

# Understanding Fungicide Resistance

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## Introduction

Chemical control is one of many tools used to manage plant diseases in an integrated pest management (IPM) strategy. Fungicides are a specific type of pesticide used to inhibit or kill some fungal pathogens. Before making any fungicide application, proper identification is essential to strategize and initiate a disease management plan.

Fungicide use is common for one of three purposes:

- disease control during crop establishment and development

- increased crop productivity and aesthetic appeal for consumers
- improved storage life after harvest

Depending on the pathogen, environmental conditions, application equipment, and producer needs, fungicides are applied as a granular, dust, smoke, fog, mist, gas, or liquid form.

Fungicides possess unique modes of action to control pathogens. Modes of action may include cell membrane disruption, interfering with metabolic processes, or target-

ing and inhibiting enzymes or proteins critical for pathogen survival and function. Certain fungicides have the ability to target one specific site in the pathogen, while others may target several sites. Each fungicide group is unique in how it targets and manages pathogens.

Fungicides may have single-site or multisite modes of action. Single-site modes of action are also referred to as “targeted” fungicides. These fungicides are considered to be medium to high risk for resistance development within a population. The risk is higher because the fungicide acts on only one site in the pathogen. Thus, a single mutation within the population can make that fungicide ineffective or less effective than before. Even with medium to high risk for resistance development, development of targeted fungicides continues because they are more environmentally friendly. They are less toxic to plants, have reduced impacts on the environment, and can move through the plant easily after application.

Multisite mode fungicides have reduced risk for resistance development as they target more than one site in the fungus. Development of resistance requires multiple mutations within the pathogen genome to allow survival. Typically, these fungicides are the older products on the market and are not considered environmentally friendly because they are not as specific, sometimes impacting nontarget species. It is important to note that several newer products now available are classified as multimode fungicides but are actually a combination of two to three single-site mode of action fungicide mixtures.

### Contact vs. Systemic and Preventative vs. Curative

Contact fungicides remain on the surface of the plant after an application. These are also referred to as “protectant” or “preventative” fungicides. They are not readily absorbed into the plant, and they control fungal pathogens on the leaf surface. Repeated applications may be required as they can wash off the leaf surface from rainfall or irrigation, or are degraded from sunlight exposure.

Systemic fungicides are more easily absorbed into the plant and can move either short distances or long distances within the plant. These also are referred to as “penetrant” or “curative” fungicides as they are more readily absorbed compared with contact fungicides, and may help control pathogens after infection occurs. Systemic fungicides target fungal pathogens growing inside the host plant. Some systemic fungicides can have both preventative and curative effects, but very few fungicides have curative properties.

#### There are four main types of systemic movements:

- Local systemic or translaminar. Products move very little throughout the system, but tend to move from the upper to the lower leaf surface.

- Xylem mobile systemic—soil applied. Products are absorbed through the root and control fungal pathogens throughout the plant.
- Xylem mobile systemic—foliar applied. Products are absorbed through the leaves/stem and move within the plant through the xylem. Thus, these products can only move “up” the plant and no product is in the plant below the point of application distribution.
- Amphimobile systemic—foliar applied. Products are absorbed through the leaves/stems and can move either up or down the phloem, ensuring protection throughout the entire plant.

## Fungicide Resistance

Fungicide resistance is when a pathogen population changes from being sensitive to a fungicide, to one that is insensitive or less sensitive to a fungicide. Fungicide resistance is not an issue isolated to one particular pathogen or plant group. It is a worldwide issue and affects several plant systems. A number of documented reports indicate some pathogen populations do not become completely resistant to a fungicide, but instead have reduced sensitivity.

Studies have shown that fungicide resistance develops through natural selection of a mutant strain of a pathogen in a population that is resistant to fungicides. It is important to remember that applying a fungicide did not cause these mutations to occur. These naturally occurring mutations occur in fungi at the rate of approximately 1 out of 100 million.

The following section was adapted from the original work by Bradley, C., et al. 2017 <https://www.plantmanagementnetwork.org/hub/soyfungicideresistance/files/FungicideResistance.pdf>.

*Cercospora sojina*, a fungus that causes frogeye leaf spot on soybean, is an example of a pathogen that has documented resistance in the United States. Under favorable conditions, a susceptible soybean variety can have a significant number of lesions per leaf with 100 or more sporulating lesions or spots on one leaf producing conidia. There can be easily 100 conidia per frogeye leaf lesion produced if one were to look at individual lesions with magnification.

Under conditions favorable for frogeye leaf spot, approximately 30 leaflets per soybean plant could be affected. Given that there are 5 million or more soybean plants in most 40-acre fields, this is a very large number of leaflets with sporulating lesions. Using these numbers, over 1.5 trillion *Cercospora sojina* conidia would be emerging from a 40-acre field. A mutation rate of 1 out of 100 million would result in 15,000 mutant isolates occurring in a heavily infested 40-acre field. While these are all naturally occurring mutants, it is



Figure 1. Spores on the leaflet are represented in two different colors. The green spores represent those still sensitive to a fungicide, and the red spores represent those that are resistant to fungicide. (Image courtesy of Iowa State University)

Table 1. Example of Fungicide Resistance Action Committee (FRAC) fungicide classification for azoxystrobin and propiconazole.

Fungicide active ingredient	FRAC Code	Group Name	Chemical group	Mode of Action
azoxystrobin	11	Quinone outside inhibitor (QoI)	Methoxy-acrylates (strobilurin)*	Respiration inhibitor
propiconazole	3	Demethylation inhibitor (DMI)	Triazole	Sterol biosynthesis in membranes

\*Fungicides in this group are commonly referred to as strobilurins; however, these active ingredients are no longer specified as strobilurins by FRAC. (Originally developed by Giesler et al., 2016).

very possible that some may be less sensitive to fungicides.

Figure 1 is a demonstration of selection pressure after the occurrence of one mutant that is able to reproduce with a fungicide applied as selection pressure to favor the mutation that has naturally occurred. The resistant isolate will continue to be favored if the same mode of action is applied in repeated applications. The resistant isolate is represented by the red colored dot in the pictorial example. As more applications are made with the same fungicide, the resistant population is favored. It will eventually dominate the population, and fungicide failure will be observed (adapted from Bradley, et al., 2017) <https://www.plantmanagementnetwork.org/hub/soyfungicideresistance/files/FungicideResistance.pdf>.

Resistance is very difficult to eliminate but can be delayed through appropriate management practices. The availability of inexpensive options with single mode of action products makes this an important issue so we do not repeat the herbicide resistance scenario currently being fought in weed management.

### Fungicide Resistance Action Committee

The organization known as the Fungicide Resistance Action Committee (FRAC) was established by industry and



Figure 2. Frog-eye leaf spot of soybeans.

research scientists to oversee and monitor fungicide resistance and provide guidelines for development of products for long-term use. This committee established the FRAC codes, which identify different target sites within specific modes of action for all active ingredients. Usually, a small rectangular box is near the top of every fungicide label where the FRAC number or numbers are located for the active ingredient (Table 1). For example, a FRAC code shown as group 7 indicates that the fungicide is a succinate dehydrogenase inhibitor (SDHI) whereas group 11 fungicides are Quinone outside inhibitors (QoI, which includes strobilurins). However, if both 7 and 11 appear in the label, it means the fungicide has active ingredients belonging to the two groups. Specific examples of fungicide resistance previously observed in different crops are discussed below. A fungus resistant to a specific active ingredient within a FRAC code will most likely be resistant to all fungicides with the other active ingredients in the same FRAC code.

## Disease Case Histories

### Frog-eye Leaf Spot of Soybean

Frog-eye leaf spot, caused by the fungus *Cercospora sojina*, is becoming a common foliar fungal disease in Nebraska (Figure 2). The disease is most severe when soybean is grown continuously in the same field, particularly in fields where tillage is reduced, since this is a residue-borne pathogen. The primary source for this fungus is infested residue, infected seed, and airborne spores.

In 2010, resistance to QoI (Quinone outside inhibiting) fungicides, also known as strobilurins (FRAC Code 11), was reported for the first time to this pathogen in Tennessee.

Since then a significant spread has occurred in the Mississippi Valley, and most recently in 2017 soybeans in eastern Iowa. Resistance has not been observed in Nebraska yet. The current distribution of confirmed resistant populations is located on the IPM PIPE website, <http://frogeye.ipmpipe.org/cgi-bin/sbr/public.cgi>. Resistance to QoI fungicides in *C. soja* populations is the result of a single-site mutation. This mutation is not known to have any fitness costs and has resulted in it persisting in the population once it occurs.

## General Management of Frogeye Leaf Spot

### *Resistance*

Soybean varieties vary in their resistance to frogeye leaf spot, and several genes are commonly used for resistance. This will reduce inoculum and exposure to fungicides for selection of resistance.

### *Cultural Practices*

Frogeye leaf spot is more severe in continuously cropped soybean fields. Reduced tillage systems will tend to have more infested debris as the pathogen overwinters in residue. This will reduce inoculum levels and exposure to fungicide for selection of resistance.

### *Fungicide Application*

Application of fungicides to manage frogeye leaf spot in Nebraska typically is not warranted in most fields. Fields with a history of frogeye leaf spot should be watched carefully. If disease develops, application of a QoI fungicide at the R3 (pod set) to early R4 growth stage is considered the most effective. Avoid applying products when disease development is significantly severe.

## Gray Leaf Spot of Corn

Gray leaf spot of corn is a common fungal disease in much of Nebraska (Figure 3). The causal agent, *Cercospora zeae-maydis* (Czm), is closely related to the fungus causing frogeye leaf spot of soybean, being in the same genus, *Cercospora soja*, albeit a different species. These pathogens have many biological characteristics in common, such as survival in infested plant debris from the previous season(s) and similar weather conditions that are favorable for disease development, namely warm temperatures and high relative humidity. Whereas fungicide resistance to strobilurin fungicides (QoI fungicides) has been well documented in the soybean frogeye leaf spot pathogen in other parts of the United States, there



Figure 3. Gray leaf spot of corn.

are no confirmed reports of fungicide resistance for the gray leaf spot pathogen of corn in the field. However, fungicide resistance has been documented in the laboratory from in vitro tests where the fungus can utilize alternative respiration pathways to overcome the effects of the fungicides, allowing for spore (conidia) germination.

Baseline QoI fungicide sensitivities were identified for the gray leaf spot fungus collected from several states, including Nebraska. The results of these experiments indicated that resistance is possible in naturally occurring populations, but that it may be less likely than in other closely related species. However, frequent applications of QoI fungicides over a large area of corn increase the probability that fungicide resistance may develop. Populations of the fungus should continue to be monitored over time to assess for a reduction in fungicide sensitivity.

## Management of Gray Leaf Spot

### *Hybrid resistance*

Corn hybrids vary widely in their resistance to gray leaf spot, which can reduce the size and number of lesions. Highly resistant hybrids may still develop some lesions. Consult ratings provided by seed companies to help predict how the hybrid will react to gray leaf spot. Position more resistant hybrids in fields with a history of severe disease and other high-risk factors, such as continuous corn and minimum tillage.

### *Cultural practices*

Residue management with tillage may provide some benefits for disease reduction, but is not practical for all



Figure 4. Premature bleaching of spikelets on a wheat head, a typical symptom of *Fusarium* head blight.

production systems or locations. Tillage buries infested crop debris, promoting degradation and reducing overwintering inoculum of the fungus-causing disease. Crop rotation to nonhost crops can provide similar benefits, although neither strategy eliminates the risk of some disease, especially during seasons with very favorable weather conditions or susceptible corn hybrids.

### *Fungicides*

Foliar fungicides can be very effective at managing gray leaf spot when applied at optimal times. Applications of fungicides are most effective when applied before severe disease development and can be economical, especially in high-yielding, susceptible hybrids. Minimizing the disease in the upper plant canopy during grain fill reduces its impact on yield.

### *Integrated management*

Deploying a combination of management strategies is more likely to provide satisfactory results. Plant hybrids that are more resistant in high-risk production systems. Monitor disease development and its progression up the plant in susceptible hybrids to make fungicide application decisions and more effectively manage gray leaf spot.

## **Fusarium Head Blight of Wheat**

*Fusarium* head blight (FHB), also known as scab, is a destructive disease of wheat. In North America, it is caused primarily by *Fusarium graminearum*. The disease causes premature bleaching of spikelets (Figure 4), causing sterility or production of discolored, shriveled kernels commonly referred to as *Fusarium*-damaged or “tombstone” kernels (Fig-



Figure 5. *Fusarium*-damaged (“tombstone”) wheat kernels (left) and healthy kernels.

ure 5). In addition, *F. graminearum* produces trichothecene mycotoxins, mainly deoxynivalenol (DON) and nivalenol, which contaminate grain and are harmful to humans and animals. FHB epidemics occur sporadically in Nebraska due to the variable climate. The disease tends to occur during years with excessive rainfall before and during flowering. The most recent major epidemics occurred in 2007, 2008, and 2015.

FHB is controlled by applying a triazole fungicide (FRAC Code 3) to the heads during flowering. Triazoles used for FHB control include tebuconazole, prothioconazole, and metconazole. In 2011, the first isolate of *F. graminearum* resistant to tebuconazole (triazole fungicide) was collected from a wheat spike during a survey in Steuben County, New York. It is the first tebuconazole-resistant field isolate of *F. graminearum* reported in the Americas. *Fusarium graminearum* resistance to triazole fungicides has not been documented in Nebraska. However, the discovery of a tebuconazole-resistant isolate in New York indicates that the potential exists for resistance to develop in Nebraska isolates.

## **Management of FHB**

### *Cultivar Selection*

The majority of wheat cultivars grown in Nebraska have little or no resistance to FHB. Breeding efforts in recent years have yielded several cultivars in the central Great Plains states with moderate resistance to FHB. They include Overland, Everest, and Lyman. Because *F. graminearum* infects wheat heads mostly during flowering, planting cultivars with different flowering dates increases the probability that some can escape infections.

### *Cultural practices*

Because FHB epidemics are initiated by inoculum produced on crop residues, reducing residue can reduce inocu-



Figure 6. *Ascochyta* blight on chickpea foliage.



Figure 7. *Ascochyta* blight on chickpea pods.

lum potential. In Nebraska, a practical cultural management practice that can reduce residue-borne inoculum is rotation with nonhost crops such as soybean and alfalfa. Irrigation management to allow the crop canopy to dry between irrigations can reduce disease severity.

### *Fungicides*

The two most effective fungicide products in controlling FHB are Prostaro® (prothioconazole + tebuconazole) and Caramba® (metconazole). Fungicide application should be timed to protect the head. Optimal timing is at approximately 15 percent flowering (Feekes 10.51). Thorough coverage of heads is essential for maximum control.

### *Biological control*

Certain bacteria and fungi have been identified that are antagonistic to *F. graminearum*, but their efficacy in the field has been poor and commercial formulations are not available. Significant progress has been made in Canada where the fungus *Clonostachys rosea* has been formulated to a product that is effective in reducing production of perithecia (sexual fruiting structures) on crop residues by *Gibberella zeae* (sexual stage of *F. graminearum*) and in suppressing FHB in the field.

### *Integrated Management*

Because of the lack of highly resistant or tolerant cultivars, integrating available FHB management strategies is the best approach to managing the disease. Use of moderately resistant cultivars with different flowering dates, residue management, crop rotation, irrigation management, and judicious use of fungicides all should be integrated into an FHB management program.

## **Ascochyta Blight of Chickpea**

*Ascochyta* blight, caused by the fungal pathogen *Ascochyta rabiei*, is the most serious and damaging disease of chickpeas worldwide. It attacks all aerial parts of the chickpea plant (Figures 6 and 7), and is considered the primary constraint to successful chickpea production wherever the crop is grown. The pathogen can survive in both crop residue and infected seeds, which are the major sources of spread and dissemination.

Resistance to strobilurin fungicides by *A. rabiei* was first noted from North Dakota and Montana in 2005 and 2007, respectively. In 2010, fields in South Dakota and Nebraska exhibited limited disease management after being treated with pyraclostrobin (Headline®, FRAC Code 11). Isolates from these locations were confirmed to contain a gene mutation that has been previously correlated with resistance to QoI fungicides in other fungal pathogens.

## **Management of Ascochyta Blight**

### *Resistance*

Until recently, only moderately resistant cultivars have been available, but none were completely resistant, requiring additional integrated techniques for better control. A new regionally adapted resistant cultivar has been developed, but is currently being increased. It will not be available for commercial use for several years. Several other cultivars also are close to release.

### *Cultural*

Due to the seed- and residue-borne nature of the pathogen, burial of residue and seeds from harvest losses from

infected crops and rotating out of chickpeas will help reduce pathogen populations.

### *Chemical*

Seed treatments will help to suppress early infection and improve stand establishment but will not provide season-long protection. Fungicide applications can also be used to reduce losses, but due to the presence of resistant pathogen populations in Nebraska, care must be taken to use the proper chemicals. Although resistance in Nebraska has only been identified to pyraclostrobin, the use of related fungicides alone, such as azoxystrobin (Quadris®), should also be discontinued. Resistance also to azoxystrobin is unproven, but still highly probable.

Optimal Ascochyta blight management in chickpeas in the future will most likely consist of an integrated approach using crop rotation, genetic resistance, fungicidal seed treatments, and foliar applications with varying modes of action other than the strobilurin fungicides.

## **Early Blight of Potato**

Early blight is a common disease of potato. This disease is caused by the fungus *Alternaria solani*. Early blight occurs over a wide range of climatic conditions and depends in large part on the frequency of leaf wetness from rainfall, fog, dew, and irrigation; nutritional status of foliage; and cultivar susceptibility. In Nebraska, the primary infections observed are in foliage; however, tuber infections can occur. Severe foliar infection by the early to mid-bulking period can result in smaller tubers, yield loss, and reduced tuber dry matter content.

The QoI (FRAC Code 11) fungicides, also known as strobilurins, were introduced for early blight management in 1999. By 2001 Nebraska and North Dakota detected resistance, and resistance was prevalent across the United States by 2006. In 2005 succinate dehydrogenase inhibitor fungicides (SDHI), also known as carboximides (FRAC Code 7), were released for early blight control. SDHI resistance was observed in Idaho in 2009 and 2010, with prevalent resistance found in Nebraska, North Dakota, Minnesota, and Texas in 2010 and 2011.

## **Management of Early Blight**

### *Resistance*

Some cultivars have good levels of field resistance. However, no completely resistant cultivars are available, thus requiring additional integrated techniques for better control.



Figure 8. Downy mildew on hops.

### *Cultural*

Crop rotation, removing and burning infected plant debris, and eradicating solanaceous weed hosts help reduce inoculum levels for subsequent years.

### *Chemical*

Foliar fungicides are the most effective control method for early blight. Protectant fungicides, such as maneb, mancozeb, chlorothalonil, iprodione and triphenyltin hydroxide, are effective when applied at approximately 7- to 10-day intervals. With resistance found in Nebraska for QoI (FRAC Code 11) and SDHI (FRAC Code 7), these products should be discontinued to control early blight.

## **Downy Mildew of Hops**

Downy mildew (*Figure 8*) is one of the most destructive diseases of hops. The fungus *Pseudoperonospora humuli* persists in infected plant material and infects all parts of the plant. It can rapidly spread with warm and wet

weather. Infected leaves have necrotic, angular lesions and the undersides may be covered by spores that are purple to black in color. Infected shoots will appear stunted and yellow, and flowers become shriveled and brown. The pathogen also infects the crown, leading to perennial, systemic infections.

Fungicide resistance of *P. humuli* has not yet been reported in the Midwest. However, in the Pacific Northwest, resistance to phenylamide fungicides (mefenoxam, FRAC Code 4) is common, and these fungicides are ineffective in many regions. Additionally, reduced sensitivity to phosphonates has been observed.

## Management of Downy Mildew

### *Resistance*

Hops vary in their tolerance to downy mildew. Though some varieties provide good resistance, many of the varieties in highest demand from brewers are very susceptible to the disease. No variety is completely resistant to downy mildew.

### *Cultural*

Cultural practices that reduce humidity—such as pruning, stripping the bottom leaves from the vines, and controlling weeds surrounding the base of the hop plant—will decrease infection. Shoots and side arms should be removed once disease is detected. Dead material should be disposed of and yards cleaned post-harvest to reduce overwintering inoculum. Removing the top inch or two of the crown removes infected buds and shoots, which serve as early-season inoculum. When sourcing new plants, growers should ensure that plants and rhizomes are disease free.

### *Chemical*

The use of fungicides can effectively control downy mildew. If yards have a history of the disease, preventative applications are recommended when weather conditions favor development. Many fungicides labeled for downy mildew have limited post-infection activity, making preventative control crucial.

### *Integrated Management*

Strict sanitation is critical for downy mildew control as infection can occur throughout the growing season. When weather favors disease development and repeated fungicide applications are necessary, rotating modes of action and



Figure 9. Dollar spot on Kentucky bluegrass.

mixing with aluminum or copper products can be effective. Carefully read labels as some products should not be used close together, tank-mixed, or may cause phytotoxicity.

## Dollar Spot of Turfgrass

Dollar spot (*Figure 9*) is a worldwide problem that affects almost every cultivated turfgrass species. More money is spent every year on chemical control worldwide for this disease than any other turfgrass disease. In Nebraska, dollar spot damage is most prevalent on golf putting greens and fairways composed of creeping bentgrass and annual bluegrass.

The first report of fungicide resistance in dollar spot occurred in 1993 and 1983 to benzimidazole (FRAC Code 1) and dicarboximide (FRAC Code 2) fungicides, respectively. In 1992, resistance to the demethylation inhibitor fungicides (DMI, 3) was detected. The latest resistance development to be reported is to the SDHI fungicides (FRAC Code 7).

## Management of Dollar Spot

### *Resistance*

No cultivars completely resistant to dollar spot are available. However, cultivars with varying degrees of susceptibility are available in perennial ryegrass, tall fescue, annual bluegrass, and creeping bentgrass. Consulting the National Turfgrass Evaluation Program ([www.ntep.org](http://www.ntep.org)) to view the level of susceptibility of specific turfgrass species and cultivars is advised.



## Cultural

Monitoring turfgrass fertility is a vital part of dollar spot management. Turfgrasses maintained under low nitrogen fertility are more susceptible to dollar spot infection and are unable to recover as quickly. In a golf course setting, light and frequent application of nitrogen is recommended to manage disease and to maintain optimal turfgrass growth.

Irrigation management includes avoiding late afternoon and evening watering to limit prolonged overnight periods of leaf wetness. To maximize irrigation efficiency, manage thatch accordingly. Thatch layers should be removed when they are greater than ½ inch deep.

## Biological control

Biological control agents have been extensively researched for the management of dollar spot. Currently, *Streptomyces*, *Pseudomonas*, *Reynoutria*, and *Bacillus* species are labeled for control of dollar spot.

## Chemical control

Numerous fungicides are labeled for dollar spot control, including the following classes: benzimidazoles, DMIs, carboximides, dicarboximides, dithiocarbamates, SDHIs, nitriles, and dinitro-aniline fluazinam. Label rates should be applied in golf course settings at either 7 to 10 day or 14 to 21 day intervals. With the known resistance to benzimidazoles, dicarboximides, and DMIs, alternating the use of the products in the established resistance management program is critical for dollar spot control.

## Risk Factors for Development of Fungicide Resistance

- Repeated applications during a single or across multiple growing seasons
- Use of products with active ingredients with only one FRAC code
- Applications made after disease symptom development
- Application of reduced rates of fungicides
- Certain fungicide classes and some fungal pathogens have been identified by FRAC as being at greater risk

## Management Recommendations

While fungicide resistance cannot be eliminated, it can be managed to reduce the potential for development. New fungicide groups are not easily identified, and currently only three main FRAC codes are used in Nebraska's main crop production systems. Therefore, it is critical that producers take steps to prolong the usefulness of the current products.

**The following recommendations should be considered when using a fungicide:**

- Fungicides should be applied when disease development is at a low level of severity to avoid high numbers of the pathogen's spores being exposed (selected) to the fungicide.
- Use fungicides only when necessary. Good agronomic practices and cultural methods could reduce the need for fungicides.
- Use fungicides containing more than one FRAC code.
- When using single mode of action fungicides, tank-mix more than one fungicide with a different FRAC code.
- Use labelled rates and avoid using reduced rates. Know the risk factors associated with reduced rates for specific FRAC codes (e.g., reduced rates of triazole fungicides increase the risk of resistance).
- Evaluate the level of disease control after an application is made. If producers suspect they are having reduced control, resistance may be occurring. Producers should contact their local Nebraska Extension employee if they believe fungicide resistance may be an issue in their field. It is important to report this quickly so that selection pressure is not continued in the region.

## Resources

Additional information on identification of common field crop diseases can be found at <http://cropwatch.unl.edu/plantdisease>

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