Fungicide Resistance and the FRAC Code

Fungicide Resistance

Fungicides have been used on field crops since the 1700s (Morton and Staub, 2008). In the 1800s, fungicides were sulfur and copper based. Mercury fungicides were developed in the early 1900s and used widely until it was discovered that they were highly toxic to animals. In the 1940s and 1950s, fungicides such as captan and mancozeb were introduced. These contact fungicides worked only if applied before infection occurred. In addition, they affected several different biochemical sites within the fungus, so fungicide resistance did not readily appear.

More recently, highly effective fungicides with very specific modes of action have been developed, such as the quinone outside inhibitors (QoIs). These products generally have several attractive properties, including being more systemic than contact fungicides while still managing a broad range of fungal pathogens. However, since these fungicides affect one specific site or function in one metabolic pathway of the pathogen, the fungus only has one barrier or one change in site or function to overcome the product’s action. Thus, the problem of fungicide resistance has emerged and continues to increase, because farmers rely more and more on these newer fungicides.

Development of fungicide resistance is a worldwide concern for the agricultural industry. Unfortunately, resistance has developed in many fungi, especially after fungicides have been used intensively on crops. Farmers of several crops—including potato, soybean, sugar beet, sunflower, and others—have dealt with fungicide failure caused by fungicide resistance (Fig. 35). Resistance can develop over decades of use or within only a few years after initial use. For example, QoI-resistant strains of Cercospora sojina, the fungus that causes frogeye leaf spot on soybean (Fig. 36), have been identified in several areas of the United States (Zhang et al., 2012). Resistance was confirmed approximately 4 years after this fungicide class was first used for management of frogeye leaf spot on soybean.

How Fungicide Resistance Develops

Fungicide resistance can occur when a selection pressure is placed on the fungal population. Characteristics of both the fungicide and the pathogen

Fig. 35. Mefenoxam and metalaxyl were once effective and widely used for sunflower downy mildew (infected plant on right), but these chemicals are no longer considered useful because of pathogen resistance. (Courtesy Samuel Markell)

Fig. 36. Strains of Cercospora sojina, the fungus that causes frogeye leaf spot on soybean, with resistance to quinone outside inhibitor (QoI) fungicides have been identified in several states. (Courtesy Daren S. Mueller)
determine the magnitude of the selection pressure and the risk of resistance occurring. Fungicides that have a single site of action typically are more at risk for selection of resistance than those that have multi-site activity. Fungal pathogens that regularly undergo sexual reproduction are more likely to have greater variability in the population, which increases the chances of developing a strain that is less sensitive to a fungicide. Additionally, fungal pathogens that have a repeating spore stage (polycyclic pathogens) are more likely to develop resistance to a fungicide, in part because of the high number of spores they produce within a season.

The applicator has control over fungicide-based selection pressure but not the variability of the pathogen. Managing selection pressure is vital to reducing the risk of fungicide resistance.

The Fungicide Resistance Action Committee and the FRAC Code

The Fungicide Resistance Action Committee (FRAC) is an international group that provides guidelines and recommendations to manage the development of fungicide resistance. FRAC developed a code of numbers and letters that can be used to distinguish different fungicide groups based on their modes of action. The FRAC code can be found on the product label of every fungicide (Fig. 5, page 4). A fungus that becomes resistant to a specific fungicide may be resistant to many or all of the fungicides with the same FRAC code—a condition that is referred to as cross-resistance. Table 6 (pages 32–33) provides the FRAC codes for the fungicide groups currently applied to field crops in the United States and Canada.

Management Practices for Fungicide Resistance

Several practices can be applied to minimize the risk that a fungus will become resistant to a fungicide. The best management program for fungicide resistance utilizes all available practices to prolong the life and effectiveness of a fungicide.

Monitoring Programs

One of the first steps in implementing a fungicide resistance management program is to develop baseline levels of sensitivity using laboratory analysis (Fig. 37). The term baseline level refers to the amount of the fungicide necessary to effectively control a fungal pathogen population that has never been exposed to the fungicide. In other words, the baseline reflects the pathogen population’s sensitivity to the fungicide when it is first used.

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1For more information on the Fungicide Resistance Action Committee (FRAC), go to www.frac.info/frac/index.htm.
<table>
<thead>
<tr>
<th>FRAC Code</th>
<th>Group Name</th>
<th>Active Ingredient Common Name</th>
<th>Risk of Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Methyl benzimidazole carbamates (MBC)</td>
<td>Thiabendazole&lt;br&gt;Thiophanate-methyl</td>
<td>High</td>
</tr>
<tr>
<td>2</td>
<td>Dicarboximides</td>
<td>Iprodione&lt;br&gt;Vinlozolin</td>
<td>Medium to high</td>
</tr>
<tr>
<td>3</td>
<td>Demethylation inhibitors (DMI)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Cyproconazole&lt;br&gt;Difenconazole&lt;br&gt;Fenbuconazole&lt;br&gt;Flutriafol&lt;br&gt;Imazalil&lt;br&gt;Metconazole&lt;br&gt;Myclobutanil&lt;br&gt;Propiconazole&lt;br&gt;Prothioconazole&lt;br&gt;Tebuconazole&lt;br&gt;Tetraconazole&lt;br&gt;Triticonazole</td>
<td>Medium</td>
</tr>
<tr>
<td>4</td>
<td>Phenylamides</td>
<td>Mefenoxam&lt;br&gt;Metalaxyl</td>
<td>High</td>
</tr>
<tr>
<td>7</td>
<td>Succinate dehydrogenase inhibitors (SDHI)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Boscalid&lt;br&gt;Carboxin&lt;br&gt;Fluopyram&lt;br&gt;Flutolanil&lt;br&gt;Fluxapyroxad&lt;br&gt;Penthiopyrad&lt;br&gt;Sedaxane</td>
<td>Medium</td>
</tr>
<tr>
<td>9</td>
<td>Anilino-pyrimidines (AP)</td>
<td>Cyprodinil&lt;br&gt;Pyrimethanil</td>
<td>Medium</td>
</tr>
<tr>
<td>11</td>
<td>Quinone outside inhibitors (QoI)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Azoxyystrobin&lt;br&gt;Famoxadone&lt;br&gt;Fenamidone&lt;br&gt;Fluoxastrobin&lt;br&gt;Picoxystrobin&lt;br&gt;Pyraclostrobin&lt;br&gt;Trifloxystrobin</td>
<td>High</td>
</tr>
<tr>
<td>12</td>
<td>Phenylpyroles (PP)</td>
<td>Fludioxonil</td>
<td>Low to medium</td>
</tr>
</tbody>
</table>

<sup>a</sup>Data from Fungicide Resistance Action Committee (2012).

<sup>b</sup>Some fungicides in the DMI group may be referred to as triazoles or imidazoles.

<sup>c</sup>Some fungicides in the SDHI group may be referred to as carboxamides.

<sup>d</sup>Some fungicides in the QoI group may be referred to as strobilurins.

(continued)
Once the baseline level has been established, a monitoring program can be implemented to determine whether the pathogen population is becoming less sensitive to the fungicide over time. Generally, a monitoring program consists of collecting samples of the pathogen and testing them periodically in a laboratory for sensitivity to the fungicide.

After every fungicide application, the field should be scouted to evaluate how well the fungicide has worked and to identify signs of product failure (Fig. 38). Although a fungicide might fail for a variety of reasons (see pages 20–24), it is important to determine if fungicide resistance is a possible factor. Doing so involves contacting the chemical company representative or personnel from local extension services.

![Fig. 38. Scouting after applying fungicides will help identify signs of product failure. (Courtesy Marcia McMullen)](image)
**Fungicide Mixtures and Alternation**

Tank mixing fungicides or applying premixed products with different modes of action can help reduce the selection pressure placed on the pathogen population compared with using only a single product. Tank mixing reduces the risk of fungicide resistance, because if a mutant spore develops resistance to one fungicide, it will be killed by the other fungicide in the mix. Tank mixing is effective only if both fungicides control the target pathogen. For example, tank mixing tetraconazole plus thiophanate-methyl would not be a good fungicide resistance management practice for soybean rust, because thiophanate-methyl is not effective against the pathogen that causes this disease.

If more than one fungicide application is required during a season, then fungicides with different modes of action should be used. For example, a QoI fungicide can be applied first, followed by a DMI fungicide later in the crop’s development. When alternating fungicides, each fungicide should be applied at the time when it will be most effective on the diseases being managed.

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**IPM Practices**

Scouting fields regularly, monitoring the development and movement of diseases regionally, and applying a recommended fungicide when there is a high risk for disease development are all parts of a successful integrated pest management (IPM) program. Applying fungicide only when necessary is important for prolonging the effective life span of a product (Fig. 39). Many fungicide products and active ingredients (or similar products with the same mode of action) are registered for use across several field crops—some of which grow in rotation with one another. Applying a fungicide when the economic yield loss from a disease is relatively low can increase the risk of selecting for a fungicide-resistant population.

Conserving the existing fungicide groups is extremely important, because few other groups are effective on the field crop pathogens that currently exist. Using IPM practices will help conserve these products for the management of field crop diseases for years to come.

*Fig. 39.* Applying fungicide only when necessary is important for resistance management. (Courtesy Gary Munkvold)
**Label Recommendations**

Another important component of fungicide resistance management is following the product label, which is the law. Some fungicides have restrictions on the number of applications that can be made during a season or restrictions on making back-to-back applications.

Following fungicide label rates is not only a key component of disease management but also important to an effective fungicide-resistance program. When sublethal doses of a fungicide are applied, the risk increases that fungal pathogens will become less sensitive to the chemical.

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**Guidelines for Management of Fungicide Resistance**

Management of fungicide resistance is important in the production of all field crops. The risk of fungicide resistance developing can be reduced by following these guidelines:

- If a fungicide is applied, monitor the crop for disease progress. Ineffective control by the fungicide can indicate resistance.
- Tank mix fungicides or use premix products with different modes of action.
- Use good agronomic practices to reduce the need for fungicides.
- Apply a fungicide only when necessary.
- Follow the label. Use recommended rates, and obey restrictions.