Types of Fungicides and Definitions

Fungicides are categorized in several ways based on different characteristics. The most common characteristics used and the categories are described below. <u>Table 1 (Adobe Acrobat PDF)</u> is a list of selected fungicides currently registered in the United States that represent the major fungicide groups and chemistry within these groups.

1. Mobility in a plant: contacts or systemics: Contact fungicides (also called protectants) remain on the surface of plants. Many contacts are potentially phytotoxic (toxic to plants) and can damage the plant if absorbed. Systemics (also called penetrants and mobile fungicides) are absorbed into plants. Most systemics move very short distances from the site of application, such as across a leaf blade from one surface to the other (local systemic or translaminar). Some fungicides are weakly systemic and can move further from the application site than local systemics, reaching all parts of the leaf the fungicide is deposited on. A few systemics move more extensively because they are mobile in xylem tissue. When applied to the root zone, these are absorbed by roots and then move upward through the plant with the transpiration stream (xylem-mobile systemic). Xylemmobile systemics applied to leaves move throughout the leaf where deposited, but cannot be redistributed out of that leaf; however, any material deposited on stems can move upwards into leaves. Phloem-mobile systemics (also known as "true" or amphimobile systemics) have bi-directional mobility, some material moves in phloem out of the leaf where deposited upwards to other leaves and downwards to roots. Systemics cannot move again after translocation.

Animated examples of fungicide mobility:

Contact fungicide - applied to foliage.

Local systemic or translaminar- applied to foliage.

Xylem mobile systemic - applied to soil.

Xylem mobile systemic - applied to foliage.

Amphimobile systemic - applied to foliage.

2. Role in protection: preventive or curative. Contacts are products suited for preventive (prophylactic) use as they work by contact action on the surface of the plant to which they have been applied. Repeated applications are needed to protect new growth of the plant and to replace material that has been washed off by rain or irrigation, or degraded by environmental factors such as sunlight. Sometimes contacts are referred to as "residual" products because the deposited fungicide remains on the plant surface, occasionally as a visible residue, for several days. Due to their ability to penetrate plants, some systemics possess both preventive and curative (eradicant or kick-back) activity, thus affecting the

pathogen after infection.

3. **Breadth of activity: single-site or multi-site.** Single-site fungicides are active against only one point in one metabolic pathway in a pathogen or against a single critical enzyme or protein needed by the fungus. Since single-site fungicides are highly specific in their toxicity, having little effect on most organisms, they can safely be absorbed into plants, thus these fungicides tend to have systemic properties. As a result of this specific activity, fungi are more likely to become resistant to the fungicide because a single mutation in the pathogen usually allows it to overcome the action of the fungicide, such as by preventing it from binding to the active site in the fungus.

Typically, older contact fungicides have multi-site activity and thus usually affect many fungi in different classes. Through the development of in vivo screens, and due to the increase in the stringency and number of regulatory tests required to register a new active ingredient, fungicide manufacturers have found it easier to develop single-site systemics recently. As a result, fungicide resistance has become a more important concern in disease management.

4. **Mode of action.** Fungicides kill fungi by damaging their cell membranes, inactivating critical enzymes or proteins, or by interfering with key processes such as energy production or respiration. Others impact specific metabolic pathways such as the production of sterols or chitin. For example, phenylamide fungicides bind to and inhibit the function of RNA polymerase in oomycetes, while the benzimidazole fungicides inhibit the formation of beta tubulin polymers used by cells during nuclear division.

Some recently developed products are unique in that they do not directly affect the pathogen itself. Many of these elicit a response from the host plant known as "systemic acquired resistance" (SAR). These SAR inducers basically mimic chemical signals in plants that activate plant defense mechanisms such as the production of thicker cell walls and anti-fungal proteins. The utility of SAR inducers, however, has been limited so far since many pathogens are capable of over-powering such defenses.

Knowledge of exactly how a fungicide affects a fungus is helpful for selecting products. First, mode of action determines which fungi will be affected by a fungicide and thus which diseases can be controlled by using the fungicide. Second, fungicides with different modes of action are needed in a disease management program to delay fungicide resistance development.

Biochemical mode of action is the primary basis used to classify fungicides into chemical groups. A list of fungicides organized by chemical group is maintained by the Fungicide Resistance Action Committee (FRAC) (http://www.frac.info/frac/index .htm) and is in Appendix II of a US Environmental Protection Agency (EPA) document (www.epa.gov/opppmsd1/PR Notices/pr2001-5.pdf). Fungicides in Table 1 (Adobe Acrobat PDF) are listed according to the FRAC/EPA classification scheme plus an additional class for biofungicides. Basic chemical information for fungicides is at the PAN Pesticide Database (www.pesticideinfo.org). All fungicides within a chemical group share a common mode of action and resistance mechanism, even though their chemical structures may be different. Two exceptions in the FRAC/EPA classification scheme are the "multi-site activity" fungicide class and the "unknown" class of fungicides with unknown modes of action.

- 5. **Breadth of activity: narrow-spectrum or broad-spectrum.** Narrow-spectrum fungicides are effective against only a few usually closely related pathogens. These usually have single-site activity and are often systemic. Broad-spectrum fungicides can often control a wide range of unrelated pathogens. These usually are contacts with multi-site activity, but some have single-site activity. Several fungicides have activity that places them on a continuum between narrow- and broad-spectrum fungicides.
- 6. **Type of chemical: inorganic or organic.** Fungicides also can be classified based upon their chemical composition. Chemically, organic molecules are those that contain carbon atoms in their structure whereas inorganic molecules do not. Many of the first fungicides developed were inorganic compounds based on sulfur or metal ions such as copper, tin, cadmium and mercury that are toxic to fungi. Copper and sulfur are still widely used. Most other fungicides used today are organic compounds and thus contain carbon. The term "organic" as used here is based on chemistry terminology and differs from "organic" used to describe a system of agriculture that strives to be holistic and to enhance agroecosystem health.

<u>Table 1 (Adobe Acrobat PDF)</u> provides a list of fungicides and their characteristics that are representative of the major chemical groups registered in the USA.

7. Additional terms.

 Active ingredient (a.i.) is the active component of a pesticide, and is that moiety which is patented, synthesized, and registered by the manufacturer.

- **Biofungicide** is a naturally based microbial or biochemical product. There are three types of biopesticides. (a) Microbial biopesticides have an active ingredient that is a biological control agent (organism capable of attacking or competing with a pathogen or pest). (b) Plant biopesticides or plantincorporated protectants are defined by the EPA as "pesticidal substances that plants produce from genetic material that has been added to the plant". (c) Biochemical biopesticides contain naturally-occurring substances. Some biochemicals may also be products of fermentation. Biochemicals can directly affect disease-causing organisms or may stimulate SAR. Biopesticides generally are narrow-spectrum, have low toxicity, decompose quickly, and thus are considered to have low potential for negative impact on the environment (www.epa.gov/pesticides/biopesticides/). Many biofungicide products are being approved for organic crop production (www.omri.org). While many have low toxicity, biopesticides are not necessarily safer than pesticides containing synthetic ingredients.
- **Chemical group or class** is the name given to a group of chemicals that share a common biochemical mode of action and may or may not have similar chemical structure.
- **Chemical name** is denoted by a nomenclature system designed by the International Union of Pure and Applied Chemistry (IUPAC); this set of rules is used to name organic, carbon-based compounds.
- **Common name** is the name proposed by the basic manufacturer for the active ingredient. This name is ratified by a committee either at IUPAC or the ACS (American Chemical Society).
- Reduced risk is a special classification approved by the EPA for specific uses of pesticides that have low risk to human health, low toxicity to non-target organisms, low potential to contaminate water or other environmental resources, and/or that broaden the adoption and effectiveness of integrated pest management strategies. Registration is expedited for uses designated as reduced risk.
- **Formulation** is the pesticide product. It is a prepared mix of active ingredient plus ingredients that improve pesticidal performance, such as carriers, solvents, wetting agents, spreaders, and stickers. Types of formulations include wettable powders, dry flowables, emulsifiable concentrates, and granules.
- **Trade name/Trademark** is the patented name under which a product is sold to the end user.

Fungicide resistance is a stable, heritable trait that results in a reduction in sensitivity to a fungicide by an individual fungus. This ability is obtained through evolutionary processes. Fungicides with single-site mode of action are at relatively high risk for resistance development compared to those with multi-side mode of action. Most fungicides being developed today have a single-site mode of action because this is associated with lower potential for negative impact on the environment, including non-target organisms.

When fungicide resistance results from modification of a single major gene, pathogen subpopulations are either sensitive or highly resistant to the pesticide. Resistance in this case is seen as complete loss of disease control that cannot be regained by using higher rates or more frequent fungicide applications. This type of resistance is commonly referred to as "qualitative resistance".

When fungicide resistance results from modification of several interacting genes, pathogen isolates exhibit a range in sensitivity to the fungicide depending on the number of gene changes. Variation in sensitivity within the population is continuous. Resistance in this case is seen as an erosion of disease control that can be regained by using higher rates or more frequent applications. Long-term selection for resistance in the pathogen by repeated applications may eventually result in the highest labeled rates and/or shortest application intervals not being able to adequately control the disease. This type of fungicide resistance is commonly referred to as "quantitative resistance". Comments about resistance risk of fungicides are included in Table 1 (Adobe Acrobat PDF) and in a table of fungicides at the FRAC web site (http://www.frac.info/home/).

Fungal isolates that are resistant to one fungicide are often also resistant to other closely-related fungicides, even when they have not been exposed to these other fungicides, because these fungicides all have similar mode of action. This is called cross resistance. Fungicides with the same <u>Group Code</u> are likely to exhibit cross resistance. Occasionally negative cross resistance occurs between unrelated fungicides because the genetic change that confers resistance to one fungicide makes the resistant isolate more sensitive to another fungicide.

Managing fungicide resistance is critically important to extend the period of time that an at-risk fungicide is effective. The primary goal of resistance management is to delay its development rather than to manage resistant fungal strains after they have been selected. Therefore, resistance management programs need to be implemented when at-risk fungicides first become available for commercial use. The objective of resistance management is to minimize use of the at-risk fungicide without sacrificing disease control. This is accomplished by using the at-risk fungicide with other fungicides and with non-chemical control measures, such as disease resistant cultivars, in an integrated disease management program.

It is critical to use an effective disease management program to delay the build-up of resistant strains. At-risk fungicides should be used at the manufacturer's recommended rate (full rate) and application interval. Using full rates is expected to minimize selection of strains with intermediate fungicide sensitivity when resistance involves several genes (quantitative resistance). At-risk fungicides should be used in alternation with other at-risk fungicides with different modes of action or different chemical groups, and they should be combined or alternated with fungicides that have a low resistance risk.

When one crop could serve as a source of inoculum for a subsequent crop, the alternation scheme among at-risk fungicides should be continued between successive crops such that the first at-risk fungicide applied to a crop belongs to a different cross-resistance group than the last at-risk fungicide applied to the previous crop. Some at-risk fungicides are formulated as premix products with other fungicides to manage resistance. At-risk fungicides should be used only when needed most. The most critical time to use them for resistance management is early in an epidemic when the pathogen population is small. Multi-site contact fungicides should be used alone late in the growing season, where they have been shown to provide sufficient disease control to protect yield. Another important component of resistance management is assessing disease control and reporting any loss of efficacy potentially due to resistance.

To promote resistance management, companies registering fungicides are voluntarily putting on the labels guidelines developed recently by EPA through a joint effort with the Canadian Pest Management Regulatory Agency (PMRA) under the North American Free Trade Agreement (NAFTA). These are described in Pesticide Registration (PR) Notice 2001-5 (www.epa.gov/opppmsd1/PR Notices/pr2001-5.pdf). Group codes for designating chemical groups were developed as part of these guidelines (see Table 1 (Adobe Acrobat PDF)).