Carboxylic Acid Amides (CAA) Working Group

Annual Meeting Season 2021 on April 4th, 2022

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
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Audrey Derumier	Belchim Crop Protection, Brussels, Belgium
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Venue:
Virtual Meeting

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

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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 CAA fungicides) and that it can be managed by appropriate product use strategies (see below).

2. CAA – Resistance Monitoring 2021

2.1. CAA – *Plasmopara viticola* – Grape downy mildew

Disease incidence

In 2021, disease pressure was high in most European countries with regional differences,

Monitoring results

(BASF, Bayer, Belchim, KI-Chemical and 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 latest assessments for each country are provided. These are in most cases from populations from the 2021 season, besides another year is mentioned. Regions of interest which are not listed here, may be found in previous meeting minutes.

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

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

Switzerland
A limited number of samples was analysed from Ticino, Vaud and Wallis with moderate to high frequency values of CAA resistance.

Austria

A limited number of samples was analysed from Austria with no resistance findings in Burgenland and heterogenous (no and high values) in Steiermark.

Italy
High frequencies of resistance were observed in Lombardia, Piemonte, Trentino, Umbria and Veneto while moderate values were found in Lazio. A limited sample number was analysed for Marche, Friuli and Campania, all with high values. For Toscany and Emilia Romagna monitoring was also limited to single samples which showed moderate frequencies of CAA resistance.

Spain:
As in the years before, a heterogenous situation with no or high frequency of CAA resistance was detected in Galicia. A limited monitoring was done for Basque, resulting in a low to moderate frequency.

Portugal
Most samples from Portugal were fully sensitive, some samples contained low or moderate frequencies of CAA resistance.

Greece
Based on limited sampling, no CAA resistance was detected in Peloponnese area and moderate frequencies of CAA resistance were detected in Makedonia.

Croatia
All samples from Croatia showed high frequency of CAA resistance.

Hungary
Samples from Hungary were heterogenous and contained no to moderate frequency of CAA resistance.

Romania
Monitoring of samples across Romania showed no to moderate values of CAA resistance.

Turkey
Limited samples from Akdeniz region showed moderate frequency while samples from Dogu Marmara region were fully sensitive.

Bulgaria
Data from 2020 season with a limited CAA monitoring showed a full sensitive situation in Bulgaria.

Slovenia
A limited monitoring from 2020 showed the presence of CAA resistance in single sites.

Slovakia
The sites, which were analysed in a limited CAA monitoring in 2020 were full sensitive.

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. CAA – *Phytophthora infestans* – Late blight

Disease incidence

In 2021, disease pressure was moderate in the main growing areas of Europe.

Monitoring results

(Belchim, KI-Chemical and Syngenta)

Sensitivity monitoring programmes showed generally a full sensitive picture over Europe. Samples were taken from tomatoes and potatoes originating from Belgium, Ctech Republic, Denmark, Germany, France, Spain, Greece, Italy, Portugal, Slovakia, Netherlands, Poland, Romania, United Kingdom. However few suspicious isolates with higher EC_{50} values have been detected and are currently under further investigation.

Sensitivity monitoring programs in previous years showed full sensitivity for *Phytophthora infestans* collected from potatoes and tomatoes in Europe (Belgium, Croatia, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Lithuania, Latvia, Netherlands, Poland, Portugal, Slovakia, Spain, Sweden, UK).. From China, data are available from 2016 (Hebei, Inner Mongolia) and all samples were sensitive.

Genotypes of *Phytophthora infestans* are classified by Euroblight. These genotypes could express variable aggressiveness, but are not necessarily linked to fungicide resistance, which is genetically independent.

Field performance

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

2.3. CAA – *Pseudoperonospora cubensis* - Downy mildew of cucurbits

(Syngenta)

In 2020 and 2021 full sensitivity was monitored in samples collected from cucumber, melon and zucchini in Croatia, Germany, Hungary, France, Greece, Poland, Switzerland. Single strains showing CAA resistance were detected in Italy in 2020 and in Spain from 2021, however most of the samples from both countries were sensitive.

All samples collected from China (6 provinces) between 2019 and 2020 confirmed full sensitivity based on molecular analysis.

Two trial sites from US (South Carolina and Florida) confirmed the presence of the previous published mutation G1105W in the cesA3 associated to CAA resistance (Blum *et al.* 2011, *Pest Management Science* 67, 1211-1214).

2.4 CAA – *Bremia lactucae* – Downy mildew of lettuce

(Syngenta, BASF)

Full sensitivity was monitored in 2020 and 2021 from samples collected in Belgium, Germany, Spain, Greece, Croatia, Hungary and Italy.

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.
In 2018 and 2019 samples collected from France, Greece, Germany, Netherlands and Italy were sensitive.

2.5 CAA – *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. CAA – Use Recommendations

3.1. CAA – *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.

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

3.2. CAA – *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. CAA – *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. CAA – 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 20 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 17th, 2023.