

## **FRAC Code List<sup>®\*</sup>: Fungicides sorted by mode of action (including FRAC Code numbering)**

### **INTRODUCTION**

The following table lists commercial fungicides according to their mode of action and resistance risk. The most important bactericides are also included.

The Table headings are defined as:

#### **MOA Code**

Different letters (A to I, with added numbers) are used to distinguish fungicide groups according to their biochemical mode of action (MOA) in the biosynthetic pathways of plant pathogens. The grouping was made according to processes in the metabolism starting from nucleic acids synthesis (A) to secondary metabolism, e.g. melanin synthesis (I) at the end of the list, followed by host plant defence inducers (P), recent molecules with an unknown mode of action and unknown resistance risk (U, transient status, mostly not longer than 8 years, until information about mode of action and mechanism of resistance becomes available), and multi-site inhibitors (M).

#### **Target Site and Code**

If available, the biochemical mode of action is given. In many cases the precise target site is not known. However, a grouping can be made due to cross resistance profiles within a group or in relation to other groups.

#### **Group Name**

The Group Names listed are based on chemical relatedness of structures which are accepted in literature (e.g. The Pesticide Manual). They are based on different sources (chemical structure, site of action, first important representative in group).

#### **Chemical Group**

Grouping is based on chemical considerations. Nomenclature is according to IUPAC and Chemical Abstract name.

#### **Common name**

BSI/ISO accepted (or proposed) common name for an individual active ingredient expected to appear on the product label as definition of the product.

## Comments on Resistance

Details are given for the (molecular) mechanism of resistance and the resistance risk. If field resistance is known to one member of the Group, it is most likely but not exclusively valid that cross resistance to other group members will be present. There is increasing evidence that the degree of cross resistance can differ between group members and pathogen species or even within species. For the latest information on resistance and cross resistance status of a particular pathogen / fungicide combination, it is advised to contact local FRAC representatives, product manufacturer's representatives or crop protection advisors. The intrinsic risk for resistance evolution to a given fungicide group is estimated to be **low, medium or high** according to the principles described in FRAC Monographs 1, 2 and 3. Resistance management is driven by intrinsic risk of fungicide, pathogen risk and agronomic risk (see FRAC pathogen risk list).

Similar classification lists of fungicides have been published by T. Locke on behalf of FRAG – UK (Fungicide Resistance, August 2001), and by P. Leroux (Classification des fongicides agricoles et résistance, Phytoma, La Défense des Végétaux, No. 554, 43-51, November 2002).

## FRAC Code

Numbers and letters are used to distinguish the fungicide groups according to their cross resistance behaviour. The numbers were assigned primarily according to the time of product introduction to the market (numbers 1 to 44, status 2008). The letters refer to P = host plant defence inducers, M = multi-site inhibitors, and U = unknown mode of action and unknown resistance risk.

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MOA	TARGET SITE AND CODE	GROUP NAME	CHEMICAL GROUP	COMMON NAME	COMMENTS	FRAC CODE
<b>A: nucleic acids synthesis</b>	A1: RNA polymerase I	PA – fungicides (PhenylAmides)	acylalanines	benalaxyl furalaxyl metalaxyl metalaxyl-M (=mefenoxam)	Resistance and cross resistance well known in various Oomycetes but mechanism unknown.  High risk. See FRAC Phenylamide Guidelines for resistance management	4
			oxazolidinones	oxadixyl		
			butyrolactones	ofurace		
	A2: adenosin-deaminase	hydroxy-(2-amino-) pyrimidines	hydroxy-(2-amino-) pyrimidines	bupirimate dimethirimol ethirimol	Medium risk Resistance and cross resistance known in powdery mildews. Resistance management required.	8
	A3: DNA/RNA synthesis (proposed)	heteroaromatics	isoxazoles	hymexazole	Resistance not known	32
			isothiazolones	octhilinone		
A4: DNA topoisomerase type II (gyrase)	carboxylic acids	carboxylic acids	oxolinic acid	Bactericide. Resistance known. Risk unknown. Resistance management required.	31	
<b>B: mitosis and cell division</b>	B1: $\beta$ -tubuline assembly in mitosis	MBC - fungicides (Methyl Benzimidazole Carbamates)	benzimidazoles	benomyl carbendazim fuberidazole thiabendazole	Resistance common in many fungal species. Several target site mutations, mostly E198A/G/K, F200Y in $\beta$ -tubulin gene  Positive cross resistance between the group members. Negative cross resistance to N-Phenylcarbamates  High risk. See FRAC Benzimidazole Guidelines for resistance management.	1
			thiophanates	thiophanate thiophanate-methyl		
	B2: $\beta$ -tubulin assembly in mitosis	N-phenyl carbamates	N-phenyl carbamates	diethofencarb	Resistance known. Target site mutation E198K. Negative cross resistance to benzimidazoles. High risk. Resistance management required.	10
	B3: $\beta$ -tubulin assembly in mitosis	benzamides	toluamides	zoxamide	Low to medium risk. Resistance management required.	22
	B4: cell division (proposed)	phenylureas	phenylureas	pencycuron	Resistance not known	20
B5: delocalisation of spectrin-like proteins	benzamides	pyridinylmethyl-benzamides	fluopicolide	Resistance not known	43	

MOA	TARGET SITE AND CODE	GROUP NAME	CHEMICAL GROUP	COMMON NAME	COMMENTS	FRAC CODE
<b>C. respiration</b>	<b>C1:</b> complex I NADH Oxido-reductase	pyrimidinamines	pyrimidinamines	diflumetorim	Resistance not known	<b>39</b>
	<b>C2:</b> complex II: succinate-dehydro-genase	SDHI (Succinate dehydrogenase inhibitors)	phenyl-benzamides	benodanil flutolanil mepronil	Resistance known for several fungal species in field populations and lab mutants. Target site mutations in <i>sdh</i> gene, e.g. H/Y (or H/L) at 257, 267, 272 or P225L, dependent on fungal species. Resistance management required. <b>Medium risk.</b> See FRAC SDHI Guidelines for resistance management.	<b>7</b>
			pyridinyl-ethyl-benzamides	fluopyram		
			furan- carboxamides	fenfuram		
			oxathiin-carboxamides	carboxin oxycarboxin		
			thiazole-carboxamides	thifluzamide		
			pyrazole-carboxamides	furametpyr penthioapyrad bixafen isopyrazam sedaxane		
			pyridine-carboxamides	boscalid		
	<b>C3:</b> complex III: cytochrome bc1 (ubiquinol oxidase) at Qo site ( <i>cyt b gene</i> )	QoI-fungicides (Quinone outside Inhibitors)	methoxy-acrylates	azoxystrobin enestrobin picoxystrobin	Resistance known in various fungal species. Target site mutations in <i>cyt b</i> gene (G143A, F129L) and additional mechanisms. Cross resistance shown between all members of the QoI group. <b>High risk.</b> See FRAC QoI Guidelines for resistance management.	<b>11</b>
			methoxy-carbamates	pyraclostrobin		
			oximino acetates	kresoxim-methyl trifloxystrobin		
			oximino-acetamides	dimoxystrobin metominostrobin orysastrobin		
			oxazolidine-diones	famoxadone		
			dihydro-dioxazines	fluoxastrobin		
			imidazolinones	fenamidone		
benzyl-carbamates			pyribencarb			
<b>C4:</b> complex III: cytochrome bc1(ubiquino-ne reductase) at Qi site	QiI - fungicides (Quinone inside Inhibitors)	cyano- imidazole	cyazofamid	Resistance risk unknown but assumed to be medium to high (mutations at target site known in model organisms). Resistance management required.	<b>21</b>	
		sulfamoyl-triazole	amisulbrom			
<b>C5:</b> uncouplers of oxidative phosphorylation		dinitrophenyl crotonates	binapacryl meptyldinocap dinocap	Resistance not known. Also acaricidal activity	<b>29</b>	
		2,6-dinitro-anilines	fluazinam	Low risk. However, resistance claimed in <i>Botrytis</i> in Japan.		
		pyrimidinone-hydrazones	ferimzone	Resistance not known		
<b>C6:</b> inhibitors of oxidative phosphorylation, ATP synthase	organo tin compounds	tri phenyl tin compounds	fentin acetate fentin chloride fentin hydroxide	Some resistance cases known. Low to medium risk.	<b>30</b>	
<b>C7:</b> ATP produc-tion (proposed)	thiophene-carboxamides	thiophene-carboxamides	silthiofam	Resistance reported. Risk low	<b>38</b>	

MOA	TARGET SITE AND CODE	GROUP NAME	CHEMICAL GROUP	COMMON NAME	COMMENTS	FRAC CODE
<b>D: amino acids and protein synthesis</b>	<b>D1:</b> methionine biosynthesis (proposed) ( <i>cgs gene</i> )	AP - fungicides (Anilino-Pyrimidines)	anilino-pyrimidines	cyprodinil mepaniprim pyrimethanil	Resistance known in <i>Botrytis</i> and <i>Venturia</i> , sporadically in <i>Oculimacula</i> .  Medium risk. See FRAC Anilinopyrimidine Guidelines for resistance management.	9
	<b>D2:</b> protein synthesis	enopyranuronic acid antibiotic	enopyranuronic acid antibiotic	blastocidin-S	Low to medium risk. Resistance management required.	23
	<b>D3:</b> protein synthesis	hexopyranosyl antibiotic	hexopyranosyl antibiotic	kasugamycin	Resistance known in fungal and bacterial ( <i>P. glumae</i> ) pathogens. Medium risk. Resistance management required.	24
	<b>D4:</b> protein synthesis	glucopyranosyl antibiotic	glucopyranosyl antibiotic	streptomycin	Bactericide. Resistance known. High risk. Resistance management required.	25
	<b>D5:</b> protein synthesis	tetracycline antibiotic	tetracycline antibiotic	oxytetracycline	Bactericide. Resistance known. High risk. Resistance management required.	41
<b>E: signal transduction</b>	<b>E1:</b> G-proteins in early cell signalling (proposed)	quinolines	quinolines	quinoxifen	Resistance known. Medium risk. Resistance management required. Cross resistance to proquinazid in <i>Erysiphe (Uncinula) necator</i> but not in <i>Blumeria graminis</i> . As a precaution, proquinazid and quinoxifen should be managed together for resistance management	13
	<b>E2:</b> MAP/Histidine-Kinase in osmotic signal transduction ( <i>os-2, HOG1</i> )	PP-fungicides (PhenylPyrroles)	phenylpyrroles	fenpiclonil fludioxonil	Resistance found sporadically, mechanism speculative. Low to medium risk. Resistance management required.	12
	<b>E3:</b> MAP/Histidine-Kinase in osmotic signal transduction ( <i>os-1, Daf1</i> )	dicarboximides	dicarboximides	chlozolinate iprodione procymidone vinclozolin	Resistance common in <i>Botrytis</i> and some other pathogens. Several mutations in OS-1, mostly I365S  Cross resistance common between the group members.  Medium to high risk. See FRAC Dicarboximide Guidelines for resistance management.	2

MOA	TARGET SITE AND CODE	GROUP NAME	CHEMICAL GROUP	COMMON NAME	COMMENTS	FRAC CODE
<b>F: lipids and membrane synthesis</b>	F1	formerly dicarboximides				
	F2: phospholipid biosynthesis, methyltransferase	phospho-thiolates	phospho-thiolates	edifenphos iprobenfos (IBP) pyrazophos	Resistance known for specific fungi. Low to medium risk. Resistance management required if used for risky pathogens.	6
		dithiolanes	dithiolanes	isoprothiolane		
	F3: lipid peroxidation (proposed)	AH-fungicides (Aromatic Hydrocarbons) (chlorophenyls, nitroanilines)	aromatic hydrocarbons	biphenyl chloroneb dicloran quintozene (PCNB) tecnazene (TCNB) tolclofos-methyl	Resistance known to some fungi. Low to medium risk. Cross resistance patterns complex due to different activity spectra.	14
		heteroaromatics	1,2,4-thiadiazoles	etridiazole		
	F4: cell membrane permeability, fatty acids (proposed)	carbarnates	carbarnates	iodocarb propamocarb prothiocarb	Low to medium risk. Resistance management required.	28
	F5: phospholipid biosynthesis and cell wall deposition (proposed)	CAA-fungicides (Carboxylic Acid Amides)	cinnamic acid amides	dimethomorph flumorph	Resistance known in <i>Plasmopara viticola</i> but not in <i>Phytophthora infestans</i> . Cross resistance between all members of the CAA group. Low to medium risk. See FRAC CAA Guidelines for resistance management	40
			valinamide carbarnates	benthiavalicarb iprovalicarb valifenalate		
mandelic acid amides			mandipropamid			
F6: microbial disrupters of pathogen cell membranes	Microbial ( <i>Bacillus</i> sp.)	<i>Bacillus subtilis</i> and the fungicidal lipopeptides they produce	<i>Bacillus subtilis</i> strain QST 713	No resistance reported. Assumed to be low risk based on mode of action of non-specific membrane disruption	44	

MOA	TARGET SITE AND CODE	GROUP NAME	CHEMICAL GROUP	COMMON NAME	COMMENTS	FRAC CODE
<b>G: sterol biosynthesis in membranes</b>	<b>G1:</b> C14- demethylase in sterol biosynthesis ( <i>erg11/cyp51</i> )	DMI-fungicides (DeMethylation Inhibitors) (SBI: Class I)	piperazines	triforine	There are big differences in the activity spectra of DMI fungicides.  Resistance is known in various fungal species. Several resistance mechanisms are known incl. target site mutations in cyp51 ( <i>erg 11</i> ) gene, e.g. V136A, Y137F, A379G, I381V; cyp51 promotor; ABC transporters and others.  Generally wise to accept that cross resistance is present between DMI fungicides active against the same fungus.  DMI fungicides are Sterol Biosynthesis Inhibitors (SBIs), but show no cross resistance to other SBI classes.  <b>Medium risk.</b> See FRAC SBI Guidelines for resistance management.	3
			pyridines	pyrifenox		
			pyrimidines	fenarimol nuarimol		
			imidazoles	imazalil oxpoconazole pefurazoate prochloraz triflumizole		
			triazoles	azaconazole bitertanol bromuconazole cyproconazole difenoconazole diniconazole epoxiconazole etaconazole fenbuconazole fluquinconazole flusilazole flutriafol hexaconazole imibenconazole ipconazole metconazole myclobutanil penconazole propiconazole prothioconazole simeconazole tebuconazole tetraconazole triadimefon triadimenol triticonazole		
	<b>G2:</b> $\Delta^{14}$ -reductase and $\Delta^8 \rightarrow \Delta^7$ -isomerase in sterol biosynthesis ( <i>erg24, erg2</i> )	Amines ("Morpholines") (SBI: Class II)	morpholines	aldimorph dodemorph fenpropimorph tridemorph	Decreased sensitivity for powdery mildews. Cross resistance within the group generally found but not to other SBI classes.  <b>Low to medium risk.</b> See FRAC SBI Guidelines for resistance management.	5
			piperidines	fenpropidin piperalin		
			spiroketal-amines	spiroxamine		
	<b>G3:</b> 3-keto reduc-tase, C4- de-methylation ( <i>erg27</i> )	hydroxyanilides (SBI: Class III)	hydroxyanilides	fenhexamid	Low to medium risk. Resistance management required.	17
	<b>G4:</b> squalene-epoxidase in sterol biosynthesis ( <i>erg1</i> )	(SBI class IV)	thiocarbamates	pyributicarb	Resistance not known, fungicidal and herbicidal activity	18
			allylamines	naftifine terbinafine	Medical fungicides only	

MOA	TARGET SITE AND CODE	GROUP NAME	CHEMICAL GROUP	COMMON NAME	COMMENTS	FRAC CODE
<b>H: glucan synthesis</b>	<b>H3:</b> trehalase and inositol-biosynthesis	glucopyranosyl antibiotic	glucopyranosyl antibiotic	validamycin	Resistance not known	<b>26</b>
	<b>H4:</b> chitin synthase	polyoxins	peptidyl pyrimidine nucleoside	polyoxin	Resistance known. Medium risk. Resistance management required.	<b>19</b>
<b>I: melanin synthesis in cell wall</b>	<b>I1:</b> reductase in melanin biosynthesis	MBI-R (Melanin Biosynthesis Inhibitors – Reductase)	isobenzo-furanone	fthalide	Resistance not known	<b>16.1</b>
			pyrrolo-quinolinone	pyroquilon		
			triazolobenzothiazole	tricyclazole		
	<b>I2:</b> dehydratase in melanin biosynthesis	MBI-D (Melanin Biosynthesis Inhibitors – Dehydratase)	cyclopropane-carboxamide	carpropamid	Resistance known. Medium risk. Resistance management required.	<b>16.2</b>
			carboxamide	diclocymet		
			propionamide	fenoxanil		
<b>P: host plant defence induction</b>	<b>P1:</b> salicylic acid pathway	benzo-thiadiazole BTH	benzo-thiadiazole BTH	acibenzolar-S-methyl	Resistance not known	<b>P</b>
	<b>P2</b>	benzisothiazole	benzisothiazole	probenazole (also antibacterial and antifungal activity)	Resistance not known	
	<b>P3</b>	thiadiazole-carboxamide	thiadiazole-carboxamide	tiadinil isotianil	Resistance unknown	
	<b>P4 (proposed)</b>	natural compound		laminarin	Resistance unknown	

MOA	TARGET SITE AND CODE	GROUP NAME	CHEMICAL GROUP	COMMON NAME	COMMENTS	FRAC CODE
Unknown mode of action (U numbers not appearing in the list derive from reclassified fungicides)	unknown	cyanoacetamide-oxime	cyanoacetamide-oxime	cymoxanil	Resistance claims described. Low to medium risk. Resistance management required.	27
	unknown	phosphonates	ethyl phosphonates	fosetyl-Al	Few resistance cases reported in few pathogens. Low risk	33
				phosphorous acid and salts		
	unknown	phthalamic acids	phthalamic acids	teclofthalam (Bactericide)	Resistance not known	34
	unknown	benzotriazines	benzotriazines	triazoxide	Resistance not known	35
	unknown	benzene-sulfonamides	benzene-sulfonamides	flusulfamide	Resistance not known	36
	unknown	pyridazinones	pyridazinones	diclomezine	Resistance not known	37
	unknown	thiocarbamate	thiocarbamate	methasulfocarb	Resistance not known	42
	microtubule disruption (proposed)	thiazole carboxamide	ethylamino-thiazole carboxamide	ethaboxam	Resistance not known	U5
	unknown	phenyl-acetamide	phenyl-acetamide	cyflufenamid	Resistance in <i>Sphaerotheca</i> . Resistance management required	U6
	unknown	quinazolinone	quinazolinone	proquinazid	Resistance known. Medium risk. Resistance management required. Cross resistance to quinoxifen in <i>Erysiphe (Uncinula) necator</i> but not in <i>Blumeria graminis</i> . As a precaution, proquinazid and quinoxifen should be managed together for resistance management	U7
	actin disruption (proposed)	benzophenone	benzophenone	metrafenone	Resistance not known	U8
						U10
					U11	
not classified	unknown	diverse	diverse	mineral oils, organic oils, potassium bicarbonate, material of biological origin	Resistance not known	NC

MOA	TARGET SITE AND CODE	GROUP NAME	CHEMICAL GROUP	COMMON NAME	COMMENTS	FRAC CODE
<b>Multi-site contact activity</b>	multi-site contact activity	inorganic	inorganic	copper (different salts)	Generally considered as a low risk group without any signs of resistance developing to the fungicides  * For dodine, resistance was reported in <i>Venturia inaequalis</i> suggesting that dodine may not be a multi-site inhibitor. Resistance management recommended  No cross resistance between group members M1 to M9	M1
		inorganic	inorganic	sulphur		M2
		dithiocarbamates and relatives	dithio-carbamates and relatives	ferbam mancozeb maneb metiram propineb thiram zineb ziram		M3
		phthalimides	phthalimides	captan captafol folpet		M4
		chloronitriles (phthalonitriles)	chloronitriles (phthalonitriles)	chlorothalonil		M5
		sulfamides	sulfamides	dichlofluanid tolylfluanid		M6
		guanidines	guanidines	dodine* guazatine iminocadine		M7
		triazines	triazines	anilazine		M8
		quinones (anthraquinones)	quinones (anthra-quinones)	dithianon		M9