted foraging and parasitising ability; use has resulted in increased damage from spider mites because it killed their natural enemies but not the mite.

*Birds:* risk to birds that eat pest insects.

*Earthworms:* acutely toxic to earthworms; sublethal effects include decreased sperm, decreased enzymes for breaking down cellulose, damage to DNA.

*Soil organisms:* risk to soil-dwelling arthropods from seed treatments. At environmental concentrations after systemic treatments, it may inhibit leaf litter breakdown because of adverse sub-lethal effects on decomposer invertebrates.

***Clothianidin:***

*Bees:* Highly toxic to bees; risk from exposure through contaminated pollen and nectar as it works its way through plant from treated seeds; attacks the nervous system of bees; has lethal and sub-lethal effects on larvae and reproductive effects on the Queen.

In Germany, beekeepers lost 2/3rds of their bees in May 2008 as the result of dust from clothianidin-treated seeds; their bodies had a build-up of clothianidin.

In the US, dead and dying bees and the pollen they had collected contained clothianidin, but healthy bees did not.

*Beneficial insects:* long-term risk.

*Soil organisms:* toxic to earthworms.

***Thiamethoxam:***

*Bees:* very toxic to honeybees; very toxic to bumblebees with sublethal effects including impaired ability to orientate, impaired foraging behaviour, lower reproduction and colony mortality due to a lack of food, as well as decreased pollination of plants.

In the US, dead and dying bees and the pollen they had collected contained thiamethoxam but healthy bees did not.

*Beneficial insects:* toxic to many beneficial insects.

## Resistance

Pest resistance has been found in a number of countries, including India, China, Thailand, and Vietnam. Resistance is worst for imidacloprid, the most commonly used of the neonicotinoids, but Colorado potato beetle is resistant to all 7 of them.

*acetamiprid* – 9 species, including cotton aphid

*clothianidin* – 2 species

*dinotefuran* – 1 species

*imidacloprid* – 12 species, including brown planthopper and white-backed planthopper on rice, whiteflies, aphids, mosquitoes, houseflies,

*nitenpyram* – 1 species

*thiacloprid* – 1 species

*thiamethoxam* – 4 species, including aphids, whitefly

## Environmental fate and contamination

***Imidacloprid:***

*Degradation:* metabolised by photo-degradation from soil and water surfaces.

*Soil:* moderate to very high persistence in soil under aerobic conditions (half life of 40-997 days); in one US field, concentrations did not decrease after 1 year.

*Aquatic*: medium to high mobility in soil, has the potential to leach to groundwater; moderate to high persistence in natural sediment-water systems (half-life of 30-162 days).

Countries reporting residues in groundwater include Netherlands and USA.

In theory breaks down in sunlight in water, faster in tropical conditions; has been found to be persistent and not very degradable in stream water samples in Slovenia.

Found in high levels in surface water in Netherlands.

*Bioaccumulation:* unlikely.

***Clothianidin:***

*Degradation:* metabolised by photo-degradation from soil and water surfaces.

*Soil:* very persistent in soil, half-life ranges from 148 to 6,931 days; residues found in soil 2 years after treated seed was sown.

*Aquatic:* medium to high mobility in soil and has high potential to leach to groundwater, and run off to surface waters. Water-sediment system, half-life = 27 days.

***Acetamiprid:***

*Soil:* rapidly biodegradable in most soils (half-life 8 days).

*Aquatic:* highly mobile in soil, potential for degradation products to leach to groundwater.

*Air:* has been measured in ambient air in Spain.

***Dinotefuran:***

*Soil:* persistent in soil, half-life up to 138 days, metabolite 459 days.

***Thiacloprid:***

*Soil:* half-life in soil is 2-27 days.

*Aquatic:* low to medium potential to leach to groundwater.

***Thiamethoxam:***

Soil: persistent in soil, half-life of 34-280 days; residues can be detected in succeeding crops.

Aquatic: potential groundwater contaminant.

## Alternatives

There are numerous cultural, mechanical and biological solutions to pest control, as well as natural sprays that can be used instead of neonicotinoids depending on the pest and the situation.

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