Fungicide Resistance Management

Part 1 – Evolution of Resistance

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Evolution of Fungicide Resistance

Individual organisms have the ability to:

- *grow*,
- *differentiate*, and
- *respond to environmental changes*

Pathogenic Fungi

"Trained" to grow at ever higher concentrations …

- Metal toxicants
- DMI fungicide triforine

Evolution of Fungicide Resistance

Phenomic Adaptation (*general*)

Physiological adjustment of an individual organism without change in genetic constitution

Non-Genetic Resistance (*specific*)

Pathogenic fungus alters its physiology, enabling growth in a fungicide amended environment

Evolution of Fungicide Resistance

Non-Genetic Resistance

Little Practical Importance for Agriculture

1. If fungicide removed … resistance immediately lost (becomes sensitive)
2. No genetic change … no inheritance of these acquired characteristics

Evolution of Genetic Resistance

Evolution of Fungicide Resistance

Development of Genetic Resistance

Probability of developing fungicide-resistant plant pathogens is dependent on:

Factors Influencing Evolution of Resistance

1. *Rate of mutation* of genes conferring resistance
2. *Rate of selection* for these mutants

Evolution of Fungicide Resistance

Definitions of Mutation

Mutation

Def. #1: A heritable change in the genetic material of an organism

Def. #2: A change in the sequence of nucleotide bases in the DNA polymer

Types of Mutations – Examples

- Deletion
- Duplication
- Insertion
- Inversion

Evolution of Fungicide Resistance

Characteristics of Mutations

- Mutation is a chemical process
- Important mutagenic agents:
  - Temperature, radiation, chemicals
- Low population frequency
  - 1×10^{-4} to 1×10^{-9}
  - Occurrence of dodine-resistant *Venturia inaequalis* mutants is 1 in 1,385,714
- Most mutations are deleterious

Evolution of Fungicide Resistance

Characteristics of Mutations

What about Fungicides?

- Some fungicides are mutagens at high concentrations, but …
- No evidence that directed mutagenesis occurs at doses used in practice

Evolution of Fungicide Resistance

Characteristics of Mutations

Do mutations result in fungicide resistance?

Not entirely …

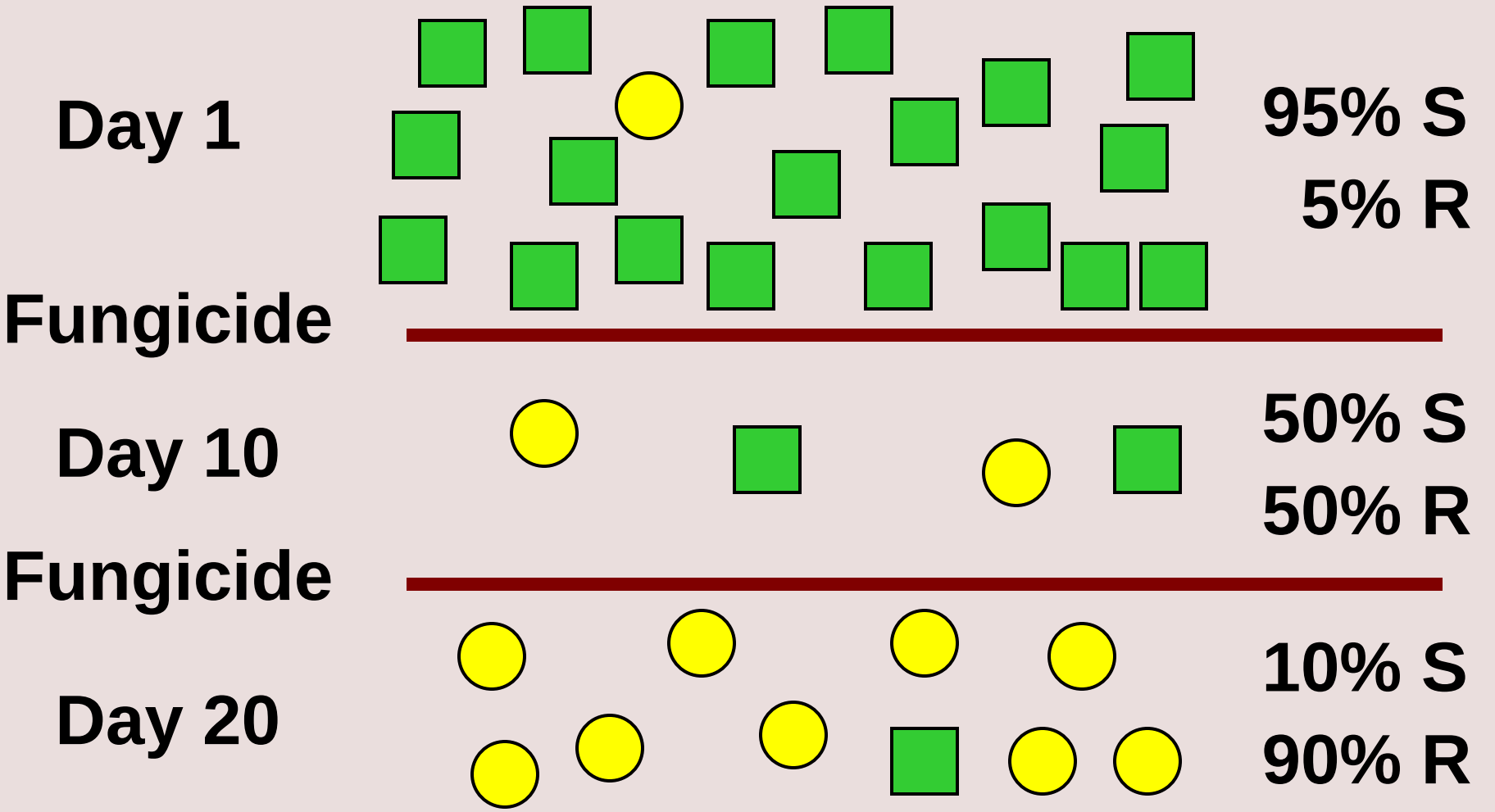
- Rate of mutation is too low to generate populations of mostly resistant strains
- *Selection* for the resistant strains must occur next …

Evolution of Fungicide Resistance

Selection for Resistant Strains

Evolution of Fungicide Resistance

Selection for Resistant Strains



Evolution of Fungicide Resistance

Selection for Resistant Strains

Fungicide-Sensitive Subpopulation

Fungicide-Resistant Subpopulation

Will application of the fungicide select for resistance?

Not necessarily!

Fungicide resistance is only one of many traits that bestow *fitness*!

Evolution of Fungicide Resistance

Selection and Fitness

One organism is more ***fit*** than another if it has:

1. Greater reproductive potential
2. Greater success of survival

Fitness – relative reproductive success

The organism with greater *fitness* will have more of its genes present in succeeding generations

Evolution of Fungicide Resistance

Fitness Attributes of Fungal Plant Pathogens

Epidemiological Fitness Parameters

- Colonization
- Sporulation
- Latent period
- Infection efficiency
- Temperature range
- Moisture range

…. and so on ….

- Fungicide resistance

Selection for other fitness parameters important to survival of newly resistant strain

Evolution of Fungicide Resistance

Selection Process

Multidimensional … consists of two phases

1. Selection for resistance regardless of other traits
2. Progressive organization of the genetic background for greater fitness (esp. via genetic recombination)

The longer the selection process in step 2 ("*aging*"), the greater the persistence of the resistant population; i.e., resistant pathogen becomes more fit

Evolution of Fungicide Resistance

Summary of Process

Development of a Resistant Population

1. Mutation in DNA bestowing resistance
2. Multidimensional selection process
   - ❖ Selection for resistance trait
   - ❖ Selection for other fitness parameters

FUNGICIDE RESISTANCE MANAGEMENT

PART 2 – FUNGICIDE CHEMISTRIES

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Fungicide Chemistries

Fungicide 101

- Fungicide Basics
  - **Protectant** vs **Penetrant**
  - **Mode of action**: **single site** vs **multi-site**

- **Fungicide Resistance Action Committee (FRAC):** Group codes
  - Knowing the fungicides
    - Group – Trade name – Fungicide family – Common Name
  - Risk

Fungicide Chemistries

Fungicide Basics: Protectant vs. Penetrant

Protectant

- "**Contact**"
- **No movement into plant**
- Applied **prior** to infection
- **Needs to be re-applied**
  - New growth
  - Not rainfast

Examples: Manzate, captan, copper

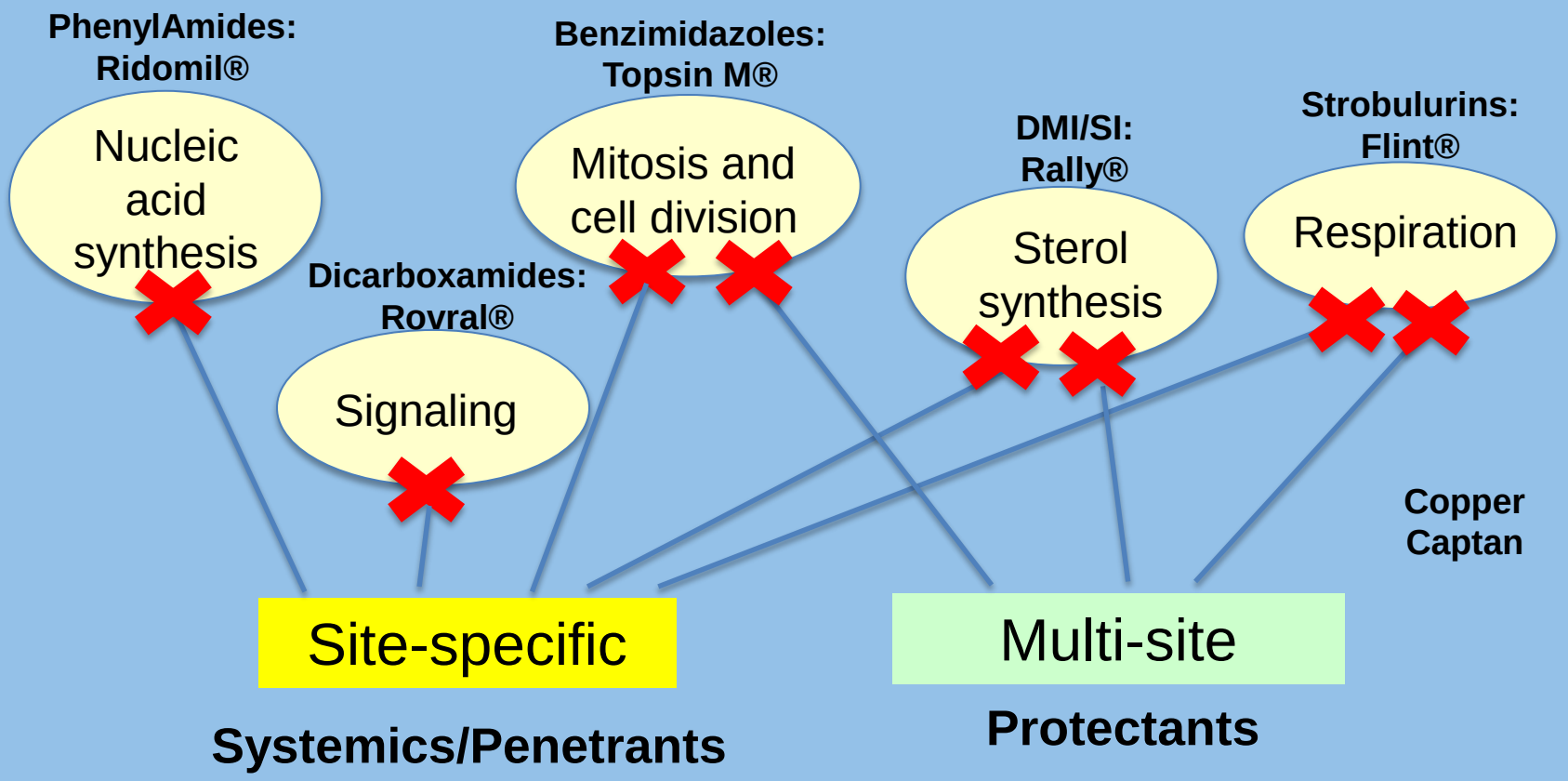
Penetrants = Systemics

- **Absorbed** into plants following application
  - **Rainfast**
- Less thorough coverage to be effective
- Protectant and/or "curative":
  - **Inhibit/slow fungal growth**
    - During early stage of infection
- **Examples**: Vangard, Flint, Pristine

Fungicide Chemistries

Fungicide Basics: Mode of Action (MOA)

The specific way fungicide poisons the fungus:
Disrupts important biochemical processes causing the fungus to die



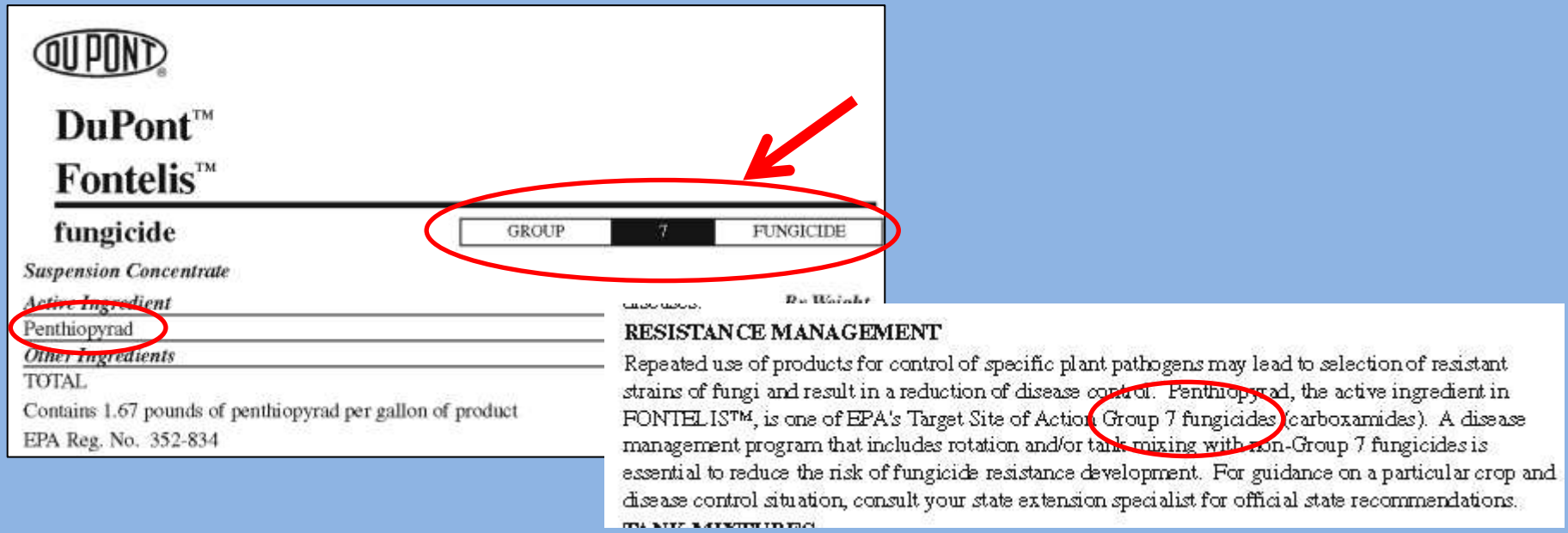
Fungicide Chemistries

Fungicide Basics: Fungicide Resistance Action Committee (FRAC)

FRAC: **www.frac.info**

- Established codes for fungicides based on their mode of action (**FRAC Code**)
- Get to know your fungicide label:

  Importance of FRAC group codes on fungicide labels



Fungicide Chemistries

Fungicide Basics: Knowing the fungicides

Mode of Action	FRAC Group	Trade Name	Fungicide Family	Common Name	Protectant /Systemic
Single-site	1	**Topsin M®**	**Benzimidazoles/MBC**	Thiophanate-methyl	Systemic
Single-site	3	**Rubigan® Indar® Rally®**	**DMI/SI**	fenarimol fenbuconazole myclobutanil	Systemic
Single-site	7	**Pristine® (7 + 11) Fontelis®**	**Carboxamides/SDHI**	boscalid penthiopyrad	Systemic
Single-site	11	**Pristine® (7 + 11) Flint®**	**Strobulurins/QoI**	pyraclostrobin trifloxystrobin	Systemic
Multi-site	M1	**Kocide®, Nu-Cop®**	**Inorganic**	copper salts	Protectant
Multi-site	M3	**Carbamate® Dithane®, Manzate®**	**Dithiocarbamates (EBDC)**	Ferbam Mancozeb	Protectant

Products with the **same FRAC number**: Behave similarly = cross resistance

*Except “M” = multi-site

Products with **different FRAC numbers**: Act differently

Fungicide Chemistries

Fungicide Basics: Fungicide-Associated Risk

Knowledge of mode of action: assessing positive indicators of risk

- Single site vs. multi-site
- Site of action known to become resistant to other fungicides

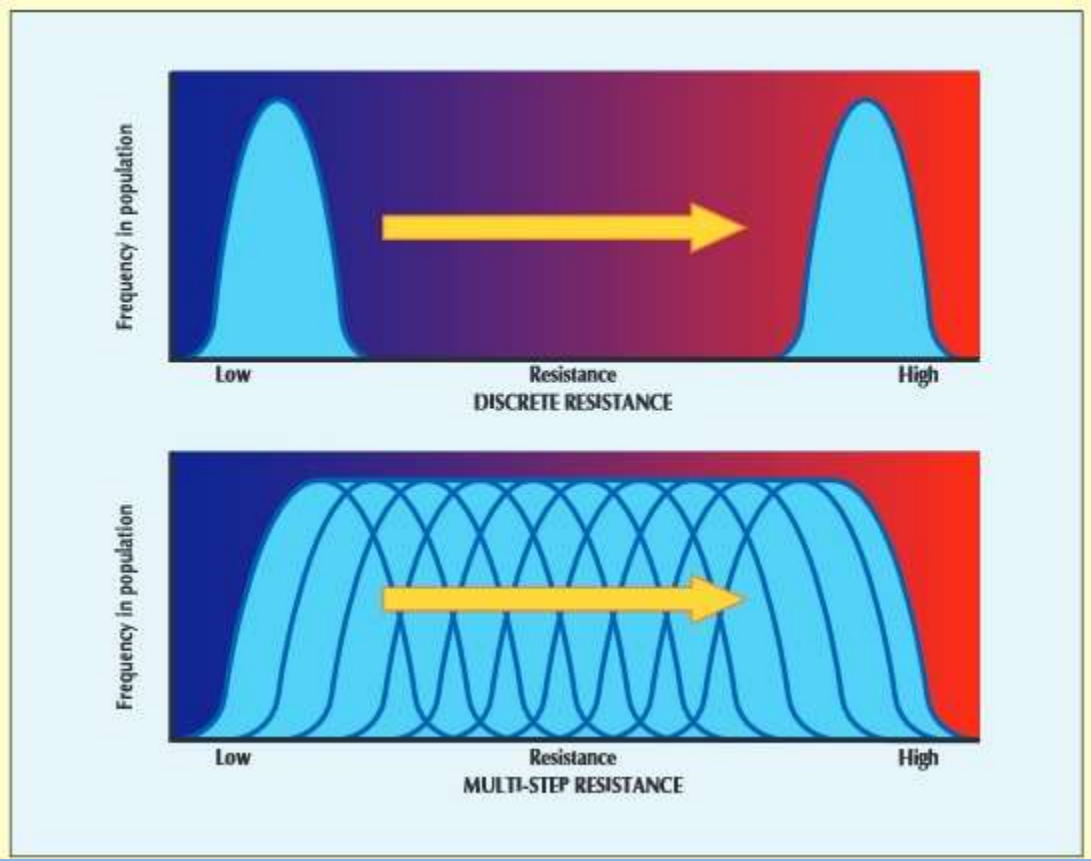
- **High:** Products having single-site of action
  Disease resistant populations have been discovered in more than one target pathogen

- **Medium:** Mutation of more than one target site
  Resistance formation is less frequent

- **Low:** Very rare or undocumented occurrence of resistance

Fungicide Chemistries

Fungicide Basics: Fungicide-Associated Risk



"Single-step" resistance
Benzimidazoles:
Mertect®
Topsin M®
= HIGH RISK

"Multi-step"
Sterol inhibitors (DMIs):
Indar®
Rally®
Procure®
=MEDIUM RISK

Brent, K.J. and Hollomon, D.W. 2007. Fungicide Resistance in Crop Pathogens: How Can It Be Managed? Fungicide Resistance Action Committee

Fungicide Chemistries

Fungicide Basics:Fungicide-Associated Risk

Mode of Action	FRAC Group	Trade Name	Fungicide Family	Common Name	Protectant /Systemic	Risk
Single-site	1	**Topsin M®**	**Benzimidazoles/MBC**	Thiophanate-methyl	Systemic	High
Single-site	3	**Rubigan®** **Indar®** **Rally®**	**SI**	fenarimol fenbucanazole myclobutanil	Systemic	Medium Medium Medium
Single-site	7	**Pristine® (7 + 11)** **Fontelis®**	**Carboxamides/SDHI**	boscalid penthiopyrad	Systemic	Low – Med Med – High
Single-site	11	**Pristine® (7 + 11)** **Flint®**	**Strobulurins/QoI**	pyraclostrobin trifloxystrobin	Systemic	Low – Med High
Multi-site	M1	**Kocide®, Nu-Cop®**	**Inorganic**	copper salts	Protectant	Low
Multi-site	M3	**Carbamate®** **Dithane®,** **Manzate®**	**Dithiocarbamates (EBDC)**	Ferbam Mancozeb	Protectant	Low

Products with the **same FRAC number**: Behave similarly = cross resistance

*Except "M" = multi-site

Products with **different FRAC numbers**: Act differently

Fungicide Chemistries

Fungicide Basics: Take Home Messages

Pay attention to FRAC codes on the fungicide label

- FRAC codes based on mode of action (MOA)
- Site-specific = systemic = Risk for resistance
- Multi-site = protectant = Low risk for resistance

Products with the **same FRAC number**:
Behave similarly = cross resistance (*Except “M” = multi-site)

Products with **different FRAC numbers**:
Act differently

Fungicide Resistance Management

Part 3 – Management Strategies

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Resistance Management Considerations

Factors affecting on-set of resistance (apple scab):

Selection pressure: heavy inoculum X heavy fungicide use

Use history – number of applications in the orchard

Long-term disease pressure- over the years; weather conditions affect selection pressure; fungicide residual

Proximity to neighboring orchards with resistance

Indications of problem:

Unexplained control failure

Lab test is best indicator of current resistance status

Ultimately YOU decide if you are satisfied with control and what to do differently if you're not

Resistance Management Considerations

On-set of resistance in an orchard:

Benzimidazoles- Topsin M, Benlate; 20 applications in orchard

QoIs (strobilurins) - Flint, Sovran- 25 apps.; Pristine?

SIs (sterol-inhibitors, DMIs, EBIs)- Rally, Rubigan, Procure; 10-30 apps at low rates, 60 or more apps. at high rates

Dodine - Syllit, (Cyprex); 60 apps.

APs (anilinopyrimidines) - Vangard, Scala

SDHI's – moderately high risk??? Fontelis, fluopyram in Luna Sensation and Luna Tranquility, fluxapyroxad in Merivon.

Koller

Classes of apple fungicides at risk for development of resistance

FRAC Chemical class	Compound	Trade name(s)
Strobilurin (Qol) (Group 11)	kresoxim-methyl trifloxystrobin pyraclostrobin + boscalid	Sovran Flint Pristine
Carboxamide (SDHI) (Group 7)	boscalid + pyraclostrobin (not a carboxamide) penthiopyrad fluopyram + trifloxystrobin fluopyram + pyrimethanil fluxapyroxad + pyraclostrobin	Pristine Fontelis Luna Sensation Luna Tranquility Merivon
Guanidine	dodine	Syllit, Cyprex
Sterol inhibitors (SI) (Group 3)	myclobutanil triflumizole fenbuconazole difenoconazole+ cyprodinil flutriafol	Rally (Nova) Procure Indar Inspire (Super) Topguard
Anilinopyrimidine (AP) (Group 9)	cyprodinil pyrimethanil cyprodinil + difenoconazole	Vangard Scala, Penbotec Inspire (Super)
Group 29	fluazinam	Omega

Resistance Management Considerations

General strategies to off-set resistance:

Selection pressure: heavy inoculum X heavy fungicide use

Reduce inoculum and break up fungicide schedules

Long-term disease pressure-

Strategy must consider overall disease spectrum

Practical Considerations for Fungicide STRATEGIES to Offset Resistance

Mid-Atlantic Fungal Apple Diseases

Early season

- Scab - drives early season spray schedule
  Resistance to SIs and QoIs common in Frederick Co. VA
- Mildew -only dry weather disease
  SI resistance since 2004 & now QoI at VT-AREC.
- Cedar-apple and quince rusts-needs for control (locally)

'Summer' diseases- more severe problems in south

- Sooty blotch / fly speck – as many as 60 different fungi
- Brooks fruit spot- 2nd cover
- Alternaria and Glomerella leaf blotches (specific cvs.)
- Rots (frogeye leaf spot/black rot, bitter, Bot, others)

Resistance Management Strategies

Reduce inoculum levels / reduce selection pressure
Choose fungicides based on disease spectrum
Include a protectant for every disease
Minimize use of “at risk” classes of fungicides
(After-infection applications increase selection pressure)
Rotate classes, always in combination with protectant

Resistance Management Strategies

Utilize copper spray for fire blight and scab (before 1/4" green on fresh market fruit; or later for processing)

Include a scab protectant with all “at risk” fungicides

Choice of general protectant based on rust pressure, cost, and compatibility with oil (EBDCs, ziram vs. captan)

Vangard or Scala, dodine?, at ½” green (don’t control rusts or mildew

Always avoid use of SIs, QoIs and SDHIs alone. Use mixtures or protectants where applicable

Consider alternating schedules of mixtures that may involve the several “at-risk” groups

Consider practices that reduce selection pressure (urea)

Use of urea to reduce scab inoculum

- Apply urea (40 lb/A) just before leaf drop
- Cover trees and ground to wet leaves which have already fallen

- Shredding leaf litter with a flail mower may have some similar effects on leaf breakdown (Also for Alternaria and Glomerella leaf blotches, and Brooks spot)

The early season management problem:

Economical control of scab, rusts and mildew
Scab- year-to-year inoculum level?; resistance status?

Powdery mildew- chronic effects on yield (20% lvs inf.)
- inoculum buildup without SI use

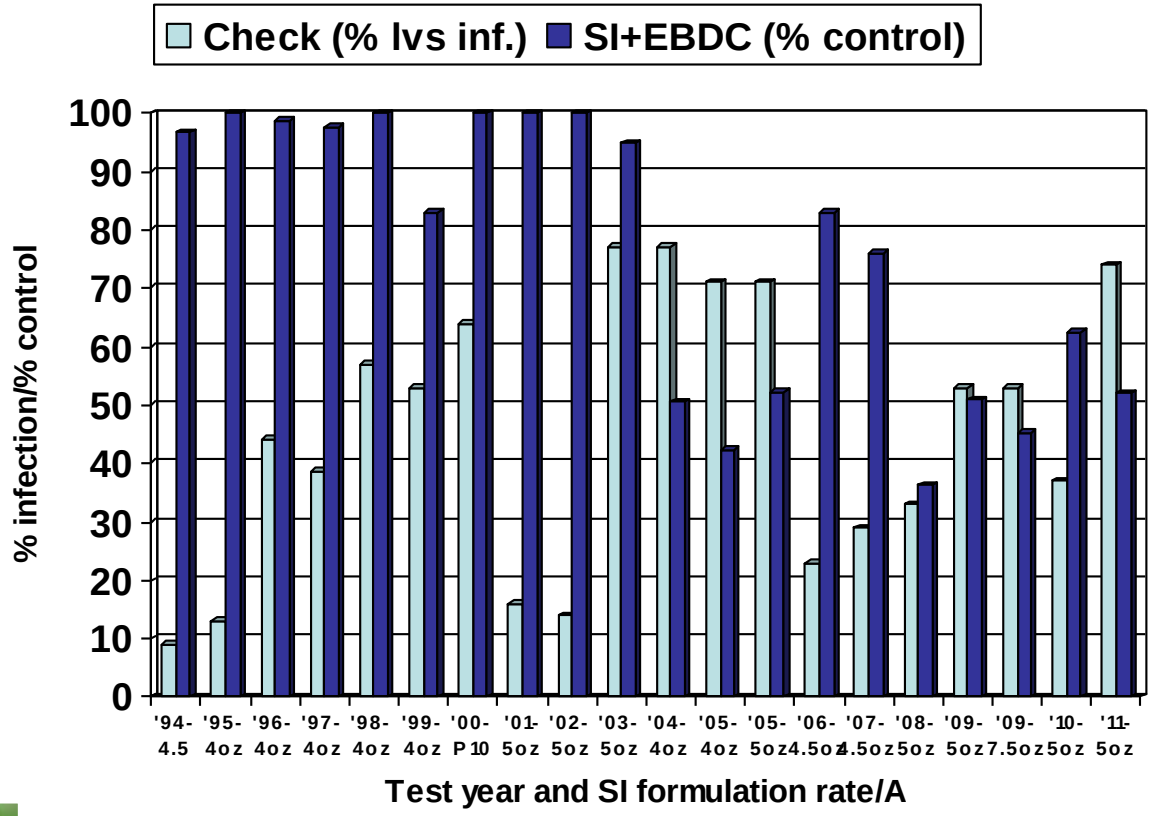
Cedar-apple and quince rusts- local problems
- leaf infection into June some years
- heavy fruit infection some years
- yield effects

Effect of Rally/Topguard, other SIs on cedar/quince rusts
Positioning of newer fungicides?
Indar 2F, Inspire Super ok if there isn't SI resistance
Luna Sensation?, Merivon?, Luna Tranquility, Fontelis?

Resistance Management Strategies

- Plan fungicide schedule with long-term use in mind
- Tight cluster- 2nd cover
  - scab first concern; esp. resistance issues;
  - Keep something in schedule for mildew, if needed (SDHI, SI, strobilurin, sulfur, other)?
  - include something for rusts, if needed
- Plan for season-long options - 1st choice; 2nd choice
- Issues about number of apps. / year (package mixes)
- Use mixtures with protectants as much as possible
  - reduce likelihood of resistance
  - reduce damage in year resistance appears
  - slows rate of epidemic; more forgiving
- Can't prescribe one program for everyone!

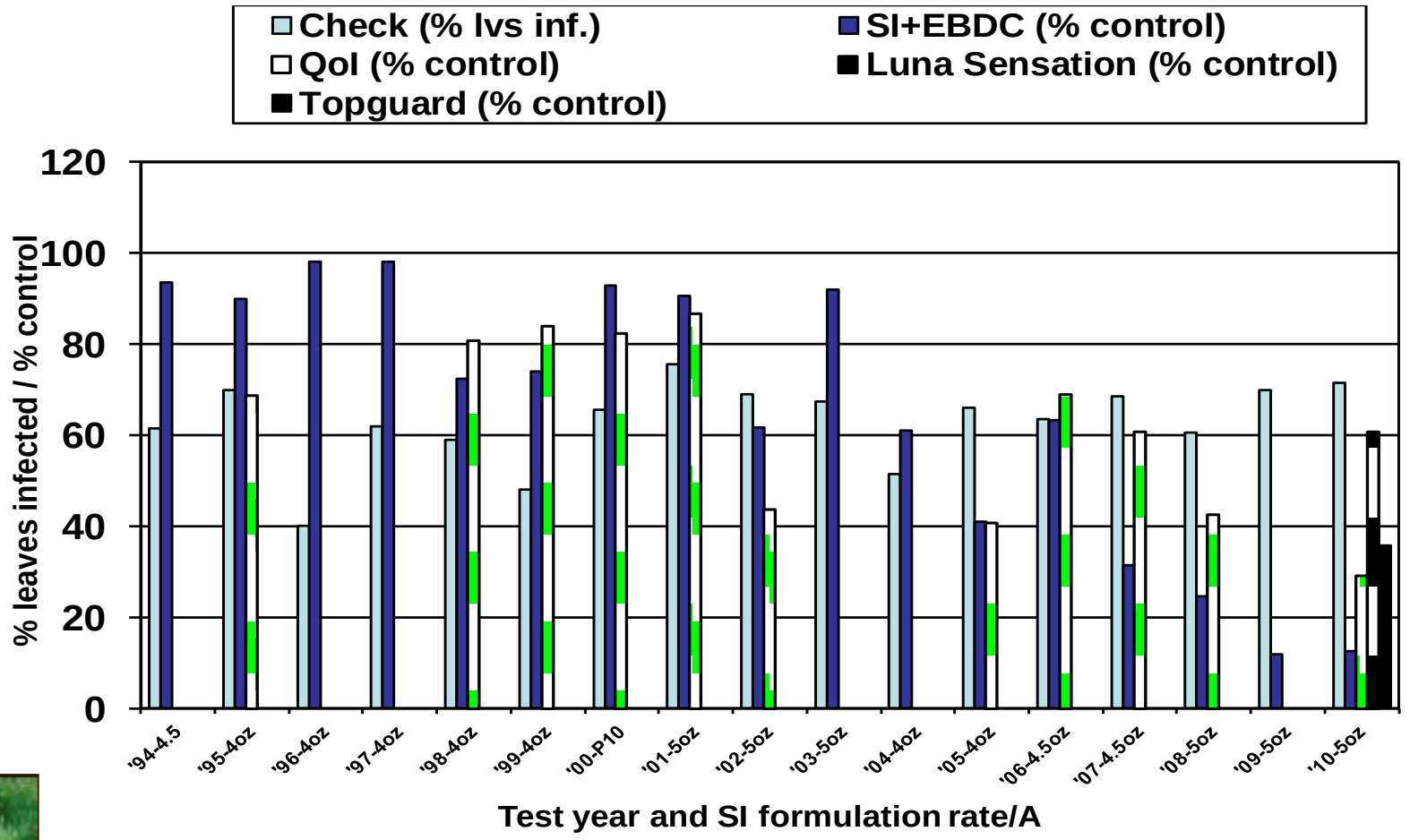
18-yr history of foliar scab control with SI+EBDC
Stayman apple, Winchester, VA (VARP)



- Generally poorer and variable control since 2004.
- Credit control in 2006-07 & ‘10 to EBDCs (dry years).

Control of % leaves infected with mildew by selected fungicides

Stayman and Idared apples, 1994-2010, Winchester, VA



‘08-09: SIs less effective after 9.8 A treated; QoIs after 4.8 A!

Questions/comments?

Evolution of Resistance