Carboxylic Acid Amides (CAA) Working Group

Annual Meeting 2018 on December 11th

Protocol of the discussions and recommendations of the CAA Working Group of the Fungicide Resistance Action Committee (FRAC)

Participants

Gerd Stammler (Chairman)	BASF SE, Limburgerhof, Germany
Nadine Riediger	BASF SE, Limburgerhof, Germany
Daniela Portz	Bayer AG, Monheim, Germany
Sophie Huvier-Boutin	Bayer AG, Monheim, Germany
Pauline Leroux	Belchim Crop Protection, Brussels, Belgium
Peter Adriaansen (excused)	Belchim Crop Protection, Brussels, Belgium
Martin Huttenlocher (excused)	ADAMA, Köln, Germany
Akihiro Moriwaki	K-I Chemical, Brussels, Belgium
Stefano Torriani	Syngenta, Basel, Switzerland
Anna Dutton (excused)	Syngenta, Basel, Switzerland

Venue:
Lindner Congress Hotel, Frankfurt am Main, Germany

Anti-trust guidelines (from FRAC constitution) were shown at the start of the meeting

1. Introduction

The FRAC CAA Working Group was set up in 2005 to generate common resistance management recommendations for the Oomycete fungicides dimethomorph, flumorph, pyrimorph, benthiavalicarb, iprovalicarb, valifenalate and mandipropamid.

All of the above-mentioned fungicides exhibit cross resistance and are grouped under the FRAC Code No. 40 in the FRAC Code List.

CODE	TARGET SITE OF ACTION	GROUP NAME	CHEMICAL GROUP	COMMON NAME	COMMENTS
40	Cellulose synthesis	**CAA**-fungicides (**C**arboxylic **a**cid **a**mides)	cinnamic acid amides	dimethomorph flumorph pyrimorph	Low to medium risk. Resistance management required.
			valinamide carbamates	benthiavalicarb iprovalicarb valifenalate	
			mandelic acid amides	mandipropamid	

As shown in the table, the group name **C**arboxylic **A**cid **A**mides (**CAA**) has been chosen. This name best represents compounds from three different chemical groups.

The mode of action of CAA compounds is directly linked to the inhibition of cellulose synthesis in the Oomycete plant pathogen (Blum *et al.* 2010, Molecular Plant Pathology 11, 227-243). Uptake studies with ^{14}C labeled mandipropamid (MPD) showed that this Oomycete control agent acts on the cell wall and does not enter the cell. Furthermore, ^{14}C glucose incorporation into cellulose was perturbed in the presence of MPD. Gene sequence analysis of cellulose synthase genes in laboratory mutants, insensitive to MPD, revealed two point mutations in the *PiCesA3* gene, known to be involved in cellulose synthesis. Both mutations in the *PiCesA3* gene result in a change to the same amino acid (Glycine-1105) in the protein.

Sensitivity monitoring studies over several years revealed that in populations of the late blight pathogen, *Phytophthora infestans*, all isolates were fully sensitive to CAA fungicides. However, in populations of the grape downy mildew pathogen, *Plasmopara viticola*, isolates can be found in certain regions, which are resistant to all CAA fungicides.

Inheritance studies (Gisi *et al.* 2007, Plant Pathology 56, 199-208) showed that sexual crosses between sensitive and CAA resistant isolates of *Plasmopara viticola* lead to a co-segregation of resistance to dimethomorph, iprovalicarb, benthiavalicarb and mandipropamid, but not to the phenylamide, mefenoxam, which was tested in parallel as an independent marker.

Further, the inheritance studies showed that the gene(s) for resistance to CAA fungicides are inherited in a recessive manner. Therefore, the entire F1 generation of crosses between sensitive and CAA resistant isolates was sensitive, and only in the F2 progeny did CAA resistance reappear in some isolates. These results suggest that the resistance risk can be classified as moderate (as compared to high for phenylamide and QoI fungicides) and that it can be managed by appropriate product use strategies (see below).

2. Resistance Monitoring 2018

2.1. *Plasmopara viticola* – Grape downy mildew

Disease incidence
In 2018, disease pressure was low in the Northern grape growing areas in Europe and high in the Southern grape growing regions in Europe.

Monitoring results
(BASF, Bayer, Belchim, K-I Chemical, Syngenta)

The following estimations are based on the data provided by the different companies. These data were generated by different laboratories including external service providers. Different methods such as *in vivo* tests, zoospore germination tests and moleculargenetic analysis were used for sensitivity assessment.
The assessments are from 2018 studies, besides another year is mentioned.

France
As in the years before, CAA resistant isolates have been detected consistently in most areas. High frequencies of resistance were detected in Armagnac, moderate to high frequencies in Cognac, Centre, Midi-Pyrenees and Savoie. Moderate frequencies were detected in Bordeaux, Bourgogne and Beaujolais, Champagne, Val de Loire, Languedoc, Alsace and Lorraine, low to moderate frequencies in Provence and Val du Rhone.

Germany
Moderate to high frequencies of resistance were found in Mosel and Pfalz. Moderate frequencies were observed in Baden, Rheinhessen and Württemberg.

Switzerland
High values were detected in Ticino, moderate to high values in Vaud.

Austria
High values were detected in Wachau and Steiermark, low values in Weinviertel and no resistance in Burgenland.

Italy
High frequencies of resistance were observed in Campania, Friuli, Piemonte, Toscana, Trentino, Umbria and Veneto, moderate values in Marche and Abruzzi, low to moderate values in Lombardia and low values in Lazio and South Italy.

Spain:
High frequencies of resistance were found in Basque region and no resistance was detected in Cataluna, Galicia and Rioja.

Portugal
An overall sensitive situation was found in Portugal in 2018.

Greece
No resistance was detected in Greece (Peleponnes and Makedonia).

Hungary
Samples from Hungary contained low to high frequency values of CAA resistance.

Romania
Samples from Romania had low values of CAA resistance.

Slovenia
Samples from Slovenia contained low frequency values of CAA resistance (2017 data).

Czech Republic
No monitoring data were presented for 2018. In 2016 sensitivity monitoring showed low frequencies of CAA resistance.

Slovakia
No monitoring data were presented for 2018. In 2016 sensitivity monitoring showed low frequency of CAA resistance in both countries.

Bulgaria
No monitoring data were presented for 2018. In 2017 sensitivity monitoring showed no CAA resistance.

Field performance
Field performance of registered products was good when applied in spray programmes using timely preventive applications, according to the FRAC recommendations.

2.2. *Phytophthora infestans* – Late blight

Disease incidence
In 2018, disease pressure was low in the main growing areas of Europe.

Monitoring results
(Belchim and Syngenta)

Sensitivity monitoring programs in 2018 showed full sensitivity for *Phytophthora infestans* collected from potatoes and tomatoes in Europe (Belgium, Denmark, France, Germany, Netherlands, Poland, Slovakia, Sweden, UK) and in 2016 in China (Hebei, Inner Mongolia). These studies document that populations of *Phytophthora infestans* are fully sensitive to CAA fungicides and confirm the observations of previous years.

Field performance
Field performance of registered products in potatoes and tomatoes was good when applied in spray programmes using timely preventive applications.

2.3. *Pseudoperonospora cubensis* - Downy mildew of cucurbits

Sensitivity monitoring programs in 2015 were carried out in Europe. No resistance has been detected in France, Italy and Poland. A case of CAA resistance was observed in Spain.

2.4 *Bremia lactucae* – Downy mildew of lettuce
(Syngenta, BASF)

Sensitivity studies were done with samples from 2013-2015 from France, Italy, Germany and Spain. All samples tested were sensitive.
In 2016, genetic analysis of the cesA3 gene showed that all samples from Spain, Germany and UK did not contain any known mutation potentially causing CAA resistance and were therefore classified as sensitive.

2.5 *Peronospora destructor* - Downy mildew of onions
(BASF)

Genetic analysis of the cesA3 gene in 2016 showed that all samples from Germany did not contain any known mutation potentially causing CAA resistance and were therefore classified as sensitive.

3. Use Recommendations

3.1. *Plasmopara viticola* – Grape downy mildew

Plasmopara viticola is classified by FRAC as a high-risk pathogen. Long-term experience with CAA fungicides demonstrates that the resistance risk of *Plasmopara viticola* to this fungicide group is moderate and can be managed through appropriate use strategies.

Use Recommendations:

- Apply CAA fungicides preferably in a preventive manner
- Apply a maximum of 50% of the total number of intended applications for disease control not exceeding a total of **4 (3?)** CAA fungicide sprays during one crop cycle. In areas of high resistance, the total number should not exceed a maximum **of 3 (2?)** applications during one crop cycle
- Always apply CAA fungicides in mixture with effective partners such as multi-site or other non-cross resistant fungicides
- An effective partner for a CAA fungicide is one that provides satisfactory disease control when used alone at the mixture rate
- Alternation with fungicides having other modes of action is recommended in spray programs

For more detailed product recommendations refer to the use guidelines published by the respective CAA manufacturers.

3.2. *Phytophthora infestans* – Late blight of potato and tomato

No resistant isolates from field populations have been found since the introduction of CAA fungicides in 1993.

Phytophthora infestans is classified by FRAC as a medium risk pathogen. Long-term experience with CAA fungicides demonstrates that the resistance risk of *Phytophthora infestans* to this fungicide group is low to moderate. For effective resistance management, a precautionary strategy has to be implemented.

Use Recommendations:

- Apply CAA fungicides preferably in a preventive manner
- Apply a maximum of 50% of the total number of intended applications for late blight control
- Alternation with fungicides having other modes of action is recommended in spray programs

For more detailed product recommendations refer to the use guidelines published by the respective CAA manufacturers.

3.3. *Pseudoperonospora cubensis* – Downy mildew of cucurbits

Pseudoperonospora cubensis is classified by FRAC as a high-risk pathogen.

Use Recommendations:

- Apply CAA fungicides preferably in a preventive manner
- Apply a maximum of 50% of the total number of intended applications for disease control not exceeding a total of 4 CAA fungicide sprays during one crop cycle. In areas of high resistance, the total number should not exceed a maximum of 3 applications during one crop cycle
- Always apply CAA fungicides in mixture with effective partners such as multi-site or other non-cross resistant fungicides
- An effective partner for a CAA fungicide is one that provides satisfactory disease control when used alone at the mixture rate
- Alternation with fungicides having other modes of action is recommended in spray programs

For product recommendations refer to the use guidelines published by the respective CAA manufacturers.

3.4. Other Oomycete pathogens

Some of the downy mildew pathogens are classified by FRAC as moderate risk pathogens (e.g. *Bremia lactucae)*. In spite of the use of CAA fungicides for more than 15 years against a range of such Oomycete pathogens, no reports on the occurrence of less sensitive field populations are available.

For effective resistance management, a precautionary strategy has to be implemented.

Use Recommendations:

- Apply CAA fungicides preferably in a preventive manner
- Apply a maximum of 50% of the total number of intended applications for disease control
- Alternation with fungicides having other modes of action is recommended in spray programs

For more detailed product recommendations refer to the use guidelines published by the respective CAA manufacturers.

4. Next Meeting

Next annual meeting is planned for January 22nd, 2020.