Resistance management in potato pathogens and updated FRAC guidelines

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Risk Factors for Resistance Development determining need for Resistance Management in Potatoes

Matrix triggers Resistance Management activities in main potato diseases

- Inherent Risk Factors classified according to FRAC as Low to High Risk for:
  - Agronomic Risk
  - Fungicide Risk
  - Pathogen Risk
- Multiple Resistance needs to be considered

➢ **Implications for Resistance Management**

Early and Late Blight Pathogens of Potatoes need to be monitored and implementation of resistance management strategies is advised

Fungicide risk

Fungicide Risk / Pathogen Risk				
High risk OSBPIs PAs QIs** SDHIs*	6	**6**	**12**	**18**
Medium risk APs CAAs* Carbamates* Cymoxanil* DMIs Fluopicolide Zoxamide	4	**4**	**8**	**12**
Low Risk fluazinam Multi-sites	1	**1**	**2**	**3**
		1	2	3
Fungicide Risk / Pathogen Risk		**Low Risk** *Rhizoctonia* *Helminthosporium* Soil borne fungi	**Medium Risk** *Alternaria solani* *Phytophthora infestans*	**High Risk** *A. alternata*

Pathogen risk

*highest risk class mentioned **QI: QiI*, QioiSI*, QoI

Setting the Stage for Resistance Development

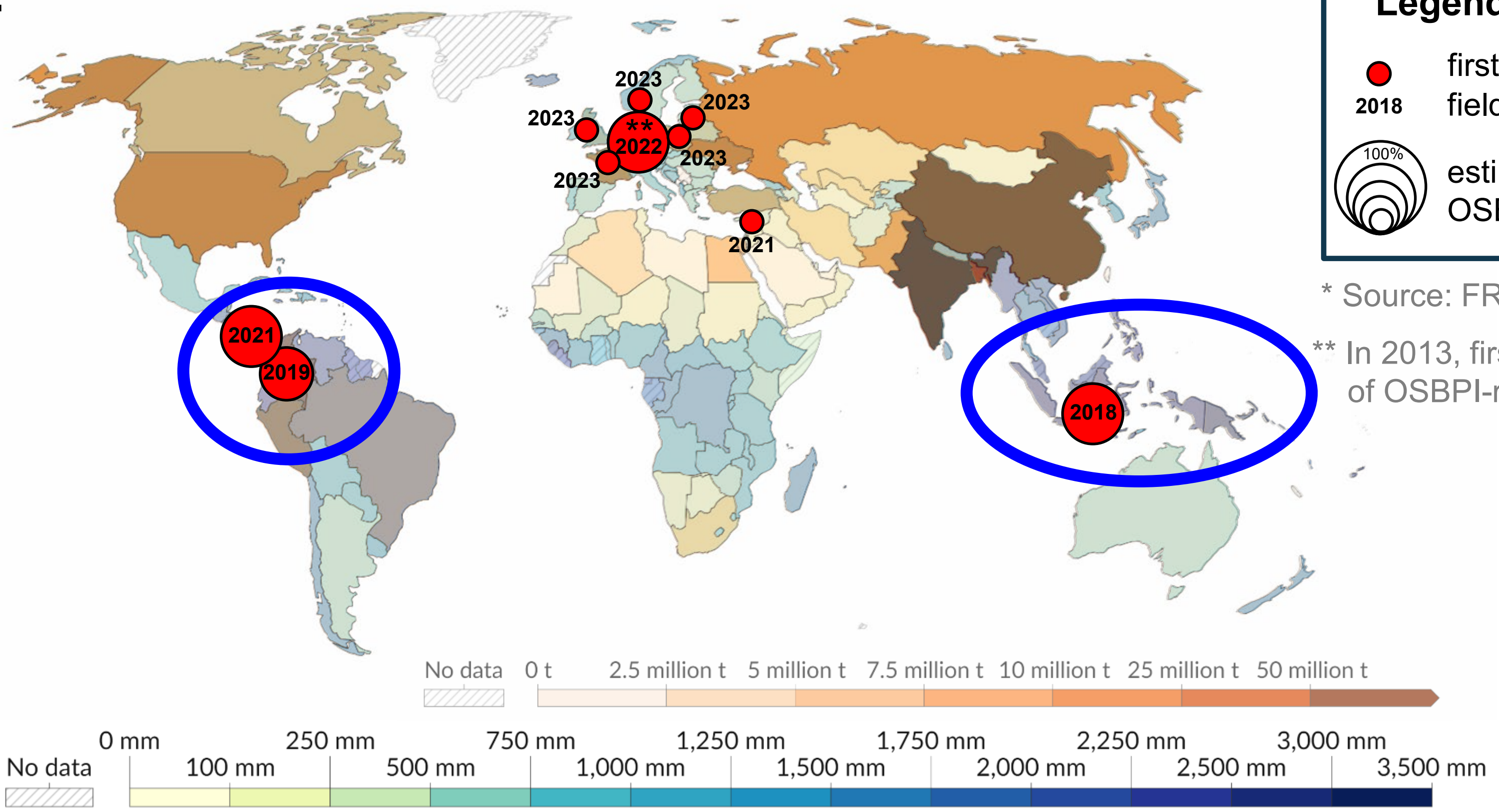
Agronomic Risk

Agronomic Risk – Environment and Agronomic practices influence Resistance Development of *P. infestans* to OSBPIs in Potatoes

Average annual precipitation [mm/a] and potato production [t/a] in 2022

Agronomic Risk defined by:

- climatic conditions favoring the disease
- agricultural practice:
  - crop rotation
  - tolerant cultivars
  - irrigation
  - sanitary measures
  - fertilization
  - adoption of IPM
  - etc.
- number registered MOA's



Legend:

- 2018 — first year of confirmed field OSBPI-resistance*
- 100% — estimated frequency of OSBPI-resistance*

* Source: FRAC OSBPI WG Minutes

** In 2013, first field trial observation of OSBPI-resistance in Netherlands (Mboup *et al.*, 2021)

- Agronomic Risk the highest in Central America and South-East Asia, also multiple potato crops per year
- first detection and spread of OSBPI-resistance in these high risk areas

Resistance Mechanism determine Evolution of Resistance

Fungicide Risk

mainly alteration at target site

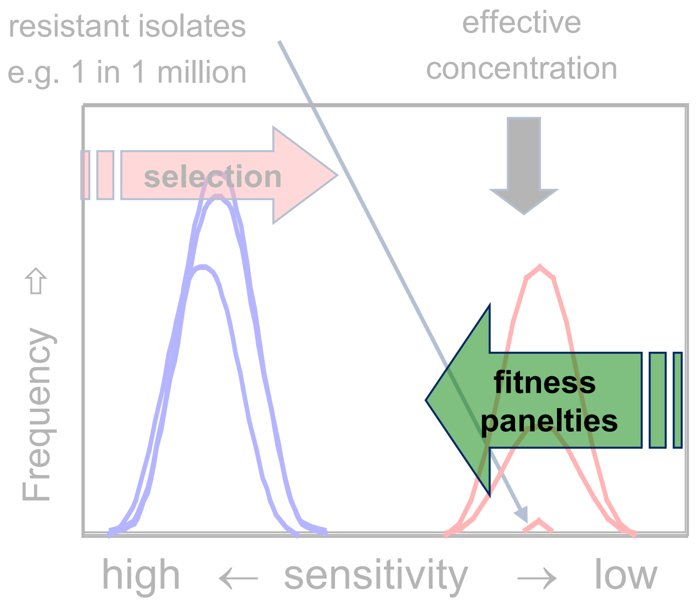
further minor mechanisms:

- increased efflux (pumps)
- target-site overexpression
- decreased demand for target-site product

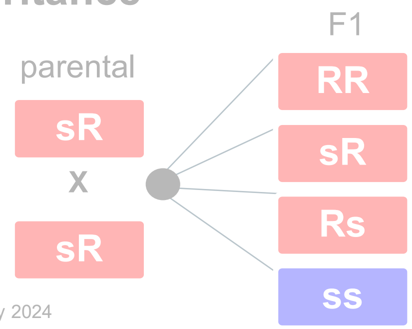
Monogenetic Resistance – Single Mutation causing high R. Factors and <u>Dominant</u> Inheritance

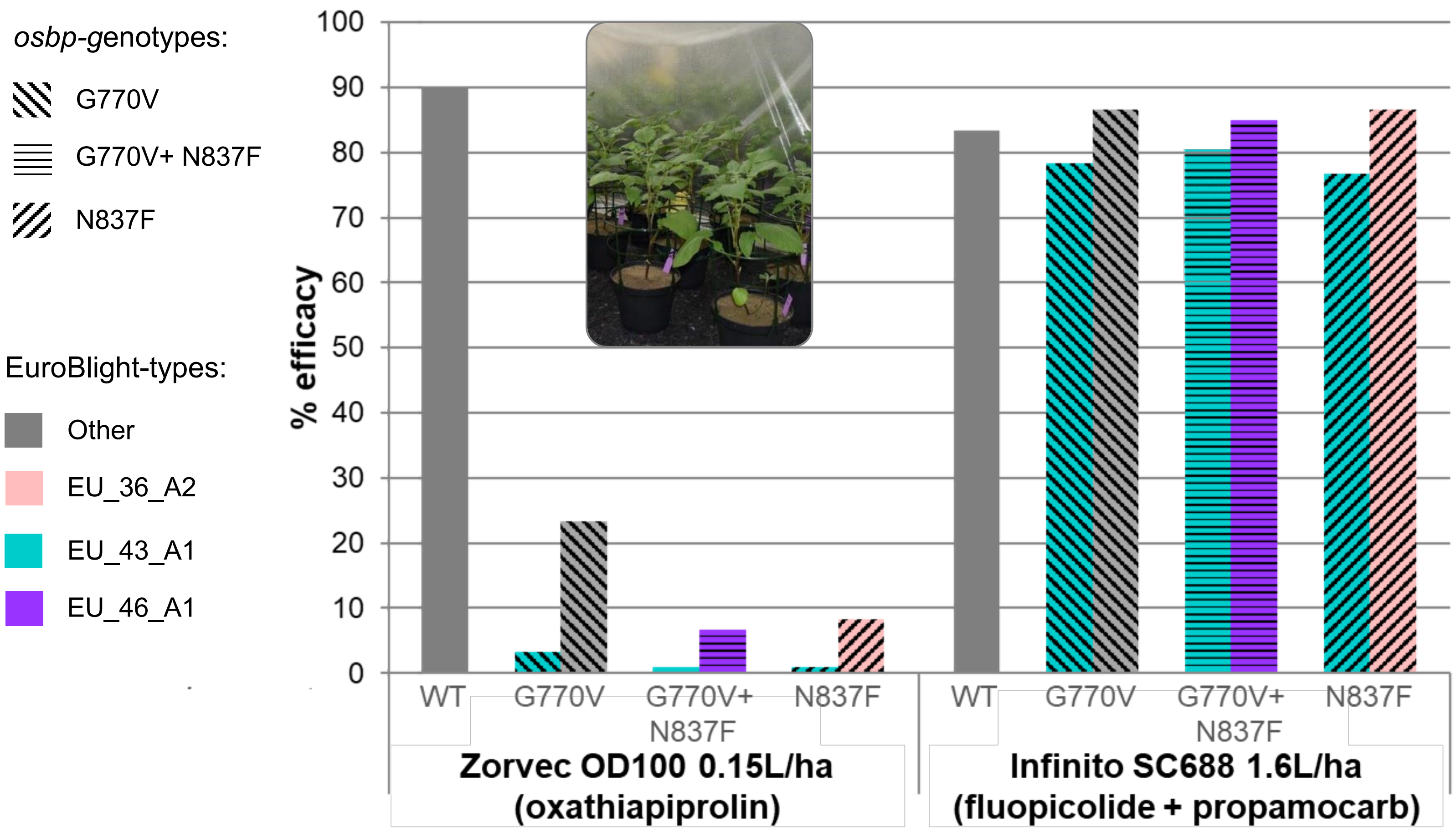
Disruptive Selection (sexual & asexual), e.g. *A. alternata* for QoI- and OSBPI-resistance in *P. infestans*

Monogenetic Resistance



Dominant Inheritance





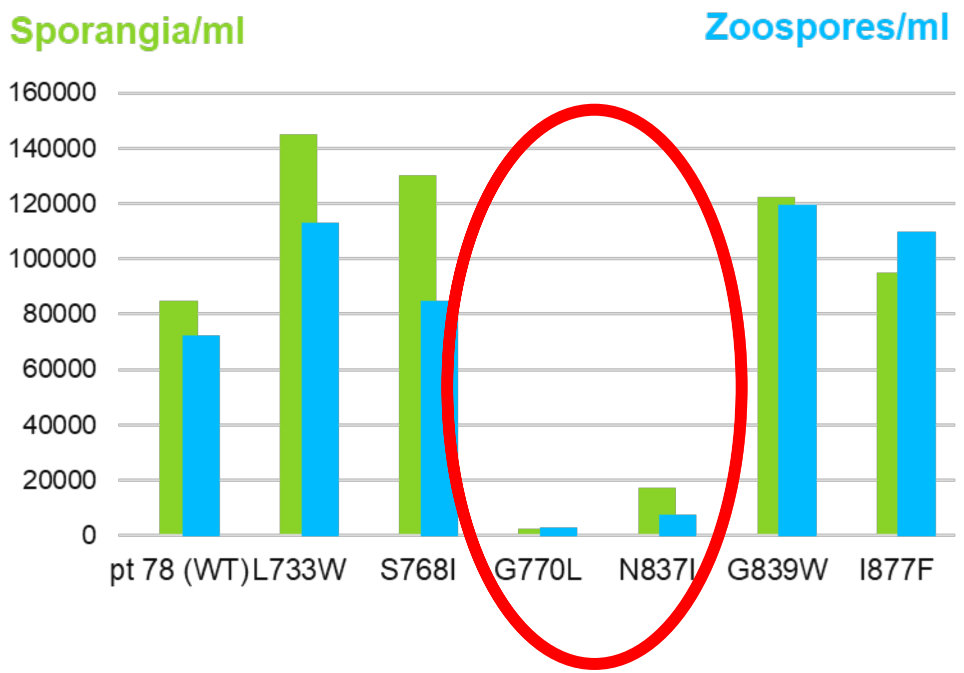
- all *osbp*-genotypes lead to a strong reduction in efficacy of solo OSBPIs
- independent of EuroBlight-types (EU_36, EU_43, EU_46 or 'Other')

Monogenetic Resistance –
Single Mutation causing high R. Factors and Dominant Inheritance

Gene editing of *P. infestans* and subsequent sensitivity and fitness penalty testing

osbp-genotype	Mean Resistance Factor (RF)	
	oxathiapiprolin	fluopicolide
L733W	36	0,5
S768I	18	1
G770L	625	1
N837I	22 (field: >100)	1
G839W	1142	1
I877F	30	0,4

transformation not for all mutations successful:
- G624R, S/G*850T, P861H, L863W/F, I954M
- also further amio acid changes possible (e.g. 770A/I/V/P, 837F/Y)

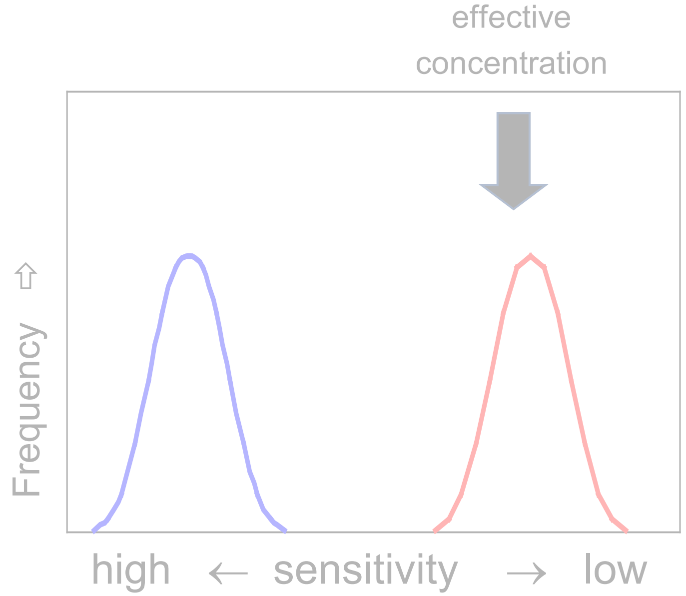


- **transformation was not successful for all amino acid substitutions (also at relevant positions)**
- **fitness penalties for substitutions at position 837 and 770 => allows resistance management !**
- **continuation of research needed…**

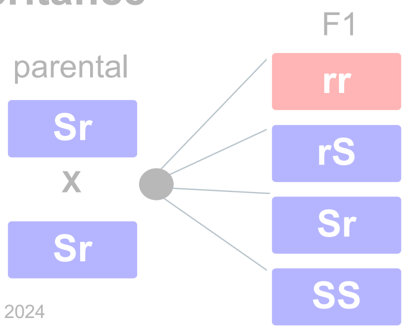
Monogenetic Resistance –
Single Mutation causing high R. Factors and Recessive Inheritance

`Disruptive Selection´ only during asexual cycles, e.g. CAA-resistance in *P. infestans*

Monogenetic Resistance



Recessive Inheritance



EU_36_A2 EU_43_A1 EU_46_A1
Revus SC250 0.6 L/ha
(mandipropamid)

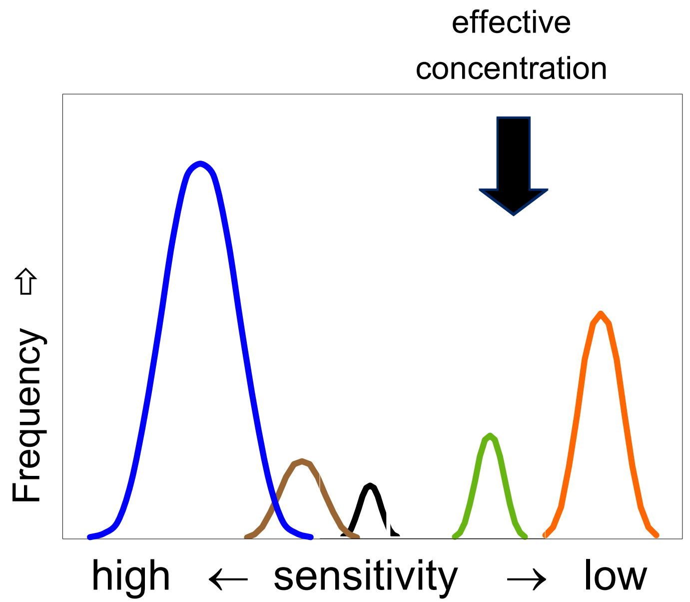
EU_36_A2 EU_43_A1 EU_46_A1
Infinito SC688 1.6L/ha
(fluopicolide + propamocarb)

- (probably) homozygote EU_43 strains showed full resistance to CAAs
- also EU_46 strains with full CAA-resistance collected in NL und DE

Monogenetic Resistance – Different mutations cause varying Resistance Factors

Depends highly on mutation and (SDHI-)fungicide tested, e.g. SDHI-resistance in *A. solani*

Monogenetic Resistance, but...



… different Resistance Factors (RF)

Genotype	n	mean RF	
		Boscalid	Fluopyram
B-H278R	9	137	
C-H134R	12	>1200	
C-H134Q	1	50	
D-D123E	1	35	
…			

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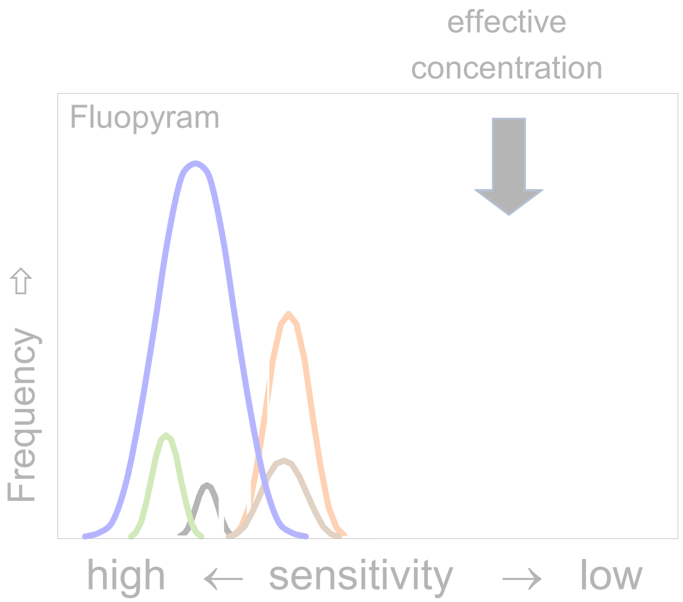
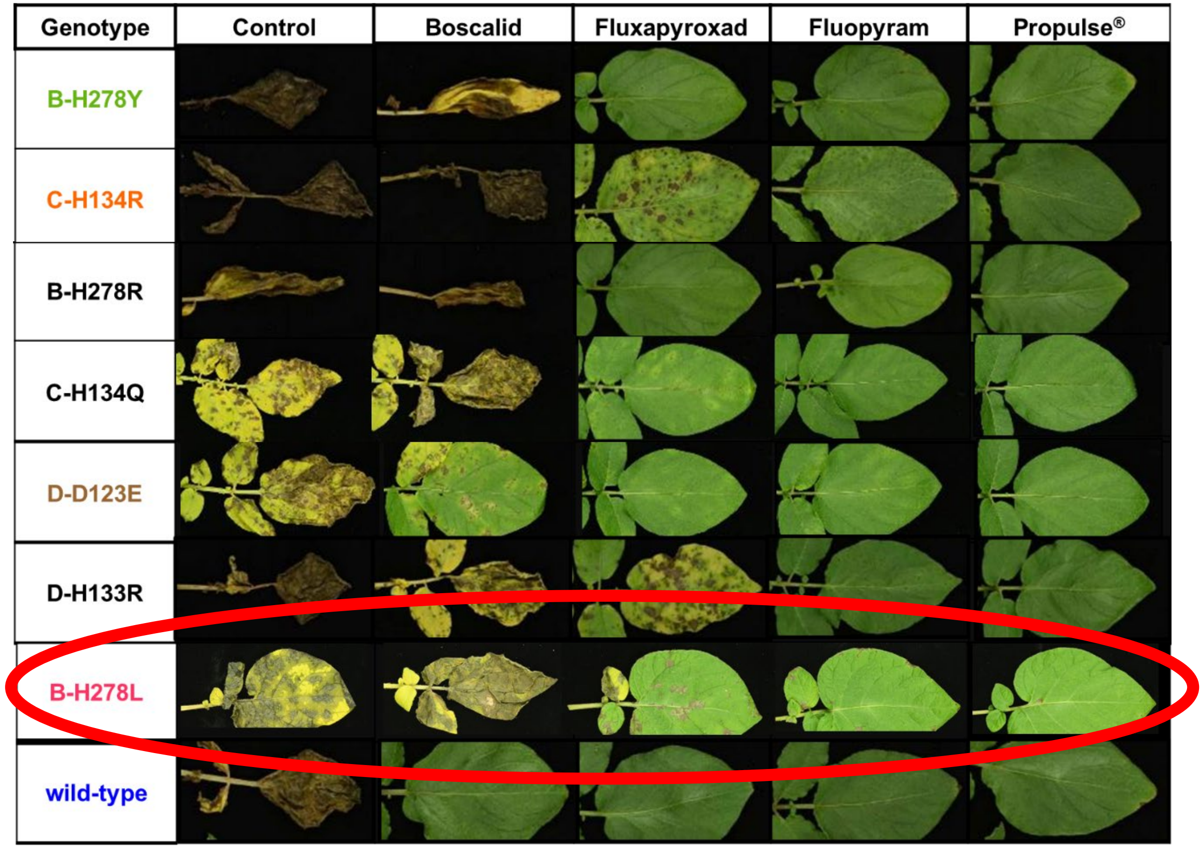


… different Resistance Factors (RF)

Genotype	n	mean RF Boscalid	mean RF Fluopyram
B-H278R	9	137	1
C-H134R	12	>1200	32
C-H134Q	1	50	10
D-D123E	1	35	31
…			

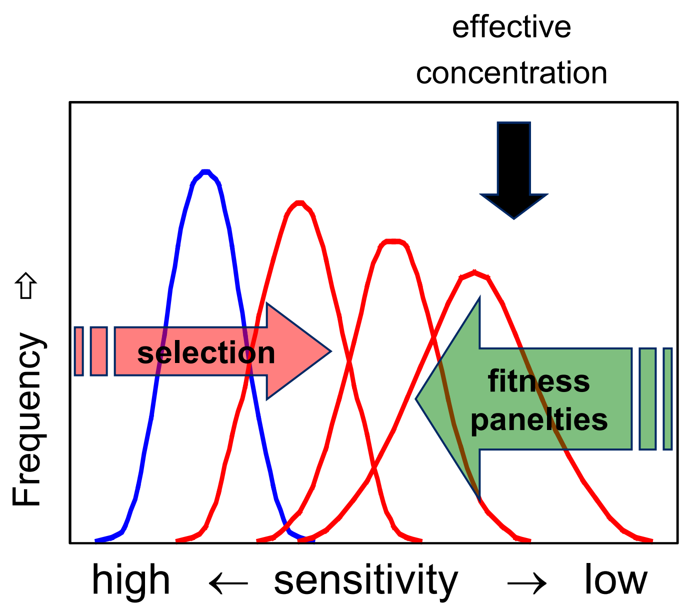


- incomplete cross-resistance explains difference in efficacy of SDHIs
- first finding of new genotype *sdh*B-H278L, also controlled by Fluopyram

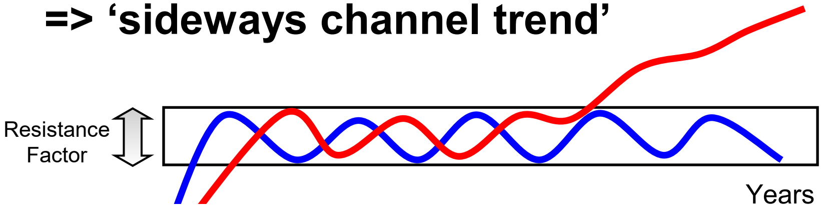
Polygenetic Resistance –
Several Mutations have to accumulate to lower sensitivity

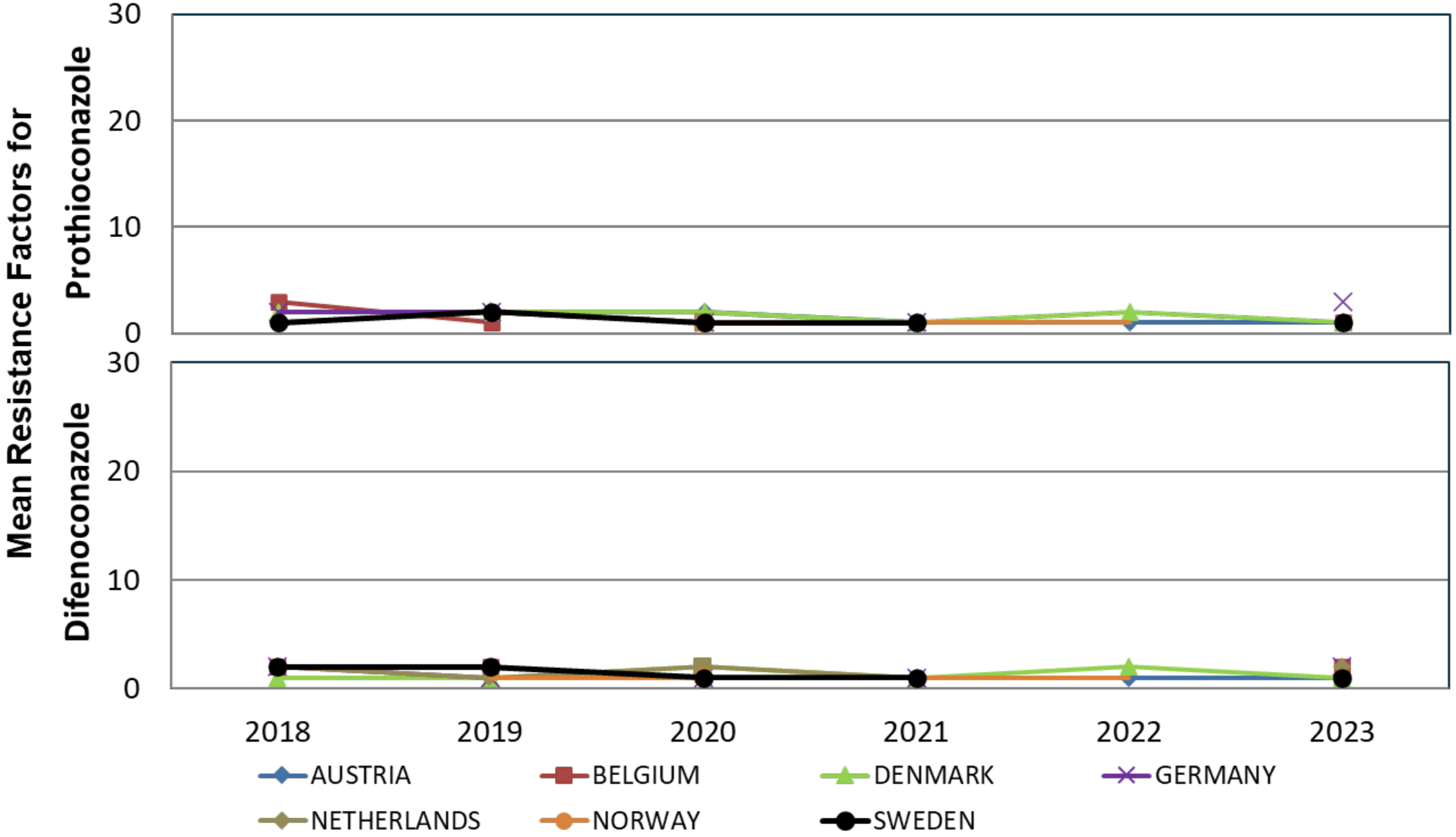
Continuous `Shifting´, but high RF unlikely to dominate population, e.g. DMI-sensitivity in *A. solani*

Polygenetic Resistance, lead to...



… shifting & back-shifting over time
=> 'sideways channel trend'





- mEC$_{50}$-values close to baseline resulting in Resistance Factors (RF) ~ 1
- no hint for relevant shifting of *A. solani* populations in Europe

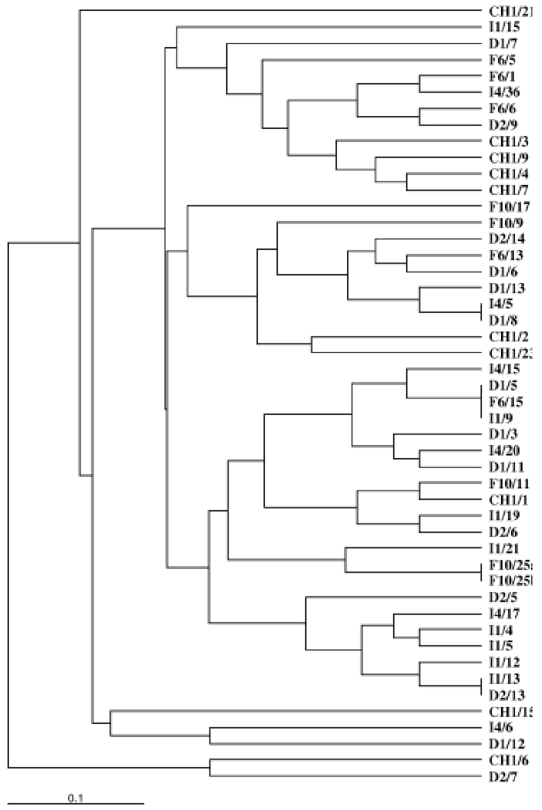
Accelerator of Emergence and/or Spread of Resistance

Pathogen Risk

Genetic diversity of *Plasmopara viticola* and *Phytophthora infestans* using SSR-markers

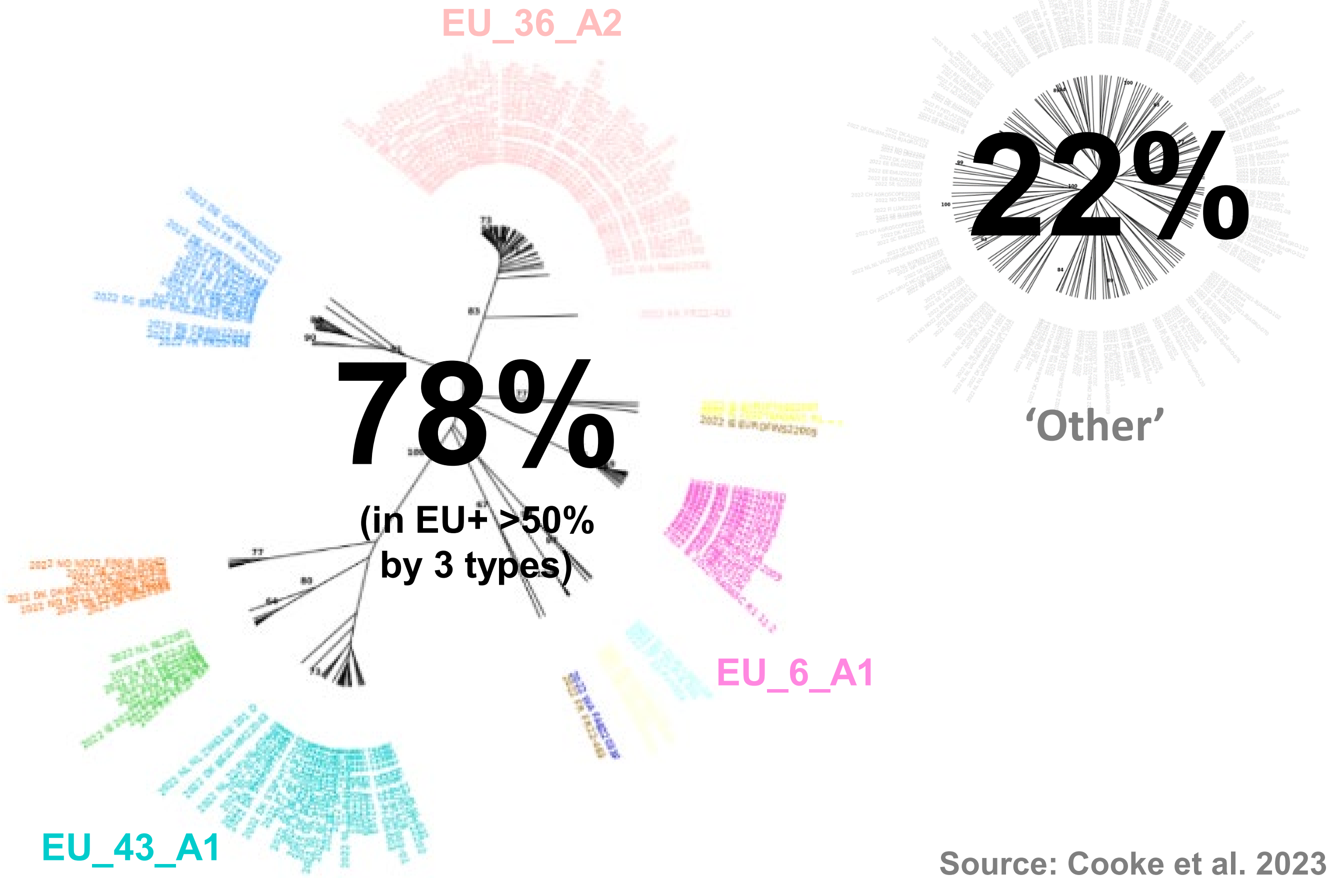
EuroBlight
A potato late blight network for Europe

Plasmopara viticola (High Risk Pathogen)



Source: Scherer & Gisi. 2006

Phytophthora infestans (Medium Risk Pathogen)



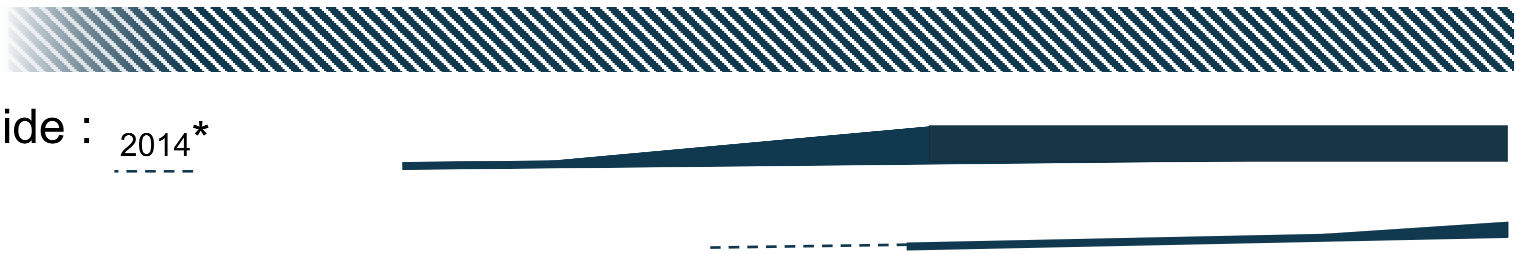
Source: Cooke et al. 2023

- high genetic diversity for *P. viticola*: a distinctive multi-locus genotype for almost each isolate
- distinct clusters of sub-clonal EuroBlight-types make up majority of *P. infestans* population in EU+ in 2022

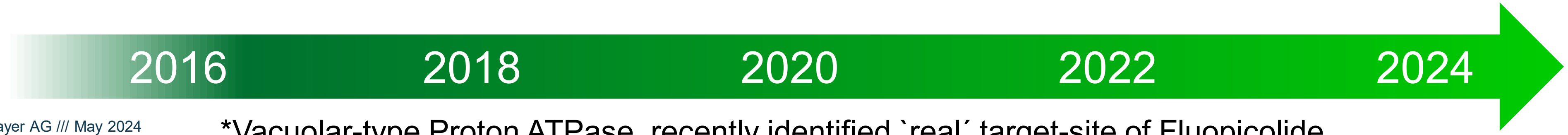
Development of resistance towards four Modes of Action by two important Oomycetes in selected EU-countries

Schematic evolution from first findings to frequencies impacting field efficacy

Plasmopara viticola**:** example France (Sources: Bayer, FRAC WGs)



- CAA: but recessive crossing
- Fluopicolide : constant low to moderate
- OSBPI: few farmers field sites
- resistance reported against seven main modes of action:
  - CAAs, fluopicolide, OSBPIs, PAs, QoIs, QiIs (e.g. amisulbrom), QioSI (ametoctradin), zoxamide
  - Isolates detected with multiple resistance towards 7 compounds of 5 modes of action



* first trial observation of field resistance

*Vacuolar-type Proton ATPase, recently identified `real´ target-site of Fluopicolide

Development of resistance towards four Modes of Action by two important Oomycetes in selected EU-countries

Schematic evolution from first findings to high frequencies impacting field efficacy

***Plasmopara viticola*: example France (Sources: Bayer, FRAC WGs)**

- CAA: but recessive crossing
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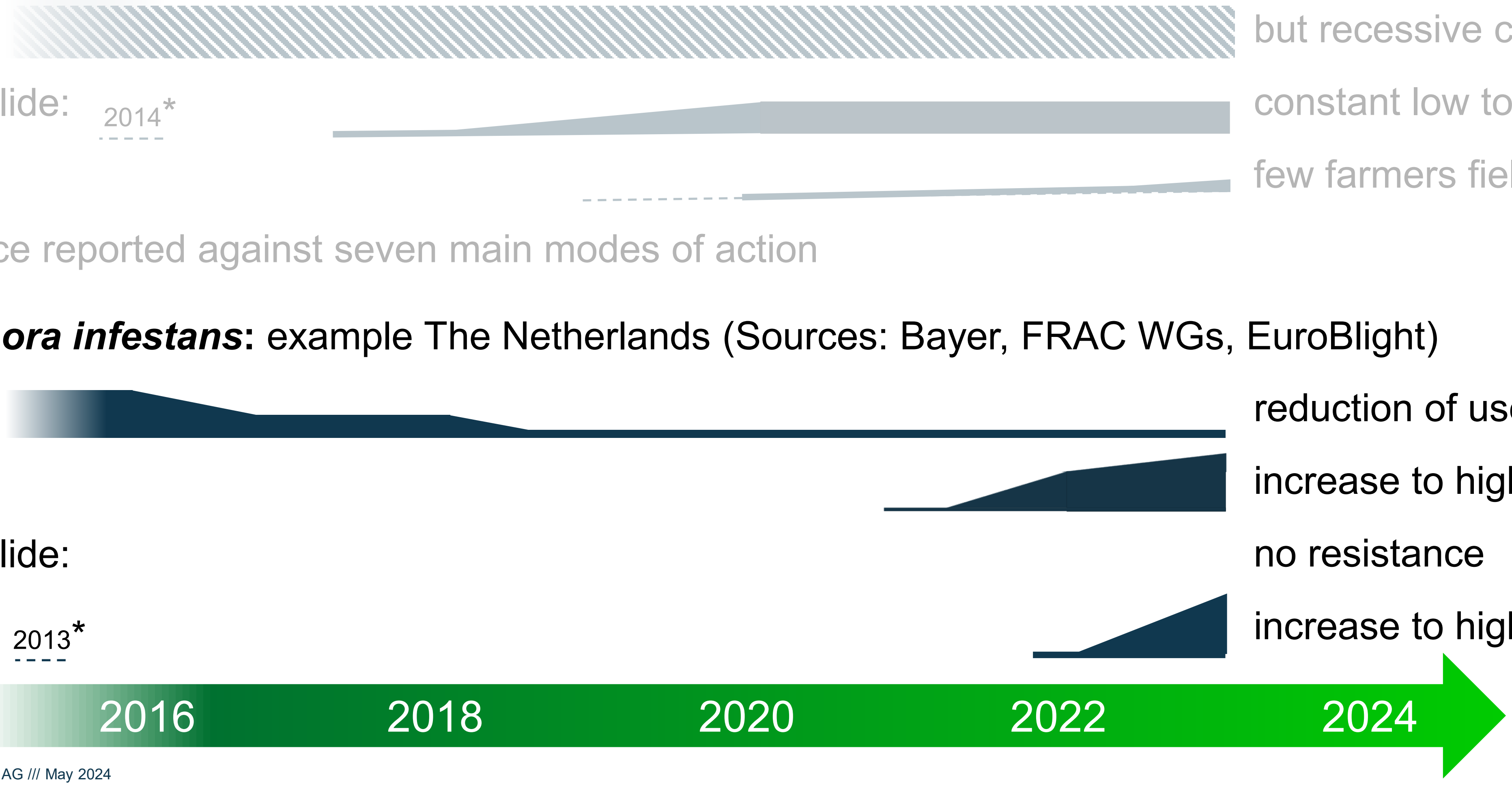
- resistance reported against seven main modes of action

***Phytophthora infestans*: example The Netherlands (Sources: Bayer, FRAC WGs, EuroBlight)**

- PA: reduction of use
- CAA: increase to high level
- Fluopicolide: no resistance
- OSBPI: increase to high level



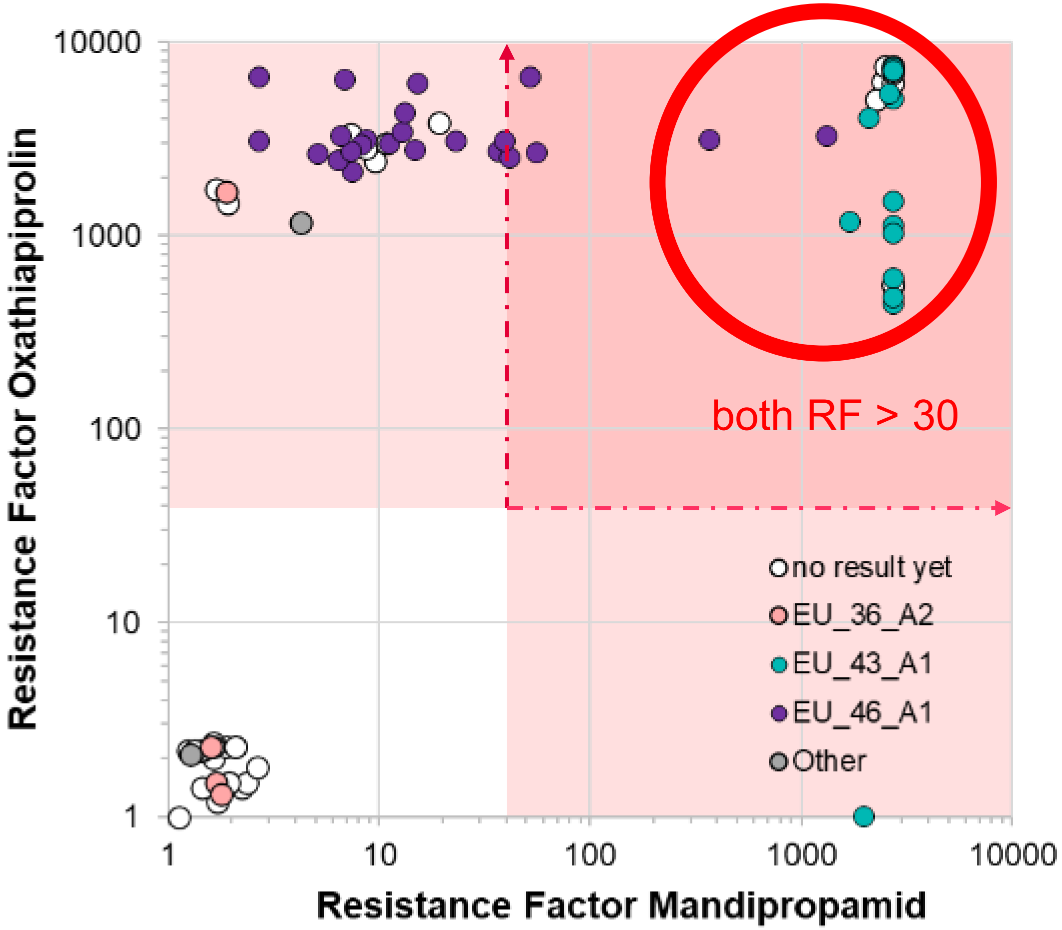
* first trial observation of field resistance

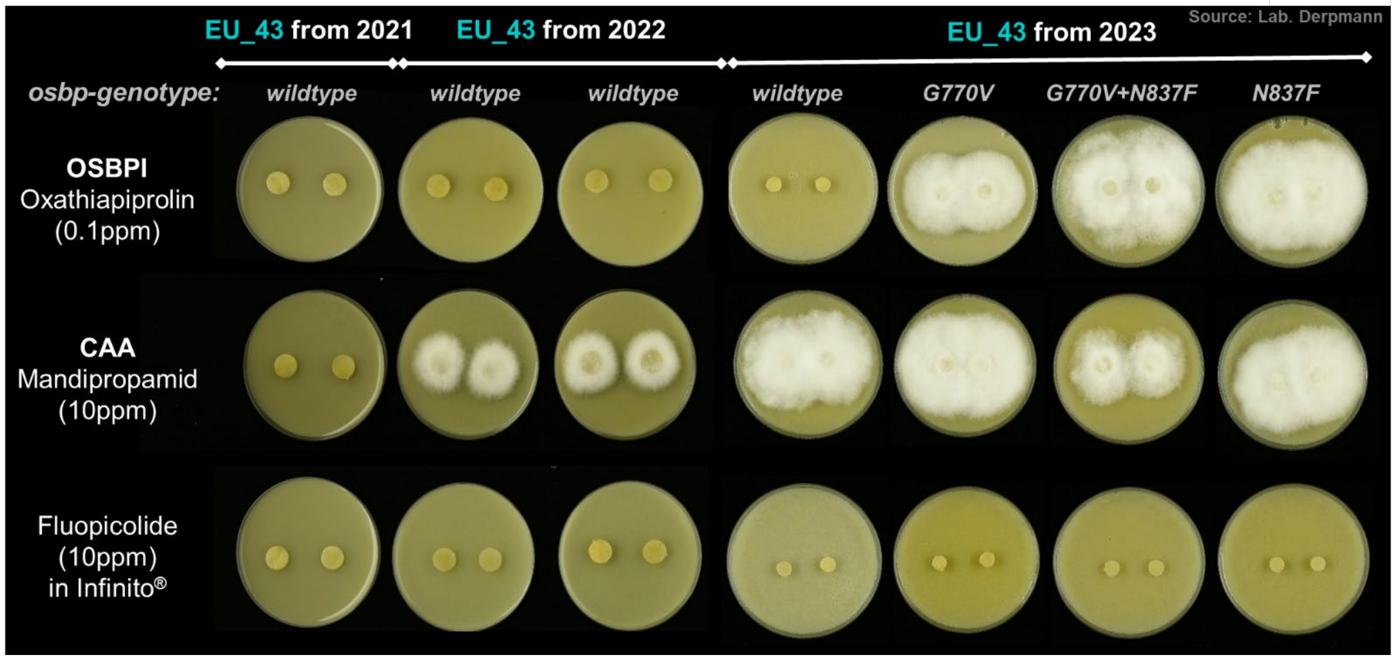
Multiple Resistance and Implications for Resistance Management

Phytophthora infestans

Multiple resistance study with two Modes of Action with different *P. infestans* strains from DE and NL collected in 2023

in-vitro Resistance Factors to CAA and OSBPI of different EuroBlight-types





- **multiple resistance (= CAAs + OSBPI) detected in EU_43, also cases of EU_46 (probably homozygote G1105S in *cesA3*)**
- **for example in NL the EU_43 sub-population accumulated multiple resistances from 2021 to 2023**

Control of *P. infestans* in EU – FRAC & Bayer perspective: Implement diverse strategy to include all available control measures

difficult to find right balance between no. of Modes of Action (MoA), in accordance to no. of applications

Fungicide or MoA	total 12 sprays	Comment
CAAs	1 – 2 (6*)	mixtures, disruptive resistance
OSBPIs	1 – 2*	mixtures, disruptive resistance
PAs	1 – 2	mixtures, disruptive resistance
Cymoxanil	2 – 4	
Fluazinam	2 – 4	reduced sensitivity detected
Fluopicolide+ Propamocarb	2 – 4	sporicidal activity
QiIs	2 – 4	sporicidal activity
QioSIs (ametoctradin)	2 – 4	sporicidal activity
QoIs (strobilurines)	2 – 4 (6*)	mixture, otherwise max. 3
Zoxamid	2 – 4	

Important considerations:

- apply recommended dose rate and adhere to spray window
- **use preferably in-tank mixtures or ready-mixtures**
- **avoid block applications**
- **do not use mixtures with MoA with known resistance at beginning of season**
- in case of known resistance to one MoA, the mixing partner should have full dose rate
- no mix of MoA in case of known resistance to both MoA

- adapt number of applications based on resistance, but be cautious not to overuse a single MoA
- the more different fungicide classes are registered and used, the more stable the system !

* max. number recommened by FRAC

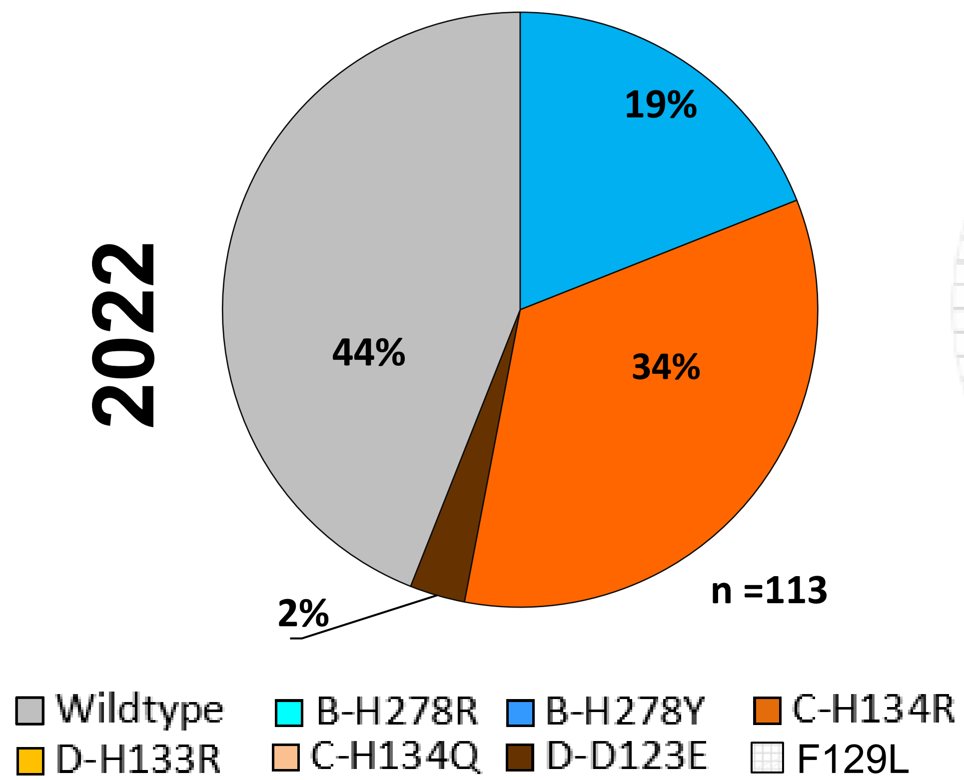
Multiple Resistance and Implications for Resistance Management

***Alteraria* spp.**

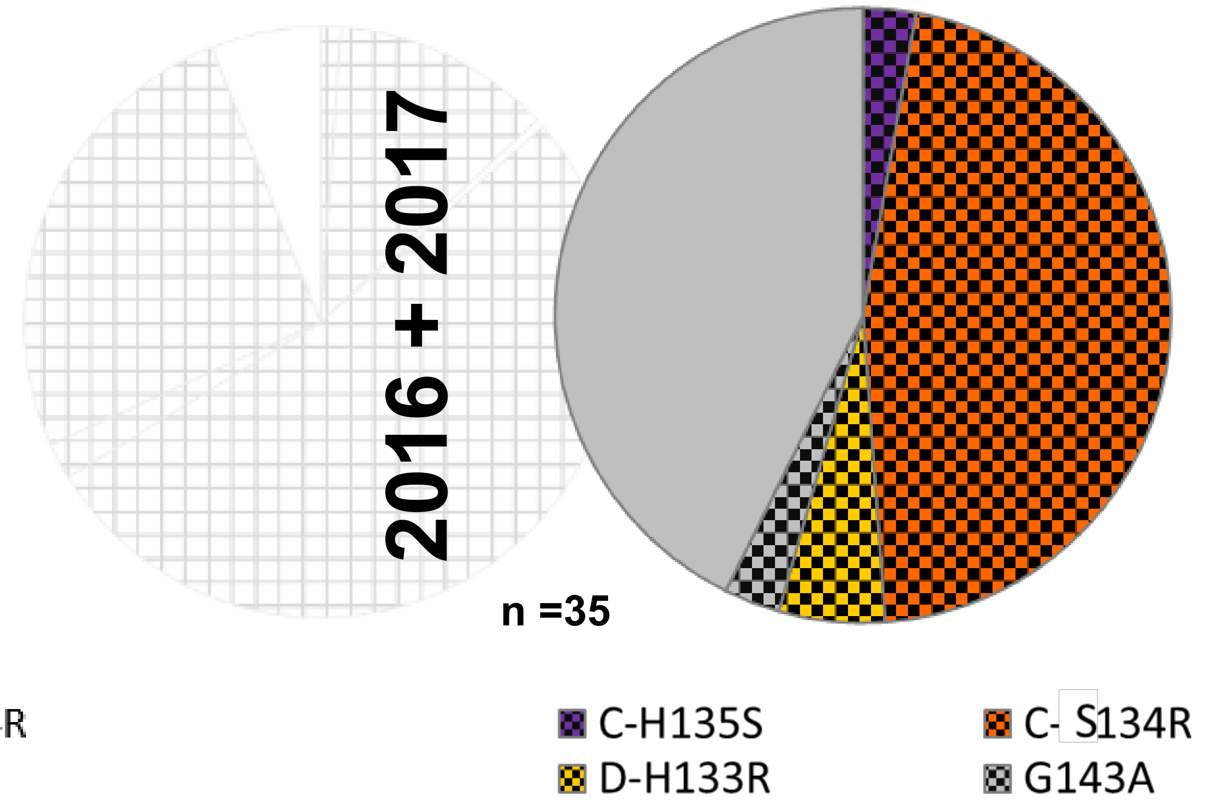
Alternaria spp. – mutation analysis for SDHIs and QoIs

frequency of different *sdh*- and *cytb*-genotypes in European potato fields

Alternaria solani:



A. alternata:



- ***A. solani:*** **majority of isolates with mutations in *sdh*-genes have F129L-mutation in *cytB*-gene**
- ***A. alternata:*** **all isolates with mutations in *sdh*-genes have G143A-mutation in *cytB*-gene**

Source: www.frac.info

Control of *Alternaria* spp. in Potatoes – FRAC Recommendations for resistance management

QoI Working Group

- resistance confirm, then must apply only in mixtures
- mixtures: do not exceed 50% or a max. of 6 QoI applications, whichever is the lower
- should be used preventive
- use in spray program with effective fungicides from different cross-resistance groups

SDHI Working Group

- mixture partner should provide satisfactory control when used alone on the target disease and must have a different MoA
- mixture: max. 2 consecutive
- guideline for no. of sprays:

Total no. of sprays in crop	1-3	4	5	6-7	8
Solo SDHI	1	1	2	2	3
SDHI in mixture	1	2	2	3	3

SBI Working Group

- users must adhere to manufacturers recommendations (e.g. dose, spray interval)
- make alternation or mixtures with. effective non cross-resistant partner
- DMIs should be used preventative and curative situations should be avoided
- fungicide use does not replace the need for GAP

Anilinopyrimidines Working Group

- max. number of applications should not exceed more than 50% of all treatments
- for sound resistance management, good agricultural practices, including phytosanitary measures and crop protection, should be followed not only in commercial practice, but also in nurseries

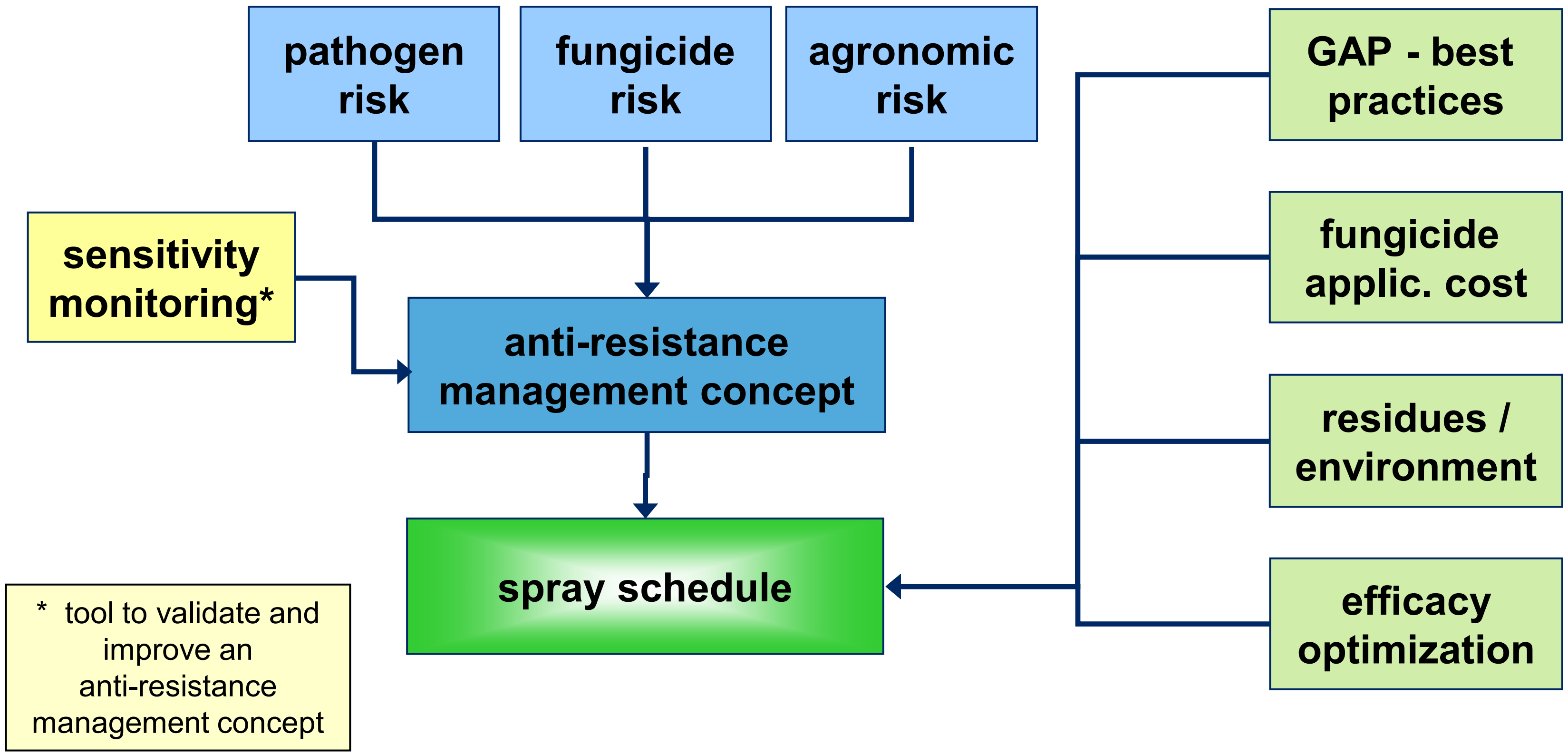
Optimal Resistance Management - following the Golden Rules:

- fully implement the FRAC guidelines
- consider the regular use of mixtures
- do not use only the top fungicides (SBIs, SDHIs)
- do not under-dose the mixing partners with different mode of action => sufficient efficacy
- lower the overall infection pressure as much as possible (best practices!)

➢ **The more different fungicide classes used, the more stable the system !**

How to define a rational Resistance Management Concept?

Resistance Management is one of multiple factors determining an effective spray schedule



Good Agronomic Practice (GAP):

- Crop Rotation
- Primary inoculum sources
- Planting time and density
- Fertilization
- Irrigation
- Cultivar tolerance
- Prediction models
- Decision Support Schemes

strategy: rational use of available control tools (incl. MoA), optimized by a high feedback from effective monitoring systems & embedded in a robust disease management concept

Thank you!