The effectiveness and safe use of the numerous brand name and generic herbicides registered for forest vegetation management in Florida (Osiecka and Minogue 2013) requires developing site-specific herbicide prescriptions made with careful consideration of site factors and knowledge of herbicide characteristics. Familiarity with chemical and physical properties of herbicides and their effects on biological systems enables the selection of appropriate herbicide products, application methods, rates, and timing.

In addition to understanding herbicide characteristics, it is crucial to understand terminology used on herbicide labels. These labels are legally binding documents for herbicide use. The single most important rule in employing herbicides is to always read and follow the label instructions, which are provided on the herbicide container and are also available at numerous websites, for example Crop Data Management Systems (CDMS) http://www.cdms.net/label-database.

Herbicide components, such as:

- mode of action
- selectivity
- activity
- mobility in soil
- volatility
- persistence in the environment
- toxicity

are determined by the active ingredients as well as by the formulations of the herbicide products in which the active ingredients are “packaged.” Herbicides contain one or more active ingredients and several inert ingredients:

- a carrier/solvent
- possibly one or more adjuvants

There are no chemical reactions involved between active and inert ingredients, but their homogenous and stable mixture ensures that the formulation is safe and efficacious when applied to target vegetation.

Herbicide Components

The term active ingredient refers to the chemical substance in the herbicide product that disrupts plant metabolism and produces the herbicidal effect. The active ingredient has the greatest influence on the properties and behavior of the herbicide, and is the primary factor to consider when selecting a herbicide product for a particular application. The active ingredient may be referred to by the common name (e.g., triclopyr) or its chemical name (e.g., for triclopyr: 3,5,6-trichloro-2-pyridinyloxyacetic acid). Many herbically-active compounds are acids that can be formulated as salts (mostly amine salts) or esters. Once a herbicide enters the plant, the salt or ester is disassociated and the parent acid may be transported throughout the plant to the site of action where the herbicidal effect is produced. The amount of an active ingredient in a herbicide product is reported either as the amount of active ingredient (a.i.) or
the free acid portion of the active ingredient known as the **acid equivalent** (a.e.). The latter is especially useful when comparing herbicides containing different derivatives of the same parent acid. The amount of active ingredient in a herbicide product is usually expressed as the pounds of active ingredient or acid equivalent per gallon (or grams per liter) and also as the percentage a.i. or a.e. by volume or mass. Several active ingredients are available in both salt and ester formulations (e.g., triclopyr as Garlon® 3A and Garlon® 4, respectively). When choosing between a salt and an ester formulation, the following characteristics should be considered.

**Salts**
- water-soluble; polar (ionic—separate into negative and positive ions when mixed with water)
- typically require a surfactant to facilitate penetration through the waxy leaf covering (cuticle)
- low volatility (less likely to move as a vapor) and thus preferable near sensitive sites, especially in hot weather

**Esters**
- low water-solubility; generally require an emulsifying agent or agitation to maintain dispersion in water-based carriers
- oil-soluble; can penetrate the outer oil-loving, or lipo-philic tissues of plants such as the waxy cuticle of the leaf surface or the suberin-rich material of the bark
- varying degrees of volatility, but generally more volatile than salts
- generally more toxic to plants and animals than salts

**Adjuvants**
Adjuvants are chemicals included in a herbicide product or added to a tank mix immediately preceding an application to enhance herbicide effectiveness, stability of the spray preparation, or to improve application efficiency. Adjuvants improve herbicide performance by increasing efficiency of spray deposition to target vegetation and improving plant uptake. Adjuvants include surfactants (see below), pH buffers and acidifiers, drift mitigation agents, spray colorants, anti-foaming agents, and compatibility agents. Before adding adjuvants to a herbicide spray preparation, refer to the labels of all products to ensure their compatibility. While adjuvants may improve herbicide performance, they may also affect non-target specie's tolerance. For instance, some surfactants increase herbicide absorption by pines, resulting in injury, thus decreasing selectivity.

**Surfactants**
Surfactants (surface-active agents) are the most commonly used adjuvants and include several groups of products described as spreaders, stickers, emulsifying agents, and crop oil concentrates. However, the term “surfactants,” is often used in a narrower sense referring to spreaders, or wetting agents, which work by reducing the surface tension of water and causing a larger portion of each spray droplet to come into contact with the surface of the target vegetation. Reducing surface tension results in enhanced wetting and penetration by a herbicide. **Ionic** surfactants separate into negative and positive ions when mixed with water and may react unfavorably with ionic herbicides. **Non-ionic** surfactants do not separate into ions when mixed with water and therefore are not likely to react with herbicides. Since many herbicides are ionic, many herbicide labels specify the use of non-ionic surfactants.

**Carriers/Solvents**
Carriers, or solvents, are the inert liquid or solid materials in a herbicide product that serve as delivery vehicles for the active ingredients. Carriers are also used to dilute or suspend an herbicide product for the application. The most common liquid carrier is water because of low cost and ease of use. Petroleum and plant oils as well as liquid fertilizers are also used as herbicide carriers. Solid (dry) carriers include attapulgite, kaolinite, vermiculite, bentonite, polymers of starch, and dry fertilizers.

**Herbicide Products or Formulations**
Herbicide products or formulations are commercial preparations of herbicides. They may contain one or more active ingredients, adjuvants, and a carrier/solvent. Formulated herbicide products are registered and marketed under various trade names intended for uses specified on the product label. Because of the multitude of existing herbicide formulations, one has to make sure that the selected formulation is appropriate for the desired application. The important determining factors include: application method, target weed species, crop tree species and environmental considerations. Knowing the formulation helps the applicator to properly dispense herbicides in an appropriate carrier, add appropriate adjuvants if necessary, and select the appropriate application method. Forestry herbicides are manufactured as liquid or solid formulations.

**Liquid Formulations**
May be used undiluted, as in the case of “ready-to-use (RTU)” herbicide products (e.g., Pathfinder® II), mixed with water to form a solution, mixed with oil, or mixed...
with water plus oil carriers to form an emulsion. In a solution, herbicide product is dissolved in water and is dispersed uniformly in the spray preparation. In an emulsion, the herbicide is suspended in minute globules of oil (micelles) in a predominately water carrier through the use of an emulsifier. The water and oil phases will separate over time without agitation. Invert emulsions are a suspension of water droplets containing herbicide in a predominately oil carrier, are very thick in nature, and provide some drift mitigation because they produce a larger droplet size.

- **Water-soluble liquids** are designated as L, SL, or WS in herbicide product names such as Velpar® L, the liquid formulation of hexazinone.

- **Emulsifiable concentrates** are commonly designated as EC in the product names such as Pendulum® EC, the emulsifiable concentrate formulation of pendimethalin.

### Solid Formulations

May be mixed with water to form solutions, suspensions, or applied as a solid.

- **Soluble powders** form a homogenous solution in water.
- **Wettable powders** such as Aatrex® 80 W are suspended in water through constant agitation.
- **Water-dispersible granules**, also known as dry flowables, such as Velpar® DF, typically disperse (but do not fully dissolve) in water, and generally require agitation to prevent precipitation in the spray tank. They are similar to wettable powders, but formulated as small, easily measured granules.
- **Granules** and pellets (e.g. Pendulum® 2G) consist of one or more active ingredients embedded in an inert solid material. When applied to the soil they slowly dissolve, gradually releasing the active ingredients.

### Herbicide Characteristics

**Mode of action** is the mechanism by which an active ingredient interferes with the metabolism of a plant in order to kill or suppress it. It largely determines the effectiveness of an herbicide in controlling a particular species, and thus the **selectivity** of the herbicide product (see Table 1). An herbicide’s mode of action includes the nature by which it is absorbed by plants (activity), the pattern of movement within the plant (translocation) and the physiological processes that are affected by the herbicide (site of action). The mode of action is generally determined by the chemical structure and properties of an active ingredient. Herbicide active ingredients that are chemically similar belong to the same “herbicide family” and tend to have the same mode of action. However, active ingredients belonging to different families may also exhibit the same mode of action. For example, triclopyr and clopyralid which are in the pyridine family, and 2,4-D within the phenoxy family, are all auxin analogs and mimic this plant hormone physiologically. Alternating between herbicides with different modes of action helps prevent creating herbicide-resistant weed populations. The most common modes of action among forestry herbicides are listed here.

- **Auxin analogs** (e.g. 2,4-D, aminopyralid, clopyralid, and triclopyr) mimic the plant growth hormone auxin, resulting in disorganized growth through many physiological processes.
- **Mitosis inhibitors** (e.g. fosamine) affect cell division, preventing new growth.
- **Photosynthesis inhibitors** (e.g. atrazine and hexazinone) interfere with electron transport in photosynthesis.
- **Amino acid synthesis inhibitors** (e.g. glyphosate, imazapic, imazapyr, metsulfuron methyl, and sulfdometuron methyl) prevent the synthesis of amino acids (the building blocks of proteins).
- **Lipid biosynthesis inhibitors** (e.g. fluazifop-p-butyl) prevent the synthesis of lipids, crucial elements of cell membranes.

**Selectivity** refers to a herbicide’s capability to affect different categories of plants to different extents due to physiological or morphological differences between species, and is largely dictated by the herbicide active ingredient’s mode of action. Ideally, differences between crop plants and weed species are exploited. **Selective** herbicides have a specific range of susceptible species and often target a particular class of plants, for example broadleaf plants (e.g. 2,4-D and aminopyralid) or grasses (e.g. fluazifop-P-butyl and clethodim). **Non-selective** or **broad-spectrum** herbicides (like glyphosate) negatively affect most species by impacting metabolic processes common to many plant groups. Non-selective herbicides, therefore are normally not used over-the-top of crop trees, especially during periods of active growth. Selectivity may also be achieved by manipulating application method, rate, and timing. For example, one can control undesirable trees by applying a non-selective herbicide directly to their stems or foliage without spraying desired vegetation. Also, some herbicides applied at lower rates may selectively control unwanted vegetation without affecting crop trees or other desired plant species. Non-selective herbicides can sometimes be
applied with selectivity over-the-top of crop trees during their dormancy.

**Activity** refers to the way a herbicide enters treated plants.

**Foliar-active** herbicides are absorbed by leaves and stems, and typically require herbicide spray coverage to most of the crown in order to be effective in controlling woody plants. Herbicides absorbed by foliage may translocate to the roots in the phloem. Some foliar-active herbicides can also be applied to stems and absorbed through bark and epidermal tissues. Many foliar-active herbicides can be injected directly into tree stems, or applied to cuts made in the stem to expose cambium and vascular tissues. This approach also includes treating surfaces of cut tree stumps. Foliar herbicides exhibit **post-emergent** weed control, meaning they have to be applied directly to established plants.

**Soil-active** herbicides are taken up from the soil solution by roots and are transported in the xylem to the upper parts of the plant. They generally require adequate soil moisture for activation of hericide properties. For annual and perennial herbaceous plant control, soil active herbicides such as sulfometuron methyl are effective with **pre-emergent** application timing, meaning before plants emerge, or with early post-emergent timing, when weeds are only a few inches tall. Pre-emergent herbicides disrupt germination or kill germinating seedlings. Other long-residual soil-active herbicides such as hexazinone and imazapyr are more effective in controlling established plants such as perennial herbaceous plants, shrubs and trees and are usually applied during the growing season.

Herbicide mobility in soil, volatility, persistence, and toxicity are very important in environmental considerations (see Table 2).

**Herbicide mobility in soil** of a herbicide is determined by its water solubility and potential for soil sorption, both important characteristics for predicting the potential for off-site movement through leaching and runoff. The potential for soil sorption is assessed primarily through two measures, usually reported for the active ingredient and sometimes for the parent acid and the salt and ester formulation, if applicable:

- **K₅₃** (Soil sorption coefficient) is defined as the ratio of sorbed herbicide to dissolved herbicide at equilibrium in water/soil slurry at a given temperature and pH.

- **K₉₅** (Soil organic carbon sorption coefficient) is calculated as **K₅₃** divided by the weight fraction of organic carbon present in the soil at a given temperature and pH.

Herbicides with small **K₉₅** values are more likely to be leached compared with those with large **K₉₅** values. However, **K₉₅** values should be used with caution, since they may be significantly affected by soil properties and environmental factors.

**Vollatility** refers to a herbicide’s tendency to go into a gaseous phase during or after application and is primarily determined by its molecular weight and presence or cyclic hydrocarbons. High volatility may result in herbicide movement off-site with negative impacts on nearby sensitive crops. The danger of herbicide volatilization increases with increasing air temperatures during and immediately following application. Of the common forestry herbicides, only triclopyr and 2,4-D can pose significant volatilization risk. In general, ester formulations are more volatile than salts.

**Persistence** defines the “lasting-power” of a herbicide and is measured in half-life. **Half-life (T₁/₂)** can be defined as the expected time after application during which half of the applied herbicide would be degraded. The half-life values for herbicide active ingredients are derived from field and laboratory experiments. These values give only a rough estimate of the persistence in the environment, since an actual half-life of a particular herbicide product also depends on the formulation and can vary significantly depending on soil characteristics, weather (especially temperature and soil moisture) and vegetation at the site. Nonetheless, average half-life values, based on herbicide active ingredient deactivation in surface soils, provide some means of comparing the relative persistence of herbicide products. The T₁/₂ values in subsoils and ground water are usually much larger and often not available.

**Herbicide toxicity** refers to the potential to cause injury, illness, or other undesirable effects in mammals, birds, fish, honey bees, or other organisms. Toxicity studies measure short term (acute), mid-term (subchronic), and long term (chronic) effects. Since most herbicides affect physiological processes exclusive to plants (like photosynthesis or plant-specific hormones or enzymes), the majority of forestry herbicides have very low toxicity to humans and animals.

The United States Environmental Protection Agency (EPA) requires results of six acute toxicity studies (acute oral, acute dermal, acute inhalation, primary eye irritation, primary skin irritation, and the dermal sensitization)
performed with the herbicide product formulation to determine the safety language appearing at the beginning of each herbicide label: an appropriate signal word, “Hazards to Humans and Domestic Animals,” “Personal Protective Equipment,” and “First Aid” statements. An herbicide is assigned a toxicity category for the results of each acute toxicity study, with exception of dermal sensitization (see Table 3). The signal word is determined by the most severe toxicity category.

The commonly used acute toxicity measures include the median lethal dose (LD$_{50}$) for oral and dermal exposure and median lethal concentration (LC$_{50}$) in air or water.

LD$_{50}$ is the dose (quantity) of a herbicide that kills 50% of a population of test animals through oral or dermal exposure and is expressed in milligrams of the herbicide per kilogram of the test animal body weight.

LC$_{50}$ is the herbicide concentration in the air (inhalation toxicity) or in the water (aquatic toxicity) that kills 50% of a population of test animals and is expressed in milligrams of the herbicide per liter of air or water (parts per million).

Chronic mammalian toxicities are determined by long term (12–24 month) feeding studies, which evaluate the potential for long-term negative effects on test animals including:

- Carcinogenicity, the potential to cause cancer.
- Potential for adverse effects on reproduction.
- Teratogenicity, the potential to cause birth defects.
- Mutagenicity, the potential to cause genetic changes.

In addition, wildlife toxicity is determined using various test organisms, including quail, duck, honey bees, Daphnia (water flea), rainbow trout, and bluegill.

Acute and chronic toxicity studies are required for the registration of an active ingredient, and most often toxicities are reported for the technical grade of the active ingredient (or the parent acid), as in Table 2. However, the formulated herbicide product may have greater or lower toxicity, depending on the concentration and formulation of the active ingredient, as well as the adjuvants and carriers. For example, some ester formulations (e.g. Garlon® 4) are much more toxic to aquatic organisms than the salt formulations (e.g. Garlon® 3A). Surfactants may also increase herbicide toxicity to aquatic organisms. For example, glyphosate formulations with surfactants (e.g. Accord® XRT II) are more toxic to aquatic organisms than formulations containing no surfactants (e.g. Foresters®).

Detailed herbicide toxicity characteristics (including ecotoxicity) are included in Safety Data Sheets (SDSs) available at http://www.cdms.net/label-database and in Pesticide Information Profiles (PIPs) in EXTOXNET available at http://extoxnet.orst.edu/pips/ghindex.html.

**References**


Table 1. Forest herbicide characteristics relative to effectiveness.

<table>
<thead>
<tr>
<th>Active Ingredient</th>
<th>Trade Name Examples</th>
<th>Herbicide Family</th>
<th>Mode of Action</th>
<th>Selectivity (target weeds)</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>2,4 D salt</td>
<td>Weedar® 64</td>
<td>Phenoxy</td>
<td>Growth regulator (auxin analog)</td>
<td>Annual &amp; perennial broadleaves; woody plants</td>
<td>Foliar</td>
</tr>
<tr>
<td>2,4 D ester</td>
<td>Barrage® HF</td>
<td>Phenoxy</td>
<td>Growth regulator (auxin analog)</td>
<td>Annual &amp; perennial broadleaves; woody plants</td>
<td>Foliar</td>
</tr>
<tr>
<td>Aminopyralid</td>
<td>Milestone®</td>
<td>Pyridine</td>
<td>Growth regulator (auxin analog)</td>
<td>Woody plants; annual &amp; perennial broadleaves</td>
<td>Foliar, some soil</td>
</tr>
<tr>
<td>Atrazine</td>
<td>AAtrex® 4L</td>
<td>Triazine</td>
<td>Photosynthesis inhibitor</td>
<td>Annual broadleaves &amp; grasses</td>
<td>Soil</td>
</tr>
<tr>
<td>Clopyralid</td>
<td>Transline®</td>
<td>Picolinic acid</td>
<td>Growth regulator (auxin analog)</td>
<td>Annual &amp; perennial broadleaves; woody plants</td>
<td>Foliar</td>
</tr>
<tr>
<td>Fluazifop-p-Butyl</td>
<td>Fusilade® DX</td>
<td>Aryloxyphenoxy-propionate</td>
<td>Lipid synthesis inhibitor</td>
<td>Annual &amp; perennial grasses</td>
<td>Foliar</td>
</tr>
<tr>
<td>Fosamine</td>
<td>Krenite® S</td>
<td>Organophosphorus</td>
<td>Mitotic inhibitor</td>
<td>Woody plants</td>
<td>Foliar</td>
</tr>
<tr>
<td>Glyphosate</td>
<td>Accord® XRT II, Foresters®</td>
<td>Organophosphorus</td>
<td>Amino acid synthesis inhibitor</td>
<td>Annual &amp; perennial broadleaves &amp; grasses; woody plants</td>
<td>Foliar</td>
</tr>
<tr>
<td>Hexazinone</td>
<td>Velpar® L</td>
<td>Triazine</td>
<td>Photosynthesis inhibitor</td>
<td>Annual &amp; perennial broadleaves &amp; grasses; woody plants</td>
<td>Soil, some foliar</td>
</tr>
<tr>
<td>Imazapic</td>
<td>Plateau®</td>
<td>Imidazolinone</td>
<td>Amino acid synthesis inhibitor</td>
<td>Annual &amp; perennial grasses &amp; broadleaves; vines</td>
<td>Foliar &amp; soil</td>
</tr>
<tr>
<td>Imazapyr</td>
<td>Arsenal® AC</td>
<td>Imidazolinone</td>
<td>Amino acid synthesis inhibitor</td>
<td>Annual &amp; perennial grasses &amp; broadleaves; woody plants; vines</td>
<td>Foliar &amp; soil</td>
</tr>
<tr>
<td>Metsulfuron methyl</td>
<td>Escort® XP</td>
<td>Sulfonylurea</td>
<td>Amino acid synthesis inhibitor</td>
<td>Annual &amp; perennial grasses &amp; broadleaves; woody plants</td>
<td>Foliar &amp; soil</td>
</tr>
<tr>
<td>Sulfometuron methyl</td>
<td>Oust® XP</td>
<td>Sulfonylurea</td>
<td>Amino acid synthesis inhibitor</td>
<td>Annual &amp; perennial grasses &amp; broadleaves</td>
<td>Foliar &amp; soil</td>
</tr>
<tr>
<td>Triclopyr salt</td>
<td>Garlon® 3A</td>
<td>Pyridine</td>
<td>Growth regulator (auxin analog)</td>
<td>Annual &amp; perennial broadleaves; woody plants</td>
<td>Foliar</td>
</tr>
<tr>
<td>Triclopyr ester</td>
<td>Garlon® 4</td>
<td>Pyridine</td>
<td>Growth regulator (auxin analog)</td>
<td>Annual &amp; perennial broadleaves; woody plants</td>
<td>Foliar</td>
</tr>
<tr>
<td>Active ingredient</td>
<td>Water solubility (mg/L)</td>
<td>Behavior in soils</td>
<td>Toxicity</td>
<td>Environmental and safety concerns</td>
<td></td>
</tr>
<tr>
<td>---------------------------</td>
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<td>----------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Soil sorption average $K_{oc}$ (mL/g)</td>
<td>Mobility</td>
<td>Oral LD$_{50}$ Rat (mg/kg)</td>
<td>Dermal LD$_{50}$ Rabbit (mg/kg)</td>
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<tr>
<td>2,4 D DMA salt</td>
<td>729,000 (20°C)</td>
<td>20</td>
<td>Moderate</td>
<td>10 (7–28)</td>
<td>949</td>
</tr>
<tr>
<td>2,4 D 2-EHE ester$^1$</td>
<td>0.087 (20°C)</td>
<td>100</td>
<td>Moderate</td>
<td>10 (7–28)</td>
<td>896</td>
</tr>
<tr>
<td>Aminopyralid</td>
<td>212,000 (pH 5); 203 (pH 9)</td>
<td>10.8</td>
<td>Low</td>
<td>32 (6–74)</td>
<td>&gt;5,000</td>
</tr>
<tr>
<td>Atrazine</td>
<td>33 (22°C, pH 7)</td>
<td>100</td>
<td>Low</td>
<td>60</td>
<td>3,090</td>
</tr>
<tr>
<td>Clopyralid$^2$</td>
<td>300,000 (25°C)</td>
<td>6 (6–60)</td>
<td>Moderate</td>
<td>40 (12–70)</td>
<td>&gt;5,000</td>
</tr>
<tr>
<td>Fluazifop-P-butyl</td>
<td>1.1 (25°C)</td>
<td>5,700</td>
<td>Low</td>
<td>not available</td>
<td>&gt;5,000$^3$</td>
</tr>
<tr>
<td>Fosamine</td>
<td>1,790,000 (25°C)</td>
<td>150</td>
<td>Low</td>
<td>8</td>
<td>24,400</td>
</tr>
<tr>
<td>Glyphosate</td>
<td>900,000 (25°C, pH 7)$^5$</td>
<td>24,000</td>
<td>Very low</td>
<td>47</td>
<td>5,600</td>
</tr>
<tr>
<td>Hexazinone</td>
<td>33,000 (25°C)</td>
<td>54</td>
<td>Moderate-high</td>
<td>90</td>
<td>1,690</td>
</tr>
<tr>
<td>Imazapic</td>
<td>2,200 (25°C)</td>
<td>112</td>
<td>Low</td>
<td>120</td>
<td>&gt; 5,000</td>
</tr>
<tr>
<td>Imazapyr</td>
<td>11,272 (25°C, pH 7)</td>
<td>poor, $K_{oc}$ not available</td>
<td>Moderate</td>
<td>25–142 days</td>
<td>&gt;5,000</td>
</tr>
<tr>
<td>Metsulfuron methyl</td>
<td>(25°C): 548 (pH 5) 2,790 (pH 7)</td>
<td>35 (pH 7)</td>
<td>Moderate</td>
<td>30 days (7–42)</td>
<td>&gt;5,000</td>
</tr>
<tr>
<td>Sulfometuron methyl</td>
<td>(25°C): 10 (pH 5) 300 (pH 7)</td>
<td>78 (pH 7)</td>
<td>Moderate-high</td>
<td>20–28 (pH 6–7)</td>
<td>&gt;5,000</td>
</tr>
<tr>
<td>Triclopyr salt$^6$</td>
<td>2,100,000 (25°C)</td>
<td>20</td>
<td>Moderate</td>
<td>30 (10–46)</td>
<td>2,574</td>
</tr>
<tr>
<td>Triclopyr ester$^7$</td>
<td>23 (25°C)</td>
<td>780</td>
<td>Low</td>
<td>30 (10–46)</td>
<td>1,581</td>
</tr>
</tbody>
</table>

$^1$ 2-EHE = 2-ethylhexyl ester
$^2$ As monoethanolamine salt
$^3$ As Fusilade DX
$^4$ As a parent acid
$^5$ Isopropylamine salt
$^6$ Triethylamine salt (Garlon® 3A)
$^7$ Butoxyethyl ester (Garlon® 4)
Table 3. Pesticide toxicity categories according to US EPA Label Review Manual (as of July 2014).

<table>
<thead>
<tr>
<th>Study</th>
<th>Category I</th>
<th>Category II</th>
<th>Category III</th>
<th>Category IV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute Oral</strong></td>
<td>Up to and including 50 mg/kg</td>
<td>&gt; 50 thru 500 mg/kg</td>
<td>&gt; 500 thru 5000 mg/kg</td>
<td>&gt; 5000 mg/kg</td>
</tr>
<tr>
<td><strong>Acute Dermal</strong></td>
<td>Up to and including 200 mg/kg</td>
<td>&gt; 200 thru 2000 mg/kg</td>
<td>&gt; 2000 thru 5000 mg/kg</td>
<td>&gt; 5000 mg/kg</td>
</tr>
<tr>
<td><strong>Acute Inhalation</strong></td>
<td>Up to and including 0.05 mg/L</td>
<td>&gt; 0.05 thru 0.5 mg/L</td>
<td>&gt; 0.5 thru 2 mg/L</td>
<td>&gt; 2 mg/L</td>
</tr>
<tr>
<td><strong>Primary Eye Irritation</strong></td>
<td>Corrosive (irreversible destruction of ocular tissue) or corneal involvement or irritation persisting for more than 21 days</td>
<td>Corneal involvement or other eye irritation clearing in 8–21 days</td>
<td>Corneal involvement or other eye irritation clearing in 7 days or less</td>
<td>Minimal effects clearing in less than 24 hours</td>
</tr>
<tr>
<td><strong>Primary Skin</strong></td>
<td>Corrosive (tissue destruction into the dermis and/or scarring)</td>
<td>Severe irritation at 72 hrs (severe erythema or edema)</td>
<td>Moderate irritation at 72 hrs (moderate erythema)</td>
<td>Mild or slight irritation at 72 hrs (no irritation or slight erythema)</td>
</tr>
<tr>
<td><strong>Signal Word</strong></td>
<td>DANGER</td>
<td>WARNING</td>
<td>CAUTION</td>
<td>CAUTION (optional)</td>
</tr>
</tbody>
</table>

1 4hr exposure