FROM TOP: D.H. Gent, M.J. Weaver (courtesy Virginia Tech Pesticide Programs, PesticidePics.org), J.D. Barbour, D.G. James

# Pesticide Toxicology and Selectivity

## Pesticide Toxicity Ratings

**Douglas B. Walsh**

Pesticides are applied in hop yard IPM programs when pest abundance or disease incidence and severity exceed established or perceived action thresholds. Approximately 250 to 300 pesticide active ingredients have national registrations that permit their use on hop in the United States if the lead state agency permits the application of that pesticide on hop in its state. Inevitably pesticide use involves some degree of exposure and risk to humans, non-target organisms, and the environment. Table 1 lists selected pesticides along with their relative human health hazard rankings and their relative impacts on non-target beneficial arthropods.

In Table 1, Column 1 lists the active ingredient of fungicides, herbicides, and insecticide/miticides that are registered for use in the major hop-producing states. Column 2 provides a common trade name or products that contain the active ingredient in Column 1. Trade names vary by region, particularly between the East and West, with the Mississippi River being a common divide. As throughout this field guide, the listing of these trade names does not represent endorsement of that particular formulation; it simply provides a frame of reference.

The "signal word" in Column 3 indicates the hazard ranking assigned to each of these active ingredients by the U.S. Environmental Protection Agency with respect to potential human (i.e., mixer or applicator) exposure. The signal word "Danger" identifies a product as being a Category I restricted use pesticide, and includes products such as 2,4-D, ethoprop, and folpet. These products have toxicological profiles that could cause injury or irritation to individuals exposed to low concentrations and often require that the applicator has received specific training or licensing to apply the product. The signal word "Warning" identifies a product as a Category II pesticide, and includes products such as clethodim, cymoxanil, and beta-cyfluthrin. These materials typically require the use of fairly extensive personal protective equipment, but exposure levels required to cause injury or irritation are substantially greater than Category I pesticides. The signal word "Caution" identifies a Category III pesticide, and includes products such as the biocontrol bacterium *Bacillus pumilus*, carfentrazone, and various Bt formulations (e.g., *Bacillus thuringiensis* subsp. *kurstaki*). A Category III pesticide is a product that can cause injury or irritation at a relatively high exposure rate. Personal protective equipment is required, typically including safety glasses, pants, rubber boots, gloves, and long-sleeved shirts. No signal word is required for a Category IV pesticide. Simple safety rules should be followed with these products to avoid exposure. No Category IV pesticides are listed in the table.

Pesticide impacts on humans do not necessarily mirror the impacts those same pesticides would have on beneficial hop yard arthropods. Human physiology differs from arthropod physiology, and substantial differences exist between and among the various arthropods as well. Differences in both susceptibility and resilience factor into a pesticide's impact on a population of beneficial arthropods. Large predatory insects, for example, may be able to survive greater doses (i.e., be less susceptible) than smaller predatory insects and mites. However, larger insects typically will complete only one or a few generations over the course of a growing season, whereas a smaller insect or mite will likely complete more generations and have a greater chance of recovering its population level (i.e., be more resilient). If a population is depressed due to pesticide exposure, it may not recover in a hop yard unless there is an immigration of new individuals from outside of the yard.

To standardize topical mortality studies, the International Organization for Biological Control (IOBC) has categorized pesticides using a ranking of 1 to 4. Columns 4, 5, and 6 in Table 1 provide IOBC toxicity ratings, where available, on three key beneficial arthropods that occur on hop: predatory mites, lady beetles, and lacewing larvae. IOBC categories 1-4 should not be confused with EPA categories I-IV relating to human exposure and indicated by signal words "Danger," "Warning," and "Caution" as described previously.

## Table 1. Signal Words and Relative Impact on Representative Non-target Beneficial Arthropods of Pesticides Registered for Use on Hop



| Active Ingredient | Trade Name | Signal Word | Beneficial Arthropod IOBC Ranking* | | |
|---|---|---|---|---|---|
| | | | Predatory Mites | Lady Beetles | Lacewing Larvae |
| **Fungicides** | | | | | |
| *Bacillus pumilus* | Sonata | Caution | 1 | ND | ND |
| *Bacillus subtilis* | Serenade | Caution | 1 | ND | ND |
| Boscalid | Pristine | Caution | 1 | ND | ND |
| Copper | Various formulations | Caution | 1 | ND | ND |
| Cyazofamid | Ranman | Caution | ND | ND | ND |
| Cymoxanil | Curzate 60DF | Warning | ND | ND | ND |
| Dimethomorph | Forum | Caution | ND | ND | ND |
| Famoxadone & cymoxanil | Tanos | Caution | ND | ND | ND |
| Fenarimol | Vintage SC | Caution | ND | ND | ND |
| Folpet | Folpan 80WDG | Danger | ND | ND | ND |
| Fosetyl-Al | Aliette WDG | Caution | ND | ND | ND |
| Kaolin | Surround | Caution | 3 | ND | ND |
| Mandipropamid | Revus | Caution | 1 | 1 | ND |
| Mefenoxam | Ridomil | Caution | ND | ND | ND |
| Metalaxyl | MetaStar | Warning | ND | ND | ND |
| Mineral oil/petroleum distillate | Various formulations | Caution | 2 | ND | ND |
| Myclobutanil | Rally 40W | Warning | 2 | 1 | ND |
| Phosphorous acid | Fosphite, other formulations | Caution | ND | ND | ND |
| Pyraclostrobin | Pristine | Caution | ND | ND | ND |
| Quinoxyfen | Quintec | Caution | 1 | ND | ND |
| Sodium borate | Prev-Am | Warning | 2 | ND | ND |
| Sulfur | Various formulations | Caution | 2 | ND | ND |
| Tebuconazole | Folicur 3.6F | Caution | 1 | ND | ND |
| Trifloxystrobin | Flint | Caution | 1 | ND | ND |
| **Herbicides** | | | | | |
| 2,4-D | Weedar 64, other formulations | Danger | ND | ND | ND |
| Carfentrazone | Aim EC | Caution | 1 | ND | ND |
| Clethodim | Select Max | Warning | 1 | ND | ND |
| Clopyralid | Stinger | Caution | 1 | ND | ND |
| Flumioxazin | Chateau | Caution | 1 | 1 | ND |
| Glyphosate | Roundup, other formulations | Caution | 1 | ND | ND |
| Norflurazon | Solicam | Caution | ND | ND | ND |
| Paraquat | Gramoxone,other formulations | Danger | 1 | ND | ND |
| Pelargonic acid | Scythe | Warning | ND | ND | ND |
| Pendamethalin | Prowl $H_2O$ | Caution | ND | ND | ND |
| Trifluralin | Treflan, other formulations | Caution | 2 | ND | ND |
| **Insecticides/Miticides** | | | | | |
| Abamectin | Agri-Mek, other formulations | Warning | 3 | 3 | ND |
| *B. thuringiensis* subsp. *aizawai* | XenTari, other formulations | Caution | 1 | 2 | ND |
| *B. thuringiensis* subsp. *kurstaki* | Dipel, other formulations | Caution | 1 | 2 | ND |
| Beta-cyfluthrin | Baythroid XL | Warning | 4 | 4 | 4 |
| Bifenazate | Acramite-50WS | Caution | 1 | 2 | ND |
| Bifenthrin | Brigade, other formulations | Warning | 4 | 4 | 4 |
| Cyfluthrin | Baythroid 2E | Danger | 4 | 4 | 4 |
| Dicofol | Dicofol | Caution | 1 | 1 | ND |
| Ethoprop | Mocap | Danger | 4 | 4 | ND |
| Etoxazole | Zeal | Caution | 1 | 1 | ND |
| Fenpyroximate | FujiMite | Warning | 1 | 3 | ND |
| Flonicamid | Beleaf 50SG | Caution | 1 | 1 | ND |
| Hexythiazox | Savey 50DF | Caution | 1 | 1 | ND |
| Imidacloprid | Admire Pro, other formulations | Caution | 1 | 3 | 3 |
| Malathion | Various formulations | Warning | 2 | 4 | 3 |
| Naled | Dibrom | Danger | 2 | 4 | 3 |
| Propargite | Omite 6E | Danger | 1 | 1 | ND |
| Pymetrozine | Fulfill | Caution | 1 | 1 | 1 |
| Pyrethrin | Pyganic, other formulations | Caution | 2 | 2 | 2 |
| Spinosad | Success, other formulations | Caution | 2 | 2 | 1 |
| Spirodiclofen | Envidor | Caution | 2 | 2 | 1 |
| Spirotetramat | Movento | Caution | 1 | 1 | 1 |
| Thiamethoxam | Platinum | Caution | 1 | 1 | ND |

* International Organization for Biological Control rankings represent relative toxicity based on data from studies conducted with tree fruit, hop, mint, and grape. 1 = "harmless," less than 30% mortality following direct exposure to the pesticide; 2 = "slightly harmful," 30 to 79% mortality; 3 = "moderately harmful," 79 to 99% mortality; 4 = "harmful," greater than 99% mortality; and ND = no data / not determined.

## Strategies to Minimize Development of Pesticide Resistance

◆ Utilize cultural practices to reduce pathogen, weed, and pest populations whenever possible.

**EXAMPLE**
Removing overwintering flag shoots and basal spikes mechanically or chemically helps reduce the inoculum level of powdery mildew and downy mildew.

**EXAMPLE**
Delay resistance development by hand weeding or cultivating annual weeds to prevent them from developing seed.

◆ Limit the number of applications of resistance-prone pesticides as directed by the label.

◆ Apply pesticides at rates specified on the label, especially for weed and arthropod pests.

◆ Adjust application volume per acre based on the size and volume of the crop to attain excellent spray coverage.

# Pesticide Resistance Management

**Mark E. Nelson, David H. Gent, Robert Parker, Rick A. Boydston, and Douglas B. Walsh**

Many of the most widely used pesticides pose an inherent risk of resistance development. Pesticide resistance is a consequence of repeated use of an herbicide, fungicide, or insecticide/miticide with the same (or, in some cases, a similar) mode of action, resulting in a lack of efficacy for a particular pesticide or pesticide group against a particular pest. Resistance has been documented among numerous pests that may affect hop. Examples include herbicide resistance in kochia and pigweed, organophosphate resistance in hop aphid, abamectin and bifenazate resistance in twospotted spider mite, and mefanoxam resistance in the downy mildew pathogen.

Resistance develops in a pest population and not in individuals. It occurs when a pesticide is applied repeatedly and susceptible pests are controlled but genetically resistant individuals of the same species reproduce and increase in absence of competition. Resistant strains of the pest become prevalent in a population over time due to this selection pressure. For example, studies have shown that kochia is a genetically diverse weed species, and in a kochia population a small number of plants (e.g., 1 in 1,000,000 plants) may be naturally resistant to a particular herbicide. Repeatedly exposing kochia populations to the same herbicide may result in a rapid buildup of resistant weeds. Weeds resistant to that herbicide will then dominate over time due to this selection pressure, and the previously effective herbicide will fail to control the population.

Resistance can be quantitative or qualitative. Quantitative resistance manifests as a gradual loss of control that occurs as a pest population becomes more tolerant to a pesticide. In these situations, a product may perform brilliantly when first used and then over a period of years slowly deteriorate in efficacy. As a result, the compound must be applied at higher rates and/or shorter intervals in order to maintain control. An example of this quantitative resistance is fosetyl-Al (Aliette WDG) against the hop downy mildew pathogen. The registered label rate for Aliette of 2.5 lbs. per acre no longer effectively controls downy mildew in some regions. Alternatively, qualitative resistance is "all or none," where a pesticide performs brilliantly for a period of time but provides no control after resistance develops. A good example of qualitative resistance is mefenoxam (Ridomil) against the hop downy mildew pathogen. Once useful, this fungicide now provides no control in yards where resistance is present.

Note that persistence of resistance in a pest population varies among pesticides and pests. For instance, resistance to mefenoxam can still be detected in the downy mildew pathogen in hop yards that have not been treated with this fungicide in over 10 years. Susceptibility to bifenazate

Pigweed. (H.F. Schwartz, Colorado State University, Bugwood.org)

Hop aphids on leaf. (D.G. James)

Twospotted spider mites. (D.G. James)

and bifenthrin is renewed more rapidly in field populations of spider mites than susceptibility to abamectin. This implies that the "cost" (from the mites' perspective) of maintaining resistance to bifenazate and bifenthrin is greater in a mite population than maintaining resistance to abamectin. Persistence of resistance in weeds depends in part on the longevity and dormancy of the weed seed in the soil. In addition, some resistance genes reduce the relative fitness of weeds in the absence of the herbicide, whereas others have no apparent effect on relative fitness.

The risk of resistance development is linked closely to the genetics and reproductive potential of a pest. Pests that have a high reproductive potential (e.g., powdery mildew and spider mites) generally have a higher risk of resistance development than pests with a low fecundity. The number of generations within a year also affects the rate of resistance development. Spider mites can produce multiple generations per growing season and are haplo-diploid. (Females emerge from eggs that have been fertilized by sperm and egg and consequently are diploid in having two sets of chromosomes. Males emerge parthenogenically from unfertilized eggs, consequently possessing only a single haploid set of chromosomes.) When acaricide resistance in a mite population is genetically based, male mites that lack the genes for resistance are killed when exposed to an acaricide, while male mites with the resistance gene survive to further contribute these resistant genes to subsequent generations. Haplodiploidy can contribute to rapid development of acaricide resistance. Most annual weeds produce only one generation a year, so the rate of resistance development tends to be slower in weeds than with many insect or plant pathogens. Other factors that influence resistance development are the fitness (relative vigor) of resistant strains versus susceptible strains, dispersal ability of the pest, availability of nearby populations of susceptible strains of the pest, the number of individuals needed to initiate an infestation or infection, and reproductive mechanisms of the pest (asexual or sexual reproduction). On hop, many pesticides used for management of powdery mildew, downy mildew, spider mites, and hop aphid have a risk of resistance due to the highly specific mode of action of the pesticides and biological characteristics of the pests.

Few pesticides with novel modes of action are being brought forward to market and field use, and increased regulatory scrutiny of new pesticides limits the registration of new pesticides. Consequently, the hop industry must judiciously use pesticides to prevent or delay resistance development to available pesticides. A key point in resistance development is that only a very small percentage of individuals in a population have the potential for resistance to a given mode of action. Therefore, the overall objectives of resistance management are to reduce the populations of pests exposed to a given mode of action, as well as reduce the duration and frequency of that exposure, thereby reducing the opportunity for those few individuals with resistance potential to become predominant in the population. Utilizing diverse modes of action and limiting the total number of applications of a particular mode of

Symptoms of downy mildew. (D.H. Gent)

## Strategies, cont.

◆ Include low-resistance-risk compounds in spray programs whenever possible. Do not rely on resistance-prone compounds to attempt to control severe pest outbreaks. For example with powdery mildew, petroleum oils and carbonates are the best eradicant fungicides.

◆ Select miticides and insecticides with a high degree of selectivity for beneficial arthropods to allow biological control to reduce populations of resistant pest strains.

◆ Utilize synthetic fungicides prone to resistance development protectively before powdery mildew or downy mildew becomes a problem. Avoid making more than two consecutive applications of synthetic fungicides (e.g., DMI, quinoline [azanaphthalene], strobilurin [QoI], or carboxamide classes).

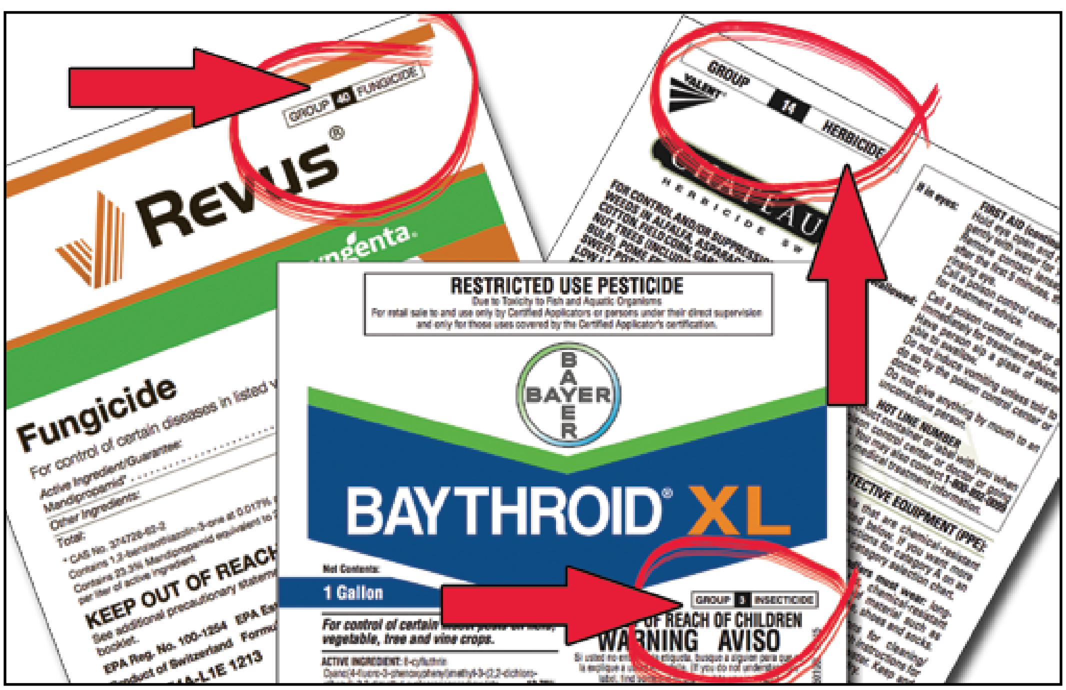
action serve to maintain a reservoir of the susceptible population, which is essential in proactive pesticide resistance management.

For downy mildew and powdery mildew, resistance generally can be delayed by limiting the number of applications of any resistance-prone fungicide class (no more than three per season and no more than two sequential applications), use of single or block applications in alternation with fungicides from a different group, tank-mixing with fungicides with different modes of action, and use early in the season before the diseases are well established. Do not alternate resistance-prone products with other products in the same fungicide class as cross-resistance has been documented in the demethylation inhibitor (DMI) and strobilurin fungicide classes. For example, a rotation of trifloxystrobin (Flint) and pyraclostrobin (Pristine) would not be effective since both fungicides have active ingredients with the same mode of action.

Similar principles apply to resistance management for spider mite and hop. Limit the number of applications of any resistance-prone product as directed by the label (ideally not more than once per two seasons in a given yard), use single or block application in alternation with products with a different mode-of-action group, target applications against the most vulnerable life stage of the pest, and integrate non-chemical control measures before pests exceed economic thresholds. Use of products with a high degree of selectivity to the target pest (i.e., preserving beneficial arthropods) can allow biological control to reduce populations of resistant pest strains, and thus help to delay resistance.

The Fungicide Resistance Action Committee (FRAC, http://www.frac.info), Insecticide Resistance Action Committee (IRAC, http://www.irac-online.org), Herbicide Resistance Action Committee (HRAC, http://www.hracglobal.com), and Weed Science Society of America (WSSA, http://wssa.net) classify pesticides according to mechanism of action and resistance risk in their respective groups. These organizations assign numeric or alphanumeric codes to pesticides, signifying groupings with similar modes of action. For groups prone to resistance problems, development of resistance to any pesticide within a group generally means there will be a loss of efficacy by all members of the group. The appropriate website and pesticide label should be consulted for current use guidelines. The pesticide group designation is often indicated on the first page of the label, as illustrated below.

Table 2 provides a list of registered pesticides commonly used on hop, their modes of action, and their resistance codes.




The pesticide group designation is often indicated on the first page of the label.

## Strategies, cont.

◆ Alternate or tank mix products with diverse modes of action within and between seasons. Make sure the alternative mode of action chosen is also active on the target species.

◆ Avoid using broad-spectrum insecticides that are disruptive to the predators and parasites of pests, particularly early in the growing season.

◆ Choose miticides and insecticides with a high degree of selectivity for beneficial arthropods to allow biological control to reduce populations of resistant pest strains.

## Table 2. Modes of Action and Resistance Codes for Pesticides Used on Hop



| Active Ingredient | Trade Name Example | Mode of Action* | Resistance Code |
|---|---|---|---|
| **Fungicides** | | | **FRAC Code** |
| Fenarimol | Vintage SC | G1: DMI (SBI class 1) | 3 |
| Myclobutanil | Rally 40W | | |
| Tebuconazole | Folicur 3.6F | | |
| Mefenoxam | Ridomil | A1: Phenylamide | 4 |
| Metalaxyl | MetaStar | | |
| Boscalid | Pristine | C2: SDHI | 7 |
| Pyraclostrobin | Pristine | C3: QoI | 11 |
| Trifloxystrobin | Flint | | |
| Famoxadone & cymoxanil | Tanos | C3: QoI & Unknown: Cyanoacetamideoxime | 11 & 27 |
| Quinoxyfen | Quintec | E1: Azanapthalene | 13 |
| Cyazofamid | Ranman | C4: QiI | 21 |
| Cymoxanil | Curzate 60DF | Unknown: Cyanoacetamideoxime | 27 |
| Fosetyl-Al | Aliette WDG | Unknown: Phosphonate | 33 |
| Phosphorous acid | Fosphite | | |
| Dimethomorph | Forum | F5: CAA fungicide | 40 |
| Mandipropamid | Revus | | |
| *Bacillus pumilus* | Sonata | F6: Microbial | 44 |
| *Bacillus subtilis* | Serenade | | |
| Copper | Various | Multi-site | M1 |
| Sulfur | Various | | M2 |
| Folpet | Folpan 80WDG | Multi-site: Phthalimide | M4 |
| Kaolin | Surround | Physical barrier | n/a |
| Mineral oil/petroleum distillate | Various | | |
| Sodium borate | Prev-Am | | |
| **Herbicides** | | | **WSSA Group** |
| Clethodim | Select Max | Inhibition of acetyl CoA carboxylase (ACCase) | 1 |
| Pendimethalin | Prowl $H_2O$ | Microtubule assembly inhibitor | 3 |
| Trifluralin | Treflan | | |
| 2,4-D | Weedar 64 | Action like indole acetic acid | 4 |
| Clopyralid | Stinger | | |
| Glyphosate | Roundup | EPSP synthase inhibitor | 9 |
| Norflurazon | Solicam | Phytoene desaturase step (PDS) | 12 |
| Carfentrazone | Aim EC | Protoporphyrinogen inhibitor | 14 |
| Flumioxazin | Chateau | | |
| Paraquat | Gramoxone | Photosystem-I-electron diverter | 22 |
| Pelargonic acid | Scythe | Other | n/a |
| **Insecticides/Miticides** | | | **IRAC Code** |
| Ethoprop | Mocap | Acetylcholinesterase inhibitor | 1B |
| Malathion | Various | | |
| Naled | Dibrom | | |
| Beta-cyfluthrin | Baythroid XL | Sodium channel modulator | 3A |
| Bifenthrin | Brigade | | |
| Cyfluthrin | Baythroid 2E | | |
| Pyrethrin | Pyganic | | |
| Imidacloprid | Admire Pro | Nicotinic acetylcholine receptor antagonist | 4A |
| Thiamethoxam | Platinum | | |
| Spinosad | Success | Nicotinic acetylcholine receptor allosteric antagonist | 5 |
| Abamectin | Agri-Mek | Chloride channel activator | 6 |
| Pymetrozine | Fulfill | Chordotonal organ modulator | 9B |
| Flonicamid | Beleaf 50SG | | 9C |
| Hexythiazox | Savey 50DF | Mite growth inhibitor | 10A |
| Etoxazole | Zeal | | 10B |
| *B. thuringiensis* subsp. *aizawai* | XenTari | Midgut membrane microbe disruptor | 11A |
| *B. thuringiensis* subsp. *kurstaki* | Dipel | | |
| Propargite | Omite 6E | Mitochondrial ATP synthase inhibitor | 12C |
| Fenpyroximate | FujiMite | Mitochondrial complex I electron transport inhibitor | 21A |
| Spirodiclofen | Envidor | Acetyl CoA carboxylase inhibitor | 23 |
| Spirotetramat | Movento | | |
| Bifenazate | Acramite-50WS | Unknown | Unknown |
| Dicofol | Dicofol | | |

* Mode of action information is provided with guidance from FRAC, HRAC, and IRAC.