

Resistance management is a strategy designed to preserve or sustain pesticide effectiveness. Although the concept of resistance usually is associated with arthropod (insect and mite) pests, there are a number of plant pathogens that have demonstrated resistance (e.g., *Botrytis cinerea* or gray mold) to certain fungicide classes. In addition, many weed species are resistant to pre- and postemergence herbicides. This fact sheet focuses on resistance management of plant-feeding arthropods. Avoiding resistance in disease and weed management is equally important.

Arthropod pests in greenhouses and nurseries are principally managed with pesticides (insecticides and miticides). These pests possess the inherent ability to adapt to various environmental and human disturbance factors such as pesticide applications. Continual reliance on pesticides leads to resistance, which is the genetic ability of some individuals in a population to survive exposure. In other words, the pesticide no longer kills a sufficient number of individuals to be considered effective.

Resistance is an international concern with expanding global trade. Plant material can spread arthropod pests as well as resistant genes associated with those pests. Resistance is an inherited trait. Evolution of resistance in a population depends on existing genetic variability that permits some individuals to survive exposure to a pesticide. Surviving individuals transfer traits to the next generation, enriching the gene pool with resistant genes. The “selection pressure,” or proportion of the population killed by a pesticide, is the main factor that influences resistance. Genetic variation related to pesticide susceptibility also is important.

Every time an arthropod pest population is exposed to a pesticide, there is potential selection for resistance, which increases the frequency or proportion of resistant genes within that population. Traits providing adaptive advantage include rare versions of genes that diminish sensitivity to a particular pesticide, or altered gene expression that results from amplification of commonly existing genes. In rare instances, no genetic variation exists that would block resistance development. Resistance to horticultural oil, for example, would require a defense against suffocation.

The speed of resistance developing in the population depends primarily on two biological factors: short

generation time and high female fecundity, which is the ability to produce large numbers of offspring in a single generation. In addition, some arthropod pests, including the twospotted spider mite (*Tetranychus urticae*) and western flower thrips (*Frankliniella occidentalis*), have haplo-diploid breeding systems that accelerate the rate of resistance development. Genes associated with resistance are fully expressed in haploid (single set of chromosomes) males in haplo-diploid species. With entirely diploid (double set of chromosomes) species, resistance may be partially hidden as recessive or co-dominant traits.

Genes for resistance typically occur at a low frequency in an arthropod pest population before a pesticide is applied. An individual does not become resistant, but frequent applications of a given pesticide over multiple generations remove susceptible individuals, leaving resistant individuals to reproduce. The result is a pest population that can no longer be controlled with a given pesticide.

Resistance also may develop as arthropod pests move within and between greenhouses and nurseries. Pest immigration enhances resistance in several ways. Migration from other crops within the greenhouse or nursery, or between greenhouses and nursery blocks, increases the chance that the pest population has been exposed to additional pesticide applications. Receiving plants from a distributor with pests that have been exposed to pesticides



Twospotted spider mite (above) and western flower thrips (below).



may increase the likelihood of resistance because a large percentage of those pests may already possess genes for resistance. Arthropod pests that enter greenhouses or nurseries from field or vegetable crops may have been exposed to agricultural pesticides similar to those used in greenhouses and nurseries.

Different mechanisms can confer resistance in various populations of the same species, and multiple resistance mechanisms may coexist in the population. This is known as “polyfactorial resistance.” The five resistance mechanisms are metabolic, physical, physiological, behavioral, and natural.

Metabolic resistance is the breakdown of the active ingredient by the arthropod pest. When the pesticide enters the body, enzymes attack and detoxify or convert the active ingredient into a nontoxic form. Detoxifying enzymes convert insecticides that are hydrophobic (water-hating) to more hydrophilic (water-loving) and less biologically active compounds that are excreted.

A number of enzymes may be involved, including large families of enzymes capable of metabolizing unusual plant chemicals, insect hormones, and pesticides. The levels of these enzymes are not static in arthropod pests. They change during development, making some life stages more susceptible to a pesticide than others.

Physical resistance is a change or alteration in the cuticle (skin) that reduces or delays pesticide penetration. Delayed penetration through the cuticle reduces insecticide concentration at the target site and prevents overloading the insect’s detoxification system.

Physiological resistance is also known as target site insensitivity. The interaction between the pesticide and its target is similar to a key (the toxin) fitting into a lock (the target site). Decreased binding associated with physiological resistance is analogous to the lock having been changed so the key no longer fits and thus the pesticide is no longer effective. Examples of this kind of resistance occur in the organophosphate, carbamate, and pyrethroid chemical classes. Insects may evolve different means to decrease susceptibility to organophosphate and carbamate insecticides, including reduced sensitivity of central nervous system enzymes that disrupt nerve signal transmission.

Some insects may possess knockdown resistance that makes them less sensitive to pyrethroid-based insecticides (e.g., bifenthrin, cyfluthrin, permethrin, fenpropathrin, fluvalinate, and lambda-cyhalothrin) due to modified sodium channels of nerve axons, which are the target site for these insecticides.

Behavioral resistance is when arthropod pests avoid contact with a pesticide. One behavior is hiding in locations such as the terminal growing points, which may

be difficult for a pesticide to penetrate. Another behavior is loss of a leg that has contacted insecticide residues. Altered behaviors may allow arthropod pests to avoid contact and exposure to pesticides.

Natural resistance is a term used to describe a pre-existing lack of susceptibility to a toxin that does not result from repeated exposure to a pesticide. This may be due to any of the previously described metabolic, physical, physiological, or behavioral traits, and includes life stages not susceptible to a pesticide. For example, most contact and systemic insecticides and miticides are not effective against the egg and pupae stages.

Two additional terms associated with resistance are cross and multiple resistance. **Cross resistance** involves insensitivity to pesticides with similar modes of action or in the same chemical class. **Multiple resistance** is when an arthropod pest population is resistant to pesticides with different modes of action or across chemical classes. Multiple resistance is a consequence of the arthropod pest population possessing more than one defense mechanism against a particular class or mode of action, or one mechanism coping with unrelated pesticides.

Because resistance often involves more than one adaptive mechanism and often several detoxification enzymes, intensive selection with any pesticide can result in adaptations that make cross resistance more likely and increase the risk of multiple resistance.

Factors that may influence the rate of resistance development can be divided into operational factors that are under the control of greenhouse or nursery managers or biological factors, which are intrinsic to the arthropod pest population.

Operational factors:

- Length of exposure to a single pesticide and pesticide residue characteristics
- Frequency of pesticide application
- Pesticide dosage (use rate)
- Spray coverage, specifically, non-uniform deposition on leaves or in growing medium
- Mortality or proportion of arthropod pest population killed
- Timing – applying pesticides when the most susceptible life stage(s) such as larva, nymph, and adult are absent
- Previous pesticide use
- Relationship of a pesticide to those previously applied
- Presence or absence of refuge sites or hiding places

Biological factors:

- Time to complete one generation from egg to adult

- Fecundity or number of offspring produced per generation
- Arthropod pest mobility – the ability of winged adults to disperse, to mate, or feed in protected habitats
- Host range – a wide range enhances the ability of arthropod pests to detoxify pesticides
- Mobility of individuals
- Genetic system (e.g., parthenogenesis, haplo-diploid, or sexual reproduction)
- Expression of resistance trait: mono- vs. multi-genic, and recessive vs. dominant

The stability of resistance in an arthropod pest population depends on several factors:

- Immigration of susceptible individuals, which may reduce gene frequency for resistance in the arthropod pest population through breeding
- Use of biological control agents (natural enemies), which may counteract resistance by removing survivors following a pesticide application
- Fitness costs associated with possessing resistance traits

If the resistance trait only enhances survival under continual pesticide exposure (e.g., *Bacillus thuringiensis* resistance) then, when pesticide exposure ends, individuals expressing non-resistance traits are better able to survive, reproduce faster, and produce more offspring. Within a few generations, susceptibility may be restored.

Greenhouse conditions can increase the rate of resistance developing in an arthropod pest population. Environmental conditions, such as temperature and relative humidity, typically are conducive for rapid arthropod pest development and reproduction. The greenhouse generally encloses arthropod pests and restricts susceptible individuals from migrating into the population. Resistant individuals within a pest population are dominant and remain in the greenhouse to breed. Susceptible individuals from areas not treated with a pesticide are unable to enter and hybridize with resistant arthropod pests. In addition, biological control agents or natural enemies – such as parasitoids and predators – often are absent and cannot immigrate into greenhouses. Intensive year-round production in many greenhouses and nurseries throughout the United States provides a continuous food supply for pests and often results in multiple generations per year and frequent pesticide exposure.

Resistance Management

Effective resistance management involves judicious selection and accurate application of pesticides and integration with other sound pest management strategies.

Below are guidelines for minimizing the prospect of arthropod pest populations developing resistance:

- Scout crops regularly and time pesticide applications to target the most susceptible life stages – larvae and adults.
- Implement sound cultural practices, such as proper watering and fertilizing, and practice good sanitation with prompt weed removal.
- If feasible, screen greenhouse openings to prevent insect pests from migrating into greenhouses.
- Use biological control agents or natural enemies.
- Use synergists when applying pesticides to inhibit detoxification enzymes. Read the label to determine whether a synergist has already been incorporated into the formulation. Certain demethylation inhibitor (DMI) fungicides and plant growth regulators may act as synergists by blocking the same enzymes as the conventionally used synergist, piperonyl butoxide (PBO). Because arthropod pests may counteract synergists through enzyme induction, effects may be temporary. Certain insecticides also may be used as synergists when mixed together. For example, organophosphate insecticides block carboxylesterase enzymes that can metabolize certain pyrethroids.
- Rotate pesticides with different modes of action.
- Use pesticides with broad modes of activity, such as insect growth regulators, insecticidal soap (potassium salts of fatty acids), horticultural oils (paraffinic, petroleum-based or methylated seed oils), selective feeding blockers (inhibitors), beneficial bacteria and fungi, and microorganisms.

In developing a resistance management program it is important to rotate common names (active ingredients) – not trade or brand names. For example, despite having different trade names, both Azatin® and Ornazin® contain the same active ingredient, azadirachtin. To alleviate the possibility of an arthropod pest population developing resistance, it is important to rotate pesticides with different modes of activity from the Insecticide Resistance Action Committee (IRAC) groups – not just active ingredients or chemical classes. This is because some chemical classes have similar modes of activity.

“Mode of action” or “mode of activity” refers to the specific target affected in an arthropod pest (e.g., sodium channel of the nerve axon, oxidative phosphorylation, or juvenile hormone). The classification of an insecticide or miticide is listed by its IRAC label designation (see Table 1).

For example, organophosphates and carbamates, despite being different chemical classes, have identical modes

of activity. These chemical classes block the action of acetylcholinesterase (AChE), an enzyme that deactivates the neurotransmitter acetylcholine (ACh) and results in total loss of nerve function. Using acephate for two consecutive spray applications during a generation and switching to methiocarb would not constitute a proper rotation scheme.

Similarly, although acequinocyl, pyridaben and fenpyroximate are in different chemical classes — naphthoquinone, pyridazinone, and phenoxy-pyrazole, respectively, all three are active on the energy production system and should not be used in succession.

The neonicotinoid chemical class contains a number of insecticides including imidacloprid, thiamethoxam, acetamiprid, and dinotefuran. Neonicotinoid-based insecticides have similar modes of action, so it is essential to avoid using them in succession. It is recommended that an insecticide with a different mode of activity be used before using a neonicotinoid-based insecticide.

Because resistance can develop due to enhanced metabolic conversion of insecticides, rotation schemes based on IRAC groupings are not fail-safe for avoiding resistance. They only take into account mode of action, not mode of detoxification. Examples of multiple resistance have demonstrated that elevated general detoxification capabilities resulting from intensive selection pressure with one insecticide can jeopardize the effectiveness of many other insecticides, including those associated with different IRAC groupings.

Another essential strategy is to rotate pesticides with specific modes of activity with those having non-specific or multiple modes of activity, such as insect growth regulators, insecticidal soaps, horticultural oils, selective feeding blockers (inhibitors), beneficial bacteria and fungi,

and microorganisms. This minimizes the possibility of resistance development. It is also important to rotate insect growth regulators with different modes of action because certain insect pests have demonstrated resistance to a number of insect growth regulators. Table 1 describes modes of activity and lists the common name (active ingredient) of pesticides in each category.

In general, modes of activity should be rotated every two to three weeks, or within one to two arthropod pest population generations. Timing will depend on the time of year because temperature influences life cycle duration from egg to adult. High temperatures during the summer shorten developmental time of most major arthropod pests of greenhouses and nurseries, including aphids, thrips, whiteflies, caterpillars, beetles, and spider mites. This often leads to overlapping generations. With various developmental stages – eggs, larvae/nymphs, pupae, and adults – present simultaneously, more frequent pesticide applications and rotations are required. During the winter, pest development is extended due to cooler temperatures and shorter days, so pesticides may not have to be rotated as often.

Combining or tank-mixing pesticides with different modes of action may delay resistance because mechanisms required to resist these pesticide mixtures may not be widespread, and it may be difficult for individuals in the arthropod pest population to develop resistance to several modes of action simultaneously. Arthropod pests in the population resistant to one or more pesticides would likely succumb to the other pesticide in the mixture. This approach, however, risks selecting for detoxification mechanisms that may permit survival to both pesticides.

Table 2 presents examples of pesticide rotation schemes that use active ingredients with dissimilar modes of activity

Table 2. Rotation programs for major arthropod pests using pesticides with different modes of action.

Aphids	Pymetrozine->	Imidacloprid->	Petroleum Oil->	Acephate
Thrips	Spinosad->	Chlorfenapyr->	Abamectin->	Pyridalyl
Twospotted Spider Mite	Bifenazate->	Chlorfenapyr->	Pyridaben->	Etoxazole
Whiteflies	Dinotefuran->	Pyriproxyfen->	Spiromesifen->	Buprofezin
Mealybugs	Acetamiprid->	Acephate->	Potassium Salts of Fatty Acids->	Kinoprene
Fungus Gnats	Pyriproxyfen->	Cyromazine->	Chlorfenapyr->	Diflubenzuron
Scales	Potassium Salts of Fatty Acids->	Petroleum Oil->	Acetamiprid->	Acephate

against various arthropod pests. Pesticide rotation will only be effective in delaying the development of resistance if pesticides used select for different resistance mechanisms as described above. For example, metabolic resistance may confer resistance to pesticides in different chemical classes that have different modes of action. Rotation schemes should encompass as many pesticides with different modes of action as possible.

Combining Resistance Management and Pest Management

The key to converting from a “pesticide management” to a “pest management” approach usually requires greater reliance on biological control and discontinuing the use of broad-spectrum pesticides, especially organophosphates, carbamates, and pyrethroids. Careful use of selective pesticides may work in concert with naturally occurring or introduced parasitoids or predators to maintain arthropod pest populations at non-damaging levels.

Ornamental crops grown in greenhouses or nurseries often have dense canopies, which makes complete spray coverage difficult. This may lead to a situation where the outer part of the plant canopy is thoroughly sprayed, but a refuge remains unsprayed in the plant interior, allowing arthropod pests to recolonize the outer foliage. Using pesticides selectively preserves natural enemies that can deal with the remaining arthropod pest population in the unsprayed refuges. This avoids pesticide resistance among arthropod pest populations by eliminating survivors through parasitism or predation. Effective arthropod pest suppression can be achieved without needing to ensure complete spray coverage.

Unfortunately, this system cannot be established where long residual, broad-spectrum pesticides have previously been applied because these pesticides generally are more



Frequent applications of pesticides may lead to resistance in arthropod pest populations.

toxic to natural enemies than arthropod pest populations. Systemic insecticides, which are taken up by plant roots, may be used in conjunction with natural enemies because residues are inside the plant, limiting direct exposure of natural enemies.

Horticultural oils are valuable for management of spider mites because all life stages – eggs, larvae, nymphs, and adults – are susceptible to suffocation by oil. An exception is predatory mites in the family Phytoseiidae, which can tolerate application rates of up to 1% horticultural oil.

Conclusion

Greenhouse and nursery producers should use pesticides judiciously, combining different modes of action and detoxification to avoid resistance and preserve the longevity of currently available pesticides. However, failure to control or regulate arthropod pest populations is not always due to resistance.

Table 1. Mode of action of pesticides registered for use in greenhouses and nurseries with the common name or active ingredient associated with that mode of action. The number and/or number and letter combinations in parentheses behind each active ingredient are the Insecticide Resistance Action Committee (IRAC) mode of action group designations.

Mode of Action of Pesticides (Common Name/Active Ingredient)

Acetylcholinesterase Inhibitors

Inhibit the enzyme acetylcholinesterase (AChE) from clearing and degrading the neurotransmitter acetylcholine (ACh). This prevents termination of nerve impulse transmission and results in acetylcholine accumulation, which leads to hyperactivity, respiratory failure, exhaustion, and death.

Pesticides: acephate (1B), chlorpyrifos (1B), and methiocarb (1A)

Sodium Channel Blockers

Interfere with nerve cell membranes in the peripheral and central nervous system by binding to sodium channel sites, delaying or preventing closure. Prolonged sodium inactivation stimulates nerve cells to discharge repetitively, leading to paralysis and death.

Pesticides: bifenthrin, cyfluthrin, fenpropathrin, fluvalinate, and lambda-cyhalothrin (3)

Nicotinic Acetylcholine Receptor Disruptors

Act on the central nervous system by binding to post-synaptic enzyme receptors and permanently blocking them. Blockage disrupts nerve transmission and contributes to rapid, uncontrolled nerve firing, leading to hyperexcitation, paralysis, and death.

Pesticides: acetamiprid, dinotefuran, imidacloprid, and thiamethoxam (4A)

Nicotinic Acetylcholine Receptor Agonist and GABA Chloride Channel Activator

Disrupt binding of acetylcholine at nicotinic acetylcholine receptors located at post-synaptic cell junctures and negatively affect gamma-amino butyric acid (GABA) gated ion channels.

Pesticide: spinosad (5)

GABA Chloride Channel Activators

Open chloride ion channels and bind to gamma-amino butyric acid (GABA) receptor sites. Increased membrane permeability to chloride ions inhibits nerve transmission, leading to paralysis, and death.

Pesticides: abamectin and milbemectin (6)

GABA-Gated Antagonist

Blocks or closes gamma-amino butyric acid (GABA) activated chloride channels in the peripheral nervous system. May inhibit the mitochondria electron transport chain, decreasing production of adenosine triphosphate (ATP).

Pesticide: bifenazate (25)

Juvenile Hormone Mimics

Arrest development, causing insects to remain in the immature stage by inhibiting metamorphosis. Toxicity is most apparent when insects are reaching the onset of metamorphosis. As a result, they fail to reach adulthood and are unable to complete their life cycle.

Pesticides: fenoxycarb (7B), kinoprene (7A), and pyriproxyfen (7C)

Chitin Synthesis Inhibitors

Inhibit formation of chitin, an essential component of an insect's exoskeleton, affecting the firmness and elasticity of the cuticle. Insects (and mites in the case of etoxazole) die while attempting to molt from one stage to the next.

Pesticides: buprofezin (16), cyromazine (17), diflubenzuron (15), etoxazole (10B), and novaluron (15)

Ecdysone Antagonist

Inhibit the release of hormones responsible for molting (eclosion hormone and bursicon) by blocking molting hormone activity. Also disrupt the molting process by inhibiting biosynthesis or metabolism of the molting hormone, ecdysone.

Pesticide: azadirachtin (18B)

Growth and Embryogenesis Inhibitors

Disrupt formation of the embryo during development or inhibit larval maturation. Specific mode of action and target site activity are not well understood.

Pesticides: clofentezine and hexythiazox (10A)

Selective Feeding Blockers

Inhibit insect feeding by interfering with neural regulation of fluid intake in the mouthparts, resulting in starvation.

Pesticides: flonicamid (9C) and pymetrozine (9B)

Disruptors of Insect Midgut Membranes

Crystals from *Bacillus thuringiensis* release proteins that are partially digested to form toxins (endotoxins). Toxins bind to the midgut membrane proteins, creating pores or channels. This paralyzes the digestive system and ruptures midgut cell walls disrupting potassium ion and pH balances. Fluids from the alkaline intestine (pH=9.0 to 10.5) pass into the blood (hemolymph) and cause pH to rise from 6.8 to >8.0. This increase in blood alkalinity leads to paralysis and death.

Pesticides: *Bacillus thuringiensis* spp. *israelensis* (11A1) and *Bacillus thuringiensis* spp. *kurstaki* (11B2)

Oxidative Phosphorylation Uncoupler

Uncouple oxidative phosphorylation, a major energy-producing step in cells, by disrupting the proton (H⁺) gradient across membranes in the mitochondria. Subsequently impairs the mitochondria's ability to produce adenosine triphosphate (ATP).

Pesticide: chlorfenapyr (13)

Oxidative Phosphorylation Inhibitor

Inhibit synthesis of adenosine triphosphate (ATP) resulting in decreased oxidative phosphorylation at the site of dinitrophenol uncoupling.

Pesticide: fenbutatin-oxide (12B)

Mitochondria Electron Transport Inhibitors

Inhibit nicotinamide adenine dinucleotide hydride (NADH) dehydrogenase (complex I) associated with electron transport or act on the NADH-CoQ reductase site, or bind to the Qo center or cytochrome bc1 (complex III) in the mitochondria. These actions reduce energy production by preventing the synthesis of adenosine triphosphate (ATP).

Pesticides: acequinocyl (20B), fenpyroximate (21), and pyridaben (21)

Lipid Biosynthesis Inhibitors

Block the production of lipids, including fatty acids, oils, and waxes. A lack of lipids disrupts cell membrane structure and reduces energy sources.

Pesticides: spiromesifen and spirotetramat (23)

Desiccation or Membrane Disruptors

Damage the waxy layer of the exoskeleton (cuticle) of soft-bodied insects and mites by altering chitin so it cannot hold fluids and dries up. Cuticle damage allows water to penetrate insect breathing pores (spiracles) and kills insects via drowning. Cuticle damage also may smother pests by covering breathing pores.

Pesticides: neem oil, paraffinic oil, petroleum oil, and potassium salts of fatty acids

Unclassified Modes of Action

Pesticides: *Beauveria bassiana* (entomopathogenic fungus) and pyridalyl

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