Collaborative note
INRA, ANSES, ARVALIS – Institut du végétal 2013 for cereals diseases resistance management

This note written by INRA, ANSES and ARVALIS – Institut du végétal, draws up the resistance situation and expresses recommendations to manage fungicide resistance and efficacy. This 2013 note stresses the changes, and especially the emergence of a new category of strains resistant to DMIs in septoria leaf blotch. It also include, an information very recently available, resulting from surveys carried out by companies, about the detection of three cases of specific resistance towards SDHI.

SEPTORIA LEAF BLOTCH

(Mycosphaerella graminicola, anamorph Zymoseptoria tritici, syn. Septoria tritici)

Resistance to QoIs (strobilurins, famoxadone) due to the mutation G143A is generalized in all regions producing cereals, including South of France. In these conditions, the efficacy of all strobilurins is strongly compromised everywhere in France.

S. tritici strains moderately resistant to triazoles (main class of DMIs) are still dominant in all French areas; these strains are weakly resistant, and for a part of them, fully susceptible, to prochloraz.
Several new emerging phenotypes, highly resistant to azoles and prochloraz, are detected since 2008. These emerging phenotypes are in progression in 2012 but stay mostly at low frequency in populations (mean frequency of 8.8 % in the whole sampling but presence in 52 % of the populations, compared to 30% in 2010). They can be divided into 2 subgroups[1]: (1) the first subgroup, in progression (called non-MDR) is constituted of strains exhibiting high resistance levels to one or a few DMIs, due to the selection of new combinations of mutations in the gene encoding the target protein of DMIs; (2) the second subgroup, in geographic expansion between 2011 and 2012, called MDR (for MultiDrug Resistance). The strains of this subgroup are highly resistant to most DMIs and a weakly resistant to SDHIs (Succinate DesHydrogenase Inhibitors, including carboxamides), following the acquiring of an additional resistance mechanism that enables these strains to excrete fungicides out of the fungal cell more efficiently. Due to the rare frequency of these new emerging phenotypes, fungicides efficacy is not affected by this recent evolution of populations. The first results from field trials show that all tested unisite fungicides (triazoles, imidazoles, SDHIs), used alone or in mixture, may exert a selective pressure, with different intensities, at least partially on these emerging populations.

Recent information resulting from surveys carried out by companies revealed the detection, among a large number of tested isolates, of one case of specific resistance towards SDHIs (mechanism distinct from MDR).
One resistant strain of *Mycosphaerella graminicola* was collected on wheat in a trial plot from Northern France. This strain bears the T79N change in the C subunit of the succinate dehydrogenase protein. The resistant phenotype present again relatively moderate resistance factors towards SDHIs.
Being given the frequency and the resistance factors observed at this stage, practical efficacy of SDHIs should not be altered in 2013.

Recommendations

Though the efficacy of triazoles in the field is decreasing, the most efficient ones (mostly epoxiconazole and prothioconazole) are still interesting. Furthermore, the efficacy of triazoles must be reinforced by some multisite fungicides (chlorothalonil, mancozeb), or prochloraz or SDHIs. To limit the fungicidal selection pressure, especially towards emerging phenotypes, modes of action, as well as molecules within a mode of action, should be diversified. In particular, we strongly recommend limiting SDHI use to one application per season, regardless of the dose[2]. For the same reason, the introduction of chlorothalonil in programs is also recommended.

(1) Leroux P, Walker AS, Multiple mechanisms account for resistance to sterol 14α-demethylation inhibitors in field isolates of *Mycosphaerella graminicola*. *Pest Manag Sci* (2011) *67(1), 44-59*
(2) The splitting of a full dose into two applications should be counted as two independent applications.

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POWDERY MILDEW ON WHEAT AND BARLEY

(B. graminis f. sp tritici and B. graminis f. sp hordei)

We have observed a low disease pressure these last years. Resistance to strobilurins is probably still deeply established in France, remaining however limited in the South. Even if resistance to SBIs (DMIs and "amines") is widespread in France, many of these molecules are still partly effective.

Some strains strongly resistant to quinoxyfen have been detected in France these last few years and are mainly located in Champagne (North–East of France) and in others European countries. If the activity of quinoxyfen can be affected, proquinazid, even if exhibiting cross-resistance with quinoxyfen, remains good in all situations.

Cyflufenamid and metrafenone present distinct modes of action. In 2012, no specific resistance to cyflufenamid has been reported. In contrast, since 2009, strains moderately resistant to metrafenone have been observed at low frequency in France. More recently, highly resistant strains to metrafenone have been detected at very low frequency in France and in other European countries.

In absence of new data since 2007, triticale powdery mildew is considered as susceptible to the whole mildewcides used on wheat.

Recommendations

Metrafenone, but also cyflufenamid and proquinazid remain efficient in practice on the current cereal mildew populations. Moreover, to slow down the selection pressure of mildewcides concerned by resistance, (metrafenone, quinoxyfen, cyprodinil, "amines"), these should be used preferentially in mixture with another mode of action. The QoI family can no longer be considered as efficient on powdery mildew in most of the French regions. Cyprodinil is no longer effective enough to be used on powdery mildew.

EYESPOT *(Oculimacula spp.)* [3]

The dominant species in France is *Oculimacula yallundae* and the strains now encountered are often resistant to most DMIs, and especially to prochloraz but not to prothioconazole.

Some strains resistant to cyprodinil can still be detected in France at significant frequency within the two species of *Oculimacula spp*. They have, however, no notable impact in practice.

Regarding prothioconazole, boscalid and cyprodinil, multiresistant strains (MDR) showing a low level of resistance have been detected regularly since a few years, without any efficacy loss. Metrafenone is not concerned by this phenomenon, neither by specific resistance.

Recommendations

Efficacy levels observed in trials are generally limited. Mixtures of several fungicides are often needed to obtain satisfactory results. Prochloraz is generally poorly efficient against eyespot and has to be kept to control *septoria* leaf blotch. As metrafenone is active against eyespot as well as against powdery mildew, limit its use to one application per season. The alternance of modes of action is recommended to limit the risk of resistance, between years or within a year, between active ingredients applied on the foot or on the leaves.
Reminder: resistant varieties constitute a good non chemical opportunity to control eyespot

(3) Leroux P,et al. Fungicide resistance status in French populations of the wheat eyespot fungi *Oculimacula acuformis* and *Oculimacula yallundae* (2012). Pest Management Science 69(1), 15-26

HELMINTHOSPORIUM ON WHEAT

(Pyrenophora tritici-repentis, anamorph Drechslera tritici-repentis)

In Northern Europe, some strains of *Helminthosporium tritici-repentis* exhibit mutations in the cytochrome b gene (the QoIs' target), either in position 129 (low level of resistance), or in position 143 (high level of resistance). These two mutations can be found both at the same time in a population. Efficacy of strobilurins could then be severely affected if the frequency of strains highly resistant is important. In France, these two mutations are regularly observed in the very limited number of analysed populations. No efficacy loss was reported for strobilurins, until now.

Recommendations

Use strobilurins in association with a triazole efficient on wheat Helminthosporium (in particular prothioconazole, tebuconazole, propiconazole) if agronomic situation is at high risk and when the disease has been formally identified.

NET BLOTCH *(Pyrenophora teres, anamorph Helminthosporium teres)*

In France, the resistance of *Helminthosporium teres* to QoI fungicides is well established and seems to remain stable since 2006. This phenomenon is determined by the mutation located in position 129 which leads to low to moderate resistance. In situation of resistance, field efficacy of all strobilurins was affected, especially for azoxystrobin, whereas pyraclostrobin is still the less affected strobilurin. Picoxystrobin and trifloxystrobin exhibit similar and intermediate results. The positive effect of fluoxastrobin used in mixture with prothioconazole is mostly less important than that of trifloxystrobin.

A shift in sensitivity to DMI has also been observed for a long time and probably induced the decrease in efficacy of this class of SBI. Today, prothioconazole remains the most efficient product of this family on this disease.

Cyprodinil and SDHI represent two other modes of action that are not affected at the moment by resistance.

Recent information resulting from surveys carried out by companies revealed the detection, among a large number of tested isolates, of 2 strains of *Pyrenorophora teres* exhibiting specific resistance to SDHIs. These were collected on barley in production plots from North Germany. These strains bear the H277Y change in the B subunit of the succinate deshydrogenase protein. The resistant phenotype presents relatively moderate resistance factors towards SDHIs. No specific resistance to SDHIs was detected in France in 2012. Therefore, practical efficacy of SDHIs should not be altered in 2013.

Recommendations

Always associate strobilurins with efficient fungicides that have other modes of action (in particular prothioconazole or cyprodinil). Diversify and alternate the modes of action. Avoid using double applications of SDHIs, strobilurins, prothioconazole, epoxiconazole, or cyprodinil, in the same year.

RAMULARIA ON BARLEY

(Ramularia collo-cygni)

Observed for the first time in France in 2002, *Ramularia* was rapidly extended to the main barley cropping areas. The analysis undertaken since 2008 revealed high frequencies of *Ramularia* highly resistant strains to strobilurins and presenting a modified cytochrome b in position 143. In practice, the efficacy of this class of fungicides is highly affected.

Recommendations

Ramularia is difficult to distinguish from physiological leaf spots and net blotch and is then controlled with the rest of the disease complex. The three most efficient active ingredients are the multisite chlorothalonil, and among unisites, prothioconazole and some SDHIs.

RHYNCHOSPORIUM ON BARLEY

(Rhynchosporium secalis)

A few resistant strains to strobilurins and presenting the G143A substitution (cytochrome b) have been detected in France in 2008 but haven't been recovered, although since then sought in the field.

Recommendations

Mix triazoles with another mode of action.

RUSTS ON CEREALS *(P. recondita, P. striiformis, P. hordei)*

As far as we can know, brown and yellow rust are not concerned by field resistance, as well as for triazoles and strobilurins.

Recommendations

Take into account the intrinsic activity on rusts of active ingredients used in treatment programs. For the time being, associations of triazoles and strobilurins provide the best efficacy against these diseases.

FUSARIUM HEAD BLIGHT *(M. majus, M. nivale, F. graminearum, F. culmorum, F. avenaceum, F. tricinctum, F. poae and F. langsethiae)*

In 2007, 2008 and 2012, heavy attacks of *Microdochium majus* and *M. nivale* were observed. Since 2007, *Microdochium* QoIs resistance is widely established with highly resistant strains. The main mechanism of resistance is the alteration of cytochrome b at location 143 (mutation G143A) but some other mechanisms occur. According to the available data, frequency and levels of resistance are very high, especially in *M. majus*, which is actually the dominant species, and are leading to field efficacy losses.

The *Microdochium* resistance to benzimidazoles and to thiophanate methyl, selected during the seventies is still detected in the survey run in 2008. . The strains concerned often, but not systematically, cumulate the resistance to strobilurins.

F. culmorum, *F. graminearum* and *F. langsethiae* strains remain almost all susceptible to benzimidazoles and thiophanate. Finally, no shift in sensitivity to DMIs have been observed for *Fusarium* spp., for which most of the strobilurins have no or poor efficacy.

Recommendations

Microdochium spp: among SBIs, only prothioconazole present good field efficacy; prochloraz and fenpropimorph present interesting activities. Thiophanate-methyl and strobilurins have no longer interest on *M. majus* and *M. nivale*, since the generalization of these resistances.

Fusarium spp.: to control the various species of *Fusarium*, it is possible to use DMIs like prothioconazole, tebuconazole or metconazole, or also thiophanate-methyl since the current populations are susceptible to these fungicides.

GENERAL RECOMMENDATIONS[4] FOR 2013

• **Give preference to varieties tolerant to relevant diseases**, and avoid using sensitive wheat or barley cultivars on the entire farm.

• **Diversify the cultivars** over years at the scale of the farm and of the local area, to enhance the durability of cultivars resistance to diseases.

• Prefer field practices that reduce the disease risk, in particular those that can **limit primary inoculum** (for example rotation, ploughing, destruction of volunteers, …) or **disease spreading** (density, nitrogen).

• **Treat only if necessary**, according to the climate, cultivation conditions, models and observations.

• Treat according to disease development, using **reliable methods** of observation and symptoms forecasting system.

• **Limit the number of applications per season of active ingredients from the same chemical family** (usually characterized by a positive cross resistance). Similarly, when the same active ingredient may be used as an ear treatment and as seed treatment, avoid if possible cumulating two treatments with the same molecule.

• **Diversify modes of action by alternating or associating molecules in treatment programs,** to minimize the risk of resistance development.

- **Use, when possible and useful, multisite inhibitors**, less prone to select resistance, in particular on septoria leaf blotch.

- **Limit the SDHI and QoI use, preferably to one application per season**

• The most efficient DMI active ingredients can be used to treat cereals diseases even in a resistance context. As far as possible**, avoid using the same molecule more than once per season**. Furthermore, their performances will be improved if they are associated with some other modes of action, or even, in the case of mixtures, between complementary DMIs.

*NB: this note do not consider SDHIs used as seed treatments. Those which are **already** registered don't have any noticeable effect on the considered foliar diseases and so have little chance to select resistance. In the other hand, as soon as seed treatment solutions, active on foliar diseases will be available, this type of treatment should be taken fully into account in the management of the risk of resistance. Finally, in both cases, the management of the resistance risk for diseases transmitted by seeds, like smut and Microdochium must also be reasoned*

(4) Our recommendations are designed, to decrease disease pressure and the risk of emergence of resistance, reduce selection by fungicides of emerging phenotypes, and manage efficiency in a situation of resistance established in practice

Annexe : Simplified classification of fungicides

MODE OF ACTION	TARGET	GROUP	HEMICAL FAMILY	MOLECULES
Mitosis and cellular division	**Microtubules**	MBC (Methyl Benzimidazole Carbamates)	benzimidazoles	thiophanate thiophanate-methyl
Respiration	**Mitochondrial complex II : succinate-déshydrogénase**	SDHI (Succinate dehydrogenase inhibitors)	phenyl-benzamides	benodanil flutolanil mepronil
			pyridinyl-ethyl-benzamides	fluopyram
			furancarboxamides	fenfuram
			oxathiin- carboxamides	carboxin oxycarboxin
			thiazole- carboxamides	thifluzamide
			pyrazole- carboxamides	bixafen furametpyr isopyrazam penflufen penthiopyrad sedaxane fluxapyroxad
			pyridine- carboxamides	boscalid
	Mitochondrial complex III: cytochrome b	QoI (Quinone Outside Inhibitors)	methoxy-acrylates	azoxystrobin picoxystrobin
			methoxy-carbamates	pyraclostrobin
			oximino-acetates	kresoxim-methyl trifloxystrobin
			oximino-acetamides	dimoxystrobin fluoxastrobin
Synthesis of amino-acids and proteins	**Methionine biosynthesis**	AP (Anilino-Pyrimidines)	anilinopyrimidines	cyprodinil
Signal transduction	**Unknown mechanism**	Aza-naphthalenes	quinolines	quinoxyfen
			quinazolinones	proquinazid
Biosynthesis of membrane lipids	**C14-demethylation of sterols**	DMI (De-Methylation Inhibitors)	imidazoles	prochloraz
			triazoles	bromuconazole cyproconazole difenoconazole epoxiconazole fluquinconazole flusilazole flutriafol metconazole myclobutanil propiconazole tébuconazole tetraconazole triadimenol triticonazole
			triazolinethiones	prothioconazole
	Δ^{14} reductase and $\Delta^{8}\rightarrow\Delta^{7}$ isomerase of stérols	Amines	morpholines	fenpropimorph
			piperidines	fenpropidin
			spiroketalamines	spiroxamine
Unknown mode of action	**Unknown mechanism**	Phenyl-acetamide	phenyl-acetamide	cyflufenamid
	Actin disruption ?	Benzophénone	benzophenone	metrafenone
Multisites	**Several action sites**	Dithiocarbamates	dithiocarbamates	mancozeb
		Chloronitriles	chloronitriles	chlorothalonil