Collaborative note
INRA, ANSES, DGAL-SDQPV, ARVALIS – Institut du végétal
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for cereals disease resistance management

This note written by INRA, ANSES and ARVALIS – Institut du végétal draws up the resistance situation and expresses recommendations. This 2012 note stresses the changes, and especially the emergence of a new category of strains resistant to DMIs in septoria leaf blotch.

SITUATION in 2011 and RECOMMENDATIONS for 2012

SEPTORIA LEAF BLOTCH (*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 2011 but stay mostly at low frequency in populations (mean frequency of 7% in the whole sampling but presence in 45% 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, stable, called MDR (for MultiDrug Resistance) is represented by strains exhibiting high levels of resistance to most DMIs and a weak cross-resistance with SDHIs (Succinate DeHydrogenase Inhibitors, including carboxamides). This phenotype selected 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, on part or all of these emerging populations.

Recommendations: Though the efficacy of triazoles in the field is decreasing, the most efficient ones (mostly epoxiconazole and

[1] Leroux P, Walker AS, Multiple mechanisms account for resistance to sterol 14α-demethylation inhibitors in field isolates of *Mycosphaerella graminicola. Pest Manag Sci* (2010). *In Press*

prothioconazole) are still interesting. Furthermore, the efficacy of triazoles must be reinforced by some multisite fungicides (chlorothalonil, mancozeb), or prochloraz or SDHIs. In all cases, when fungicides are needed, the introduction of chlorothalonil in programs is highly recommended. 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 should try to limit SDHI application to one per season.

POWDERY MILDEW (*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). 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. Since 2009, strains moderately resistant to metrafenone have been observed at low frequency in France. Highly resistant strains have been detected in Champagne in 2010 and 2011 at very low frequency and in other European countries since 2009.
However, triticale powdery mildew is still susceptible to the whole mildewcides used on wheat.

Recommendations: Metrafenone, cyflufenamid and proquinazid remain efficient on the current cereal mildew populations. Moreover, to slow donwn 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 QoIs 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 yallundae* and *O. acuformis*.)
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.

Multiresistant strains exhibiting low levels of resistance towards prothioconazole, boscalid and cyprodinil are regularly observed 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 and has to be used in priority 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. More generally, the associations of several modes of action are more effective. However, for the first treatment, it is recommended to alternate the use of different types of products, either active on foot or leaves, over years to limit the risk of resistance. Reminder: resistant varieties constitute a good non chemical opportunity to control eyespot

HELMINTHOSPORIUM ON WHEAT (*H. 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. But no efficacy loss was reported for strobilurins.

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

HELMINTHOSPORIUM ON BARLEY (*H. teres*)
In France, the resistance of *Helminthosporium teres* to QoIs 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 boscalid represent two other modes of action that are not affected at the moment by resistance.

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 strobilurins, prothioconazole, epoxyconazole, cyprodinil, or boscalid in the same year.

RAMULARIA ON BARLEY (*Ramularia collo-cyni*)
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 boscalid.

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 in 2009, neither in 2010 and 2011.
Recommendations: Triazoles alone or in mixture with cyprodinil are giving good results.

RUSTS (*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 and 2008 and to a lesser extend in 2009 and 2010, 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.
Most ***Microdochium*** *strains are resistant to* benzimidazoles and thiophanates. They often 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 TO MANAGE CEREALS DISEASES RESISTANCE IN 2012

Based on this updated view of the situation, we renew our practical recommendations of prophylaxis to:

- Reduce parasitical risks,
- Limit the use of fungicides and thus the selective pressure on pathogen fungus,
- Manage situations of practical resistance

• **Give preference to varieties tolerant to relevant diseases**, and avoid using sensitive wheat or barley cultivars over wide areas.

• **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, sowing date…) 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.

• **Avoid unnecessary application** of active substance by adjusting the spectrum of products used at real risk.

• **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.

- **Use preferably SDHIs only once a season**. This is also recommended for QoIs.

• The most efficient DMI active ingredients can be used to treat cereals diseases in a resistance context. As far as possible**, avoid to use 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.*

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